195 Influenza

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- *respiratory* illness accompanied by systemic symptoms of fever, malaise, and myalgia

- orthomyxoviruses

- many features distinguish influenza from these other illnesses:
most particularly its systemic symptoms
its propensity to cause sharply peaked winter epidemics
and its capacity to spread rapidly among close contacts

■ETIOLOGIC AGENTS

- Three influenza viruses occur in humans
- A, B, and C
- irregularly circular in shape, measure 80–120 nm in diameter, and have a lipid envelope and prominent spikes that are formed by the two surface glycoproteins, hemagglutinin (H) and neuraminidase (N)

- Influenza A viruses have eight single-strand negative-sense RNA segments in their genomes that encode hemagglutinin and neuraminidase as well as internal genes, including polymerase, matrix, nucleoprotein, and nonstructural genes.

- Among the influenza viruses, the A viruses are of paramount importance for several reasons:
- (1) (*antigenic drift)*
- *(2)* (*antigenic shift)*
- *(3) their extensive mammalian and avian reservoirs, in which* multiple variants with distinct hemagglutinin and neuraminidase genes lie in wait
- As a result of all of these factors, influenza A virus has the ability, particularly after an antigenic shift, to cause a worldwide epidemic (*pandemic)*
- *The most severe influenza A pandemic in modern* history took place in 1918; ~50 million deaths were attributed to the culpable influenza A H1N1 virus in the years surrounding 1918

■EPIDEMIOLOGY

- outbreaks during the cooler months of the year
- mirror-image season in the antipodes compared with that in the Northern Hemisphere
- The circulation of strains in the Southern Hemisphere has some predictive value for vaccine composition in the Northern Hemisphere, and vice versa.
- This information is important as the degree of antigenic drift is one determinate of vaccine efficacy.
- Vaccine composition typically must change in at least one component yearly in anticipation of the predicted circulating strains

- A typical outbreak begins in early winter and lasts 4–5 weeks in a given community, although its impact on the country as a whole will be of considerably longer duration
- When excess mortality occurs, an influenza outbreak increased school and work absenteeism, increased visits to emergency rooms and primary care physicians, and increased hospitalizations, particularly of elderly patients and individuals with underlying cardiopulmonary disease.
- Despite efforts to limit influenza spread through vaccination, cohorting, use of masks, and hand washing, long-term-care facilities house another sentinel population, including many elderly patients who are at increased risk of complicated disease.
- Influenza is largely spread by small- and large-particle droplets;
- spread is undoubtedly facilitated by the coughing and sneezing that accompany the illness
- Within families, the illness is often introduced by a preschool or school-aged child

TABLE 195-2 High-Risk Groups Who Should Be Assigned a High Priority for Influenza Immunization and Treatment[a]

High-Risk Group
Children 6–59 months of age
Adults ≥50 years of age
Persons with chronic pulmonary (including asthma), cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
Persons who are immunocompromised (any cause, including medications or HIV infection)
Women who are or plan to be pregnant during the influenza season
Children and adolescents (6 months through 18 years of age) who are receiving aspirin- or salicylate-containing medications and who might be at risk for Reye syndrome
Residents of nursing homes and other long-term-care facilities
Native Americans, including Alaska Natives
Persons who are extremely obese (BMI ≥40)
Contacts and Caregivers
Caregivers and contacts of those at risk: health care personnel in inpatient and outpatient care settings, medical emergency-response workers, employees of nursing home and long-term-care facilities who have contact with patients or residents, and students in these professions who have contact with patients
Household contacts and caregivers of children ≤59 months (i.e., <5 years) of age (particularly contacts of infants <6 months old) and adults ≥50 years of age
Household contacts and caregivers of persons who are in a high-risk group

- Influenza infection is initiated in the upper respiratory tract via aerosolized virus.
- The cells infected with influenza virus are primarily the ciliated cells of the respiratory tract
- The onset of symptoms follows an incubation period that, for a viral illness, is very short:48–72 h
- The infection spreads to the lungs but, even there, remains confined to the epithelial layer

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- These manifestations are presumed to be mediated by cytokines
- The immune response to influenza virus occurs at the systemic and mucosal levels and involves both T and B cells
- The symptoms typically begin within 48–72 h of exposure

■■CLINICAL MANIFESTATIONS

- primarily a respiratory illness causing rhinorrhea , sore throat, conjunctivitis, and cough
- sudden onset and is epidemiologically linked to close contact with persons who have similar symptoms and often to community-wide respiratory illness
- What distinguishes influenza from other respiratory illnesses is the degree of accompanying fever, fatigue, myalgia, and malaise

- Respiratory symptoms, particularly recurrent cough, persist well beyond the 2–5 days of systemic symptoms
- Pulmonary function is persistently decreased after acute influenza
- Persons with a regular exercise routine (e.g., runners) note a decrease from their prior level of performance that typically lasts for a month or more
- In the elderly, the respiratory presentation may be less prominent, but there is often a decline in baseline activity and a loss of appetite

COMPLICATIONS

- Complications of influenza occur most commonly in persons >65 years of age, those with underlying cardiopulmonary disease, those with immunosuppression, and women who are in the second or third trimester of pregnancy.
- In recent years, there has been mortality attributable to influenza among often previously healthy children <5 years of age in the United States, with ~100 deaths per year

Respiratory Complications

- Pneumonia characterized by progressive air hunger, localized pulmonary findings on physical examination , and radiographic findings of infiltrates and consolidation is the most common complication of influenza.
- primary influenza viral pneumonia
- secondary bacterial pneumonia,
- or mixed viral and bacterial pneumonia

- Primary viral pneumonia :

increasing dyspnea , persistent fever, and—in more severe cases—cyanosis

secondary bacterial pneumonia or mixed viral and bacterial

- may be biphasic, with evidence of recovery from the primary influenza illness followed by recrudescence of fever and pulmonary symptoms
- Another proposed mechanism for bacterial/viral enhancement is the production by *Staphylococcus and Pseudomonas of proteases that* enhance cleavage of the influenza hemagglutinin and thereby facilitate viral replication
- The risk of secondary bacterial disease is greatest in elderly patients and those with chronic obstructive pulmonary disease.
- Some influenza strains cause laryngotracheobronchitis or croup in children
- Otitis media—a common accompaniment to influenza in children—may also be due to a combination of influenza virus and bacteria

Extrapulmonary Complications

- The most common extrapulmonary manifestation of influenza is myositis, which is seen more often in influenza B and is characterized by severe muscle pain, elevated creatinine phosphokinase levels, and myoglobinuria that can lead to renal failure
- The muscles are extremely tender to touch
- Myo/pericarditis is seen less frequently
- acute demyelinating encephalomyelitis
- Encephalitis and transverse myelitis
- Guillain-Barre syndrome
- Until aspirin was recognized as a co-factor in its precipitation, Reye syndrome, an acute hepatic decompensation, was seen commonly in children and adolescents with influenza, particularly those infected with influenza B virus

■■LABORATORY FINDINGS AND DIAGNOSIS

- Influenza virus is most easily recovered from nasopharygeal specimens.

- These tests are highly specific

- sensitivity of only 50–70%
- Their sensitivity is strongly dependent:
- on sample collection early in the course of illness—ideally within 48 h of the onset of symptoms

- The most useful clinical approach :PCR-based

- Other laboratory tests are of limited value. Mild leukopenia is seen in influenza, and a white blood cell count above 15,000/μL suggests a secondary bacterial component in influenzal pneumonia

■PROPHYLAXIS

- The major intervention to limit influenza illness is vaccination, which is conducted on a yearly
- The overall accuracy of the prediction is at least 70% for all strains in the recommended vaccine.
- Influenza vaccine is unique in being given seasonally in the months immediately preceding an outbreak. In the United States, vaccine is typically available from September
- The protection (and licensure) of all influenza vaccines depend on their
- stimulation of antibodies to the hemagglutinin; all are 50–75% effective at preventing clinical influenza
- The contraindications to inactivated influenza vaccine administration are limited to individuals who have experienced a Guillain-Barre reaction within 6 weeks of a prior influenza vaccination.
- Egg allergy is not considered a contraindication to vaccination

- LAIV had no demonstrable efficacy assignable to the vaccine's H1N1 component
- the recommendation is that all individuals >6 months of age receive inactivated influenza vaccine yearly and that two doses of vaccine be given to children <9 years of age who are getting their first or second yearly vaccination
- Face masks and hand hygiene in the hospital setting

TREATMENT

- In the past, influenza A infection could be treated with the M-2 channel blockers amantadine and rimantadine. Widespread resistance has currently relegated these compounds to historical interest only
- The currently available class of drugs for treatment of influenza A and B viruses consists of neuraminidase inhibitors
- These drugs hasten the resolution of symptoms if given within 48 h of infection.
- There are indications for their use both prophylactically—either throughout the season or, when a case is recognized in a close contact, in the short term—and therapeutically
- resolution of symptoms 1–2 days sooner than without treatment

- The available neuraminidase inhibitors are oral oseltamivir, nasal-spray zanamivir, and intravenous peramivir and zanamivir.
- Gastrointestinal symptoms, especially nausea, may accompany the administration of oseltamivir.
- Because zanamivir is not orally bioavailable, it is given as an inhaled dry powder dispersed through a Diskhaler device.
- The usual duration of therapy with either oral oseltamivir or intranasal zanamivir is 5 days, with twice-a-day dosing.
- Oseltamivir is preferred for treatment of pregnant women and is approved for children ≥1 year of age
- Poor oral intake or absorption is a contraindication to the use of oseltamivir, although this drug can also be given by oro/nasal tube.
- Asthma and chronic obstructive pulmonary disease are relative contraindications to the use of intranasal zanamivir;

THE END