**INFLUENZA**

Epidemiology

Every year in the US, influenza causes:

* 200,000 hospitalizations
* 36,000 deaths
* Infection in 5-20% of the population
* $12 billion in expenditures and lost productivity

The Influenza Virus

* Family: *Orthomyxoviridae*
* Genera: A, B, and C
  + A causes seasonal flu
  + B causes sporadic outbreaks
* ssRNA (-) virus
* Genome contains 8 RNA segments (7 for C)
* 11 proteins, 2 major surface antigens
  + Hemagglutinin
  + Neuraminidase
* Mutates very rapidly and often

Microbiology

Influenza A

* Characterized by mix of major antigens
  + 16 HA, 9 NA
* Primary reservoir of influenza A = birds; some also in pigs

Named as

* genus/±species/location/strain #/year/(subtype)
  + e.g. A/California/07/2009/(H1N1)

Antigenic drift

* Minor changes in viral antigens
* Due to evolutionary pressures
* Attenuated memory immune response
* Reason for annual vaccination and epidemics

Antigenic shift

* Major changes in viral antigens
* Due to reassortment/cross-species events
* Minimal memory immune response
* Reason for pandemics

Pathogenesis

* Spread primarily from respiratory droplets
  + Secondary route: contact -> respiratory
* Respiratory tissues invaded
* Interferons and interleukins released
* Antibodies produced
  + Most important – vs HA
* Symptoms caused by cellular destruction and cytokine release
* Incubation period – 1-4 days
* Viral shedding starts 1 day before Sx and lasts ~5+ days after

The Flu or Cold? Comparison of Influenza and the Common Cold

Complications

* Primary viral pneumonia
  + Less common, most severe
  + Risks: cardiac disease, pregnancy (?)
* Secondary bacterial pneumonia
  + Common causes: *S. pneumoniae, S. aureus, H. influenzae*
  + Risks: cardiac or pulmonary disease, advanced age
* Pulmonary complications
  + COPD, asthma exacerbations
* Reye’s syndrome (influenza B)
  + Avoid ASA in children

Risk Factors

* Acquisition
  + Age (young and old)
  + Lack of immunity
  + Health care and child care workers
  + Crowded living conditions
  + Nursing homes, dorms, barracks
  + Pregnancy
  + Immunocompromised
* Severe Disease After Infection
  + Chronic cardiac or pulmonary disease
  + Advanced age
  + Pregnancy
  + Chronic renal or metabolic disease
  + Immunocompromised

Diagnosis

* Often diagnosed based on symptoms alone
* Rapid tests available
  + Nasopharygeal swab
  + 15 min answer… or not
* Gold standard: viral culture
  + 5-7 days: the answer!
* CBC, “standard” labs not useful

Immunity

* Immunoglobulins directed mainly towards surface antigens of specific strains of specific subtypes
* Mutations lead to decreased or eliminated immunity

The Drugs – M2 Ion Channel Inhibitors

* Amantidine, Rimantidine
* Inhibit viral uncoating and HA processing by interfering with M2 protein, an ion channel
  + Only active against influenza A
* Well absorbed, eliminated renally
* GI and CNS adverse effects (anxiety, lightheadedness, difficulty concentrating)
  + Amantadine>Rimantidine
* Rimantidine 4-10x Amantadine in potency
* Dose: 100mg PO BID; 100mg PO daily ≥65 YO
* Clinically, reduce duration of symptoms by 1-2 days in susceptible strains
* Used in prophylaxis when dominant strains are susceptible
* Resistance
  + Emerges *during therapy*
  + >90% of US strains are resistant *before therapy*
* Best use: Parkinson’s disease (amantadine)

M2 Ion Channel Inhibitor Efficacy

The Drugs – Neuraminidase Inhibitors

* Oseltamivir, Zanamavir
* Destroy NA receptors, preventing release of virions from infected cells and slowing replication
* Active against influenza A and B
* Resistance does occur, but is currently uncommon in dominant strain (2009-11)
  + ~10% in 2008-9
* Most effective when started early; little utility >48 hr after symptoms start
* Table: formulation, indications, dose TX, prophylaxis, AR
* Zanamivir – How to Use

<http://www.relenza.com/using-your-diskhaler/how-to-use-relenza.html>

* Peramavir
  + Non-FDA-approved IV neuraminidase inhibitor
  + Emergency use authorizations (EUAs) granted by FDA in 2009-10 flu season for novel H1H1 infection
* Efficacy

Treatment – General Approach

Who should ALWAYS be treated?

* Severe disease
* Patients requiring hospitalization
* Progressive disease
* Children (especially <5)
* Children <19 on long-term aspirin therapy
* Adults >65
* Patients with asthma and other comorbidities
  + Diabetes, renal disease, CV disease, pulmonary disease, etc
* Pregnant women
* Immunosuppressed

Treatment - Protocol

* How long?
  + 5 days
  + Longer in immunocompromised?
* What if >48 hours?
  + Judgment call
  + Treat if at risk
* What if influenza is not confirmed?
  + Treat anyway

Treatment – Symptomatic Care

* Rest, rest, and more rest
* APAP/NSAIDs for myalgias
* Antihistamines for rhinitis
* Warm chicken soup, teas
* Throat lozenges
* STAY HOME!!

Resistance

Vaccination – Dose, Age

Who should be vaccinated?

* In short, everyone (6 mos and up)
* 85% of US population has an indication for vaccination
* <50% of US pop is vaccinated annually
  + <40% with pH1N1 09-10
* Children receiving 1st influenza vaccination should receive a 2nd

Who REALLY needs to be vaccinated? Priority populations in the event of a shortage

* Children 0.5-5 yrs old
* Pregnant women
* Age >50
* Children on chronic ASA
* Anyone with chronic pulmonary or CV dz (not HTN)
* Pts with chronic dz that requires medical F/U
* LTCF residents
* Healthcare workers
* Family/caregivers of children <7 YO

Influenza Vaccine – Efficacy

* Efficacy depends on host status and antigen matching
* If vaccine is well matched, efficacy rates of 70-90% are in <65 YO
* If vaccine is poorly matched, efficacy rates are 50-60% in <65 YO
* Flu-related hospitalizations decrease even more
* Efficacy is lower in elderly
  + 30-40% in preventing influenza
  + 50-60% effective in preventing flu-related hospitalization or pneumonia
  + 80% effective in preventing flu-related death
* LTCF residents – lower effectiveness
  + Vaccination rates >80% + HCWs -> better outcomes

Influenza Vaccine – Safety

* 1976, new H1N1 strain in NJ killed one soldier and infected >200
* National reaction to possible pandemic occurred
* Reports of Guillain–Barré Syndrome (GBS) associated with vaccination appeared
  + 1 per 100,000 additional (1-2 per 100,000 normally)
* GBS risk may be higher post-influenza that with vaccination
* Systemic reactions can be seen after vaccination
  + Immune response
* Complications after vaccination are very rare
* No association with thimerosol and autism

Influenza Vaccine – Production

* Decision on strains to include made in February by WHO
* Virus cultured in chicken eggs
* Scaled up for mass vaccination in October

Chemoprophylaxis

* Administration of antiviral drugs to prevent influenza in at risk patients
  + Unable to be vaccinated
  + Exposed family members
* Amantadine, Rimantidine not recommended
* Oseltamivir, Zanamivir both effective
  + Doses: oseltamivir 75 mg PO daily; zanamivir 10 mg inhaled daily
  + Duration: 10 days after exposure, or entire influenza season

Prevention

* Avoid inhaling influenza virus
  + Stay away from sick patients
  + Encourage coughing/sneezing into tissues, or mask wearing
  + Wear a mask
* Avoid transmitting flu virus to your nose and mouth
  + Wash those hands!
  + Don’t touch your face and nose
  + Avoid sick people

Summary

* Influenza is a highly contagious, largely preventable disease
* Vaccination is the key component of control
* Antivirals are useful early in therapy
* Pharmacists can and should have an active role in vaccination and triaging