Going Viral: Something Catchy for Your Old Age 2017

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Objectives

• Recite the common causes of viral pneumonia in the elderly
• Recognize and manage norovirus infection
• Apply appropriate preventive measures to avoid viral infections in the elderly
Virus: diseases of the young?

- URIs
- Sinusitis
- Pharyngitis
- Conjunctivitis
- Otitis media
- Meningitis
- Skin: HSV, HZV
- Pneumonia/pneumonitis
- Pleuritis
- Hepatitis
- Myocarditis
- Viremia
- Gastroenteritis
- Cancer: HPV, hep C & B
NEJM Pneumonia: 2488 patients

A. Specific Pathogens Detected

- Patients with a Positive Result (%)
- Pathogens:
  - Human rhinovirus
  - Influenza A or B
  - S. pneumoniae
  - Respiratory syncytial virus
  - Parainfluenza virus
  - Coronavirus
  - Mycoplasma pneumoniae
  - S. aureus
  - Adenovirus
  - Legionella pneumophila
  - Enterobacteriaceae
  - Other

- Specific Pathogen Detection:
  - Viral pathogen only (22%)
  - Viral-viral co-detection (2%)
  - Bacterial-viral co-detection (3%)
  - Bacterial pathogen only (11%)
  - Fungal or mycobacterial detection (1%)
  - No pathogen detected (62%)

- Patients with a Positive Result (%): 9.194, 8.132, 7.115, 6.88, 6.68, 6.67, 5.53, 4.43, 3.37, 3.32, 3.32, 3.31, 3.74
RSV Pneumonia

RNA Virus; Proteins G+F; Subgroup A+B
RSV
Respiratory Syncytial Virus

- **Transmission**: large particle droplets at short distances (3 to 6 feet)
- **Spread via direct contact or fomites**: childcare centers, schools, hospitals, workplace
- **Fomites**: viable on surfaces for several hours and more than 30 minutes on hands (dog)
- **Contact**: hand to eye or hand to nasal epithelium results in self-inoculation
- **42% of infected persons are asymptomatic**
Respiratory Syncytial Virus

- Annual epidemics during late fall, winter, early spring
- Infants infected during the 1st year of life; 100% of infants infected at least once by 2nd birthday
- Most experience only URI symptoms
- 30% develop LRI disease: bronchiolitis and/or pneumonia; just like the nose clogging then unclogging, chest x-ray of pneumonia may change from day to day
Respiratory Syncytial Virus

- Incubation period: 2-8 days, 5 days most common
- Viral shedding: 3-8 days, longer in young infants and immunocompromised, especially HIV infection, where shedding may last 4 weeks or longer

Respiratory Syncytial Virus in Older Adults: A Hidden Annual Epidemic Sept 2016

Respiratory Syncytial Virus

- About 2% of all children are hospitalized for RSV during their first 12 months of life, usually in the first 3 months of life.

- About 100 children die from RSV every year but highest mortality is in elderly!

- Disease in infants is a major reservoir for disease in adults.

Respiratory Syncytial Virus Burden

- 18% office visits by elderly adults for respiratory illnesses during winter are RSV related
- RSV: roughly 177,000 hospital admissions per year in US
- 11% of hospitalizations for pneumonia
- 11% of chronic obstructive pulmonary disease
- 5% of congestive heart failure
- 7% of asthma
- 8% death rate: **14,000 deaths annually in elderly**

Diagnosis of RSV

- Chest radiograph, pulse O2, blood gas, ESR, CRP, CBC, procalcitonin

- Rapid diagnostic antigen assays: (See list of products at https://www.google.com/?gws_rd=ssl#q=rapid+rsv+test&tbn=shop&*)
  - On site antigen detection tests like QuickVue or Binax: sensitivity 80%; but low in older adults: 30%
  - Lab antigen detection tests: more sensitive ≥90%

- Cell culture: sensitivity to temperature, results vary

- RT-PCR: most reliable and expensive (billing = $2700)

- Serologic testing: paired sera mandatory; rarely used
  
  J Clin Microbiol 2015; 53: 3738–3749
  
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4652120/
RSV Treatment

• Symptomatic care
• **Ribavirin:** really debatable efficacy
• Drugs under study: presatovir, ALS-008176, ALX-0171
• Prophylaxis in high-risk groups in pediatrics:
  – **Palivizumab:** monoclonal antibody, monthly IM injections during RSV season
RSV Vaccine Trials

- RSV-F target vaccines
- Older adults
- Infants
- Pregnant women

Novavax F protein failure 2016

http://ir.novavax.com/phoenix.zhtml?c=71178&p=irolnewsArticle&ID=2202271
VIRAL Pneumonia Multitude

- Parainfluenza virus: 4 types
- Human metapneumovirus: 4 genotypes
- Rhinovirus: ≥100 serotypes
- Adenovirus: 7 species
- Coronavirus: 4 genera; SARS
- Varicella, measles, mumps, rubella, CMV, EBV, dengue
- RVP: cost high!
Diagnosis?

Case courtesy of Dr Jayanth Keshavamurthy, Radiopaedia.org, rID:44612
Herpes zoster: Chickenpox & Shingles

Acute HZV: more dangerous in adults; lasting consequences.

Shingles: 50% risk in elderly; 1 million/yr; PHN 9-25%

NEJM 2010:362: 1128,1227
Shingles vaccine: 1 dose: give within 30 mins.

- 24% vaccine rate 2016
- No need to take history of past chicken pox or shingles
- No need to give chickenpox vaccine first but you can if no CP history, 2 doses 4 weeks apart
- When to give: age ≥50 years vs age ≥60 years
- Role of the pharmacist: age ≥65 yrs.
- Concomitant use with PPSV23/ PCV13 okay
- Use with immunocompromised person in household okay
- Use after personal history of zoster (shingles): may give (+/- benefit) in 1 year or wait at least five years; recurrence rate 6% within 5 yrs. time; benefit may be better after that
- Standing order increases vaccination rate;
- VE 51% against zoster; 67% against PHN
- Contraindications: pregnancy, immune deficiency (HIV), chronic steroid use; cancer, chemotherapy, radiation therapy
- New killed vaccine: GSK 2 doses two months apart: VE 91%
Hepatitis A & B Vaccines

Vaccinate those who are adopted internationally

Salads and fruits: hepatitis A
Liver disease: cirrhosis, alcoholism
Diabetes mellitus: ≤59 yrs. routine; 60 and over elective

**Vaccines:**

Hepatitis A: 0, 6 mos
Hepatitis B: 0, 1, 6 mos
Twinrix (A+B): 0, 1, 6 mos

Must give all 3 doses to cover both Hep A +B.
NOROVIRUS

- RNA virus: 6 genogroups: 3 genogroups affect humans: 25 genotypes; you can be infected multiple times; new Q3-5 yrs
- 12-48 hour incubation; duration 24-72 hours; can shed virus for up to 2 wks after recovery
- One gram stool: 1 trillion viral copies; NNTI = 18
- Vomiting, nausea, cramps, fever, headache, myalgia
- Dehydration, death
NOROVIRUS

- 19-21 million cases/yr in US; Nov-Apr
- 1.7-1.9 million visits; 70,000 hospitalizations; 500-800 deaths (world 50,000 children die/yr)
- 50% of food-related disease d/t norovirus: leafy greens (lettuce), fresh fruits, shellfish (oysters); any food served raw or handled after cooking;
- Person to person; water any where
- Stool specimen: RT-qPCR assay; enzyme immunoassay for outbreaks: RIDASCREEN Norovirus 3rd Generation EIA; up to 16% carry
NOROVIRUS: Kaplan Criteria

1. A mean (or median) illness duration of 12 to 60 hours,
2. A mean (or median) incubation period of 24 to 48 hours,
3. More than 50% of people with vomiting, and
4. No bacterial agent found.

When all 4 criteria present, very likely norovirus. About 30% of norovirus outbreaks do not meet these criteria. If criteria not met, it does not mean that outbreak was not caused by norovirus.
### Setting of Norovirus Outbreaks

**Reported Through the National Outbreak Reporting System (NORS), 2009-2012**

<table>
<thead>
<tr>
<th>Exposure Setting</th>
<th>Number of Outbreaks</th>
<th>Percentage of Outbreaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health care facility</td>
<td>2189</td>
<td>62.7%</td>
</tr>
<tr>
<td>Restaurant or banquet facility</td>
<td>771</td>
<td>22.1%</td>
</tr>
<tr>
<td>School or day-care facility</td>
<td>214</td>
<td>6.1%</td>
</tr>
<tr>
<td>Private residence</td>
<td>69</td>
<td>1.9%</td>
</tr>
<tr>
<td>Other/multiple settings</td>
<td>251</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

Data on specific settings are restricted to outbreaks with a single exposure setting; for foodborne outbreaks, setting refers to the setting where implicated food was consumed.
NOROVIRUS Management

- Fluids; ondansetron; acetaminophen; loperamide; bismuth subsalicylate
- Hand hygiene: soap/water; alcohol products ???
- Surface cleansing: overall role?
- Cohort ill patients; contact precautions; suspend group activities
- Staff off until 48 hours after illness resolves
- Surveillance for new cases

Annual Flu Epidemic

- **Prevention:**
  - Hygiene
  - Vaccine
  - Antiviral drugs

- **Treatment:**
  - Supportive care
  - Antiviral drugs
  - Respirators/ECMO
Influenza: An Annual Epidemic

• 5%-20% of the US population becomes ill with influenza each year (subclinical or mild cases difficult to identify)
  o 15-60 million cases overall
• 3000-49,000: Estimated annual influenza-related deaths (attributed to flu or flu complications) in US; link to MI, stroke
• 250,000-500,000 deaths world wide
• Influenza and pneumonia: Eighth leading cause of death in the US (all ages)
• 55,000-431,000: Range of estimated annual influenza-related hospitalizations in US
• 90% of hospitalized adults have underlying health condition

MMWR 2017; 66:159-166
https://www.cdc.gov/mmwr/volumes/66/wr/mm6606a2.htm?s_cid=mm6606a2_w
Underlying Medical Conditions in Laboratory-Confirmed Flu: 2013-14

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>22%</td>
</tr>
<tr>
<td>COPD</td>
<td>34%</td>
</tr>
<tr>
<td>Metabolic (DM, etc.)</td>
<td>36%</td>
</tr>
<tr>
<td>Neurologic</td>
<td>21%</td>
</tr>
<tr>
<td>CV</td>
<td>34%</td>
</tr>
<tr>
<td>Obesity</td>
<td>43%</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>22%</td>
</tr>
<tr>
<td>Immune disorder</td>
<td>19%</td>
</tr>
<tr>
<td>NONE</td>
<td>15%</td>
</tr>
</tbody>
</table>

http://www.cdc.gov/flu/weekly/
Older Adults: High Disease Burden

• Older adults represent 13.7% of the US population
• But 63% of influenza-related hospitalizations
• And >90% of influenza-related deaths: most due to type A strains; B strains play little role in death of elderly
• Influenza and pneumonia: No. 7 cause of death in US in persons ≥65 years of age
• Vaccination rates for seniors have hovered in the 65%-70% range for a decade
• Despite having the highest vaccination rate, seniors have highest disease rate
Influenza-related Hospitalizations and Deaths


Influenza and Comorbidities

- Influenza may lead to hospitalization or death from other causes, such as heart failure, myocardial infarction, stroke, or respiratory collapse.
- Influenza causes complications like pneumonia, sepsis, sinusitis, otitis media, viremia.
- The pivotal contributing role of influenza in these clinical consequences is often unrecognized.
- Age itself is a comorbidity: immunosenescence: lower antibody levels post-vaccination.
- Medications may interfere with response to flu vaccine: statins.

J Infect Dis (2016) 214 (8): 1150-1158
Influenza vaccination has been shown to reduce mortality related to specific diseases in adults:

- Cardiovascular disease\(^1\)-\(^3\)
- Stroke\(^1\)
- Renal disease\(^1\)
- Diabetes\(^1\)
- Pneumonia, other acute respiratory disease\(^1\)-\(^3\)
- Chronic obstructive pulmonary disease (COPD)\(^1\)

Impact of influenza vaccination on cause-specific mortality; 10-month follow-up of 35,637 vaccinated and 67,061 unvaccinated persons ≥65 years of age in Taiwan\(^1\)

2013-14 Flu Vaccine Coverage

Figure 1. Early season and end of season flu vaccination coverage estimates, National Immunization Survey and National Internet Flu Survey, United States, 2012-13 and 2013-14 flu seasons

2013-14 Season
Health Care Workers: 63%
Doctors: 92%
Nurses: 90%
Pharmacists: 86%
Admin.: 54%
SNF: 52%
Aides: 49%

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6337a1.htm?s_cid=mm6337a1_w.pdf
Flu Vaccines

(one egg for each type made in eggs)

- **IM (IIV): trivalent (2xAs + 1xB);** Fluvirin® (≥4 yrs); Afluria® (≥9 yrs)
- **IM (IIV): quadrivalent (2xAs + 2xBs);** Fluarix®/Fluzone®/FluLaval® (≥6 mos); Afluria® (≥18 yrs)
- **High-dose IM: trivalent;** Fluzone High-Dose® (≥65 yrs)
- **Adjuvant enhanced IM: trivalent;** Fluad® (≥65 yrs)
- **Intradermal (ID): trivalent;** Fluzone ID® (18-64 yrs)
- **Needle-free jet:** Afluria® (18-64 yrs)
- **Baculovirus produced (RIV): trivalent;** egg free; FluBlok® (≥18 yrs)
- **Dog kidney cell produced:** trivalent; low egg protein: 50 femtograms (5X10 [-14]); Flucelvax® (≥4 yrs)
Adult Flu Vaccines: Fun Facts!

- **Flublok**: baculovirus; for egg anaphylaxis; age 18-64 yrs; cost 3X IIV

- **Needle-phobic**: trivalent ID, 18-64 yrs; injector jet

- **Fluzone ID**: lower antigen content; almost no pain; same side effects with more local reaction, visible in skin but generally NOT more irritating than IIV; trivalent only; cost slightly more

- **Fluzone High-Dose**: 4 times antigen content but same frequency of side effects as IIV with exception of increased local tenderness; trivalent only; B strain of little import to seniors; cost 2X IIV; adjuvanted (Fluad) role not clear as yet

- **Give as soon as available**: a second dose is not proven to help; stop vaccinating as late as 6/30/next year

- **Flucelvax**: dog kidney; useful for epidemics; age ≥18 yrs; might be okay for egg allergy; cost = IIV
Contraindications and Side Effects

• Anaphylaxis to eggs or vaccine component: use RIV
• Persons who experience only hives with exposure to eggs may receive RIV (if age ≥18) or, with additional safety precautions, IIV
• Side effects: local and systemic; pain, swelling, nasal congestion; fainting
• Precautions:
  o Guillain-Barré syndrome within 6 weeks of previous dose
  o Moderate or severe illness with/without fever
Problems with Flu Vaccine

- Antigenic drift and shift in circulating flu viruses
- Inaccurate vaccine match to current circulating flu strains
- Overcrowding and poor hygiene; higher viral load exposure?; co-infection?
- Poor immune response: older age or immunocompromising conditions
- High-risk medical conditions; anatomic issues; smoking
- One answer: high-dose (antigen) vaccine induces higher antibody titers than regular-dose vaccine and reduces lab-confirmed influenza by 24% (NNTV= 220)

NEJM 2014;371(7):635-645
Effectiveness of Influenza Vaccines Against Influenza-like Illness, by Age

During these 7 influenza seasons, the range of vaccine effectiveness was 26%-52% in persons ≥65 years of age and 62%-76% in those 15-64 years of age.

Estimates of Flu Vaccine Effectiveness (VE) 2016-2017

- Against influenza A and influenza B virus infection associated with medically attended ARI was 48% (95% confidence interval [CI] = 37%–57%)
- Most influenza infections were caused by A (H3N2) viruses.
- VE estimated to be 43% (CI = 29%–54%) against illness caused by influenza A (H3N2) virus and 73% (CI = 54%–84%) against influenza B virus.
- High dose may be more effective for seniors: 2017 report of 24% effective in reducing mortality
  
  (J Infect Dis jiw641. DOI:https://doi.org/10.1093/infdis/jiw641)
- VE for hospitalization, death under study now through CDC
  
  MMWR, 2017; 66:167-171

https://www.cdc.gov/mmwr/volumes/66/wr/mm6606a3.htm?s_cid=mm6606a3_w