Acute Respiratory Infection

Dr Anthony Gibson
Range of Conditions – Upper tract

- Common Cold – coryza
- Sore Throat - Pharyngitis
- Sinusitis
- Epiglottitis
Range of Conditions – Lower

• Acute Bronchitis
• Acute Exacerbation of COPD
• Pneumonia
• Influenza
Influenza

• Annual epidemics
• Rates of serious illness and death highest in:
  – >65yrs
  – <2yrs
  – Significant co-morbidities such as diabetes, cardiovascular disease and chronic respiratory disease.

  – Immunization of high risk groups, over 65’s health workers and carers.
Nice guidelines for the Use of Antivirals in influenza

- oseltamivir and zanamivir are recommended, within their marketing authorisations, for the treatment of influenza in adults and children if all the following circumstances apply:
  - national surveillance schemes indicate that influenza virus A or B is circulating
  - the person is in an 'at-risk' group as defined
  - the person presents with an influenza-like illness and can start treatment within 48 hours (or within 36 hours for zanamivir treatment in children) of the onset of symptoms as per licensed indications

- during localised outbreaks of influenza-like illness (outside the periods when national surveillance indicates that influenza virus is circulating in the community), oseltamivir and zanamivir may be offered for the treatment of influenza in 'at-risk' people who live in long-term residential or nursing homes. However, these treatments should be offered only if there is a high level of certainty that the causative agent in a localised outbreak is influenza (usually based on virological evidence of influenza infection in the initial case).
Neuraminidase inhibitors for preventing and treating influenza in adults and children (Review)

Time to alleviation of first symptom

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Zanamivir</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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<td>Mean</td>
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<td>Mean</td>
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<td>7.32</td>
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Total (95% CI) 3031 2380 100.0% -0.60 [-0.81, -0.39]

Heterogeneity: Tau² = 0.01; Chi² = 13.24, df = 12 (P = 0.35); I² = 9%
Test for overall effect: Z = 5.69 (P < 0.00001)
### Time to alleviation of first symptom

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Oseltamivir Mean [hours]</th>
<th>SD [hours]</th>
<th>Total</th>
<th>Placebo Mean [hours]</th>
<th>SD [hours]</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI [hours]</th>
<th>Mean Difference IV, Random, 95% CI [hours]</th>
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<td>M76001</td>
<td>140.6</td>
<td>125.2</td>
<td>933</td>
<td>165.5</td>
<td>156.5</td>
<td>473</td>
<td>26.4%</td>
<td>-24.90 [-41.13, -8.67]</td>
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<td>WV15670</td>
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<td>240</td>
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<td>235</td>
<td>15.9%</td>
<td>-15.50 [-36.42, 5.42]</td>
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<tr>
<td>WV15671</td>
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<td>204</td>
<td>125.3</td>
<td>98.9</td>
<td>200</td>
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<tr>
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<td>134.4</td>
<td>9</td>
<td>0.5%</td>
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<td>145.6</td>
<td>358</td>
<td>192.4</td>
<td>145.2</td>
<td>375</td>
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<td>-7.40 [-28.46, 13.66]</td>
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<tr>
<td>WV16277</td>
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<td>136.4</td>
<td>226</td>
<td>143.7</td>
<td>125.4</td>
<td>225</td>
<td>11.7%</td>
<td>-5.00 [-29.37, 19.37]</td>
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<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>2208</td>
<td></td>
<td></td>
<td>1746</td>
<td>100.0%</td>
<td>-16.76 [-25.10, -8.42]</td>
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</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 6.33, df = 7 (P = 0.50); i² = 0%

Test for overall effect: Z = 3.94 (P < 0.0001)

For the overall effect:
- **Favours oseltamivir**
- **Favours placebo**
Cochrane review conclusions

• There is a reduction to symptomatic improvement in adults: approximately ½ a day
• No evidence of reduction in risk of complications – particularly pneumonia, risk of hospitalisation or death
• No evidence of increased benefit in high risk groups
• When used as a prophylactic agent minimal effect on prevention
Implications of the 2014 Cochrane Review:

The Cochrane review has been reported as suggesting that antivirals are not effective for influenza. This is not the case because of the following aspects of the review:

- variation in outcomes, patient groups, and settings studied limits the conclusions of the review
- the review includes evidence only from RCTs, which by their nature are usually carried out in an otherwise healthy population in the community setting. The review is therefore useful in interpreting the modest effects that NAIs have on the duration of acute symptoms in uncomplicated infection. However, it has limitations in understanding hospitalisations, complications, and the prevention of complications occurring in cases of severe infection, and mortality
- traditional RCTs for non-seasonal influenza viruses with high case fatality rates, or a novel influenza virus with pandemic potential, are by nature not ethical or feasible. No RCTs were carried out on severely ill patients as part of the licensure of these drugs and it would now not be possible to do this
- in the absence of appropriate RCT data on severe influenza, observational studies have important contributions to make to policy development
- a substantial volume of observational data was not considered in the Cochrane Review, including evidence of the ability of NAIs to stop the progression of severe cases of H5N1 or pandemic H1N1 infection.

It is essential that physicians treating severely unwell patients in any setting are not deterred from prescribing NAI drugs as a result of confusion over efficacy. This is especially true for patients hospitalised with proven or suspected influenza.
Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data

Stella G Muthuri, PhD, Sudhir Venkatesan, MPH, Puja R Myles, PHD, Jo Leonardi-Bee, PhD, Tarig S A Al Khuwaitir, FRCP, Adbullah Al Mamun, MPH, Ashish P Anovadiya, MD Pharm, Eduardo Azziz-Baumgartner, MD, Clarisa Báez, Especialista en Epidemiología, Prof Matteo Bassetti, MD, Prof Bojana Beovic, PhD, Barbara Bertisch, MD, Isabelle Bonmarin, MD, Prof Robert Booy, MD, Victor H Borja-Aburto, PhD, Prof Heinz Burgmann, MD, Prof Bin Cao, MD, Prof Jordi Carratala, PhD,
Findings included:

- among patients aged >16 years, treatment with a NAI was associated with a 25% reduction in the likelihood of death compared with no antiviral treatment
- early treatment with NAIs (ie within 48 hours of development of illness) halved the risk of death compared with no antiviral treatment

This supports findings from previous observational studies in hospitalized influenza patients that the clinical benefit of NAI treatment is greatest when started within two days of onset of illness.⁴,⁵, vi
Pneumonia
Pneumonia - introduction

• Significant risk of fatal outcome
  – 5-10% mortality from pneumococcal pneumonia
  – 30% if bacteraemic

• 2600 deaths from pneumococcal pneumonia in UK every year

• 1 million hospital admissions for CAP per year in EU
Age standardized rate per 1000,00 population
% of Streptococcus Pnemoniae isolates resistant to:

macrolides

Penicillin
Right lower lobe pneumonia can present with abdominal pain
Variables associated with mortality

- Over 65 years of age
- Female > Male
- Use of oral corticosteroids
- Pleural effusion
- Atypical pneumonia
- HAP (0.5-2% incidence, 30-70% mortality)
- Recent hospitalisation
- ARF
- Multilobar involvement
- Impaired alertness
CURB 65 severity score

• C  new onset confusion
• U  urea >7
• R  Resp rate >30/min
• B  systolic BP <90 or diastolic <61
• 65  age 65 or older

• Score one point for each of above
CURB 65 and outcome

- 0 or 1  less than 3%
- 2  3-15%
- >/= 3  more than 15%
What do we do well and not so well when managing pneumonia?
BTS national audit data

- Key findings:
  - Reduction in in patient mortality since 2009 to 17.7%
  - Low concordance with local antimicrobial recommendations (40% not in line)
  - High level of miscoding of the diagnosis of pneumonia – 1/3rd patients did not have clinico-radiological changes consistent with CAP
1. 42.5% of patients receiving supplemental oxygen had no valid prescription, despite 70% of hospitals having a policy of setting a target saturation range for all patients at the time of admission to hospital.

2. Only 69% of patients with a prescribed target range had a saturation within the intended range. 9.5% of patients were below the target range and 21.5% were above the target range.

3. 8.8% of patients using oxygen were found to be at risk of iatrogenic hypercapnia due to being above their target range by more than 2% despite recognised hypercapnic risk (prescribed target range of 88-92% or less).

4. Oxygen saturation was reliably documented during observation rounds (104% of expected frequency) but oxygen was signed for on only 28% of drug rounds.
Why use CURB scoring?

• In hospitals with good documentation of CURB scores there is higher concordance with antimicrobial guidance.

• Helps identify those potentially suitable for ambulatory management.

• Helps identify those at highest risk and who require the closest monitoring.
Mortality

Figure 6 – Mortality rate for pneumonia in adults. Data from the World Health Organization World and Europe Mortality Databases, November 2011 update.
Complications of pneumonia

• Respiratory failure

• Pleural effusion - upto 57% (majority resolve)

• Empyema – predisposing factors
  • Diabetes mellitus
  • Immunosuppression
  • GORD
  • Alcohol and drug misuse
empyema
Diagnostic algorithm for the management of patients with pleural infection

1. History, examination & Chest X Ray
   - Pleural effusion and evidence of infection?
     - YES
     - Involve Respiratory Physician
       - Nutrition and DVT prophylaxis
     - Start antibiotics
       - Diagnostic pleural aspiration using Ultrasound guidance
       - Pus?
         - NO
         - Fluid pH Send M/C & S
         - Poor clinical response
         - Repeat fluid sampling
         - Gram stain & culture positive &/or pH < 7.2
         - YES
         - Observe unless clinical indication for chest tube
         - Insert chest tube
       - NO
         - Is the patient better?
           - CXR fluid drained & sepsis improved
             - YES
             - Remove tube
             - Remove tube
           - Day 5-7
         - NO
           - 1. Check tube position on chest X ray
             - 2. Assess tube, residual collection with contrast enhanced CT imaging
             - 3. Early liaison with thoracic surgeons
           - Is the patient fit for radical treatment?
             - YES
             - Surgical therapy
             - Consider large bore drain insertion; less radical surgical techniques, palliative care measures
           - NO
             - Prolonged antibiotics
             - Outpatient review

2. Failed Sampling?
   - Small, loculated effusion?
     - YES
     - Consider CT scan and further image guided aspiration
What to tell patients on discharge

| Recommendations | 23. Explain to patients with community-acquired pneumonia that after starting treatment their symptoms should steadily improve, although the rate of improvement will vary with the severity of the pneumonia, and most people can expect that by:
|                 | • 1 week: fever should have resolved
|                 | • 4 weeks: chest pain and sputum production should have substantially reduced
|                 | • 6 weeks: cough and breathlessness should have substantially reduced
|                 | • 3 months: most symptoms should have resolved but fatigue may still be present
|                 | • 6 months: most people will feel back to normal.
| 24. Advise patients with community-acquired pneumonia to consult their healthcare professional if they feel that their condition is deteriorating or not improving as expected. |
Exacerbations of COPD

COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

Classification

mild (treated with short acting bronchodilators only)
moderate (treated with SDABDs plus antibiotics and/or corticosteroids)
severe (patient requires hospitalisation)
Significance

• 5 year mortality following hospitalization for COPD exacerbation is around 50%

• Factors associated with poor outcome include:
  • Age
  • Low BMI
  • Comorbidities
  • Previous hospitalization for COPD
  • Need for LTOT at discharge
  • High frequency of exacerbations
Treatment

• Short acting bronchodilators

• Systemic corticosteroids can improve lung function and oxygenation and shorten recovery time and hospitalization. Duration of therapy should be 5-7 days (GOLD 2017)

• Oxygen sats 88-92%

• NIV should be the first mode of ventilation in COPD with acute respiratory failure
Use of antibiotics in COPD exacerbations

- Antibiotics when indicated can shorten recovery time and reduce the risk of early relapse, treatment failure and hospital stay.
- Duration should be 5-7 days.
- Thought around 50% of exacerbations caused by infectious agents (bacterial and viral)
- Difficult to determine when to use antibiotics
Kaplan–Meier estimates of the cumulative incidence of developing a second (A) or third (B) exacerbation stratified according to treatment type.

B M Roede et al. Thorax 2008;63:968-973
When to use antibiotics?

• Use in patients with 3 cardinal symptoms:
  – Increase in dypsnoea
  – Increase in sputum volume
  – Sputum purulence

• Have 2 cardinal symptoms if increased purulence of sputum is one of them.

• Or require mechanical ventilation (invasive or non invasive)
  • GOLD 2017
Questions?