Pertussis

Epidemiology
Surveillance
Diagnostics
Maternal Immunization
Current dilemmas
Conclusions

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Flinders University, Adelaide, South Australia
How worried should we be about the whooping cough epidemic?

Mary-Rose MacColl  The Australian  April 28, 2012 12:00AM

Dana McCaffery, who died from whooping cough at four weeks. Source: Supplied
Epidemiology of Pertussis

• Pertussis remains endemic worldwide.¹
  – Estimated 50 million cases and 300,000 deaths each year.

• Pertussis is an important public health problem, even in countries with sustained high vaccination coverage.²⁻⁴
  – Incidences vary widely from <0.1/100,000 in Japan to 150/100,000 in Australia.

• Worldwide, infants bear the greatest disease burden and mortality, making disease prevention an important public health goal.
  – Hospitalization rate for infants <12 months of age are higher at 38.8 per 100,000 population compared with those <16 years old at 2.6 per 100,000.⁵
  – Of 809 hospitalizations for pertussis in California in 2010, most occurred in infants younger than 3 months; all 10 deaths occurred in this age group.⁶

Reported NNDSS pertussis cases: 1922-2013*

Number of cases

Year

*2013 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Incidence of pertussis in Australia


Thanks to Ruiting Lan
Figure 55: Notifications and notification rates for pertussis, Australia, 1993 to 2012

- Whole cell pertussis containing vaccines used exclusively prior to 1997
- Nucleic acid testing included in pertussis case definition
- Acellular pertussis containing vaccines used for the primary schedule
- 18 month booster dose removed from the routine schedule
Figure 59: Notification rate for pertussis, Australia, 2012, by year and age group

Rate per 100,000 population

Year of diagnosis

- <1
- 1-4
- 5-9
- 10-14
- 15-19
- 20-59
- 60+
Changing Age Distribution of Pertussis

Proportion of pertussis notifications, %

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence per 100,000 individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>197</td>
</tr>
</tbody>
</table>

Pertussis notification rates and deaths, 1995-2010  Australia

From: McIntyre P, NCIRS
Pertussis: A Resurgent Problem

- Despite routine and widespread vaccination, a resurgence of pertussis cases has been observed in the post-vaccination era.
  - Pertussis resurgence reported in many countries, including Argentina, Australia, Austria, Brazil, Canada, Chile, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Japan, Netherlands, Nigeria, Norway, Poland, South Korea, Spain, Switzerland, United Kingdom, and the United States.\(^1\)\(^-\)\(^7\)

- Hypotheses for this resurgence include:
  - Improved surveillance, diagnostic methods and disease awareness.\(^8\)
  - Incomplete vaccination.\(^9\)
  - Waning vaccine- or natural infection-induced immunity.\(^10\)\(^-\)\(^15\)
  - Adaptability of bacterium to immunity conferred by vaccines.\(^10\)\(^-\)\(^15\)
  - The acellular vaccine may not fully prevent pertussis transmission.\(^16\)

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Regional Epidemiological Trends

• Despite the stable number of cases reported worldwide between 2000 to 2012, many regions experienced a resurgence in pertussis cases\(^1\)–\(^7\)

Regional Epidemiological Trends (cont.)

• Four of six regions showed an increase in number of reported cases from 2011 to 2012.

### Pertussis Control in the Asia-Pacific Region

#### Table 1
Epidemiology of pertussis in Asia-Pacific.

<table>
<thead>
<tr>
<th>Country</th>
<th>Age cohort with the highest pertussis burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>0-14 year olds</td>
</tr>
<tr>
<td>China</td>
<td>&lt;4-year olds</td>
</tr>
<tr>
<td>India</td>
<td>&lt;5 year olds, but beginning to be recognized in older children and adults</td>
</tr>
<tr>
<td>Indonesia</td>
<td>&lt;1 year olds</td>
</tr>
<tr>
<td>Japan</td>
<td>Previously infants, but incidence increasing in older cohorts</td>
</tr>
<tr>
<td>New Zealand</td>
<td>School-aged children</td>
</tr>
<tr>
<td>Pakistan</td>
<td>&lt;5 years</td>
</tr>
<tr>
<td>Philippines</td>
<td>Infants</td>
</tr>
<tr>
<td>Singapore</td>
<td>&lt;5 years</td>
</tr>
<tr>
<td>South Korea</td>
<td>&lt;1 year olds</td>
</tr>
<tr>
<td>Taiwan</td>
<td>&lt;1 year olds</td>
</tr>
<tr>
<td>Thailand</td>
<td>&lt;4 year olds</td>
</tr>
<tr>
<td>Vietnam</td>
<td>&lt;5 year olds</td>
</tr>
</tbody>
</table>
Surveillance
Surveillance and Epidemiological Trends in the Western Pacific

• Australia has a national surveillance system that implements active surveillance, and pertussis is a notifiable disease.\(^1\)
  – The notification rate increased from 4.4 per 100,000 in 1991 to 161.6 per 100,000 in 2012.\(^1\)
  – In infants <1 yr, rate was 200–400 (2010), 300–500 (2011) and 200–300 (2012).

• In the Western Pacific region as a whole, the number of reported cases increased from 25,282 in 2000 to 43,213 in 2012.\(^2\)

• In China, pertussis is a reportable disease but surveillance is passive and variable.\(^1\)

• In Japan, pertussis incidence has increased since 2008 corresponding to an outbreak that lasted until 2011.\(^3,4\)
  – Adolescent and adult cases accounted for 40–52% of all cases; however, increased disease burden also observed in primary and junior high school aged children.

Surveillance and Epidemiological Trends in Southeast Asia

• Surveillance in the region is effected by a lack of diagnostic laboratories and adequate healthcare infrastructure.
• Since 2000, the number of reported cases has remained stable at around 40,000 cases except in 2009 when it increased to 63,798.¹
  – Child mortality rates from pertussis have fluctuated from 4% of child deaths in 2008 to <1% in 2010.
• South Korea has a national passive surveillance system.²
  – Reported pertussis cases have increased since 2000, especially in adolescents ≥15 years old and adults who account for 29% of cases.
  – This shift in incidence to an older age group is attributed to waning vaccine or natural immunity.
• In 2007, an outbreak occurred in India affecting children ≤5 years old; none were vaccinated.³

Under-Reporting of Pertussis

Reported cases are the tip of the iceberg\(^1\)–\(^4\)

Atypical forms

Wide disease variability

Under-reporting

Under-diagnosis

Inconsistent case definitions

Low physician awareness

Unreported pertussis

Only 1–36% of pertussis cases are reported\(^5\)–\(^6\)

Problems with Under-reporting and Surveillance Systems

- Although a mandatory notifiable disease in most countries, pertussis is likely to be significantly under-reported (especially in adolescents and adults).1,2
- Passive surveillance statistics underestimate incidence by 10- to 1000-fold, depending on quality of surveillance system.3-5
- Under-reporting in some countries may be exacerbated by weak healthcare infrastructure, lack of diagnostic tools, and challenges of poverty.6,7
- Although both WHO and CDC have established pertussis case definitions,8,9 these are difficult to apply.2,10

Epidemiology & Surveillance

Conclusions

• No clear picture currently of worldwide epidemiology of pertussis.\(^1\)
  – Global epidemiology is complex and differs from country to country.
• Although it is evident that infants bear the greatest disease burden, poor reporting and dubious statistics from many countries confound efforts to discern patterns.\(^1\)
• Key findings:
  – Despite routine and worldwide vaccination, pertussis remains a serious health concern in all age groups.\(^1\)
  – In many regions, there has been an increase in cases in older children, adolescents, and adults.\(^1,2\)
  – Although not surprising to see an increase in regions with lower DTP3 coverage, the findings in Europe and the US where vaccine coverage is high suggests other factors are responsible for the increase in pertussis cases.\(^1\)
    • Waning vaccine immunity?

Epidemiology & Surveillance

Conclusions

• Key findings (cont.)
  – Waning immunity is a problem in countries using acellular vaccines.\(^1\text{–}\text{3}\)
  – The situation in countries still using whole cell vaccines is less clear.\(^1\text{,}\text{2}\)
  – It is likely both acellular and whole cell vaccines give impermanent immunity.

• The situation today:
  – Pertussis disease is widespread, even in countries with high vaccine coverage.\(^1\text{,}\text{4}\)
  – Pertussis vaccines, and especially acellular vaccines, are currently imperfect in that they do not provide prolonged immunity.
  – \textit{B. pertussis} is likely evolving to escape the protection offered by natural immunity and vaccination.

Conclusions

• What needs to be done:\(^1,^2\)
  – Improvement in infant primary- and booster-vaccine coverage rates are needed in many countries.
  – Strategies to decrease the reservoir for disease transmission to infants are needed, such as booster vaccination of adolescents and adults, immunizing healthcare workers and maternal immunization.
  – Additional studies are needed to evaluate:
    • The duration of immunity of current vaccines in order to optimize vaccination schedules.
    • The impact that antigenic and genotypic changes in circulating \(B.\ pertussis\) organisms are having on pertussis epidemiology.
  – More systematic and standardized epidemiological evaluation of pertussis is needed throughout the world to better elucidate the problem, compare between countries, and to find possible solutions.
  – Improvement and implementation of surveillance systems, particularly in Africa and Asia, are needed to provide accurate epidemiological data.

Vaccines
## Pertussis vaccination schedules in Asia-Pacific.

<table>
<thead>
<tr>
<th>Country</th>
<th>Primary series</th>
<th>Booster dose</th>
<th>Adolescent/adult immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Australia</strong></td>
<td>2, 4 and 6 months</td>
<td>-</td>
<td>15-17 years</td>
</tr>
<tr>
<td><strong>China</strong></td>
<td>3, 4 and 5 months</td>
<td>18 months</td>
<td>-</td>
</tr>
<tr>
<td><strong>India</strong></td>
<td>Public: 6, 10 and 14 weeks</td>
<td>Public: 16-24 months</td>
<td>Private: 10 years</td>
</tr>
<tr>
<td></td>
<td>Private: 6, 10 and 14 weeks</td>
<td>Private: 18 months</td>
<td></td>
</tr>
<tr>
<td><strong>Indonesia</strong></td>
<td>2, 4 and 6 months</td>
<td>18-24 months</td>
<td>5 years</td>
</tr>
<tr>
<td><strong>Japan</strong></td>
<td>3, 4-5 and 6-7 months</td>
<td>18 months</td>
<td>-</td>
</tr>
<tr>
<td><strong>New Zealand</strong></td>
<td>6 weeks, 3 and 5 months</td>
<td>-</td>
<td>11 years</td>
</tr>
<tr>
<td><strong>Pakistan</strong></td>
<td>Public: 6, 10 and 14 weeks</td>
<td>Private: 18 months</td>
<td>Private: 10 years</td>
</tr>
<tr>
<td></td>
<td>Private: 6, 10 and 14 weeks or 2, 4 and 6 months</td>
<td>Private: 4-5 years</td>
<td></td>
</tr>
<tr>
<td><strong>Philippines</strong></td>
<td>Public: 6, 10 and 14 weeks</td>
<td>Private: 15 months</td>
<td>Private: 10 years</td>
</tr>
<tr>
<td><strong>Singapore</strong></td>
<td>3, 4 and 5 months</td>
<td>18 months</td>
<td>10-11 years</td>
</tr>
<tr>
<td><strong>South Korea</strong></td>
<td>2, 4 and 6 months</td>
<td>15-18 months</td>
<td>Private: Available</td>
</tr>
<tr>
<td><strong>Taiwan</strong></td>
<td>2, 4 and 6 months</td>
<td>18 months</td>
<td>6 years</td>
</tr>
<tr>
<td><strong>Thailand</strong></td>
<td>2, 4 and 6 months</td>
<td>18-24 months</td>
<td>4-5 years</td>
</tr>
<tr>
<td><strong>Vietnam</strong></td>
<td>2, 3 and 4 months</td>
<td>18 months (as of June 2011)</td>
<td>-</td>
</tr>
</tbody>
</table>

*a* The primary series can be started as late as 8 months of age in Japan.

*b* In Singapore, the booster dose administered to children 10 to 11 years of age can be either Td or Tdap.

4. [http://www.idai.or.id/](http://www.idai.or.id/)
Current worldwide use of wP and aP vaccines

DTwPHBV-Hib vaccines are the cornerstone of Global Immunization programs

<table>
<thead>
<tr>
<th>Country</th>
<th>Pertussis vaccines available</th>
<th>Vaccine trade name</th>
<th>DTP3 coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia*</td>
<td>DTap, DTap+IPV, DTap+HepB+IPV, DTap+HepB+Hib+IPV, Tdap, Tdap+IPV</td>
<td>ADACEL [5], Sanofi Pasteur; ADACEL-Polio [5], Sanofi Pasteur; BOOSTRIX [3], GSK; BOOSTRIX-IPV [3], GSK; INFANRIX hexa [3], GSK; INFANRIX-IPV [3], GSK; INFANRIX penta [3], GSK</td>
<td>92%</td>
</tr>
<tr>
<td>China*</td>
<td>DTwP, DTap, DTap+Hib+IPV</td>
<td>BOOSTRIX [3], GSK; INFANRIX [3], GSK; INFANRIX-Hib [3], GSK; PENTAXIM [2], Sanofi Pasteur</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>China National Biotec Group DTap [2]; Wuhan Institute of Biological Products DTap [2]; Chengdu Institute of Biological Products (wP); Shanghai Institute of Biological Products (wP); Wuhan Institute of Biological Products, (wP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India*</td>
<td>DTwP, DTwP+HepB, DTwP+Hib, DTwP+Hib+HepB, DTap (private sector), DTap+Hib+IPV (private sector)</td>
<td>ADACEL [5], Sanofi Pasteur; BOOSTRIX [3], GSK; EASY FOUR (wP), Chiron Panacea; EASY FIVE (wP), Chiron Panacea; INFANRIX [3] GSK; PENTAXIM [2], Sanofi Pasteur; TetrACT-Hib (wP), Sanofi Pasteur; TRIPACEL [5], Sanofi Pasteur</td>
<td>66%</td>
</tr>
<tr>
<td></td>
<td>Bharat Biotech: COMVAC4-HB (wP), COMVAC5 (wP) Serum Institute of India: Q-VAC (wP), PENTAVAC (wP), QUADROVAX (wP), TRIPLE (wP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indonesia*</td>
<td>DTwP+HepB, DTwP, DTap (private sector), DTap+Hib (private sector), DTap+Hib+IPV (private sector), DTwP+Hib (private sector)</td>
<td>INFANRIX [3], GSK; INFANRIX-Hib [3], GSK; PEDIACEL [5], Sanofi Pasteur; TetrACT-Hib (wP), Sanofi Pasteur; TRIPACEL [5], Sanofi Pasteur</td>
<td>82%</td>
</tr>
<tr>
<td></td>
<td>Bio Farma (wP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>Vaccines</td>
<td>Local production</td>
<td>Coverage</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Japan</td>
<td>DTaP</td>
<td>Biken [2], Denka [4], Kaketsuken [2], Kitasato [4], Takeda [4]</td>
<td>98%</td>
</tr>
<tr>
<td>New Zealand</td>
<td>DTaP+HepB+Hib+IPV, Tdap</td>
<td>BOOSTRIX [3], GSK; INFANRIX hexa [3], GSK</td>
<td>92%</td>
</tr>
<tr>
<td>Pakistan</td>
<td>DTwP+HepB+Hib, DTaP+Hib+IPV (private sector), DTaP+HepB+Hib+IPV (private sector)</td>
<td>INFANRIX hexa [3], GSK; PENTAXIM [2], Sanofi Pasteur; QUINVAXIM (wP), Novartis</td>
<td>85%</td>
</tr>
<tr>
<td>Philippines</td>
<td>DTwP, DTaP (private sector), Tdap (private sector)</td>
<td>ADACEL [5], Sanofi-Pasteur; BOOSTRIX [3], GSK; INFANRIX hexa [3], GSK; PENTAct-Hib [2], Sanofi Pasteur; PENTAXIM [2], Sanofi Pasteur; QUINVAXEM (wP), Novartis; TETRAXIM [2], Sanofi Pasteur</td>
<td>87%</td>
</tr>
<tr>
<td>Singapore</td>
<td>DTaP, DTaP+IPV, DTaP+HepB+Hib+IPV, DTaP+Hib, DTaP+IPV+Hib, Tdap</td>
<td>ADACEL [5], Sanofi Pasteur; BOOSTRIX [3], GSK; BOOSTRIX-IPV [3], GSK; INFANRIX [3], GSK; INFANRIX hexa [3], GSK; INFANRIX-Hib [3], GSK; INFANRIX-IPV-Hib [3], GSK; PEDIACEL [5], Sanofi Pasteur; PENTAXIM [2], Sanofi Pasteur</td>
<td>97%</td>
</tr>
<tr>
<td>Country</td>
<td>Pertussis vaccines available</td>
<td>Vaccine trade name (number of pertussis components), Manufacturer</td>
<td>DTP3 coverage</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------------------</td>
<td>------------------------------------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>South Korea</td>
<td>DTaP, Tdap (private sector), Tdap+IPV (private sector)</td>
<td>ADACEL [5], Sanofi Pasteur; BOOSTRIX [3], GSK; INFANRIX [3], GSK; KINRIX [3], GSK; TETRAXIM [2], Sanofi Pasteur</td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td>DTaP+IPV+Hib, Tdap</td>
<td>ADACEL [5], Sanofi Pasteur; BOOSTRIX [3], GSK; PEDIACEL [5], Sanofi Pasteur</td>
<td>96%</td>
</tr>
<tr>
<td>Thailand</td>
<td>DTwP, DTaP (private sector), DTaP+IPV+Hib (private sector), DTaP+IPV+Hib+HepB (private sector)</td>
<td>ADACEL [5], Sanofi Pasteur; ADACEL-Polio [5], Sanofi Pasteur; BOOSTRIX [3], GSK; BOOSTRIX-IPV [3], GSK; D.T.COQ/DTP (wp), Sanofi Pasteur; INFANRIX hexa [3], GSK; INFANRIX-IPV [3], GSK; INFANRIX [3]-IPV+Hib, GSK; PEDIACEL [5], Sanofi Pasteur; PENTAXIM [2], Sanofi Pasteur; TETRAXIM [2], Sanofi Pasteur; TRIPACEL [5], Sanofi Pasteur; TRITANRIX HepB (wp), GSK</td>
<td>99%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>DPwT, DPwT+Hib+HepB, Tdap (private sector), Tdap</td>
<td>ADACEL [5], Sanofi Pasteur; INFANRIX hexa [3], GSK; PENTAXIM [2], Sanofi Pasteur; TETRAXIM [2], Sanofi Pasteur</td>
<td>96%</td>
</tr>
</tbody>
</table>

Regional Pertussis Vaccine Coverage

- DTP3 coverage in infants differs according to region

Are Current Vaccines and Vaccination Strategies the Future of Pertussis Control?
• Although it is accepted that currently-used pertussis vaccines (acP and wcP) are effective in preventing disease, some data suggest duration of protection is shorter with acP.¹,²
  • caution needs to be applied in interpreting these data due to little or no information regarding efficacy of current wcP vaccines.
• The reasons for this are unclear, but may include a different quality of immune response to acP versus wcP.
  – Priming with acP induces a Th2 cellular response.³
  – Optimum protection against B. pertussis requires induction of Th1/Th17 cells.⁴
  – T-cell memory is more robust following wcP versus acP vaccination.⁵

acP, acellular pertussis vaccine. wcP, whole cell pertussis vaccine.
Pertussis Diagnosis
Method(s) used to diagnose pertussis in Asia-Pacific.

<table>
<thead>
<tr>
<th>Country</th>
<th>Method(s) used to diagnose pertussis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Clinical and laboratory (culture, RT-PCR, serology)</td>
</tr>
<tr>
<td>China</td>
<td>Clinical and laboratory (culture, serology)</td>
</tr>
<tr>
<td>India</td>
<td>Clinical only</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Clinical only (majority of cases)</td>
</tr>
<tr>
<td>Japan</td>
<td>Clinical and laboratory [culture, serology (whole cell bacterial agglutination, not ELISA); RT-PCR available, but not widely used]</td>
</tr>
<tr>
<td>New Zealand</td>
<td>Clinical and laboratory (culture; RT-PCR; serology, but ELISA has low specificity)</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Clinical only</td>
</tr>
<tr>
<td>Philippines</td>
<td>Clinical only</td>
</tr>
<tr>
<td>Singapore</td>
<td>Clinical and laboratory (culture, immunofluorescence, RT-PCR)</td>
</tr>
<tr>
<td>South Korea</td>
<td>Clinical and laboratory (culture; serology; RT-PCR, but not routinely used)</td>
</tr>
<tr>
<td>Taiwan</td>
<td>Clinical and laboratory (culture, RT-PCR, serology)</td>
</tr>
<tr>
<td>Thailand</td>
<td>Clinical only (majority of cases)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>Clinical only</td>
</tr>
</tbody>
</table>
GPI Algorithm for Diagnosis of Pertussis Infection\(^a\): Clinical Capabilities Only

**0–3 mo**
- Cough of any duration that is not improving (may or may not be paroxysmal)
- Coryza which does not become purulent
- Afebrile/low-grade fever
- Cough + apnea
- Cough + seizures
- Cough + cyanosis
- Cough + emesis
- Pneumonia
- Coinfection with RSV or adenovirus can lead to expiratory distress and fever

**4 mo–9 yr**
- Paroxysmal non-productive cough of ≥7 days’ duration
- Coryza which does not become purulent
- Afebrile/low-grade fever
- Whoop
- Apnea
- Posttussive emesis
- Subconjunctival hemorrhage
- Cyanosis
- Sleep disturbance

**≥10 yr**
- Sweating episodes between paroxysms

\(^a\)In a person with cough illness with no or minimal fever. GPI, Global Pertussis Initiative; 1. Cherry JD, et al. *Clin Infect Dis.* 2012;54:1756–64.
GPI Algorithm for Diagnosis of Pertussis Infection\(^a\): Access to Laboratory Facilities\(^1\)

**Early stage (cough <3 weeks’ duration)**
- 0–3 mo
  - Increased WBC count (\(\geq 20,000\) with \(\geq 10,000\) lymphocytes)
  - PCR and culture\(^b\)
- 4 mo–9 y
  - PCR
- \(\geq 10\) y
  - PCR and serology (IgG-PT), if \(\geq 1\) year post-pertussis vaccination

**Late stage (cough >3 weeks’ duration)**
- 0–3 mo
  - PCR
- 4 mo–9 y
  - PCR and culture\(^c,d\)
- \(\geq 10\) y
  - PCR
  - Serology (IgG-PT), if \(\geq 1\) year post-pertussis vaccination

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\(a\)In a person with cough illness with no or minimal fever; \(b\)In resource-limited areas where PCR is not available, samples may be sent to a reference laboratory for culture confirmation; \(c\)False-negatives possible; \(d\)Serology not useful in this age cohort.

IgG, immunoglobulin G; PCR, polymerase chain reaction; PT, pertussis toxin; RSV, respiratory syncytial virus; WBC, white blood cell.

Current Pertussis Case Definitions: Summary

- Laboratory confirmation tests include:\(^1,^2\)
  - Culture (considered the “gold standard”)
  - PCR
  - Serology (generally more useful for diagnosis later in disease)

- The optimal timing for laboratory confirmation tests differs\(^2\)

- However, not all definitions require serology:\(^1\)
  - CDC definition does not include serology
  - WHO definition allows paired serology
  - EU definition allows \(B.\) pertussis-specific antibody response

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CDC, Centers for Disease Control and Prevention; EU, European Union; PCR, polymerase chain reaction; WHO, World Health Organization.

General Comments on Laboratory Diagnosis of Pertussis

• PCR and culture have the greatest utility in the first 3–4 weeks after onset of illness\(^1,2\)
  – Serology is useful later in the disease\(^2\)
• Serology is inappropriate for diagnosing pertussis in patients <1 year after immunization with an acellular or whole-cell vaccine\(^1\)
• Anti-PT IgG ELISA is preferred to IgA because the IgA response following infection is less common\(^1\)
  – A negative anti-PT IgA test is unreliable for diagnosing pertussis infection.

DFA, direct fluorescent antibody; ELISA, enzyme-linked immunosorbent assay; IgA, immunoglobulin A; IgG, immunoglobulin G; PCR, polymerase chain reaction; PT, pertussis toxin.
Maternal Immunization
Adolescents and Adults: a Major Source of \textit{B. pertussis} Infection for Infants

Young Infants Bear the Greatest Disease Burden

- Infants have the highest risk for pertussis-related complications and death,¹ and the highest rates of disease and hospitalization.²–⁴

<table>
<thead>
<tr>
<th>Age, months</th>
<th>Incidence/month / 100,000</th>
<th>Hospitalization with respiratory illness</th>
<th>Hospitalization with neurologic illness</th>
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Maternal Immunization: Rationale

• Maternal immunization during pregnancy has the potential to directly protect infants against pertussis through the passive transfer of maternal antibodies.¹
• This approach offers an important benefit in that it can protect the very young from birth.
  – Protection provided until the beginning of primary diphtheria, tetanus, and pertussis (DTaP) series.
• Several studies have demonstrated maternal transfer of anti-pertussis antibodies to the fetus following maternal vaccination or natural infection.²–⁶

GPI Algorithm to Avoid Newborn and Infant Pertussis Deaths and Severe Disease

1. Forsyth K et al, Pediatrics. 2015 Jun;135(6):e1475-82
Whooping cough vaccination in the third trimester of pregnancy is the first step you can take to provide early protection for your baby against whooping cough.

The second step is to make sure you have your baby vaccinated on time at 6 weeks, 4 months and 6 months of age.
Conclusions

• When pertussis is looked for, it is found
• To better inform vaccination approaches at the country level, surveillance is necessary
• Current vaccines are imperfect, but a vast improvement on the pre-vaccine era
• Maternal immunization is an important new development in protection of infants from pertussis
• Adherence to vaccine schedules is a critical public health intervention