The Influence of Influenza

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The Influence of Influenza

• Introduction
• Pandemic
• Transmission
• Clinical presentation and treatment
• POCT
Characteristics of flu

• Orthomyxovirus A and B (C very mild)
• Undergo reassortment of surface proteins due to inefficient RNA dependent RNA polymerase
  – Drift
  – Shift
## Flu Pandemics

<table>
<thead>
<tr>
<th>Name of pandemic</th>
<th>Date</th>
<th>Deaths</th>
<th>Fatality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spanish Flu (H1N1)</td>
<td>1918-1920</td>
<td>40 -100 million</td>
<td>2-3%</td>
</tr>
<tr>
<td>Asian Flu (H2N2)</td>
<td>1957-1958</td>
<td>1 - 1.5 million</td>
<td>&lt;0.2%</td>
</tr>
<tr>
<td>Hong Kong Flu (H3N2)</td>
<td>1968-1969</td>
<td>0.75 - 1 million</td>
<td>&lt;0.2%</td>
</tr>
<tr>
<td>‘Swine Flu’ (H1N1)</td>
<td>2009-2010</td>
<td>150 000+</td>
<td>0.03%</td>
</tr>
<tr>
<td>Seasonal (H3N2/H1N1)</td>
<td>seasonal</td>
<td>250 000-500 000</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

Information taken from en.wikipedia.org/wiki/influenza
Pandemic Influenza
The H1N1

The A/H1N1 virus

An unusual cocktail of avian, swine and human viruses

Bird flu

Human flu

Swine flu

Pigs may harbour several flu viruses simultaneously. The pathogens may mix to create a new viral strain

Transmission

Pig to human

By inhaling viral particles (there is no risk from eating cooked pork)

Human to human

By inhaling viral particles

Symptoms

High fever
Coughing, sneezing
Breathing difficulties
Loss of appetite

AFP 290409
WHO report

New Influenza A (H1N1),
Number of laboratory confirmed cases as reported to WHO

Status as of 24 June 2009
06:00 GMT

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Map produced: 24 June 2009 10:00 GMT

Source: WHO
Pandemic Influenza

• In Top 10 Global health risk
  – Vaccine hesitancy, Pandemic and AMR
  – 153 institutions in 114 countries involved in monitoring

• All institutions in UK have pandemic plan
  – Staffing- acute services, ITU
  – Treatment of patients
  – Isolation
  – IPCC
  – Mortuary
  – Services
Areas with confirmed human cases of H5N1 avian influenza since 2003 *

Country, area or territory
Cases: cumulative number
Deaths: cumulative number

- Turkey: Cases: 12, Deaths: 4
- Azerbaijan: Cases: 8, Deaths: 5
- Iraq: Cases: 3, Deaths: 2
- Pakistan: Cases: 3, Deaths: 1
- Egypt: Cases: 50, Deaths: 22
- Djibouti: Case: 1, Death: 0
- Bangladesh: Cases: 137, Deaths: 112
- China: Cases: 30, Deaths: 20
- Lao People’s Democratic Republic: Cases: 2, Deaths: 2
- Viet Nam: Cases: 106, Deaths: 52
- Myanmar: Cases: 1, Deaths: 0
- Cambodia: Cases: 7, Deaths: 7
- Thailand: Cases: 25, Deaths: 17

* All dates refer to onset of illness

Data Source: WHO
Map Production: Public Health Information and Geographic Information System (GIS)
World Health Organization
Transmission

(a) Graph showing the comparison of respiratory dose through long-range airborne and intranasal dose through fomites for different surfaces: private surfaces, top five high-touch surfaces, desktop, public surfaces, and floor.

(b) Graph showing the respiratory dose (TCID50) and intranasal dose (TCID50) over surface clean interval (h) for respiratory dose through long-range airborne and intranasal dose through fomites.

Viable virus

- Plastic control
- Telephone handset
- Pine
- Computer Keyboard
- Stainless steel
- J-cloth

B

Graph showing the virus titre (PFU/mL) over time (h) with different surface materials and time intervals.
Transmission

- Can be asymptomatic, symptoms normally within 1-4 days of transmission
- Transmission occurs 1 day prior to Symptoms
- Decreases rapidly after 5 days
- 30% elderly can secrete virus for 1 week, immunocompromised for longer
- Antivirals reduce shedding
- Attack rate in outbreak 20-30% in patients, 11-29% in healthcare workers
A Yearly Problem
Clinical Presentation

• Temp, rigors, fever, headache, myalgia, sore throat, nasal discharge, non-productive cough.

• Many DO NOT present with classical symptoms
Complications

- Primary viral pneumonitis
- Myocarditis, pericarditis
- Secondary bacterial pneumonia
- Rhabdomyolysis
- Transverse myelitis
- Meningoencephalitis
- Aseptic meningitis
Infection Prevention

- 6/8 randomised studies show no difference
- FFP3 fit tested masks should be used when aerosol generation occurs

Loeb et al. JAMA 2009 302(17)
Treatment

• Neuraminidase inhibitors
  – Oseltamavir- oral
    • Resistance seen in immunosuppressed, H1N1
  – Zanamavir- IV or intranasal

• Adamantane
  – Rimitadine or Amantadine- pan resistance
Treatment and Prevention

• Cochrane 2014- reduced time of symptoms by 16.8hrs (8.4-25.1hrs)

• no difference in treatment on:
  – Hospital admissions (RD 0.15%; 95% CI -0.78 to 0.91)
  – Serious complication (RD 0.07%; -0.78 to 0.44)

• Prophylaxis reduced transmission:
  – Individuals prevention (RD 1.48%; 1.83-3.88)
  – Household contacts (RD 13.6%; 12.8-16.55)
Treatment

• In Intention to Treat with Infection metanalysis:
  – 44% reduction in LRTI (RR 0.56; 0.42-0.75)
  – 63% reduction in hospitalisation (0.37; 0.17-0.81)
• In hospitalised patients
  – Lower risk of mortality (OR 0.8; 0.7-0.95)
• Generally treatment needs to be given within 48hrs

Dobson J. Lancet 2015; 385
Muthuri SG Lancet resp dis 2014; 2
Vaccination

- Over 65 aTIV
- HCW or needing QIV
- 2-18 LAIV
- CQUIN

Figure 1. Seasonal Flu Vaccination Coverage, by Age Group and Season, United States, 2010-2017

Error bars represent 95% confidence intervals around the estimates. Starting with the 2011-12 season, adult estimates reflect changes in NHIS survey methods: the addition of cellular telephone samples and a new weighting method.
• Autism rates through the roof--why doesn't the Obama administration do something about doctor-inflicted autism. We lose nothing to try.
• Massive combined inoculations to small children is the cause for big increase in autism....
• "@P01YN0NYM0U55: @jamandatrtl #vaccines #Shills insist #Autism starts in utero or genetic, but parents insist sudden onset after #vaccine"
• "@OnlineOnTheAir: My friend's son, immediate #autism after #vaccines 10 yrs ago. So sad. Keep up good work Nay-sayers will understand soon."
• So many people who have children with autism have thanked me—amazing response. They know far better than fudged up reports!
• I'm not against vaccinations for your children, I'm against them in 1 massive dose. Spread them out over a period of time & autism will drop!
• With autism being way up, what do we have to lose by having doctors give small dose vaccines vs. big pump doses into those tiny bodies?
Point of care tests for flu

Concerns with point of care testing:
- Accuracy
- Usability
- Up-skilling of clinical staff
- Low throughput
- Infection control
- Cost
Turn around time of results

- Time delay for standard lab test result in:
  - District general Hospital: > 5 days
  - Hosp with offsite lab: > 40 hours
  - Hosp with onsite lab: > 25 hours
Data recorded

- Time to result reference test (standard laboratory test) and the index test (Alere NPT test).
  - Time to standard test result 2.8 days vs. 60 minutes (Alere NPT).

- Isolation precautions used.
  - 75% (68/91) of patients with influenza, were not isolated
  - 69% (343/489) of patients without influenza, were isolated.

- Antivirals given.
  - 54% (49/91) of patients with influenza, were given antivirals
  - 12% (59/498) of patients without influenza, were given antivirals.
Results (n=1000)

<table>
<thead>
<tr>
<th>Cost</th>
<th>Isolation accuracy = study experience</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCR</td>
</tr>
<tr>
<td>Isolation cost</td>
<td>£41,180</td>
</tr>
<tr>
<td>Laboratory testing cost</td>
<td>£70,000</td>
</tr>
<tr>
<td>Antivirals</td>
<td>£1700</td>
</tr>
<tr>
<td>Nosocomial infection</td>
<td>£20,970</td>
</tr>
<tr>
<td>Total</td>
<td>£133,850</td>
</tr>
</tbody>
</table>

- Isolation and antiviral treatment costs £15,330 greater with Alere i NPT than PCR testing.
- Testing costs and onward transmission costs were less in NPT testing strategy.
- Overall saving of **£43,190** per 1000 cases of suspected influenza
Isolation and antiviral treatment costs £221,630 less with Alere i NPT than PCR testing.
- Costs of onward transmission (false negative results) were £6,590 more with Alere.
- Total savings with Alere i NPT are £261,590 per 1000 cases.
Number of patients with influenza (A and B) admitted to the trust (by week 2018/2019)
Patients with COPD admitted with Influenza

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Flu A or B Positive n = 115</th>
<th>Flu A or B Negative n = 180</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 Day Readmission, n (%)</td>
<td>41 (35.6)</td>
<td>96 (53.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>NIV, n (%)</td>
<td>20 (6.8)</td>
<td>19 (10.6)</td>
<td>0.09</td>
</tr>
<tr>
<td>ITU Admission, n (%)</td>
<td>4 (3.5)</td>
<td>9 (5.0)</td>
<td>0.54</td>
</tr>
<tr>
<td>90 Day Mortality, n (%)</td>
<td>12 (10.4)</td>
<td>34 (18.8)</td>
<td>0.69</td>
</tr>
<tr>
<td>90 Day Readmission or Death, n (%)</td>
<td>50 (43.5)</td>
<td>96 (53.3)</td>
<td>0.1</td>
</tr>
<tr>
<td>Length of Stay, days</td>
<td>4 (2-8)</td>
<td>5.5 (2-10)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flu A or B Positive n = 115</th>
<th>Flu A or B Negative n = 180</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinopenia (&lt;0.05x10/l), n (%)</td>
<td>81 (70.4)</td>
<td>99 (55.0)</td>
<td>1.9 (1.19-3.2)</td>
</tr>
<tr>
<td>CRP&gt;100, n (%)</td>
<td>24 (20.9)</td>
<td>59 (32.8)</td>
<td>0.19</td>
</tr>
<tr>
<td>WCC&gt;11, n (%)</td>
<td>44 (38.3)</td>
<td>100 (55.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Consolidation</td>
<td></td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Acute Oxygen, n (%)</td>
<td>16 (13.9)</td>
<td>35 (19.4)</td>
<td>0.67 (0.35-1.28)</td>
</tr>
<tr>
<td>Treatment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics</td>
<td>88 (76.5)</td>
<td>133 (73.9)</td>
<td></td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>66 (57.4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Antibiotics + Oseltamivir</td>
<td>45 (39.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>
Influenza

- Major impact yearly on hospitals
- Vaccine reduces infection
- Antivirals may help with acute infection, certainly help to prevent
- Pandemics will occur again
- Risk ever present of sporadic avian Influenza
- POC testing may be helpful