CHILDHOOD PNEUMONIA IN LOW INCOME COUNTRIES

Freddy Karup Pedersen
University Clinic of Children and Adolescents, Copenhagen

ECTMIH 2013
Burden of Childhood Pneumonia

- Causes 20% of deaths in children in LIC
- Only 4.3% of deaths in high income countries
- Globally 0.29 events per child year or 150 million new episodes annually.
- 75% of new cases in just 15 countries, more than 50% in just 6 countries (India, China, Pakistan, Bangladesh, Indonesia and Nigeria).
- Severe pneumonia requiring hospitalization accounts for 7-13% of cases.
WHO diagnostic guidelines:

- Developed as case management guidelines to ensure recognition and appropriate treatment of pneumonia in community settings.
- Sensitive for identifying pneumonia but lacking specificity.
- Problematic in asthma, viral bronchiolitis, malaria with tachypnoea, acidosis a.o.
<table>
<thead>
<tr>
<th>WHO Classification</th>
<th>IMCI Classification</th>
<th>Clinical Signs</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pneumonia</td>
<td>Cough or cold</td>
<td>No signs of pneumonia or very severe disease</td>
<td>Symptomatic treatment, advise carer when to return immediately, follow up in 5 days if not improving</td>
</tr>
<tr>
<td>Non-severe pneumonia</td>
<td>Pneumonia</td>
<td>Fast breathing</td>
<td>Give oral antibiotics for 3 days, advise the carer when to return immediately, follow up in 2 days</td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td>Severe pneumonia or very severe disease</td>
<td>Chest indrawing</td>
<td>Give first dose of antibiotic Refer urgently to hospital</td>
</tr>
<tr>
<td>Very severe disease</td>
<td>Any general danger sign</td>
<td></td>
<td>Give first dose of antibiotic Refer urgently to hospital</td>
</tr>
</tbody>
</table>
Methodological difficulties

- 1983 multicenter needlepuncture studies and later smaller studies documents LIC countries pneumonia frequently caused by bacterial pathogens (50%) in contrast to HIC pneumonia (15%)
Most frequent bacterial pathogens:
- Streptococcus pneumonia
- Haemophilus influenzae
- (Staph. Aureus, Klebsiella pneumoniae, non-typhoidal Salmonellae in tropical Africa)
- Main viral causes (rural Kenyan study): RSV, influenza type A and parainfluenza type III, adenovirus, coronavirus, metapneumonia virus
- Often multiple pathogens
Burden of childhood pneumonia increased in high HIV prevalence areas

Pneumonia related mortality is sixfold higher in HIV infected, higher risk of severe pneumonia, high prevalence of TB
Burden of disease

Research needed in:

- Better tools for pneumonia diagnosis
- Rapid and reliable methods for etiological diagnosis
- Existing estimates of disease burden affected by some uncertainty but still depicts childhood pneumonia as a major problem
WHO and UNICEF global action plan for prevention and control of pneumonia (GAPP)

- Highlights Pneumonia as a major cause of deaths in children
- Aims at scaling up interventions with proven benefit
**Strategies to Reduce Childhood Pneumonia**

### General Strategies

Nutrition and micronutrient supplementation

- Exclusive breastfeeding for 6 months in HIV-uninfected mothers
- Adequate nutrition
- Vitamin A supplementation
- Zinc supplementation

### Environmental factors

- Avoidance of indoor air pollution
- Hand washing
## Specific Strategies

### Immunisation
- Measles
- Haemophilus influenzae type b
- Pneumococcal
- Pertussis

### Antibiotic prophylaxis
- Cotrimoxazole for HIV infected or exposed children
- Isoniazide for mycobacterial disease

### Prevention of HIV infection in children
- Upscaling mother to child transmission programs

### HAART in HIV-infected children early
Decreases infant mortality, early neonatal sepsis, ARI and diarrhoea

Bangladesh study:
- 2.4 times higher ARI risk
- 2.2 times higher risk of infant death

Coverage of exclusive breastfeeding only 40% in the 90 countries with more than 90% of child deaths

Potential reduction of pneumonia incidence 15-23%
Stunting, Underweight and Micronutrient deficiency identified as risk factors for pneumonia, severe pneumonia and poor outcome

Lack of interventional research but one study: 6% reduction in mortality with complimentary feeding 6-23 months
Micronutrients

- Zinc supplementation 70 mg one weekly in Bangladesh study: 17% reduction in pneumonia, 49% reduction in severe pneumonia. Its role in treatment is less clear.
- Vitamin A reduces pneumonia morbidity and mortality associated with measles but has no effect on non-measles associated pneumonia.
Recent meta-analysis of exposure to indoor air pollution showed increased risk of pneumonia and severe pneumonia (OR 1.78). Interventions by switching to cleaner fuels or improved combustion and increased ventilation reduces pneumonia incidence by 20-40%.
- Reduces the risk of ARI and diarrhoea
- Randomized Pakistan trial: 50% reduction in pneumonia episodes with provision of training and soap, no difference between plain and antibacterial soap
Measles vaccination eliminates measles associated pneumonia. Vaccination, however, often delayed significantly beyond 9 months.

Pertussis pneumonia and pertussis related mortality greatest in the first 6 months of live. Timely vaccination important.
Hib conjugate vaccine reduces radiologically confirmed pneumonia and nasopharyngeal carriage.

PCV7 reduces the incidence of bacteremic pneumonia, radiologically confirmed pneumonia and clinical pneumonia. After introduction in the US hospitalized cases of pneumonia was reduced by 30%. In rural Gambia PCV9 reduced childhood mortality by 16% and radiologically confirmed pneumonia by more than 20%. PCV9 has proven effective in HIV infected children in South Africa though less than in immunocompetent children.
TMP-SMX prophylaxis against PCP is effective. A randomized controlled trial in Zambia in HIV-infected children found a 43% reduction in mortality and a 23% reduction in hospitalization in children on prophylaxis.

Prophylaxis indicated in HIV exposed uninfected children until 6 months of age.

Prophylaxis may be discontinued in HIV infected children older than 18 months with sustained immune reconstitution on HAART.
INH prophylaxis in a South African trial of HIV infected children not on HAART living in an area of high TB prevalence showed reduction in TB by 72% and mortality by 54%
HAART in HIV infected children reduces the incidence of bacterial pneumonia and respiratory opportunistic infections fivefold.
WHO case management guidelines assume:

- Most fatal pneumonia caused by bacterial infection
- These can be treated effectively with antibiotics
- Children can access health care facilities
- Clinical signs can be taught to health care workers.
- Incorporated into IMCI guidelines
<table>
<thead>
<tr>
<th>WHO Classification</th>
<th>IMCI Classification</th>
<th>Clinical Signs</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pneumonia</td>
<td>Cough or cold</td>
<td>No signs of pneumonia or very severe disease</td>
<td>Symptomatic treatment, advise carer when to return immediately, follow up in 5 days if not improving</td>
</tr>
<tr>
<td>Non-severe pneumonia</td>
<td>Pneumonia</td>
<td>Fast breathing</td>
<td>Give oral antibiotics for 3 days, advise the carer when to return immediately, follow up in 2 days</td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td>Severe pneumonia or very severe disease</td>
<td>Chest indrawing</td>
<td>Give first dose of antibiotic Refur urgently to hospital</td>
</tr>
<tr>
<td>Very severe disease</td>
<td></td>
<td>Any general danger sign</td>
<td>Give first dose of antibiotic Refer urgently to hospital</td>
</tr>
</tbody>
</table>
Impact of case management

A meta analysis has estimated the impact of case management to 24% reduction in total child mortality and 36% reduction in pneumonia related mortality in children under 5.

Challenges:

- Limited scale IMCI implementation
- Delayed care seeking
- Insufficient dosing with low quality drugs
- Poor quality care in district hospitals
- Lack of access to antibiotics and oxygen
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Drug</th>
<th>Route</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pneumonia</strong></td>
<td>Amoxicillin or Trimethoprim-sulpha</td>
<td>Oral</td>
<td>15 mg/kg or 30 mg/kg</td>
<td>3 times daily</td>
<td>5 days</td>
</tr>
<tr>
<td></td>
<td>methoxazole</td>
<td>Oral</td>
<td>4 mg/kg trimethoprim component</td>
<td>2 daily</td>
<td>3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 daily</td>
<td>3 or 5 days</td>
</tr>
<tr>
<td><strong>Severe pneumonia</strong></td>
<td>Beta lactam antibiotic: Benzyl penicillin Ampicillin</td>
<td>Intravenous</td>
<td>50 000 units/kg 25 mg/kg</td>
<td>4 times daily</td>
<td>Until child improves then change to oral amoxicillin, total 5 days</td>
</tr>
<tr>
<td><strong>Very severe pneumonia</strong></td>
<td>Beta lactam antibiotic: Benzyl penicillin or Ampicillin AND Gentamicin</td>
<td>Intravenous</td>
<td>50 000 units/kg 50 mg/kg</td>
<td>4 times daily</td>
<td>10 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intravenous</td>
<td>7,5 mg/kg</td>
<td>1 daily</td>
<td>10 days</td>
</tr>
</tbody>
</table>
Hypoxia is best identified by pulse oximetry. If not available, a respiratory rate above 60/minute and altered mental state may be used as clinical indicators. Routine screening for hypoxia with pulse oximetry and improved oxygen delivery systems have shown to significantly reduce pneumonia mortality.

Challenges in pneumonia treatment:
- How to identify children that fail to respond adequately to antibiotic treatment (9-20%)
- Proper management in HIV infected children.
Summary

- Childhood pneumonia continues to be a major cause of mortality in LIC and MIC.
- Effective preventive strategies must be intensified.
- Case management strategies should be more widely implemented at community level.
- Better access to pulse oximetry and oxygen delivery systems needed.
- Interventions specific for HIV infected children are needed.
- Further research to develop better diagnostic tests and reliable methods for etiological diagnosis are needed.