Influenza in Pregnancy
See also Community Acquired Pneumonia in Pregnancy

Background
1. General information
   o Common infectious disease, usually self-limited
     ▪ Estimated U.S. annual mortality: 20,000 people/year

Pathophysiology
1. Pathology of disease
   o Infection by one of 3 viruses, Influenza A, B or C
     ▪ Influenza A & B have the most severe symptoms in humans
     ▪ Family Orthomyxoviridae
       • Single stranded enveloped RNA viruses
       • Virus strain typing based on 2 major surface proteins:
         Hemagglutinin (H) and neuraminidase (N)
         ▪ Alteration of these antigen structures may lead to variants in
           the virus to which there is no resistance in the human
           population
     o Primarily spread person-to-person through small-particle aerosols (<10 um
       mass median diameter)
     o Once virus is inhaled and penetrates columnar epithelial cells, virus
       replication begins and cell death ensues
     o Respiratory tract becomes inflamed
     o Cytokines are released by infected cells and the responding immune system
       which leads to systemic symptoms.
     o Acute onset of symptoms after 1-2 day incubation period

2. Incidence, prevalence
   o Influenza epidemics tend to occur in winter months
     ▪ Seen year round in the tropics
   o During epidemics the attack rate may reach 10-20%

3. Risk factors
   o Infection rates highest in the young
   o Mortality highest in the elderly

4. Morbidity / mortality
   o Morbidity
     ▪ Hospitalizations during epidemic years 54,000 - 430,000
     ▪ Typical case in a young, healthy individual
       • 3-4 days bed rest
       • 5-6 days restricted activity
       • 3 days of work lost
     ▪ Excess risk of complications and severe disease
       • Pregnant women
         ▪ Evidence for this is primarily anecdotal with some support
           from retrospective case studies
       • Children aged 6-59 months
       • Adults over age 50
- Persons with certain chronic medical conditions
  - Immunosuppression
  - Lung Disease including asthma and COPD
  - Certain cardiovascular conditions
  - Renal dysfunction
  - Hemoglobinopathies
- Persons who live with or care for persons at high risk
  - Mortality
    - Excess deaths of pregnant women in pandemics of 1918-19 and 1957-58
    - Most deaths are in persons over 65 or with co-morbid conditions
    - 20,000 deaths annually

**Diagnostics**

1. **History**
   - Predominance of systemic symptoms is a major feature distinguishing influenza from other viral URIs
   - Abrupt onset
     - Fever, chills
     - Headache
     - Myalgia, malaise, arthralgia
     - Anorexia
     - Eye pain, burning, tearing
     - Systemic Sx resolve in 3 days
   - As systemic Sx resolve, respiratory Sx begin to dominate
     - Dry cough
     - Pharyngeal pain
     - Nasal discharge
     - Hoarseness
     - Respiratory Sx may last for weeks

2. **Physical exam**
   - Fever most important physical finding
     - Peaks of 100°-104° F within 12 hrs of onset
   - General: toxic, flushed
   - Skin hot and moist
   - Mucous membranes hyperemic
   - Eyes watery
   - Nose with clear nasal discharge but nasal obstruction is uncommon
   - Small, tender cervical lymph nodes
   - Lungs: rhonchi or localized areas of rales are found in less than 20% of cases

3. **Diagnostic testing**
   - Laboratory evaluation
     - Rapid antigen testing
       - Respiratory secretions
         - Nasal swab or throat swab or both
         - Throat swab less sensitive
         - Sputum sample if available
       - Rapid Tests, results available within 30 minutes
         - 40-80% sensitive
o 85-100% specific
o All detect influenza A and B
o Perform better in children because they shed more virus in nasal secretions
o Tests
  ▪ Directigen Flu A+B (Becton-Dickenson)
  ▪ Flu OIA (BioStar)
  ▪ QuickVue Influenza A+B test (Quidel Corporation)
  ▪ Viral culture of nasopharynx / throat
    • Gold standard
    • Requires 3-7 days
    • Too slow for effective drug therapy
  ▪ Serological Testing also available
    • PCR and immunofluorescence
o Diagnostic imaging
  ▪ CXR if pneumonia suspected
o Other studies
  ▪ If atypical presentation or co-morbid conditions, consider
    • CBC w/diff
    • Electrolytes, BUN, creatinine

4. Diagnostic criteria
o Presence of influenza virus is confirmed in a region or community
o Healthy adult with acute influenza-like symptoms
o Accuracy of clinical dx in healthy adults during influenza outbreak reaches 80-90%

Differential Diagnosis
1. Key Differential Diagnoses
   o Viral URI
   o Pneumonia, bacterial or viral
   o Mononucleosis
2. Extensive Differential Diagnoses
   o SARS
   o Encephalitis
   o Meningitis
   o HIV infection

Therapeutics
1. Acute treatment
   o Supportive care
     ▪ Acetaminophen and nasal decongestants
     ▪ Fluid resuscitation
     ▪ Electrolyte management
     ▪ Supplemental oxygen
     ▪ Intubation, tracheotomy, assisted ventilation, depending on the severity presentation
If possible bacterial supra-infection
  • Appropriate antibiotic Tx to cover S. pneumoniae and H. influenzae, and possibly S. aureus
  • Sputum culture and sensitivities

Antiviral therapy
  • Best if used within 24 hrs of onset but may be used up to 48 hrs after onset
  • Reduces duration / severity of illness, especially in high-risk patients
  • Decreases secondary complications in high-risk patients
  • All have a "C" rating for use during pregnancy and unknown effects on lactation
  • Risk versus benefit analysis for each individual who is pregnant or nursing
  • Neuraminidase inhibitors
    • Active against both influenza A and B
    • Less viral resistance than M2 inhibitors
    • Oseltamivir (Tamiflu) 75 mg bid for 5 days
    • Zanamivir rotadisk inhaler (Relenza) 2 puffs bid for 5 days

M2 inhibitors
  • Not currently recommended to use in the United State because of high levels of resistance
  • Active against influenza Type A
  • No use against influenza Type B
    • Amantadine
    • Rimantadine

2. Further management
  • Complications
    • Respiratory symptoms >5 days may suggest pneumonia and need for CXR
    • Exacerbation of chronic bronchitis or asthma
    • Primary viral pneumonia
    • Secondary bacterial pneumonia
    • Other bacterial superinfections
    • Myositis, myoglobinuria, elevated serum creatine phosphokinase
    • Guillain-Barré syndrome
    • In children:
      • Croup
      • Otitis media
      • Reye's syndrome

Follow-Up

1. Return to office
  • Most pts can be treated at home
  • Pts should return to office if:
    • Systemic symptoms do not resolve within 5 days
    • Respiratory symptoms do not improve within 5 days
  • Recommendations for earlier follow-up
    • Worsening or severe dyspnea
    • Fever is not controlled by antipyretics
- Unable to maintain adequate hydration
- Mental status changes
- Worsening headache or neck ache

2. Refer to specialist
   - Severe respiratory compromise
   - Co-morbid respiratory conditions
   - Neurologic deficits

3. Admit to hospital
   - Patients with exacerbations of underlying respiratory dz
   - Elderly with signs of pneumonia or rehydration
   - Pts with significant respiratory compromise

**Prognosis**
1. Very good for pregnant women but lack of randomized, controlled trials limits definitive prognosis
2. Complications
   - Pneumonia, bacterial superinfection, myositis

**Prevention**
1. Avoidance of sick contacts
2. Hand washing
3. Vaccine
   - Two types
     - Inactivated influenza vaccine
       - Recommended for MOST persons receiving the vaccine including pregnant women and nursing mothers
       - No adverse fetal effects
     - Live-attenuated vaccine via nasal spray
       - Approved for ages 5-49 years only
       - NOT recommended for pregnant women or nursing mothers
     - Updated yearly to reflect the influenza A and B virus strains in circulation
     - 70-90% effective in preventing influenza in healthy adults under 65 years old
   - Annual vaccinations for:
     - Persons at high risk for influenza-related complications
       - Pregnant women during influenza season
       - Children aged 6-59 months
       - Adults over age 50
       - Persons with certain chronic medical conditions
       - Immunosuppression
       - Lung dz (incl. asthma, COPD)
       - Certain cardiovascular conditions
       - Renal dysfunction
       - Hemoglobinopathies
       - Metabolic disorders including diabetes
     - Persons who live with or care for persons at high risk
       - Household contacts of those persons at high risk
       - Health-care workers
4. Prophylaxis
   o Oseltamivir in persons >1 year OR zanamivir in persons >5 years
     ▪ Can be used seasonally or to limit transmission of influenza within
       institutions during outbreaks

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