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THE RESPIRATORY VIRUSES: INFLUENZA, RSV, AND RHINOVIRUSES

Introduction: Respiratory viruses are among the most common causes of symptomatic human infections. Although viral upper respiratory tract infections are generally mild and self-limited, they are associated with significant morbidity and result in nearly twenty-six million days of school absence and twenty-three million days of work absence in the United States annually. This section will cover some of the most prevalent viral causes of respiratory illness; however, it should be remembered that a large number of other viruses can lead to symptoms of the common cold including coronaviruses (colds and SARS), adenoviruses, enteroviruses (discussed in GI viruses section) and parainfluenza viruses.

Influenza viruses

Influenza viruses cause acute, usually self-limited febrile illnesses most often in the winter months. They belong to the orthomyxoviridae family and are classified into 3 distinct types- influenza A, influenza B and influenza C. Influenza A and B cause human disease with significant morbidity and mortality. Influenza C infections are generally subclinical.

Molecular Biology and Pathogenesis: influenza viruses are enveloped viruses with segmented. negative sense RNA genomes. The genomes of influenza A and B have 8 segments while influenza C has 7 (it lacks a neuraminidase protein). Viral proteins encoded by these segments include:

I. PB I, PB2, and PA which are viral polymerase proteins and allow the virus to replicate its RNA
2. NA which is the neuraminidase protein. This protein protrudes through the viral envelope and catalyzes the removal of sialic acid residues which allows the virus to escape from its host cell and to move through mucous.
3. HA is the hemagglutinin protein which also protrudes through the viral envelope. It binds to sialic acid residues and is the major attachment protein for the virus. It also mediates fusion between the viral envelope and the endosome by which influenza gains entry into cells. NA and HA are the two major antigenic proteins (the proteins against which neutralizing antibodies are made) of influenza.
4. NP is the nucleocapsid protein and covers the genome of the virus.
5. M protein(s) are located just inside the viral envelope. Ml which is found in both influenza A and B provides stability to the virion. M2 which is found only in influenza A acts as an ion channel within the endosome.
6. NS are nonstructural proteins whose function is not yet entirely clear.

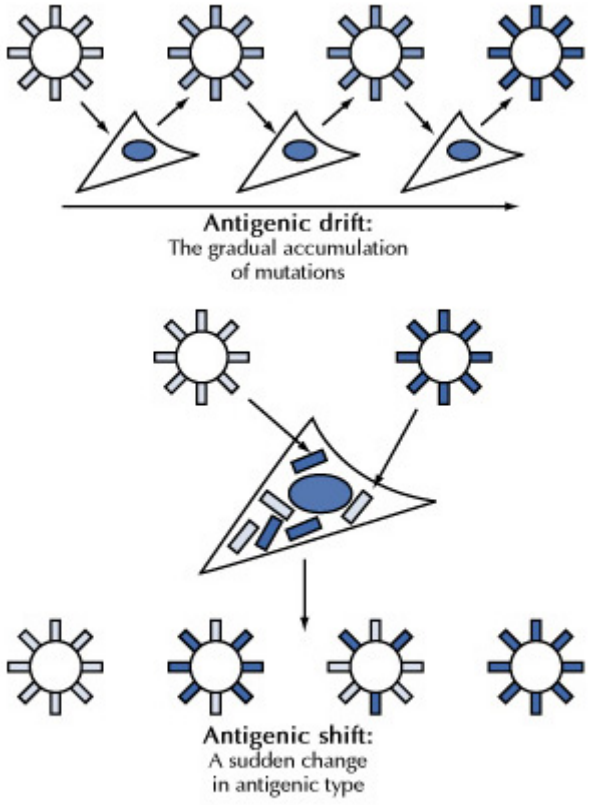
See figure I for influenza virus replication

Immune evasion and the concepts of antigenic drift and shift: Influenza is constantly changing in order to avoid immune detection. This accounts for annual flu seasons and periodic pandemics. The mechanisms that the virus uses to change its antigenic sites are called *drift* and *shift.* These concepts are very important and a favorite of people who write boards questions.

Antigenic Drift: The HA and NA proteins of influenza viruses are the major sites for antibody recognition on the virus. To help the virus evade antibody detection, the RNA segments that encode HA and NA are able to mutate so that their functions are kept intact but they are less well recognized by antibodies. This ongoing mutation is called antigenic drift and it occurs in both influenza A and B viruses. This drift is responsible for the year-to-year variation in influenza viruses and is the reason we need to keep changing the makeup of the influenza vaccine.

Antigenic Shift: Because the RNA genomes of influenza viruses are segmented they can undergo reassortment (mixing up) if two different influenza viruses infect the same cell. This concept is very important in understanding how influenza is able to cause pandemics. When a circulating human influenza virus infects a host (usually an animal or bird) already infected with its own virus, the segments of the two viruses can be mixed up and packaged together. When a foreign HA and/or NA ends up in a virus with human segments

encoding the other proteins you end up with a virus that can replicate in human cells but is not recognized at all by any human antibodies. When human populations are faced with influenza viruses to which they have no immunity, pandemics occur. Although shift can theoretically happen with any influenza virus, in practice it only occurs with influenza A as these viruses infect both humans and animals.



The consequences of antigenic shift can be deadly. The 1918 Spanish flu which killed 20-40 million people wood-wide in a single flu season was the result of antigenic shift. The most recent shift occurred in 1968 with the Hong Kong flu. Drifted variants of this flu (A/H3N2) are still the predominant strains circulating today. Flu shifts occur approximately every thirty years so we are currently overdue for a pandemic. The obvious concern at present is that the next pandemic will be due to "Avian flu" A/H5N1. (A note on nomenclature: influenza viruses are named for the type of flu (A or B)/place of initial isolation/strain designation/year of isolation/HA and NA subtype. Therefore an influenza strain isolated in Texas in 1991 of the H3N2 subtype is designated A/Texas/1991/H3N2). Influenza A/H5N1 first came to the public's attention in the late 1990's after an outbreak in Hong Kong in which 5 people and millions of birds lost their lives. H5N1 had been known to be circulating in birds (along with a number of other flu strains- birds are the largest reservoir for flu) for some time but this strain of H5N1 was different. First, it killed the birds. Second, humans could (with close contact with an infected bird) be infected and the mortality rate in humans was over 50%. Further study showed that this influenza strain had several virulence factors including a highly cleavable hemagglutinin that can be activated by multiple cellular proteases, a specific substitution in the polymerase basic protein 2 (Glu627Lys) that enhances replication, and a substitution in nonstructural protein 1 (Asp92Glu) that confers increased resistance to inhibition by interferons and tumor necrosis factor α(TNF-α) in vitro and prolonged replication in swine, as well as greater elaboration of cytokines, particularly TNF-α, in human macrophages exposed to the virus. Humans infected with the virus tend to have exaggerated symptoms of the flu and most die of primary

influenza pneumonia. In order, however, for this virus to make the jump to pandemic status it will need to be efficiently transmitted from person to person. Luckily this has yet to occur (although there are a few reports of transmission within families).

Clinical Manifestations: Influenza is a generally nasty, self-limited infection. Classic presentations require the presence of fever above 101 along with at least one systemic symptom (myalgias, chills, malaise) and at least one respiratory symptom (cough, nasal discharge). The onset of symptoms is usually abrupt and occurs 1-2 days after acquisition of the virus. Systemic symptoms usually dissipate after 3-4 days but other symptoms can persist for up to two weeks. Gastrointestinal symptoms other than anorexia are rare (there is no such thing as stomach flu- it's a different virus or bacteria). Complications are quite common and can be deadly.

Pneumonia is the most common complication of influenza infection. It can be either primary viral pneumonia or secondary bacterial pneumonia. In primary influenza pneunonia influenza virus directly infects the lower respiratory tract causing a rapidly progressive bilateral pneumonia which is very often fatal. Influenza pneumonia is responsible for the overwhelming majority of deaths in pandemics especially in otherwise healthy young adults. In older adults and those with chronic medical conditions, secondary bacterial pneumonia is the major cause of mortality. In this group of patients influenza infection allows pathogenic bacteria to secondarily infect the lung with a resulting bacterial pneumonia. Strep pneumoniae and staph aureus (seems to have a particular predilection for post-influenza lung tissue) are common post-influenza pulmonary pathogens.
Myositis, or inflammation of the muscles, is seen in children following some influenza B infections. The muscles of the legs are particularly involved.
Neurologic complications include a post-infectious encephalitis and the Guillain-Barre syndrome.
Reyes syndrome which involves changes in mental status and liver dysfunction is seen in children with influenza and other viruses who are given aspirin. Mortality from increased intracranial pressure is high and aspirin is no longer recommended as an antipyretic in children.

Diagnosis: In most individuals self-diagnosis on the basis of clinical symptoms is adequate. The gold standard for laboratory diagnosis is virus culture however this is time and labor consuming and is used primarily nowadays by state labs to monitor outbreaks. Rapid antigen tests are currently the diagnostic tests of choice for influenza. These tests are performed directly on patient samples and can be highly sensitive and specific. PCR is now available for influenza although it is not yet in widespread.

Treatment: While most people require only rest and fluids, some people will benefit from specific antiviral agents. Amantidine and rimantadine are primary symmetric amines which interfere with viral uncoating by blocking the action of influenza A's M2 protein. These drugs are only effective against influenza A as influenza B lacks an M2 protein. If given within 48 hour's of the onset of symptoms, these drugs can reduce the duration of symptoms by 1-2 days. They are also very effective at preventing infection if given during influenza outbreak. Unfortunately a number of viruses are now resistant to amantidine and rimantadine and this limits their effectiveness. Side effects especially CNS effects are a problem with these agents and dose adjustments have to be made in elderly patients and in people with renal insufficiency. Newer agents, the neuraminidase inhibitors, are also able to decrease the duration of symptoms of influenza and to prevent infections. These agents block neuraminidase activity and are effective against both influenza A and B (although their effectiveness against influenza B may be much less than against influenza A). Their side effects are generally milder than amantidine and rimantadine and they are efficacious against amantidine and rimantadine resistant viruses. None of these agents has been shown to prevent the complications of influenza infection.

Prevention: The mainstay of prevention is the trivalent inactivated influenza vaccine. This vaccine is made up of inactivated viruses which are thought likely to be circulating in the coming flu season (there's a bit of guesswork involved). Because the viruses are inactivated, it is impossible to get flu from the flu vaccine (although you'd be amazed at the number of people who claim they did). The efficacy of the vaccine is 50-80 % and is lower in the elderly and immunosuppressed populations. Despite this, the vaccine does reduce hospitalizations by 70 % and death by 80% in these groups so it's definitely worth giving. It is currently

recommended that all individuals over the age of 50 receive the vaccine (except in years when the supply is limited when the age limit is increased to 65) along with anyone with cardiac, pulmonary (asthma included), or renal disease and people with diabetes, hemoglobinopathies and immunosuppressive illnesses. Residents of nursing homes should also be vaccinated as should caregivers of any of the above groups (that's going to be all of you). It takes two weeks for protective antibody to develop and antibody titers decline over several months. The optimal time to get the flu vaccine is from October to mid-November in this country. Yearly revaccination is required for continued protection. Up to 5% of vaccinees will experience low grade fever and mild systemic symptoms- this is not the flu! Up to 30% will notice some tenderness at the vaccination site. A live attenuated nasally administered vaccine was approved 2 years ago for the prevention of influenza in healthy individuals aged 5-49 years of age. It is anticipated that it will soon be approved for infants as young as 6 months and for older adults. It is highly efficacious; however, shedding and some limited transmission of vaccine virus has been seen (however it remained attenuated and no-one got sick). A vaccine against H5N1 was recently approved by the FDA. It is only 50% efficacious at high dose, but it appears that boosting with a heterologous vaccine after a several year period increases response rates dramatically.

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) is a member of the paramyxoviridae family which also includes parainfluenza viruses (major causes of croup), mumps and measles viruses. It is the most common cause of bronchiolitis in infants and is a major contributor to morbidity and mortality especially in premature infants and the elderly.

Molecular Biology and Pathogenesis: RSV is an enveloped, single stranded, negative sense RNA virus. Its genome encodes 10 viral proteins:

- The glycosylated surface proteins F, G, and SH which mediate attachment of the virus to its host cell and fusion of the viral and host membranes.
- Proteins N, L and P which are associated with the nucleocapsid.
- M and M2 which are non-glycosylated matrix proteins.
- NS 1 and NS2 which are highly conserved nonstructural proteins that may play a role in RNA replication.

RSV grows well in several human cell lines. Its presence is detected by characteristic formation of syncytia (cells which have fused together to form multinucleated giant cells). Two groups of RSV isolates have been identified and are designated group A and group B. Viruses of both groups circulate simultaneously during outbreaks. RSV is inoculated through the eyes or nose and infection is generally confined to the respiratory tract. Infection may involve only the upper respiratory tract or it may spread to involve the entire lower respiratory tract. In lower tract involvement, pathology shows a lymphocytic peribronchiolar infiltrate with edema of the bronchial walls. Later proliferation and necrosis of the bronchioles develops. Collections of sloughed epithelium lead to obstruction of small bronchioles and subsequent air trapping. Reabsorption of trapped air leads to atelectasis (collapse of parts of the lung) especially in young children. Viral infection in the alveolar spaces can lead to frank viral pneumonia with characteristic syncytia formation. The role of the virus itself in the pathology is not clear. Most severe infections occur at times in our lives when antibody levels are high but cellular immunity is low (e.g. during early infancy or late adulthood). This observation along with the finding that infants given an RSV vaccine in the 1960s had more serious illness than unvaccinated infants suggests that immunologic mechanisms, especially the humoral immune system, may play a role in the pathogenesis of RSV infection. Immunity to RSV is incomplete and reinfections are common. Cell mediated immunity is likely to be of importance in protection against severe disease.

Epidemiology: RSV is ubiquitous having been found in every geographic area studied. Outbreaks occur every year with a distinct seasonality in the winter and early spring. In the US, outbreaks begin in November, peak in January and continue until April. Virtually all children have been infected by the age of 2 and serious illness is most common in young infants. Boys and children from lower socioeconomic backgrounds appear to be at more risk for serious disease. Particularly at risk are premature infants, especially if they have

bronchopulmonary dysplasia, children with congenital heart disease, and children with pulmonary disease. It has recently been discovered that RSV is an important pathogen in the elderly with hospitalizations for complications of RSV disease being as common in this group as hospitalizations for influenza.

Clinical manifestations: Primary infection with RSV is usually symptomatic. Involvement of the lower respiratory tract is most often seen in primary infections. Pneumonia and bronchiolitis are seen most commonly in infants with primary infection. Symptoms usually start with nasal congestion, sore throat and fever. Cough develops in the first few days and becomes deeper and more prominent as infection proceeds. Increased respiratory rate and retraction of the lower intercostal muscles herald lower respiratory tract involvement. In most infants, the duration of symptoms is 7 to 21 days. Hospitalization rates due to lower respiratory tract involvement can approach 40% in infants under 6 months. Infection in adults and older children is rarely asymptomatic despite previous immunity. Nasal congestion and cough mimicking the common cold are the most common manifestations. Older adults are at higher risk of serious infection than younger adults. Mortality from RSV pneumonia can reach 20% in older adults. Immunocompromised individuals are at particular risk from RSV infection. Children with severe combined immunodeficiency and adults with transplants and hematologic malignancies are at particular risk of fatal lower respiratory infections. Many of these infections are acquired nosocomially as RSV spreads very efficiently in hospitals.

Treatment: Supportive care is the mainstay of therapy in the management of severely ill infants. Supplemental oxygen should be given to hypoxic infants. Bronchodilators have been used for many years but their efficacy is questioned. Ribavirin, a broad spectrum antiviral agent which works by interfering with viral RNA polymerase activity and inhibiting inosine 5'- monophosphate dehydrogenase which depletes intracellular nucleotide pools, is currently approved for the treatment of lower respiratory RSV disease. It is usually administered by aerosol and is generally reserved for high-risk patients.

Prevention: Prevention of transmission requires strict hand washing and avoidance of secretions. This is difficult to accomplish in the home setting but in hospitals use of gown and glove isolation, strict hand washing and cohorting of infected patients is warranted. To prevent RSV infection in high risk infants, RSV immune globulin or a monoclonal antibody against RSV (pa1ivizumab) may be used. Either preparation (although palivizumab is currently the preferred agent) given once a month to high risk infants has been shown to significantly reduce the severity and number of RSV infections. Their use should be considered in any preterm infant of less than 32 weeks gestation who will be less than six months of age at the onset of RSV season. It is also used in RSV outbreaks jn neonatal intensive care units and in young children with bronchopulmonary dysplasia who require 02 or who have been off 02 for less than six months at the start of RSV season. Unfortunately. RSV immune globulin does not appear to benefit children with congenital heart disease. As yet, there is no vaccine against RSV.

Rhinoviruses

Rhinoviruses are the etiologic agents most frequently associated with common cold symptoms, being responsible for approximately 30 percent of all upper respiratory viral infections.

Molecular Biology and Pathogenesis: Rhinoviruses are small, nonenveloped single-stranded RNA viruses. They are members of the picornaviridae family (pico, very small; RNA) which also include the enteroviruses (polioviruses, coxsackieviruses, echoviruses, and other enteroviruses), and hepatitis A virus. We will cover picornavirus biology in more detail in the enterovirus section of the course. Over 110 different rhinovirus serotypes have been described, and this enormous diversity has made development of a vaccine almost impossible. Rhinoviruses display optimal growth at 33^{o}C which corresponds to the temperature of the nose and large airways. The majority of rhinovirus serotypes utilize a single cellular receptor- intercellular adhesion molecule-1 (ICAM-l). ICAM-l is found on the surfaces of many cell types throughout the body; it acts as the cell surface ligand for lymphocyte function associated antigen-l (LFA-I) and plays an important role in immunologic and inflammatory reactions. A smaller group utilizes members of the low-density lipoprotein receptor family.

Rhinoviruses enter the nasopharynx through the nasal or ophthalmic mucosal (by touching your nose or eyes). Viral replication takes place primarily in nonciliated lymphoepithelial cells of the nasopharynx with primary infection thought to involve the adenoidal tissues. Only a small number of epithelial cells are infected, and viremia does not occur. Rhinoviruses enter cells through specific cell surface receptors, mainly ICAM -I as noted above. This receptor. which is expressed on many different cell types, is found on the luminal surface of nonciliated lymphoepithelial cells in the nasopharynx, in endothelial cells of the microvasculature, and in the geminal centers of pharyngeal lymph nodes. It has been postulated that virus is deposited in the nares or conjunctiva of the host and is transported to the nasopharynx via mucociliary action where it encounters the ICAM-I rich adenoidal crypts. Infection then spreads anteriorly along the nasal passages. Whether lower airway epithelial cells are infected is uncertain, but rhinoviruses have been detected by PCR of epithelial cells in bronchoalveolar lavage specimens (obtained during bronchoscopy). Further evidence of a direct lower respiratory tract epithelial involvement has been recently shown in vitro by exposing primary human bronchial epithelial cells to rhinoviruses and in vivo after experimental upper respiratory infection of human volunteers. Infection of the lower airways may be more common in children; fatal rhinovirus pneumonia and histologic evidence of rhinovirus in alveolar cells have been described in infants.

For many years after the discovery of rhinoviruses, it was assumed that, like influenza and adenovirus, the associated symptoms resulted from direct cytopathic effects on infected epithelial cells. However, in situ hybridization of nasal mucosa biopsy specimens suggests that only a few cells are infected and cytopathology is conspicuously absent. The lack of cytopathology suggests that the host inflammatory reaction and not direct viral damage is responsible for the symptoms of the common cold. In studies of nasal washes in subjects with both natural and experimental rhinovirus infection, elevated levels of the proinflammatory cytokines, interleukins (IL-6, IL-8), tumor necrosis factor alpha and granulocyte-macrophage colony stimulating factor (GMCSF) have been documented. IL-8 is thought to induce many of the proinflammatory changes associated with symptomatic rhinovirus infection. In one study in normal subjects, the IL-8 concentration tended to increase in proportion to the severity of rhinorrhea and nasal obstruction. Release of IL-8 from rhinovirus infected cells appears to be dependent upon interaction of the virus with its receptor.

Epidemiology: Respiratory illness accounts for roughly one-half of all annual acute symptomatic illnesses in the community. Several large surveys of communities, workplaces, and military personnel have shown that most adults experience between one and three acute respiratory illnesses a year. Infants less than one year of age had the highest rates of illness with an average of 6.1 infections per year. Rates declined steadily with increased age with the exception of a slight increase in the 20 to 29 year-old age group. This increase is accounted for by the presence of children in the home and is supported by a slightly higher rate of illness in women in this age group who act as the primary caregivers for their children. The presence of multiple serotypes simultaneously in a community, antigenic drift, and the possibility for reinfection permit multiple infections within a single individual and contribute to the frequency of rhinovirus infections. Approximately 80 percent of these infections are associated with clinical illness; however, in comparison to other respiratory viruses, the illness is generally mild and most infected persons do not seek medical attention.
Rhinoviruses have a worldwide distribution with a well-established seasonal pattern in temperate climates. Peaks of infection are seen in the early fall and spring. Rhinovirus activity is generally low in the winter with coronaviruses and other agents being responsible for the generally more debilitating winter colds. In tropical climates, rhinovirus activity is greatest in the rainy season. It is not known why rhinoviruses show this seasonal variability. It has been postulated that seasonal changes in living conditions may account for outbreaks. Environmental temperatures do not appear to affect infection rates or the severity of illness, and despite popular belief exposure to cold or rainy weather does not affect host resistance to rhinovirus infection (getting cold or wet will not give you a cold).

Transmission: Rhinoviruses are spread from person-to-person throughout communities via virally contaminated respiratory secretions. In relatively closed communities such as homes and schools, spread is quite efficient with secondary attack rates ranging from 25 to 70%; in comparison, spread of rhinovirus colds among people at work does not appear to be as common. Studies of transmission under experimental conditions have shown that direct contact with infected secretions and aerosols are efficient means of spread of rhinoviruses. Rhinoviruses can survive on environmental surfaces for several hours, and spread from

contaminated surfaces has been described under experimental conditions. Interestingly, porous materials such as tissues and cotton handkerchiefs do not appear to allow virus survival and are not efficient modes of virus transmission. Decontamination of environmental surfaces with virucidal disinfectants such as Lysol decreases the rate of transmission.

Clinical Manifestations: Rhinovirus infections have been associated with the common cold, acute sinusitis, otitis media, exacerbations of chronic bronchitis, and acute asthma attacks. Studies in large cohorts of naturally infected individuals demonstrate that rhinorrhea, congestion, and sneezing are the most common complaints occurring in 50 to 70 percent of individuals in the first three days of infection. Sore throat, present in approximately one-half of cases within the first two days, is the next most common manifestation. Pharyngitis can be severe, and exudative rhinovirus pharyngitis has been described. Many people have come to associate a sore or "scratchy" throat with the imminent onset of a cold, an observation which correlates well with the detection of virus in nasal secretions as early as ten hours after inoculation. Hoarseness and cough are less common manifestations of the common cold; however, they may be more persistent, lasting up to several weeks, especially if a complication such as sinusitis or bronchitis arises. High fevers, myalgias, and chills are not usually seen in rhinovirus infection and should prompt a search for another cause. Symptoms peak on the second, third, and fourth days of infection; the median duration of illness is one week. Up to 20 percent of infected individuals have symptoms for a longer period of time, and virus can be shed for up to three weeks.

Complications: Most rhinovirus infections are mild and self-limited; however, complications can occur. Up to 87 percent of individuals with natural rhinovirus infection develop disease in the paranasal sinuses as demonstrated by CT scan. This form of sinusitis is generally asymptomatic and resolves spontaneously within two to three weeks. In only a small number of patients does bacterial superinfection necessitate antibiotic therapy. Exacerbation of chronic bronchitis is another well-established sequela of rhinovirus infection. Such exacerbations are usually due to inflammatory responses to the virus; antibiotics are not indicated unless there is clear evidence of bacterial superinfection. A yellow or green color in sputum or nasal discharge is not a good predictor of bacterial superinfection of the lower airways or sinuses. Neutrophils, which are present in sputum and nasal discharge in uncomplicated rhinovirus infections, cause yellow-green discoloration through natural myeloperoxidase activity. Viral upper respiratory infections (URIs) have long been known to precipitate asthma attacks in children and have been linked to up to 40 percent of acute asthma attacks in adults. It is uncertain whether the rhinovirus-induced increase in airway hyperreactivity is the result of local inflammation caused by rhinovirus infection of lower airway epithelial cells or if infection is limited to the upper airway with inflammatory mediators acting distantly in the lower airways. Rhinovirus-induced changes in airway reactivity may persist for up to four weeks following infection. This may explain the often persistent cough seen in many individuals following upper respiratory tract infections. It is important to note that this cough is not bacterial bronchitis and will spontaneously resolve.

Treatment: There is no cure for rhinovirus infection other than the passage of time during which virus is cleared by the host immune system. Unfortunately it is this host response that is responsible for most of the symptoms of the common cold. As a result, most modern cold remedies are aimed at attenuating the effects of the immune response. Decongestants both alone and in combination with either antihistamines or anticholinergics appear to decrease rhinorrhea, nasal discharge, and subjective congestion. Nonsteriodal anti-inflammatory drugs and acetaminophen may provide significant symptomatic relief, especially in combination with antihistamines or decongestants. Studies using drugs that directly impact viral replication have been disappointing to date. These agents must be used within a short period of time after infection (preferably before symptoms have appeared) in order to reduce symptoms; however, they have been more successful at decreasing spread of infection in households. Zinc lozenges have been hailed in the popular press as highly effective for treating rhinovirus colds; however, several large double blind trials involving both natura1 and experimental colds have failed to show any benefit. Echinacea, the purple coneflower, bas been a popular herbal cold remedy for decades; however, few modern studies support its effectiveness. Like echinacea, vitamin C has been touted as a popular preventive and therapeutic agent for the common cold. Also like echinacea the data on the effectiveness of vitamin C are mixed. Analysis of the six largest vitamin C supplementation studies (> 1 g per day) fail to show any benefit in decreasing the incidence of the common cold. Some of these trials suggest a modest benefit in improvement of symptoms; however, the improvements are no greater than are seen with standard over-the-counter cold remedies. There is NO role for antibiotics in

treating uncomplicated viral upper respiratory tract infections (URIs), and there is no evidence to suggest that antibiotics prevent secondary bacterial complications of viral URIs. Despite this antibiotics continue to be prescribed for uncomplicated URIs at alarmingly high rates and have probably contributed to antibiotic resistance. Unless there is fever and good objective evidence of a bacterial superinfection, DO NOT prescribe antibiotics for URIs (this will be harder than you think).

Prevention: Rhinoviruses are transmitted through aerosol and hand contact. Control of nasal secretions and the use of virucidal tissues decreased rhinovirus transmission in one study. Proper handwashing, use of virucidal agents, and avoidance of hand-to-mucous membrane exposure (this is almost impossible) also decrease transmission rates. There are no current rhinovirus vaccines, and because more than 100 serotypes of rhinovirus can cause disease in humans, it is unlikely that a rhinovirus vaccine will be developed. Thus, prevention must rely upon avoidance of the virus.