Common Infectious Diseases in Pediatrics

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Respiratory Tract Infections

Upper RTIs
- Rhinitis
- Influenza
- Pharyngitis / tonsillitis
- Rhinosinusitis

Lower RTIs
- Bronchitis
- Bronchiolitis
- Pneumonia
# Respiratory Virus Infections

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Commonly Associated Viruses</th>
<th>Less Commonly Associated Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coryza</td>
<td>Rhinoviruses, coronaviruses</td>
<td>Influenza viruses, parainfluenza viruses, enteroviruses, adenoviruses</td>
</tr>
<tr>
<td>Influenza</td>
<td>Influenza viruses</td>
<td>Parainfluenza viruses, adenoviruses</td>
</tr>
<tr>
<td>Croup</td>
<td>Parainfluenza viruses</td>
<td>Influenza viruses, RSV, adenoviruses</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>RSV, rhinoviruses</td>
<td>Influenza viruses, parainfluenza viruses, adenoviruses, hMPV</td>
</tr>
</tbody>
</table>
Influenza Virus

- 3 types: A, B, and C
- Type A undergoes antigenic shift and drift
- Influenza A subtypes: HA and NA
- Type B undergoes antigenic drift only and type C is relatively stable
Influenza A Virus

- Antigenic shifts of the HA results in pandemics
- Antigenic drifts in the HA and NA result in epidemics
Influenza: Laboratory Diagnosis

- Rapid diagnosis: Detection of antigen from nasopharyngeal aspirates and throat washings
  - Sensitivity 50-70%, specificity >90%
- Virus Isolation – Culture or PCR from nasopharyngeal aspirates and throat swabs
Treatment Recommendation

- Treatment with oseltamivir, zanamivir, or baloxavir is recommended for:
  - Persons with suspected or confirmed influenza with severe illness (e.g. hospitalized patients)
  - Persons with suspected or confirmed influenza who have risk factors for severe illness
Risk Factors For Severe Influenza Illness

- Aged <2 yrs, \( \geq 65 \) yrs
- Person with medical conditions, immunosuppression, conditions that compromise respiratory function
- Obesity
- Pregnant women and <2 weeks postpartum
- Receiving long term aspirin therapy
Types of seasonal influenza vaccine

Type of vaccines
Inactivated, Live-attenuated, Cell culture

Trivalent (TIV)
- A-H1N1
- A-H3N2

B-Yamagata OR B-Victoria

Tetravalent (QIV)
- A/H1N1
- A/H3N2

B-Yamagata AND B-Victoria

WHO 2019 (Southern hemisphere)
- A/Michigan/45/2015 (H1N1)pdm09-like virus
- A/Switzerland/8060/2017 (H3N2)-like virus
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
- B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)

WHO 2019/20 (Northern hemisphere)
- A/Brisbane/02/2018 (H1N1)pdm09-like virus
- A/Kansas/14/2017 (H3N2)-like virus
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
- B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)
Acute Otitis Media
Acute Otitis Media: Bacterial Etiology

- *S. pneumoniae*: 50%
- *M. catarrhalis*: 15%
- *H. influenzae*: 30%
- Other: 5%

Haemophilus influenzae type b as an important cause of culture-positive acute otitis media in young children in Thailand: a tympanocentesis-based, multi-center, cross-sectional study

Pavinee Intakorn¹, Nuntigar Sonsuwan², Suwiwan Noknu³, Greetha Moungthong⁴, Jean-Yves Pirçon⁵, Yanfang Liu⁶,⁷, Melissa K Van Dyke⁵,⁸ and William P Hausdorff⁵
Figure 2 Culture results and pathogens under study identified from middle ear fluid samples (N = 118). Culture results from middle ear fluid samples including serotype distribution for *S. pneumoniae* (Spn, n = 27), and *H. influenzae* (H. inf, n = 21). There were two co-infected samples due to one co-infection of *S. pneumoniae* 23F and *H. influenzae* serotype a, and one co-infection of Hib and *M. catarrhalis*. 
AOM spontaneous resolution rate varies by pathogen

<table>
<thead>
<tr>
<th>Organism</th>
<th>Spontaneous bacteriologic clearance rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em></td>
<td>19%</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>48%</td>
</tr>
<tr>
<td><em>M. catarrhalis</em></td>
<td>75%</td>
</tr>
</tbody>
</table>

Risk Factors for Resistant S. *pneumoniae* Infection

- Age (≤2 years)
- Attendance at day-care centers
- Siblings of children attending day-care centers
- Not vaccinated with pneumococcal conjugate vaccine (PCV)
- Prior AOM within the past six months
- Receipt of antibiotics within the last three months

### SOAR S/SE Asia (2012-14): main CA-RTI isolates

#### SOAR Study 2012-2014, Thailand

**S. pneumoniae**

<table>
<thead>
<tr>
<th>Antimicrobial (N)</th>
<th>CLSI (%S)</th>
<th>EUCAST (%S)</th>
<th>PK/PD (%S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC(^{b,c}) (N=208)</td>
<td>97.1</td>
<td>NA</td>
<td>97.1(99)</td>
</tr>
<tr>
<td>Penicillin (IV) (N=208)</td>
<td>98.1</td>
<td>84.1-98.1</td>
<td>NA</td>
</tr>
<tr>
<td>Penicillin oral (N=208)</td>
<td>49.0</td>
<td>49.0</td>
<td>NA</td>
</tr>
<tr>
<td>Cefuroxime(^{e}) (N=208)</td>
<td>77.9</td>
<td>59.1</td>
<td>77.9</td>
</tr>
<tr>
<td>Levofloxacin (N=208)</td>
<td>98.1</td>
<td>98.1</td>
<td>98.1</td>
</tr>
<tr>
<td>Azithromycin(^{d}) (N=208)</td>
<td>53.4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Clarithromycin(^{d}) (N=208)</td>
<td>52.4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Erythromycin(^{f}) (N=208)</td>
<td>51.9</td>
<td>51.9</td>
<td>NA</td>
</tr>
</tbody>
</table>

**AMC=Amoxicillin/clavulanate**

SOAR Study 2012-2014, Thailand

**H. influenzae**

<table>
<thead>
<tr>
<th>Antimicrobial (N)</th>
<th>CLSI (%S)</th>
<th>EUCAST (%S)</th>
<th>PK/PD (%S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amp All (N=263)</td>
<td>51.7</td>
<td>51.7</td>
<td>NA</td>
</tr>
<tr>
<td>Amp BL+ (N=96)</td>
<td>1.0</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>Amp BL- (N=167)</td>
<td>80.8</td>
<td>80.8</td>
<td>NA</td>
</tr>
<tr>
<td>AMC&lt;sup&gt;a,b&lt;/sup&gt; All (N=263)</td>
<td>97.7 (93.5)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>90.5 (81.4)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>90.5 (97.7)</td>
</tr>
<tr>
<td>AMC BL+ (N=96)</td>
<td>96.9</td>
<td>85.4</td>
<td>85.4 (96.9)</td>
</tr>
<tr>
<td>AMC BL- (N=167)</td>
<td>98.2</td>
<td>93.4</td>
<td>93.4 (98.2)</td>
</tr>
<tr>
<td>Cefuroxime&lt;sup&gt;a,b&lt;/sup&gt; All (N=263)</td>
<td>96.2 (92.4)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>7.2</td>
<td>79.5</td>
</tr>
<tr>
<td>Cefuroxime BL+ (N=96)</td>
<td>97.9</td>
<td>2.1</td>
<td>80.2</td>
</tr>
<tr>
<td>Cefuroxime BL- (N=167)</td>
<td>95.2</td>
<td>10.1</td>
<td>79.0</td>
</tr>
<tr>
<td>Azithromycin&lt;sup&gt;d&lt;/sup&gt; ALL (N=263)</td>
<td>99.6</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Clarithromycin&lt;sup&gt;d&lt;/sup&gt; ALL (N=263)</td>
<td>79.5</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Levofloxacin ALL (N=263)</td>
<td>99.6</td>
<td>99.2</td>
<td>99.6</td>
</tr>
</tbody>
</table>

AMC=Amoxicillin/clavulanate

SOAR Study 2012-2014, 4 centers in Thailand

*Moraxella catarrhalis*, 100% beta-lactamase production

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>N</th>
<th>MIC (mg/L)</th>
<th>Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>50%</td>
<td>90%</td>
</tr>
<tr>
<td>AMC</td>
<td>49</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>49</td>
<td>0.25</td>
<td>1</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>49</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>49</td>
<td>0.25</td>
<td>1</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>49</td>
<td>0.06</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Management of AOM

### TABLE 4: Recommendations for Initial Management for Uncomplicated AOM

<table>
<thead>
<tr>
<th>Age</th>
<th>Otorrhea With AOM&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Unilateral or Bilateral AOM&lt;sup&gt;a&lt;/sup&gt; With Severe Symptoms&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Bilateral AOM&lt;sup&gt;a&lt;/sup&gt; Without Otorrhea</th>
<th>Unilateral AOM&lt;sup&gt;a&lt;/sup&gt; Without Otorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mo to 2 y</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy or additional observation</td>
</tr>
<tr>
<td>≥2 y</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy or additional observation</td>
<td>Antibiotic therapy or additional observation&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Applies only to children with well-documented AOM with high certainty of diagnosis (see Diagnosis section).

<sup>b</sup> A toxic-appearing child, persistent otalgia more than 48 h, temperature ≥39°C (102.2°F) in the past 48 h, or if there is uncertain access to follow-up after the visit.

<sup>c</sup> This plan of initial management provides an opportunity for shared decision-making with the child’s family for those categories appropriate for additional observation. If observation is offered, a mechanism must be in place to ensure follow-up and begin antibiotics if the child worsens or fails to improve within 48 to 72 h of AOM onset.

Management of AOM

Antibiotic Therapy

### TABLE 5 Recommended Antibiotics for (Initial or Delayed) Treatment and for Patients Who Have Failed Initial Antibiotic Treatment

<table>
<thead>
<tr>
<th>Recommended Immediate or Delayed Antibiotic Treatment</th>
<th>Alternative Treatment (if Penicillin Allergy)</th>
<th>Antibiotic Treatment After 48–72 h of Failure of Initial Antibiotic Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended First-line Treatment</strong></td>
<td><strong>Amoxicillin (60–90 mg/ kg per day in 2 divided doses)</strong></td>
<td><strong>Amoxicillin-clavulanate</strong>&lt;sup&gt;a&lt;/sup&gt; (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate)</td>
</tr>
<tr>
<td></td>
<td><strong>Cefdinir (14 mg/kg per day in 1 or 2 doses)</strong></td>
<td><strong>Ceftiraxone, 3 d Clindamycin</strong>&lt;sup&gt;b&lt;/sup&gt; (30–40 mg/kg per day in 3 divided doses), with or without third-generation cephalosporin</td>
</tr>
<tr>
<td></td>
<td><strong>Cefuroxime (30 mg/kg per day in 2 divided doses)</strong></td>
<td><strong>Failure of second antibiotic</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Cefpodoxime (10 mg/kg per day in 2 divided doses)</strong></td>
<td><strong>Ceftiraxone (50 mg IM or IV for 3 d)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Ceftriaxone (50 mg IM or IV per day for 1 or 3 d)</strong></td>
<td><strong>Clindamycin (30–40 mg/kg per day in 3 divided doses) plus third-generation cephalosporin</strong></td>
</tr>
</tbody>
</table>

Notes:
- IM, intramuscular; IV, intravenous.
- May be considered in patients who have received amoxicillin in the previous 30 d or who have the otitis-conjunctivitis syndrome.
- Perform tympanocentesis/drainage if skilled in the procedure, or seek a consultation from an otolaryngologist for tympanocentesis/drainage. If the tympanocentesis reveals multidrug-resistant bacteria, seek an infectious disease specialist consultation.
- Cefdinir, cefuroxime, cefpodoxime, and ceftriaxone are highly unlikely to be associated with cross-reactivity with penicillin allergy on the basis of their distinct chemical structures. See text for more information.

Management of AOM

Duration of Therapy

- In children $\leq 2$ years and children with severe symptoms, a standard 10-day course is recommended.
- In children 2 to 5 years with mild or moderate AOM, A 7-day course of oral antibiotic appears to be equally effective.
- In children $\geq 6$ years with mild to moderate symptoms, a 5- to 7-day course is adequate treatment.

Acute Bacterial Rhinosinusitis
Microbiology of Acute Bacterial Rhinosinusitis (Children)

- **S. pneumoniae**: 30%
- **H. influenzae**: 20%
- **M. catarrhalis**: 20%
- **S. pyogenes**: 5%
- **Anaerobes**: 5%
- **Sterile**: 20%
- **Other**: 20%
Criteria for the Diagnosis of Sinusitis

- Presence of at least 2 major or 1 major and ≥2 minor symptoms

<table>
<thead>
<tr>
<th>Major Symptoms</th>
<th>Minor Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Purulent anterior nasal discharge</td>
<td>• Headache</td>
</tr>
<tr>
<td>• Purulent or discolored posterior nasal discharge</td>
<td>• Ear pain, pressure, or fullness</td>
</tr>
<tr>
<td>• Nasal congestion or obstruction</td>
<td>• Halitosis</td>
</tr>
<tr>
<td>• Facial congestion or fullness</td>
<td>• Dental pain</td>
</tr>
<tr>
<td>• Facial pain or pressure</td>
<td>• Cough</td>
</tr>
<tr>
<td>• Hyposmia or anosmia</td>
<td>• Fever (for subacute or chronic sinusitis)</td>
</tr>
<tr>
<td>• Fever (for acute sinusitis only)</td>
<td>• Fatigue</td>
</tr>
</tbody>
</table>

Modified from Meltzer et al [7].

Algorithm for the Management of Acute Bacterial Rhinosinusitis: IDSA 2012

### TABLE 2 Recommendations for Initial Use of Antibiotics for Acute Bacterial Sinusitis

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Severe Acute Bacterial Sinusitis&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Worsening Acute Bacterial Sinusitis&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Persistent Acute Bacterial Sinusitis&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated acute bacterial sinusitis without coexisting illness</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy or additional observation for 3 days&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acute bacterial sinusitis with orbital or intracranial complications</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
</tr>
<tr>
<td>Acute bacterial sinusitis with coexisting acute otitis media, pneumonia, adenitis, or streptococcal pharyngitis</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
</tr>
</tbody>
</table>

<sup>a</sup> Defined as temperature $\geq 39^\circ$C and purulent (thick, colored, and opaque) nasal discharge present concurrently for at least 3 consecutive days.

<sup>b</sup> Defined as nasal discharge or daytime cough with sudden worsening of symptoms (manifested by new-onset fever $\geq 38^\circ$C/100.4$^\circ$F or substantial increase in nasal discharge or cough) after having experienced transient improvement of symptoms.

<sup>c</sup> Defined as nasal discharge (of any quality), daytime cough (which may be worse at night), or both, persisting for >10 days without improvement.

<sup>d</sup> Opportunity for shared decision-making with the child’s family; if observation is offered, a mechanism must be in place to ensure follow-up and begin antibiotics if the child worsens at any time or fails to improve within 3 days of observation.

### IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis

Prevalence (Mean Percentage of Positive Specimens) of Various Respiratory Pathogens From Sinus Aspirates in Patients With Acute Bacterial Rhinosinusitis

<table>
<thead>
<tr>
<th>Microbial Agent</th>
<th>Publications Before 2000</th>
<th>Publications in 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults (^a) (%)</td>
<td>Children (^b) (%)</td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td>30–43</td>
<td>44</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong></td>
<td>31–35</td>
<td>30</td>
</tr>
<tr>
<td><strong>Moraxella catarrhalis</strong></td>
<td>2–10</td>
<td>30</td>
</tr>
<tr>
<td><strong>Streptococcus pyogenes</strong></td>
<td>2–7</td>
<td>2</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>2–3</td>
<td>...</td>
</tr>
<tr>
<td>Gram-negative bacilli (includes Enterobacteriaceae spp)</td>
<td>0–24</td>
<td>2</td>
</tr>
<tr>
<td><strong>Anaerobes (Bacteroides, Fusobacterium, Peptostreptococcus)</strong></td>
<td>0–12</td>
<td>2</td>
</tr>
<tr>
<td><strong>Respiratory viruses</strong></td>
<td>3–15</td>
<td>...</td>
</tr>
<tr>
<td><strong>No growth</strong></td>
<td>40–50</td>
<td>30</td>
</tr>
</tbody>
</table>

Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Children

<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line (Daily Dose)</th>
<th>Second-line (Daily Dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial empirical therapy</td>
<td>● Amoxicillin-clavulanate (45 mg/kg/day PO bid)</td>
<td>● Amoxicillin-clavulanate (90 mg/kg/day PO bid)</td>
</tr>
<tr>
<td>β-lactam allergy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type I hypersensitivity</td>
<td>● Levofloxacin (10–20 mg/kg/day PO every 12–24 h)</td>
<td></td>
</tr>
<tr>
<td>Non-type I hypersensitivity</td>
<td>● Clindamycin (30–40 mg/kg/day PO tid) plus cefixime (8 mg/kg/day PO bid) or cefpodoxime (10 mg/kg/day PO bid)</td>
<td></td>
</tr>
<tr>
<td>Risk for antibiotic resistance or failed initial therapy</td>
<td>● Amoxicillin-clavulanate (90 mg/kg/day PO bid)</td>
<td></td>
</tr>
<tr>
<td>Severe infection requiring hospitalization</td>
<td>● Clindamycin (30–40 mg/kg/day PO tid) plus cefixime (8 mg/kg/day PO bid) or cefpodoxime (10 mg/kg/day PO bid)</td>
<td>● Levofloxacin (10–20 mg/kg/day PO every 12–24 h)</td>
</tr>
<tr>
<td>Severe infection requiring hospitalization</td>
<td>● Ampicillin/sulbactam (200–400 mg/kg/day IV every 6 h)</td>
<td>● Ceftriaxone (50 mg/kg/day IV every 12 h)</td>
</tr>
<tr>
<td></td>
<td>● Cefotaxime (100–200 mg/kg/day IV every 6 h)</td>
<td>● Levofloxacin (10–20 mg/kg/day IV every 12–24 h)</td>
</tr>
</tbody>
</table>

Abbreviations: bid, twice daily; IV, intravenously; PO, orally; qd, daily; tid, 3 times a day.

* Resistance to clindamycin (~31%) is found frequently among *Streptococcus pneumoniae* serotype 19A isolates in different regions of the United States [94].

Pneumonia
Causes – 1 to 3 months

- Viruses: RSV, parainfluenza virus
- *Chlamydia trachomatis* (2-8 weeks)
  - Afebrile, tachypnea, CXR with interstitial infiltrates, eosinophilia
- *B. pertussis*
  - Tracheobronchitis with severe paroxysmal cough, no fever
  - Pneumonia usually related to aspiration
Causes – 3 months to 4 years

- Viruses: RSV, parainfluenza, influenza, adenovirus, hMPV, rhinovirus, coronaviruses
- *S. pneumoniae*: Related suppurative complications
- *H. influenzae* type B
- *S. aureus*
- *M. pneumoniae, C. pneumoniae*
Causes – 5 years through adolescence

- *M. pneumoniae*
- *C. pneumoniae*
- *S. pneumoniae*
- Viruses: Smaller percentage
The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America

John S. Bradley,1,a Carrie L. Byington,2,a Samir S. Shah,3,a Brian Alverson,4 Edward R. Carter,5 Christopher Harrison,6 Sheldon L. Kaplan,7 Sharon E. Mace,8 George H. McCracken Jr,9 Matthew R. Moore,10 Shawn D. St Peter,11 Jana A. Stockwell,12 and Jack T. Swanson13

Table 7. Empiric Therapy for Pediatric Community-Acquired Pneumonia (CAP)

<table>
<thead>
<tr>
<th>Site of care</th>
<th>Presumed bacterial pneumonia</th>
<th>Presumed atypical pneumonia</th>
<th>Presumed influenza pneumoniaa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outpatient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years old (preschool)</td>
<td>Amoxicillin, oral (90 mg/kg/day in 2 dosesb)</td>
<td>Azithromycin oral (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5); Alternatives: oral clarithromycin (15 mg/kg/day in 2 doses for 7–14 days) or oral erythromycin (40 mg/kg/day in 4 doses)</td>
<td>Oseltamivir</td>
</tr>
<tr>
<td></td>
<td>Alternative: oral amoxicillin clavulanate (amoxicillin component, 90 mg/kg/day in 2 dosesb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5 years old</td>
<td>Oral amoxicillin (90 mg/kg/day in 2 dosesb to a maximum of 4 g/dayc); for children with presumed bacterial CAP who do not have clinical, laboratory, or radiographic evidence that distinguishes bacterial CAP from atypical CAP, a macrolide can be added to a β-lactam antibiotic for empiric therapy; alternative: oral amoxicillin clavulanate (amoxicillin component, 90 mg/kg/day in 2 dosesb to a maximum dose of 4000 mg/day, eg, one 2000-mg tablet twice dailyb)</td>
<td>Oral azithromycin (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5 to a maximum of 500 mg on day 1, followed by 250 mg on days 2–5); alternatives: oral clarithromycin (15 mg/kg/day in 2 doses to a maximum of 1 g/day); erythromycin, doxycycline for children &gt;7 years old</td>
<td>Oseltamivir or zanamivir (for children 7 years and older); alternatives: peramivir, oseltamivir and zanamivir (all intravenous) are under clinical investigation in children; intravenous zanamivir available for compassionate use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Site of care</th>
<th>Empiric therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient (all ages)</td>
<td>Presumed bacterial pneumonia</td>
</tr>
<tr>
<td>Fully immunized with conjugate vaccines for <em>Haemophilus influenzae</em> type b and <em>Streptococcus pneumoniae</em>; local penicillin resistance in invasive strains of pneumococcus is minimal</td>
<td>Ampicillin or penicillin G; alternatives: ceftriaxone or cefotaxime; addition of vancomycin or clindamycin for suspected CA-MRSA</td>
</tr>
<tr>
<td>Not fully immunized for <em>H. influenzae</em> type b and <em>S. pneumoniae</em>; local penicillin resistance in invasive strains of pneumococcus is significant</td>
<td>Ceftriaxone or cefotaxime; addition of vancomycin or clindamycin for suspected CA-MRSA; alternative: levofloxacin; addition of vancomycin or clindamycin for suspected CA-MRSA</td>
</tr>
</tbody>
</table>
Recommendations: Duration of Antimicrobial Therapy

- Treatment courses of 10 days have been best studied, although shorter courses may be just as effective, particularly for more mild disease managed on an outpatient basis. (strong recommendation; moderate-quality evidence)

- Infections caused by certain pathogens, notably CA-MRSA, may require longer treatment than those caused by *S. pneumoniae*. (strong recommendation; moderate-quality evidence)

Pertussis in Thai Children

- QSNIC, Prospective study
- Subjects:
  - Children with cough > 7 days (Paroxysm, whooping cough, vomiting)
  - 96 patients: NB-15.4 yrs, median 7.7 mo.
  - DTP = 3 doses 49%, <3 doses 46.9%
  - PCR for pertussis: Positive 19%

Santarattivong P, PIDST Meeting, May 2013
Bordetella pertussis

- 3 stages
  - Catarrhal stage: similar to common cold
  - Paroxysmal stage: whooping cough, post-tussis emesis, apnea, cyanosis, paroxysmal events
  - Convalescent stage: symptoms wane gradually
- Fever is absent or minimal
- Conjunctival hemorrhage, petechiae on the upper body
Complications of Pertussis

**Infants < 12 months of age**
- 1 in 5 Pneumonia
- 1 in 100 Convulsions
- 1 in 2 Apnea
- 1 in 300 Encephalopathy
- 1 in 100 Die

**Adolescents and Adults**
- Weight loss (33%)
- Urinary incontinence (28%)
- Syncope (6%)
- Rib fractures (4%)

Hospitalization is most common in infants <6 months of age.

**Bordetella pertussis**

- CBC: leukocytosis, lymphocytosis and thrombocytosis
- CXR: perihilar infiltration or interstitial edema
- Diagnosis: culture remains gold-standard, PCR
- Treatment: erythromycin, clarithromycin, azithromycin, TMP/SMX (alternative drugs)
Tuberculosis
## Risk of Disease Following Primary Infection

<table>
<thead>
<tr>
<th>Risk of disease following primary infection</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated tuberculosis/tuberculosis meningitis</td>
<td>Pulmonary tuberculosis</td>
</tr>
<tr>
<td>&lt;1 years</td>
<td>10–20%</td>
</tr>
<tr>
<td>1–2 years</td>
<td>2–5%</td>
</tr>
<tr>
<td>2–5 years</td>
<td>0·5%</td>
</tr>
<tr>
<td>5–10 years</td>
<td>&lt;0·5%</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>&lt;0·5%</td>
</tr>
</tbody>
</table>

Adapted from reference 30.

**Table 1:** Risk of pulmonary and extrapulmonary disease in children following infection with *Mycobacterium tuberculosis*
Clinical Manifestations

- The most common site of infection is the lung (up to 80%)
- Extrapulmonary manifestation
  - Lymphadenopathy 67%
  - Meningitis 13%
  - Pleural TB 6%
  - Miliary TB 5%
  - Skeletal TB 4%
Pulmonary Disease

- Intrathoracic lymphadenopathy and parenchymal disease
- Progressive primary disease: Lung tissue destruction and cavity formation
- Reactivation disease: More common in adolescents
Tuberculosis: Chest X-Ray

Miliary tuberculosis

Consolidation
Tuberculosis: Chest X-Ray

Consolidation

Cavitary lesion
Miliary Disease

- Younger or immunocompromised child
- Multiorgan involvement is common
- Most affected children have constitutional symptoms, hepatosplenomegaly
- CNS involvement: Up to 20% of children
- TST: Insensitive (TST anergy)
- AFB culture from gastric aspirates: Yield as high as 50%
Are children with TB ever contagious?

• Difficult to answer in the community

• Orphanages – caretaker with TB led to transmission; a child with TB did not

• Schools – only 2 reported “epidemics” caused by children <13 years old

• Children’s Hospitals – rare case reports of transmission, all with special circumstances, none has been patient-to-patient
Features of Contagious Pediatric Tuberculosis

• Cavitary lung lesion

• Sputum production

• Positive acid-fast stain of sputum smear

• Bronchoscopy

• Draining lesions or surgical drainage of an abscess
Diagnosis

- Tuberculin skin test
- T-cell assays (IGRA): Measure IFN-$\gamma$ released by sensitized T-lymphocytes after stimulation by antigens
- Laboratory diagnosis
  - Culture
  - Molecular amplification methodology: PCR, GeneXpert MTB/RIF
Tuberculin Skin Test

- False-positive TST result: Children exposed to non-tuberculous mycobacteria, recently received BCG vaccine
- False-negative TST result: Recent measles infection, high-dose corticosteroid, irradiation, immunosuppressive therapy, or immunocompromising conditions
Interferon-Gamma Release Assays (IGRAs)

• Unable to distinguish between active disease and latent tuberculosis infection

• For immunocompetent children, IGRAs can be used in place of a TST to confirm cases of TB or LTBI, likely will yield fewer false-positive test

• Higher specificity than TST: Antigens used are not found in BCG or most pathogenic non-TB mycobacteria (eg, are not found in M. avium complex but are found in M. kansasii, M. fortuitum, and M. marinum)
Culture

- Most important laboratory test for the diagnosis and management of TB
- Positive of cultures from early-morning gastric aspirates from children with pulmonary TB is <40%
- Culture is most important when the source case is unknown or is known to have drug-resistant TB
GeneXpert MTB/RIF

1. Sputum liquefaction and inactivation with 2:1 sample reagent
2. Transfer of 2 ml material into test cartridge
3. Cartridge inserted into MTB-RIF test platform (end of hands-on work)
4. Sample automatically filtered and washed
5. Ultrasonic lysis of filter-captured organisms to release DNA
6. DNA molecules mixed with dry PCR reagents
7. Seminested real-time amplification and detection in integrated reaction tube
8. Printable test result

Time to result, 1 hour 45 minutes

Distribution of MDR-TB determining mutations

90% of RIF-R associated with \( rpoB \)

Most of INH-R associated with \( katG \): high level-R but not cross to Ethionamide

Rapid Molecular Detection of Multidrug-Resistant Tuberculosis by PCR-Nucleic Acid Lateral Flow Immunoassay

## Treatment of Drug-Susceptible TB

<table>
<thead>
<tr>
<th>Sites/Characteristics of TB Diseases</th>
<th>Treatment Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary, lymph node</td>
<td>2 IRZE/4-7 IR</td>
</tr>
<tr>
<td>Bone/joint, CNS, miliary</td>
<td>2 IRZE/10 IR</td>
</tr>
<tr>
<td>CNS, miliary, pericardium, pleural, endobronchial</td>
<td>Add prednisolone 1-2 MKD for 4-6 weeks</td>
</tr>
</tbody>
</table>
Infectious Diarrhea
Pathogens

- **Bacteria:** *Salmonella*, *Shigella*, *Vibrio cholerae*, *Clostridium perfringens*, *S. aureus*, Shiga toxin-producing *E. coli*, *Yersinia*, *Vibrio parahemolyticus*, *Vibrio vulnificus*, *Campylobacter*, *Clostridium difficile*, *Aeromonas*, *Plesiomonas shigeloides*

- **Virus:** Rotavirus, Norwalk agent, calicivirus, adenovirus, astrovirus, coronavirus

- **Parasites:** *Entamoeba histolytica*, *Giardia lamblia*, *Cryptosporidium parvum*, *Isospora belli*, *Blastocystis hominis*, *Microsporidium*
Invasive Bacterial Diarrhea

- Caused by infection due to pathogens having an ability to invade the mucosa of the distal small intestine and colon
  - *Shigella* spp.
  - *Salmonella* spp.
  - *Campylobacter* spp.
  - *E. coli*
Acute Diarrhea: Antimicrobial Treatment

- Antimicrobial therapy is not usually indicated in children.
- Antimicrobials are reliably helpful only for children with bloody diarrhea (most likely shigellosis) and suspected cholera with severe dehydration.
- Antiprotozoal drugs can be very effective for diarrhea in children, especially for *Giardia*, *Entamoeba histolytica*, and now *Cryptosporidium*, with nitazoxanide.
Acute Diarrhea: Empirical Antimicrobial Treatment

- Antimicrobial therapy should be considered for severe invasive diarrhea (acute onset of bloody/mucous diarrhea or fecal polymorphonuclear leukocytes with high fever)
- Suspected septicemia or complications
Shigellosis

- Most common cause of dysentery
- Generally self-limited course, diarrhea usually resolves within 5-7 days
- Antimicrobial therapy is effective in shortening duration of diarrhea and hastening eradication of organisms from feces
- Most strains are resistant to ampicillin, TMP/SMX and nalidixic acid
- For cases in which treatment is required and susceptibility is unknown, azithromycin, ceftriaxone, or a fluoroquinolone should be administered

Authors’ conclusions
There appears to be no evidence of a clinical benefit of antibiotic therapy in otherwise healthy children and adults with non-severe salmonella diarrhoea. Antibiotics appear to increase adverse effects and they also tend to prolong salmonella detection in stools.

Cochrane Database Syst Rev. 2000;(2):CD001167
Salmonella Infections

- Antimicrobial therapy may be recommended for gastroenteritis caused by nontyphoidal *Salmonella* serotypes in people at increased risk of invasive disease (e.g., age <3 months, patients with chronic gastrointestinal tract disease, malignant neoplasms, hemoglobinopathies, HIV infection, or other immunosuppressive illnesses or therapies)

Dengue Fever / Dengue Hemorrhagic Fever
Dengue Virus Infection

- Dengue viruses: 4 serotypes
- Transmission: *Aedes aegypti*, *Aedes albopictus*
- Each serotype produces type-specific immunity but not immunity against other types
Revised Dengue Classification: WHO 2009

**DENGUE ± Warning Signs**

- Without
- With WARNING SIGNS

**SEVERE DENGUE**

1. Severe plasma leakage leading to:
   - Shock (DSS)
   - Fluid accumulation with respiratory distress
2. Severe bleeding as evaluated by clinician
3. Severe organ involvement
   - Liver: AST or ALT>=1000
   - CNS: Impaired consciousness
   - Heart and other organs

---

**Probable Dengue**
Live in / travel to dengue endemic area. Fever and 2 of the following criteria:
- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test +ve
- Leucopenia
- Any warning sign

**Warning Signs***
- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy; restlessness
- Liver enlargement >2cm
- Laboratory: Increase in HCT concurrent with rapid decrease in platelet count

**Lab. confirmed dengue**
(important when no sign of plasma leakage)

* Requiring strict observation and medical intervention
Box 5: Manifestations of dengue virus infection

Dengue virus infection

- Asymptomatic
- Symptomatic

Undifferentiated Fever (viral syndrome)
- Without haemorrhage
- With unusual haemorrhage

Dengue fever (DF)

Dengue haemorrhagic fever (DHF)
- With plasma leakage
  - DHF non-shock
  - DHF with shock
    - Dengue shock syndrome (DSS)

Expanded dengue Syndrome/Isolated organopathy (unusual manifestation)
Dengue Virus Infection: Treatment

- No specific treatment
- Supportive treatment
  - Oral or IV fluid rehydration
  - Avoid use of aspirin, and other NSAIDs to minimize the potential for bleeding
  - Blood transfusion: In patients with significant bleeding
  - Platelet transfusions: In patients with severe thrombocytopenia (<10,000/mm$^3$) and active bleeding
- Adjunctive therapy
  - Meta-analysis of 4 trials found that corticosteroids were no more effective than placebo in reducing the number of deaths, the need for blood transfusion, or the number of serious complications$^1$

Measles

- High fever, cough, conjunctivitis, and coryza followed by the development of rash
- Rash: morbilliform, blanching rash, which begins on the face and spreads cephalocaudally and centrifugally to involve the neck, upper and lower aspect of the trunk, and extremities 2 to 4 days after onset of fever
Measles

- Koplik spots, guttate minute white macules on the buccal mucosa: Pathognomonic
Measles elimination by 2020

- Thailand is one of 11 member states in the WHO's South-East Asia Region. The region set a goal to eliminate measles by 2020.

- WHO's South-East Asia Region 11 Member States: Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste.
Incidence 5,642 cases (8.62 / 100,000 populations)
Death 11 cases
Most common age group:
: 15-24 years (18.34%),
: 25-34 years (15.99%) and
: 1 years (9.22%)
Potential complications associated with measles

- Potential complications vary in frequency and severity: \(^1\)–\(^3\)

  - Diarrhea\(^1\) 8%
  - Otitis media\(^1\) (mainly children) 7%
  - Pneumonia\(^1\) 6%
  - Encephalitis\(^1\) (high case mortality) 0.1%
  - SSPE\(^*\)\(^2,3\) 0.01–0.001%

- In developing countries, measles can be worsened by malnutrition, vitamin A deficiency and simultaneous infections\(^1,2,4\)
  - Persistent diarrhoea, deafness and blindness can also occur\(^2,4,5\)

\* SSPE, subacute sclerosing panencephalitis

Measles: Diagnosis

- Diagnosis of measles virus should be performed
  - IgM antibodies: High sensitivity and specificity
  - RT-PCR: High specificity but low sensitivity
Measles: Treatment

- In developing countries where the morbidity and mortality associated with measles are high, administration of vitamin A to children with active measles decreases measles complications such as diarrhea and pneumonia\(^1-3\)

- **Vitamin A** can function as an immunomodulator by boosting antibody responses to measles\(^4-6\)

Measles: Treatment

- Populations at increased risk for complications
  - Children hospitalized 6 months to 2 years of age
  - Older than 6 months with immunodeficiency
  - Evidence of vitamin A deficiency
  - Impaired intestinal absorption
  - Moderate to severe malnutrition
Measles: Vitamin A Treatment

- WHO currently recommends vitamin A for all children with acute measles, regardless of their country of residence.
- Vitamin A treatment: Once daily for 2 days
  - 200,000 IU for children 12 months or older
  - 100,000 IU for infants 6 through 11 months of age
  - 50,000 IU for infants younger than 6 months
- An additional (ie, a third) age-specific dose should be given 2 through 4 weeks later to children with clinical signs and symptoms of vitamin A deficiency
Hand, Foot and Mouth Disease: Complications

- Brainstem encephalitis
- Myocarditis
Coxsackie Virus

- **CV-A16**: Classic HFMD
- **CV-A6**: Atypical HFMD, associated with widespread, severe vesiculobullous disease, localization to areas of atopic dermatitis (so-called eczema coxsackium), high rates of onychomadesis, and a perioral eruption, unlike CV-A16.
- Increasing reports of HFMD in adults caused by the more virulent CV-A6
HFMD: CV-A6

HFMD: CV-A6 infection in adults

Herpes Simplex Encephalitis (HSE)

- Usually caused by HSV type 1
- Fever, confusion, seizures
- Diagnosis
  - MRI of the brain – Temporal lobe involvement
  - EEG: Periodic lateralized epileptiform discharges
  - Positive HSV PCR from CSF
# Neonatal HSV Infection

<table>
<thead>
<tr>
<th>Route of Infection</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Utero</td>
<td>5</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>85</td>
</tr>
<tr>
<td>Postpartum</td>
<td>10</td>
</tr>
</tbody>
</table>


## Neonatal HSV Infection

<table>
<thead>
<tr>
<th>Disease</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated disease</td>
<td>~25</td>
</tr>
<tr>
<td>- DIC</td>
<td></td>
</tr>
<tr>
<td>- Pneumonia</td>
<td></td>
</tr>
<tr>
<td>- Hepatitis</td>
<td></td>
</tr>
<tr>
<td>- CNS involvement (60-75%)</td>
<td></td>
</tr>
<tr>
<td>Encephalitis (CNS disease)</td>
<td>~30</td>
</tr>
<tr>
<td>- Seizures</td>
<td></td>
</tr>
<tr>
<td>- Lethargy</td>
<td></td>
</tr>
<tr>
<td>- Irritability</td>
<td></td>
</tr>
<tr>
<td>- Poor feeding</td>
<td></td>
</tr>
<tr>
<td>- Temperature instability</td>
<td></td>
</tr>
<tr>
<td>Skin, eyes, and/or mouth (SEM disease)</td>
<td>~45</td>
</tr>
</tbody>
</table>

Neonatal HSV Disease
Diagnosis of Neonate Born to Maternal Active Genital Herpes Lesions

At 24 hours of age obtain from the neonate:

- HSV surface cultures (and PCRs if desired)
  - Swabs of mouth, nasopharynx, conjunctivae, anus
- HSV blood PCR
- CSF cell count, chemistries, and HSV PCR
- Serum ALT

Neonatal HSV disease

- Delivery by cesarean section is recommended if active genital lesions are present at the end of pregnancy.
- Treatment: IV acyclovir 60 mg/kg/day for 14 days in SEM disease and for 21 days in CNS disease or disseminated disease.
- Oral acyclovir suppressive therapy for 6 months may improve neurodevelopmental outcomes in neonatal HSV disease with CNS involvement\(^1\)

Varicella Zoster Virus

- Primary infection: Chickenpox
  - Incubation period: 14-16 days, occasionally 10-21 days
- Recurrent disease: Herpes zoster
  - Associated with aging, immunosuppression, intrauterine exposure, varicella at <18 mo of age
# In Utero Varicella Infection

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Neonatal Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 20 weeks (1\textsuperscript{st} or early 2\textsuperscript{nd} trimester)</td>
<td>Fetal death, congenital varicella syndrome (1-2%) (limb hypoplasia, cutaneous scarring, eye abnormalities)</td>
</tr>
<tr>
<td>After 20 weeks (3\textsuperscript{rd} trimester to 21 days before delivery)</td>
<td>Can develop zoster early in life without varicella</td>
</tr>
<tr>
<td>Perinatal</td>
<td></td>
</tr>
<tr>
<td>• 6-21 days before delivery</td>
<td>• Passive VZV Ab</td>
</tr>
<tr>
<td>• GA &gt;28 weeks</td>
<td>• No passive VZV Ab</td>
</tr>
<tr>
<td>• GA &lt;28 weeks</td>
<td>• Neonatal varicella (untreated mortality rate 30%)</td>
</tr>
<tr>
<td>• 5 days before to 2 days after delivery</td>
<td></td>
</tr>
</tbody>
</table>
Varicella: Treatment

- Oral acyclovir is not recommended for routine use in otherwise healthy children with varicella
- Oral acyclovir should be considered for otherwise healthy people at increased risk of moderate to severe varicella
  - Age >12 years
  - Chronic cutaneous or pulmonary disorders
  - Receiving long-term salicylate therapy
  - Receiving short, intermittent, or aerosolized courses of corticosteroids
Varicella: Treatment

IV acyclovir: Indication

- Immunocompromised patients including chronic corticosteroids
Zika Virus

- Arthropod-borne flavivirus transmitted by *Aedes* mosquitoes
- Clinical manifestations of Zika virus infection occur in approximately 20% of patients and include acute onset of low-grade fever with maculopapular rash, arthralgia (notably small joints of hands and feet), or conjunctivitis (nonpurulent)
Zika Virus: Intrauterine Infection

- Intrauterine Zika virus infection in pregnant women has been associated with microcephaly and fetal loss (in the first trimester)\(^1\)

Zika Virus: Intrauterine Infection

- Retrospective analysis from French Polynesia estimated a baseline microcephaly prevalence of 2 cases per 10,000 neonates and risk of microcephaly associated with Zika virus infection rate of 95 cases per 10,000 women infected in the first trimester\(^1\)

# Zika virus and Microcephaly

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Countries (Yr of Publication)</th>
<th>No. of Studies</th>
<th>Main Findings</th>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcephaly</td>
<td>Brazil: Paraíba, Bahia (2016)</td>
<td>2</td>
<td>Paraíba: retrospective review 2012–2015: 16,208 births; higher-than-expected (2–8%) incidence of microcephaly; Bahia: ecologic association between reports of acute rash, March–June 2015 and microcephaly cases October 2015–January 2016</td>
<td>Temporal associations; large number of births; Bahia data suggest association with late first and early second trimester</td>
<td>Ecologic associations only; no confirmed Zika cases; alternative explanations not excluded</td>
</tr>
<tr>
<td>Case reports or case series</td>
<td>French Polynesia (2015)</td>
<td>1</td>
<td>Retrospective review of 2013–2014 Zika outbreak period: 17 cases of congenital brain malformations, including microcephaly</td>
<td>Temporal association with Zika outbreak; other congenital brain abnormalities observed</td>
<td>No documented maternal infection; retrospective; most not tested for ZIKV; no control group</td>
</tr>
<tr>
<td>Case reports or case series</td>
<td>Brazil: several states (2015–2016)</td>
<td>11</td>
<td>93 Cases of microcephaly, 70 with history of maternal symptoms (laboratory-confirmed in 1 of 3 tested); 9 with ZIKV in amniotic fluid, fetal or neonatal brain; 4 with ZIKV in brain but not other organs</td>
<td>Biologic evidence of ZIKV in fetal or neonatal brain tissues and neurotropism</td>
<td>Most maternal ZIKV exposures were self-reported; other congenital infections not always excluded; no control group</td>
</tr>
<tr>
<td>Case reports or case series</td>
<td>Various countries (2016)</td>
<td>1</td>
<td>9 Women returning to United States from Zika-affected countries, August 2015–February 2016; all reported symptoms, all laboratory-confirmed recent ZIKV infection; 2 early pregnancy losses, 2 terminations, 1 microcephaly, 2 healthy newborns, 2 still pregnant</td>
<td>Temporal association; biologic evidence of maternal ZIKV infections</td>
<td>Alternative explanations not excluded; no control group</td>
</tr>
<tr>
<td>Cohort study</td>
<td>Brazil: Rio de Janeiro (2016)</td>
<td>1</td>
<td>88 Women with rash during pregnancy, 72 ZIKV-positive on RT-PCR; ultrasound normal in all 16 ZIKV-negative women; ultrasound abnormal in 12 of 42 ZIKV-positive women at all stages of pregnancy (29%); microcephaly mostly in association with intruterine growth restriction</td>
<td>Temporal association; biologic evidence; strong association with abnormal ultrasound or neonatal outcome</td>
<td>Small study; control group presumed to have other causes for rash; some congenital infections not excluded</td>
</tr>
</tbody>
</table>

Zika Virus Infection

- Neurotropism of Zika virus has been demonstrated in vivo and in vitro\textsuperscript{1-4}
- Zika virus infection has been associated with neurologic complications\textsuperscript{5}
  - Congenital microcephaly
  - Developmental problems among babies born to infected pregnant women
  - Guillain-Barré syndrome
  - Myelitis
  - Meningoencephalitis
  - Acute disseminated encephalomyelitis (ADEM)

Laboratory testing for Zika virus infection in the neonate

- Serum and urine for Zika virus RNA via real-time reverse transcription PCR (rRT-PCR).
- Serum Zika virus IgM enzyme-linked immunosorbent assay (ELISA).
- If CSF is available, test CSF for Zika virus RNA (via rRT-PCR) as well as Zika virus IgM.
ขอบคุณครับ

ขอบคุณครับ