Pertussis vaccination for pregnant women – successes and challenges

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Disclosure Statement

I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.
Rationale

- Despite high vaccine coverage globally (in 2015, 86% coverage with 3 doses of a pertussis containing vaccine\(^1\)), pertussis remains endemic in all countries and continues to be a public health concern.
- Highest rates of disease observed in unimmunised infants <3 months.
- Immunising in pregnancy aims to sufficiently boost immunity to optimise transplacental transfer of maternal Abs and passively protect infants in first months of life.
- Additionally these women are unlikely to be a source of infection for their babies.
- In 2015 WHO Position paper\(^1\)

\textit{‘Vaccination of pregnant women is likely to be the most cost effective additional strategy for preventing disease in infants too young to be vaccinated and appears to be more effective and favourable than cocooning.’}

Maternal Pertussis Immunisation Programmes: Country Specific Recommendations

**Australia (2013):**
20-32 weeks gestation

**New Zealand (2013):**
28-38 weeks gestation

**Brazil (2014):**
20-36 weeks gestation

**Panama (2012):**
>28 weeks gestation

**Columbia (2013):**
>26 weeks gestation

**USA (2011):**
27-36 weeks gestation

**Mexico (2012):**
20-32 weeks gestation

**El Salvador:**
>20 weeks gestation

**Honduras:**
26-37 weeks gestation

**Costa Rica (2008):**
>20 weeks gestation

**Panama (2012):**
>28 weeks gestation

**Columbia (2013):**
>26 weeks gestation

**Chile (2016):**
27-36 weeks gestation *

**Argentina (2012):**
>20 weeks gestation

**Bahamas:**
20-32 weeks gestation

**Nicaragua:**
>20 weeks gestation

**El Salvador:**
>20 weeks gestation

**Honduras:**
26-37 weeks gestation

**Nicaragua:**
26-37 weeks gestation

**Uruguay:**
20-36 weeks gestation

**New Zealand (2013):**
28-38 weeks gestation

**Uruguay:**
20-36 weeks gestation

**Israel:**
27-36 weeks gestation

**Canada (2018):**
27-32 weeks gestation

**Uruguay:**
20-36 weeks gestation

**Singapore (2017):**
16-32 weeks gestation

**Australia (2013):**
20-32 weeks gestation

*Recommendation made in Oct 2016. Ministry of Health is in the process of adopting recommendations.*

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Maternal Pertussis immunisation programmes in Europe

- UK (2012): 16-32 weeks gestation
- Belgium (2013): 24-32 weeks gestation
- Spain (2013): 20-36 weeks gestation
- Portugal (2013): 20-36 weeks gestation
- Czech Republic (2016): 28-36 weeks gestation
- Ireland (2013): 27-36 weeks gestation
- Greece (2017): 27-36 weeks gestation
- Switzerland (2017): >13 weeks gestation
- Italy (2017): >28 weeks gestation

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UK Maternal Programme was introduced as an outbreak response measure

2011/12¹

Major increase in pertussis reports

Increase in deaths and hospitalisation, mainly in young infants before age of routine vaccination

Oct 2012¹

Emergency programme introduced for pregnant women

Offer a single dose of Repevax (dT5aP/IPV) ideally between 28–32 weeks pregnancy, in every pregnancy

July 2014

Vaccine changed to Boostrix-IPV (dT3aP/IPV)

Guidance updated to vaccination from 16 weeks, (ideally from 20–32 weeks)

April 2016

Offers more opportunities for women to be vaccinated

Success of Maternal Pertussis Immunisation Programme in England

- Rapid implementation of programme
- Rapid achievement of & sustained high coverage
- Public and Professional communications
- Early evaluation of effectiveness and impact
Success of UK maternal vaccination - the role of general practice

~95% of the UK population are registered with a general practice

- providing basis for **coordination** and **continuity** of care
- Antenatal care often delivered in general practice for low risk pregnancies
- dedicated and professional nursing workforce who deliver most routine vaccine programmes in the UK

Rapid implementation of the emergency programme (6 weeks)

- National procurement and distribution of vaccine
- Use of existing national stock of vaccine (pre-school booster)

Highly systematic use of information technology in general practice

- To support population health interventions
- Identify eligible population
- Undertake call and recall

Can rapidly implement and monitor uptake of vaccine programmes
Monthly pertussis vaccination coverage (%) in pregnant women: England, 2013 - 2019
Success of Maternal Pertussis Immunisation Programme in England

- Rapid implementation of programme
- Rapid achievement of & sustained high coverage
- Public and Professional communications
- Early evaluation of effectiveness and impact
Vaccination against pertussis (whooping cough) for pregnant women

An update for healthcare professionals

May 2016
High Awareness of maternal vaccination programmes

Parents of 0y2m - 3y3m (1158)

- Yes, I knew about both vaccines: 83%
- Yes, I knew about the whooping cough vaccine only: 1%
- Yes, I knew about the flu vaccine only: 3%
- Yes, I knew pregnant women are being vaccinated but not which diseases this was for: 1%
- No, I did not know that: 12%

Q. Did you know that whooping cough and flu vaccines are being offered to all pregnant women in England at the moment?
Success of Maternal Pertussis Immunisation Programme in England

- Rapid implementation of programme
- Rapid achievement of & sustained high coverage
- Public and Professional communications
- Early evaluation of effectiveness and impact
Pertussis maternal vaccine effectiveness in prevention of infant disease: England

(3) Amirthalingam G et al CID 2016

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Cases vaccinated / total</th>
<th>Matched / control coverage</th>
<th>Adjusted VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2M age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening method (1)</td>
<td>12/82 (15%)</td>
<td>62%</td>
<td>90% (82% to 95%)</td>
</tr>
<tr>
<td>Case-control study (2)</td>
<td>10/58 (17%)</td>
<td>39/55 (71%)</td>
<td>93% (81% to 97%)</td>
</tr>
<tr>
<td>Screening Method (3)</td>
<td>35/243 (14.4%)</td>
<td>64.8%</td>
<td>91% (88% to 94%)</td>
</tr>
</tbody>
</table>
Growing evidence of effectiveness of maternal immunisation programmes

- Vaccine Effectiveness (VE) of maternal Tdap was 91.4% (95% CI: 19.5-99.1%) in infants <2 months of age and 69.0% (95% CI: 43.6-82.9%) for first year of life\(^1\)

- Infants born to vaccinated mothers had lower risk of hospitalisation, ICU admission and shorter hospital stays. Adjusted VE for preventing hospitalisation was 58% (95% CI: 15-80%)\(^2\)

Reconciled deaths from pertussis in infants, England 2001–2019*

Sources: Public Health England, unpublished data. Lab confirmed cases, certified deaths, Hospital episode statistics, GP registration details, HPZone

* 2019 to end May
Extensive data show that Tdap and Tdap/IPV have reassuring safety profiles in maternal immunisation. 16 studies from multiple countries (mostly in Europe and North America) investigated:

<table>
<thead>
<tr>
<th>Safety in &gt;150,000 vaccinated pregnancies</th>
<th>Tdap and Tdap/IPV vaccines with either 3- or 5- pertussis components</th>
<th>A range of maternal, foetal and infant outcomes</th>
</tr>
</thead>
</table>

Findings generally consistent, with similar risks of safety outcomes in vaccinated and unvaccinated pregnancies

Mixed findings for PPH & Chorioamnionitis observed, but not 1) transient tachypnoea; 2) neonatal sepsis; 3) neonatal pneumonia; 4) respiratory distress syndrome; 5) newborn convulsions

**Mixed findings for postpartum haemorrhage and chorioamnionitis**

<table>
<thead>
<tr>
<th>Study</th>
<th>Cases/vaccinated (%)</th>
<th>Cases/unvaccinated (%)</th>
<th>Adjusted estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Postpartum haemorrhage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donegan 2014</td>
<td>59/6,185 (1.0)</td>
<td>181/18,523 (1.0)</td>
<td>0.98 (0.73–1.31)</td>
</tr>
<tr>
<td>Layton 2017</td>
<td>3,814/ 123,780 (3.1)</td>
<td>21,120/ 871,177 (2.3)</td>
<td>1.23 (1.18–1.28)</td>
</tr>
<tr>
<td>Griffin 2018</td>
<td>715/8,178 (8.7%)</td>
<td>4,611/60,372 (7.7)</td>
<td>1.05 (0.96–1.15)</td>
</tr>
<tr>
<td><strong>Chorioamnionitis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kharbanda 2014</td>
<td>1,596/26,229 (6.1)</td>
<td>5,329/97,265 (5.5)</td>
<td>1.19 (1.13–1.26)</td>
</tr>
<tr>
<td>Morgan 2015</td>
<td>421/7,152 (6)</td>
<td>9/226 (4.0)</td>
<td>P=0.3</td>
</tr>
<tr>
<td>Berenson 2016</td>
<td>39/1,109 (3.5)</td>
<td>14/650 (2.2)</td>
<td>1.53 (0.80–2.90)</td>
</tr>
<tr>
<td>Layton 2017</td>
<td>4,529/ 123,780 (3.7)</td>
<td>21,120/ 871,177 (2.3)</td>
<td>1.11 (1.07–1.15)</td>
</tr>
<tr>
<td>DeSilva 2017</td>
<td>2,883/45,008 (6.4)</td>
<td>7,970/152,556 (5.2)</td>
<td>1.23 (1.17–1.28)</td>
</tr>
<tr>
<td>Griffin 2018</td>
<td>26/8,178 (0.3)</td>
<td>198/60,372 (0.3)</td>
<td>1.10 (0.70–1.75)</td>
</tr>
</tbody>
</table>

- No evidence of increased risk of the adverse neonatal outcomes that would be expected as a consequence of chorioamnionitis (such as preterm birth, neonatal sepsis, NICU admission).
Changing model of delivery and accurate assessment of vaccine uptake are key challenges

- Antenatal care in England shared between maternity services (midwives) and general practice and care pathways vary across the country. Timely vaccination relies on good communication.
- Increasingly model of delivery in England moving to maternity settings
- Requires data on vaccines administered in maternity units to be transferred and recorded in General Practice systems.
Conclusions

• Despite success of childhood immunisation programmes, pertussis remains a global public health concern.

• Immunising pregnant women has been shown to be a highly effective strategy in protecting young infants in the first months of life.

• In June 2019, JCVI concluded that the UK emergency maternal pertussis immunisation programme become permanent.

Ongoing efforts needed to:

a) Achieve and sustain high coverage
   • Understanding attitudes of women & health professionals important to tailor effective communication strategies and training resources
   • Accurate assessment of vaccine coverage (timely transfer of data on vaccines administered outside of general practice)

b) Continue evaluating impact of blunting
   • Particular relevance in UK with no booster in 2\textsuperscript{nd} year of life
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