Medicine, Nursing and Health Sciences

Introduction to Immunisation

Assoc. Prof. Alex Tang
Clinical School Johor Bahru
Senior Consultant Paediatrician, KPJ Johor Specialist Hospital
www.alextang.org
Objective

• Overview of the immunisation schedules
• Basis of immunisation
• Infections
• Concerns of parents
• The cold chain
WHO: Major causes of death in children younger than age 5 years and in neonates

- Neonatal 37%
  - Preterm 28%
  - Asphyxia 23%
  - Congenital 8%
  - Sepsis or pneumonia 26%
- Other 7%
- Tetanus 7%
- Diarrhoea 3%

- Malaria 8%
- Measles 4%
- Diarrhoea 17%
- Injuries 3%
- Other 10%
- HIV/AIDS 3%

Lancet 2005; 365: 1147–52
Causes of deaths among children under 5 years, 2013

- Neonatal (0-27 days)
  - Neonatal sepsis: 7%
  - Prematurity: 15%
- Postneonatal (1-59 months)
  - Pneumonia: 13%
  - Other group 1 conditions: 10%
  - Injuries: 5%
  - HIV/AIDS: 2%
  - Malaria: 7%
  - Measles: 2%
  - Diarrhoea: 9%
  - Prematurity: 2%
  - Other: 4%
  - Congenital anomalies and other non-communicable diseases: 7%
  - Intrapartum-related complications, including birth asphyxia: 11%

Major Causes of Neonatal Deaths

1. Prematurity & low birth weight (31%)
2. Infections (25%)
3. Birth asphyxia & birth trauma (23%)
4. Congenital anomalies (9%)
5. Neonatal tetanus (3%)
6. Diarrheal diseases (3%)
7. Other neonatal (8%)

1-3 causes ~80%
Global Leading Causes of Vaccine-Preventable Death in Children < 5 yrs old (2008)

- Pneumococcal Disease
- Rotavirus
- Hib
- Pertussis
- Measles
- Tetanus

Vaccination schedule

## Immunisation Schedule in Malaysia

<table>
<thead>
<tr>
<th>Immunisation</th>
<th>Umur (Bulan)</th>
<th>(Tahun)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 5 6</td>
<td>0 12 19 21</td>
</tr>
<tr>
<td>BCG</td>
<td>Dos 1</td>
<td>Tiada parut</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Dos 1 Dos 2</td>
<td>Dos 3</td>
</tr>
<tr>
<td>DTaP</td>
<td>Dos 1 Dos 2</td>
<td>Dos 3</td>
</tr>
<tr>
<td>Hib</td>
<td>Dos 1 Dos 2</td>
<td>Dos 3</td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>Dos 1 Dos 2</td>
<td>Dos 3</td>
</tr>
<tr>
<td>Measles</td>
<td></td>
<td>Sebahagia</td>
</tr>
<tr>
<td>MMR</td>
<td>Dos 1</td>
<td></td>
</tr>
<tr>
<td>MR</td>
<td></td>
<td>Booster</td>
</tr>
<tr>
<td>DT</td>
<td></td>
<td>Booster</td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td></td>
<td>Perempuan sehatja</td>
</tr>
<tr>
<td>Tetanus</td>
<td></td>
<td>Booster</td>
</tr>
</tbody>
</table>
## Perubahan Jadual Imunisasi MMR

### Jadual Lama:

<table>
<thead>
<tr>
<th>IMUNISASI</th>
<th>Umur (Bulan)</th>
<th>(Tahun)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>BCG</td>
<td>Dos 1</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>DTaP</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>Hib</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>Measles</td>
<td>Sabah sahaja</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Jadual Baru:

<table>
<thead>
<tr>
<th>IMUNISASI</th>
<th>Umur (Bulan)</th>
<th>(Tahun)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>BCG</td>
<td>Dos 1</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>DTaP</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>Hib</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
<tr>
<td>Measles</td>
<td>Sabah sahaja</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JE (Sarawak)</td>
<td>Dos 1</td>
<td>Dos 2</td>
</tr>
</tbody>
</table>

**Jadual baru Imunisasi MMR digunakan bermula tahun 2016**
# Optional Vaccines in Malaysia

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Pneumococcal Vaccine</td>
<td></td>
</tr>
<tr>
<td>Chickenpox Vaccine</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A Vaccine</td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>red</td>
</tr>
</tbody>
</table>
# National Childhood and Adolescent Immunisation Schedule, Singapore

## For persons aged 0 to <18 years

<table>
<thead>
<tr>
<th>Vaccination against</th>
<th>Birth</th>
<th>1 month</th>
<th>3 months</th>
<th>4 months</th>
<th>5 months</th>
<th>6 months</th>
<th>12 months</th>
<th>15 months</th>
<th>18 months</th>
<th>6-7 years</th>
<th>10-11 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>BCG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B&lt;sup&gt;a&lt;/sup&gt;</td>
<td>HepB (D1)</td>
<td>HepB (D2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis</td>
<td>DTaP (D1)</td>
<td>DTaP (D2)</td>
<td>DTaP (D3)</td>
<td></td>
<td></td>
<td>DTaP (B1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tdap (B2)</td>
</tr>
<tr>
<td>Poliovirus</td>
<td>OPV (D1)</td>
<td>OPV (D2)</td>
<td>OPV (D3)</td>
<td></td>
<td></td>
<td>OPV (B1)</td>
<td></td>
<td></td>
<td></td>
<td>OPV (B2)</td>
<td>OPV (B3)</td>
</tr>
<tr>
<td>Measles, Mumps, Rubella</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MMR (D1)</td>
<td></td>
<td></td>
<td>MMR (D2)&lt;sup&gt;**&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal Disease&lt;sup&gt;**&lt;/sup&gt;</td>
<td>PCV (D1)</td>
<td>PCV (D2)</td>
<td></td>
<td></td>
<td></td>
<td>PCV (B1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human Papillomavirus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Recommended for females 9 to 26 years; three doses are required at intervals of 0, 2, 6 months*

**Recommended annually for all children aged 6 months to <5 years and children aged 6 months to <18 years in high-risk groups***

---

National Immunisation Registry, Health promotion Board, Singapore, update 23/06/2011
<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>Hepatitis B (hepB)</td>
</tr>
<tr>
<td>2 months</td>
<td>• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), <em>Haemophilus influenzae</em> type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)</td>
</tr>
<tr>
<td></td>
<td>• Pneumococcal conjugate (13vPCV)</td>
</tr>
<tr>
<td></td>
<td>• Rotavirus</td>
</tr>
<tr>
<td>4 months</td>
<td>• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), <em>Haemophilus influenzae</em> type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)</td>
</tr>
<tr>
<td></td>
<td>• Pneumococcal conjugate (13vPCV)</td>
</tr>
<tr>
<td></td>
<td>• Rotavirus</td>
</tr>
<tr>
<td>6 months</td>
<td>• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), <em>Haemophilus influenzae</em> type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)</td>
</tr>
<tr>
<td></td>
<td>• Pneumococcal conjugate (13vPCV)</td>
</tr>
<tr>
<td></td>
<td>• Rotavirus</td>
</tr>
<tr>
<td>12 months</td>
<td>• <em>Haemophilus influenzae</em> type b (Hib)</td>
</tr>
<tr>
<td></td>
<td>• Meningococcal C (MenCCV)</td>
</tr>
<tr>
<td></td>
<td>• Measles, mumps and rubella (MMR)</td>
</tr>
<tr>
<td>18 months</td>
<td>• Varicella (chickenpox)</td>
</tr>
<tr>
<td>4 years</td>
<td>• Diphtheria, tetanus, acellular pertussis (whooping cough) and inactivated poliomyelitis (polio) (DTPa-IPV)</td>
</tr>
<tr>
<td></td>
<td>• Measles, mumps and rubella (MMR)</td>
</tr>
<tr>
<td>Age</td>
<td>Vaccines</td>
</tr>
<tr>
<td>------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Birth</td>
<td>Hepatitis B (hepB)</td>
</tr>
</tbody>
</table>
| 2 months | • Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)  
  • Pneumococcal conjugate (13vPCV)  
  • Rotavirus |
| 4 months | • Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)  
  • Pneumococcal conjugate (13vPCV)  
  • Rotavirus |
| 6 months | • Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)  
  • Pneumococcal conjugate (13vPCV)  
  • Rotavirus |
| 12 months | • *Haemophilus influenzae* type b (Hib)  
  • Meningococcal C (MenCCV)  
  • Measles, mumps and rubella (MMR) |
| 18 months | • Measles, mumps, rubella and varicella (chickenpox) (MMRV) |
| 4 years | • Diphtheria, tetanus, acellular pertussis (whooping cough) and inactivated poliomyelitis (polio) (DTPa-IPV)  
  • Measles, mumps and rubella (MMR) |
2016 Recommended Immunizations for Children from Birth Through 6 Years Old

<table>
<thead>
<tr>
<th>Age</th>
<th>HepB</th>
<th>RV</th>
<th>DTaP</th>
<th>Hib</th>
<th>PCV</th>
<th>IPV</th>
<th>MMR</th>
<th>Varicella</th>
<th>HepA*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>HepB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>HepB</td>
<td>RV</td>
<td>DTaP</td>
<td>Hib</td>
<td>PCV</td>
<td>IPV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td></td>
<td>RV</td>
<td>DTaP</td>
<td>Hib</td>
<td>PCV</td>
<td>IPV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19–23 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–3 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–6 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Is your family growing? To protect your new baby and yourself against whooping cough, get a Tdap vaccine in the third trimester of each pregnancy. Talk to your doctor for more details.

Shaded boxes indicate the vaccine can be given during shown age range.

NOTE: If your child misses a shot, you don’t need to start over, just go back to your child’s doctor for the next shot. Talk with your child’s doctor if you have questions about vaccines.

FOOTNOTES:
1 Two doses given at least four weeks apart are recommended for children aged 6 months through 8 years of age who are getting an influenza (flu) vaccine for the first time and for some other children in this age group.
2 Two doses of HepA vaccine are needed for lasting protection. The first dose of HepA vaccine should be given between 12 months and 23 months of age. The second dose should be given 6 to 18 months later. HepA vaccination may be given to any child 12 months and older to protect against HepA. Children and adolescents who did not receive the HepA vaccine and are at high-risk should be vaccinated against HepA.

If your child has any medical conditions that put him at risk for infection or is traveling outside the United States, talk to your child’s doctor about additional vaccines that he may need.

For more information, call toll free 1-800-CDC-INFO (1-800-232-4636) or visit http://www.cdc.gov/vaccines

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

American Academy of Family Physicians
Strong Medicine for America

American Academy of Pediatrics
Dedicated to the health of all children
2015 Recommended Immunizations for Children from 7 Through 18 Years Old

7-10 YEARS
- Tdap
- MCV4

11-12 YEARS
- Tetanus, Diphtheria, Pertussis (Tdap) Vaccine
- Human Papillomavirus (HPV) Vaccine (3 doses)*
- Meningococcal Conjugate Vaccine (MCV4) Dose 1

13-18 YEARS
- Tdap
- HPV
- MCV4 Dose 1
- Booster at age 16 years

Influenza (Yearly)*

Pneumococcal Vaccine

Hepatitis A (HepA) Vaccine Series

Hepatitis B (HepB) Vaccine Series

Inactivated Polio Vaccine (IPV) Series

Measles, Mumps, Rubella (MMR) Vaccine Series

Varicella Vaccine Series

These shaded boxes indicate when the vaccine is recommended for all children unless your doctor tells you that your child cannot safely receive the vaccine. These shaded boxes indicate the vaccine should be given if a child is catching-up on missed vaccines. These shaded boxes indicate the vaccine is recommended for children with certain health conditions that put them at high risk for serious diseases. Note that healthy children can get the HepA series*. See vaccine-specific recommendations at www.cdc.gov/vaccines/pubs/ACIP-1st.htm.

FOOTNOTES
1 Tdap vaccine is recommended at age 11 or 12 to protect against tetanus, diphtheria and pertussis. If your child has not received any or all of the DTaP vaccine series, or if you don’t know if your child has received these shots, your child needs a single dose of Tdap when they are 7-10 years old. Talk to your child’s health care provider to find out if they need additional catch-up vaccines.
2 All 11 or 12 year olds—both girls and boys—should receive 3 doses of HPV vaccine to protect against HPV-related disease. The full HPV vaccine series should be given as recommended for best protection.
3 Meningococcal conjugate vaccine (MCV) is recommended at age 11 or 12. A booster shot is recommended at age 16. Teens who received MCV for the first time at age 13 through 15 years will need a one-time booster dose between the ages of 16 and 18 years. If your teenager missed getting the vaccine altogether, ask their health care provider about getting it now, especially if your teenager is about to move into a college dorm or military barracks.
4 Everyone 6 months of age and older—including preteens and teens—should get a flu vaccine every year. Children under the age of 9 years may require more than one dose. Talk to your child’s health care provider to find out if they need more than one dose.
5 Pneumococcal Conjugate Vaccine (PCV13) and Pneumococcal Polyaccharide Vaccine (PPSV23) are recommended for some children 6 through 18 years old with certain medical conditions that place them at high risk. Talk to your healthcare provider about pneumococcal vaccines and what factors may place your child at high risk for pneumococcal disease.
6 Hepatitis A vaccination is recommended for older children with certain medical conditions that place them at high risk. HepA vaccine is licensed, safe, and effective for all children of all ages. Even if your child is not at high risk, you may decide you want your child protected against HepA. Talk to your healthcare provider about HepA vaccine and what factors may place your child at high risk for HepA.

For more information, call toll free 1-800-CDC-INFO (1-800-232-4636) or visit http://www.cdc.gov/vaccines/teens
### Recommended Immunisation Schedule

<table>
<thead>
<tr>
<th>Age (month)</th>
<th>Immunisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>• General checkup. No injection 菸検。无注射</td>
</tr>
</tbody>
</table>
| 2           | • Triple antigen+polio+Hep B+ Hib (6 in 1) 三种并合针，小兒麻痺症，乙型肝炎及腦膜炎疫苗 (6 合 1)  
              • Rotavirus 轮状病毒口服疫苗 |
| 3           | • Pneumococcal (PncV) 肺炎链球菌疫苗 |
| 4           | • Triple antigen+polio+Hep B+ Hib (6 in 1) 三种并合针，小兒麻痺症，乙型肝炎及腦膜炎疫苗 (6 合 1)  
              • Rotavirus 轮状病毒口服疫苗 |
| 5           | • Pneumococcal (PncV) 肺炎链球菌疫苗 |
| 6           | • Triple antigen+polio+Hep B+ Hib (6 in 1) 三种并合针，小兒麻痺症，乙型肝炎及腦膜炎疫苗 (6 合 1)  
              • ±Rotavirus 轮状病毒口服疫苗 |
| 7           | • ±Pneumococcal (PncV) 肺炎链球菌疫苗 |
| 9           | • MMR 麻疹，腮腺炎及風疹 |
| 12          | • MMR-Chickenpox/MMR 麻疹，腮腺炎及風疹 /水痘 |
| 13          | • ±Chickenpox 水痘 (see above) |
| 15          | • Booster Pneumococcal (PncV) 肺炎链球菌疫苗 |
| 18          | • Booster Double antigen+polio+ Hib 二種并合针，小兒麻痺症及腦膜炎疫苗 |

<table>
<thead>
<tr>
<th>Years</th>
<th>Immunisation</th>
</tr>
</thead>
</table>
| 6     | • Booster Double antigen+polio 二種并合针及小兒麻痺症  
             • MMR 麻疹，腮腺炎及風疹 |
| 9-13  | • HPV (for girls) 人类乳头状瘤病毒疫苗 |
| 15    | • Tetanus 破伤风 |

(updated Jan 2016)
Vaccination successes

- Vaccination has:
  - Eradicated smallpox\textsuperscript{5}
  - Nearly eradicated polio\textsuperscript{8}
  - Controlled many major diseases\textsuperscript{3}

Ref 3: Plotkin, p 1
Ref 5: AAP, p 554
Ref 8: CDC, p 721
**Immunological Memory**

Vaccine stimulates an immune response to an antigen.

- **Humoral immunity** = actions of B-lymphocytes to produce antibodies.
- **Cellular immunity** = specialized T-lymphocytes to combat the antigen.

Long-term acquired immunity = “Immunological Memory”

Secondary immune response = reestablish protection.
The Main Cell Types in the Immune Response

Phagocytes
- Monocytes
- Macrophages
- Polymorphonuclear neutrophils (PMNs)

Lymphocytes
- B cells
- T cells
  - Helper
  - Killer
- Natural Killer cells
Indirect Effect of Vaccination

Vaccines help to reduce the spread of disease through indirect effect, sometimes called “herd immunity” or “community immunity.”

– Once a person is vaccinated against a disease, they are less likely to develop it as well as pass it on to someone who is not immunized.
## Vaccine-Preventable Diseases and the Vaccines that Prevent Them

<table>
<thead>
<tr>
<th>Disease</th>
<th>Vaccine</th>
<th>Disease spread by</th>
<th>Disease symptoms</th>
<th>Disease complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chickenpox</td>
<td>Varicella vaccine protects against chickenpox.</td>
<td>Air, direct contact</td>
<td>Rash, tiredness, headache, fever</td>
<td>Infected blisters, bleeding disorders, encephalitis (brain swelling), pneumonia (infection in the lungs)</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>DTaP* vaccine protects against diphtheria.</td>
<td>Air, direct contact</td>
<td>Sore throat, mild fever, weakness, swollen glands in neck</td>
<td>Swelling of the heart muscle, heart failure, coma, paralysis, death</td>
</tr>
<tr>
<td>Hib</td>
<td>Hib vaccine protects against <em>Haemophilus influenzae</em> type b.</td>
<td>Air, direct contact</td>
<td>May be no symptoms unless bacteria enter the blood</td>
<td>Meningitis (infection of the covering around the brain and spinal cord), intellectual disability, epiglottitis (life-threatening infection that can block the windpipe and lead to serious breathing problems), pneumonia (infection in the lungs), death</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>HepA vaccine protects against hepatitis A.</td>
<td>Direct contact, contaminated food or water</td>
<td>May be no symptoms, fever, stomach pain, loss of appetite, fatigue, vomiting, jaundice (yellowing of skin and eyes), dark urine</td>
<td>Liver failure, arthralgia (joint pain), kidney, pancreatic, and blood disorders</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>HepB vaccine protects against hepatitis B.</td>
<td>Contact with blood or body fluids</td>
<td>May be no symptoms, fever, headache, weakness, vomiting, jaundice (yellowing of skin and eyes), joint pain</td>
<td>Chronic liver infection, liver failure, liver cancer</td>
</tr>
<tr>
<td>Influenza (Flu)</td>
<td>Flu vaccine protects against influenza.</td>
<td>Air, direct contact</td>
<td>Fever, muscle pain, sore throat, cough, extreme fatigue</td>
<td>Pneumonia (infection in the lungs)</td>
</tr>
<tr>
<td>Measles</td>
<td>MMR** vaccine protects against measles.</td>
<td>Air, direct contact</td>
<td>Rash, fever, cough, runny nose, pinkeye</td>
<td>Encephalitis (brain swelling), pneumonia (infection in the lungs), death</td>
</tr>
<tr>
<td>Mumps</td>
<td>MMR** vaccine protects against mumps.</td>
<td>Air, direct contact</td>
<td>Swollen salivary glands (under the jaw), fever, headache, tiredness, muscle pain</td>
<td>Meningitis (infection of the covering around the brain and spinal cord), encephalitis (brain swelling), inflammation of testicles or ovaries, deafness</td>
</tr>
<tr>
<td>Pertussis</td>
<td>DTaP* vaccine protects against pertussis (whooping cough).</td>
<td>Air, direct contact</td>
<td>Severe cough, runny nose, apnea (a pause in breathing in infants)</td>
<td>Pneumonia (infection in the lungs), death</td>
</tr>
<tr>
<td>Polio</td>
<td>IPV vaccine protects against polio.</td>
<td>Air, direct contact, through the mouth</td>
<td>May be no symptoms, sore throat, fever, nausea, headache</td>
<td>Paralysis, death</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>PCV vaccine protects against pneumococcus.</td>
<td>Air, direct contact</td>
<td>May be no symptoms, pneumonia (infection in the lungs)</td>
<td>Bacteremia (blood infection), meningitis (infection of the covering around the brain and spinal cord), death</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>RV vaccine protects against rotavirus.</td>
<td>Through the mouth</td>
<td>Diarrhea, fever, vomiting</td>
<td>Severe diarrhea, dehydration</td>
</tr>
<tr>
<td>Rubella</td>
<td>MMR** vaccine protects against rubella.</td>
<td>Air, direct contact</td>
<td>Children infected with rubella virus sometimes have a rash, fever, swollen lymph nodes</td>
<td>Very serious in pregnant women—can lead to miscarriage, stillbirth, premature delivery, birth defects</td>
</tr>
<tr>
<td>Tetanus</td>
<td>DTaP* vaccine protects against tetanus.</td>
<td>Exposure through cuts in skin</td>
<td>Stiffness in neck and abdominal muscles, difficulty swallowing, muscle spasms, fever</td>
<td>Broken bones, breathing difficulty, death</td>
</tr>
</tbody>
</table>

* DTaP combines protection against diphtheria, tetanus, and pertussis.
** MMR combines protection against measles, mumps, and rubella.
Polio

- Affects the nervous system and spinal cord, causing paralysis
- \( \approx 1/200 \) infections lead to paralysis
- Two types of vaccine
- In 1994, wild polio transmission was interrupted in the Americas
POLIO IN MALAYSIA

Figure 1: Incidence of paralytic poliomyelitis in Malaysia (Ministry Of Health)
GLOBAL INCIDENCE OF POLIO

Reported cases of acute poliomyelitis per year

Prior to 1988 - over 350,000

To date there have been 74 polio cases in 2005

Improved reporting

http://www.who.int/vaccines/casecount/afpextractnew.cfm
MMR – THE FACTS

- Measles, Mumps & Rubella
- Short memories of deadly Measles epidemic
- 1990 – 45 million Measles; 1 million dead
- 32.8/100,000 (1987) – 2.6/100,000 (1997)
- National epidemic 1999-2000; 10 deaths
- 2004 – PI 270 cases in 6 mths.
- 2 deaths, 45 pneumonia, 8 bro. obliterans
Smallpox

- Caused by variola virus
- A deadly disease
- Most survivors scarred with residual facial marks, some left blind
Last Person Infected with Naturally Occurring Smallpox in Somalia in 1977
Tetanus

- Known as lockjaw
- Caused by *Clostridium tetani*
  - Releases a toxin causing muscle spasms
  - May lead to death by suffocation
- Neonatal tetanus occurs most often in developing countries
Diphtheria

- Caused by *Corynebacterium diphtheriae*
- Affects upper respiratory tract, also other organs
- Mortality rate 5-10 percent
  - If early treatment, < 1 percent

Kuala Lumpur, Nov 2015
Pertussis ("Whooping Cough")

- Caused by *Bordetella pertussis*
- Characteristic cough
- Three phases
  - Catartrhal phase
  - Paroxysmal phase
  - Convalescent phase
- Greatest risk in infants and young children
Rubella
(“German Measles”)

- A generally mild childhood disease caused by a virus
- Infection during pregnancy may result in fetal infection (congenital rubella syndrome)
  - Multiple defects in infants
    - Brain, Heart, Hearing, Liver
Hepatitis B

Countries using HepB vaccine in their national infant immunization system, as of December 2003

Routine HepB implementation status
- Yes (108 countries or 72%)
- Yes in part of the country (9 countries or 5%)
- No (45* countries or 31%)

*5 countries use HepB among adolescents

Source: WHO/UNICEF Joint Reporting Form, 2004. Data collected from 192 WHO Member States and as of 30 September 2004
Date of slide: 20 September 2004
Hepatitis B Immune Response Level Through 5 Years Post-Vaccination

- Protection against hepatitis B virus (HBV) is based on the presence of specific antibodies against anti-HBs antigen.\(^2\)
  - Anti-HBs levels disappear in 10-50% of vaccinees after a few years.\(^2\)
  - No booster has been recommended to date.\(^3\)

Anti-HBs After Immune Challenge

- Immune memory persists beyond the time at which anti-HBs levels may no longer be detectable.
- Immune memory leads to a rapid anamnestic response after exposure to HBV, which prevents acute infection (and disease).

Haemophilus influenzae type b (Hib)

- Causes severe infection in many organs
- Before routine use of effective vaccines, Hib was the leading cause of bacterial meningitis in young children
Neisseria Meningitidis

Typical rash of meningococcal septicemia

In this picture, confluent purpuric areas have formed with blistering and necrosis
N. meningitidis\textsuperscript{63}

Custom Medical Stock Photo, 2003
Streptococcus pneumoniae

- Gram-positive, facultative, encapsulated
- Capsular polysaccharides form the basis of serogroup and serotype classifications
- 90 serotypes
- Leading cause of vaccine-preventable bacterial disease in children
- The most common bacterial cause of
  - Community-acquired pneumonia (17-28%)
  - AOM (25-50%)
  - Sinusitis

Pediatr Infect Dis J 1992;11:S7--11
**S. pneumoniae Disease Classification**

<table>
<thead>
<tr>
<th>Mucosal Disease</th>
<th>Invasive Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>Pneumonia*</td>
</tr>
<tr>
<td>Acute otitis media (AOM)</td>
<td>Bacteremia/sepsis</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Meningitis</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Other focal, sterile-site infections from hematogenous dissemination</td>
</tr>
</tbody>
</table>

*S. pneumoniae disease may be classified as mucosal or invasive*

*Pneumonia may be classified as mucosal or invasive disease. It is invasive if accompanied by bacteremia, pleural effusion, or other invasive complication.*

Impact of Pneumococcal Disease on Children

- Pneumococcal disease can result in:
  - Death
  - Paralysis
  - Mental retardation
  - Seizures
  - Learning disabilities
  - Hearing loss
  - Other sequelae

## Risk Factors for IPD

<table>
<thead>
<tr>
<th>Age(^1)</th>
<th>Underlying Medical Conditions(^2,3)</th>
<th>Demographic Features(^3,4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children ≤2 years of age</strong>&lt;br&gt;<strong>Adults ≥65 years of age</strong></td>
<td>• Congenital or acquired immunodeficiency&lt;br&gt;• Sickle cell disease, asplenia, HIV&lt;br&gt;• Pulmonary disease&lt;br&gt;• Chronic heart disease&lt;br&gt;• Chronic renal insufficiency, nephrotic syndrome&lt;br&gt;• Diabetes&lt;br&gt;• Cerebrospinal fistula&lt;br&gt;• Existing or cochlear implants</td>
<td>• Day care attendance&lt;br&gt;• Ethnicity</td>
</tr>
</tbody>
</table>

**Age is the most important risk factor for pneumococcal disease\(^1\)**

---

Nasopharyngeal Colonization

- *S. pneumoniae* can be a normal inhabitant of the nasopharynx\(^1\)
- Global nasopharyngeal (NP) colonization/carriage ranges:
  - 10% to 85% in children <5 years of age\(^2,3\)
  - 4% to 45% in adults\(^2-4\)

NP colonization is generally a prerequisite for mucosal and invasive pneumococcal disease\(^2,4\)


Infection Pathogenesis

Nose → Sinus → Tympanic membrane → Blood vessel → Lung → Meninges → Bone

Nose
Sinus
Tympanic membrane
Blood vessel
Lung
Meninges
Bone
Invasive Pneumococcal Diseases among Malaysian Children

Tan Kah Kee MD
Pediatric Infectious Disease Consultant
Hospital Tuanku Ja’afar
70300 Seremban

Presented at National Pneumococcal workshop 28 March 2015
Pneumococcal Infections

- Burden of disease highest in youngest & oldest sections of population
- Annual deaths: 1 million < 5 years old
- High case fatality rates in meningitis (20-50%)
- 30-60% of survivors with long-term sequelae
- Treatment complicated by worldwide emergence of penicillin-resistance (IMR 2011: 36.9% penicillin-nonsusceptible)
**Streptococcus Pneumoniae**

- Common inhabitants of respiratory tract
- > 90 known serotypes
- 6-11 most common serotypes account for >70% of invasive disease worldwide.
- Polysaccharide capsule important virulence factor
- Type-specific antibody is protective

*Weekly Epidemiol Record 2012; 87:129-144*
*Johnson HL et al; PLoS Med 2010*
Annual incidence of invasive pneumococcal disease in <2 year olds
~150/100,00, United States

For each case of pneumococcal meningitis in a year

Invasive

Disease severity

Invasive

Non-invasive

Otitis media

Meningitis

Bacteremia

Pneumonia

Annual incidence of invasive pneumococcal disease in <2 year olds
~150/100,00, United States

Invasive Pneumococcal Disease Syndromes

- Bacteremia
- Meningitis
- Pneumonia
- Septic arthritis
- Hemolytic uremic syndrome

Copelovitch L et al; Pediatrics 2010; 125
Pneumococcal serotypes in Malaysia

N=433 strains, 33.5% < 5 years

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>1.80%</td>
</tr>
<tr>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>18C</td>
<td>3.90%</td>
</tr>
<tr>
<td>23F</td>
<td>4.80%</td>
</tr>
<tr>
<td>6A</td>
<td>5%</td>
</tr>
<tr>
<td>1</td>
<td>5%</td>
</tr>
<tr>
<td>14</td>
<td>6.70%</td>
</tr>
<tr>
<td>19A</td>
<td>6.90%</td>
</tr>
<tr>
<td>6B</td>
<td>10.60%</td>
</tr>
<tr>
<td>19F</td>
<td>15.00%</td>
</tr>
</tbody>
</table>

PCV 7 : 44% covered
PCV 10 : 56% covered
PCV 13 : 78% covered

Yasin MR et al; Vaccine 2011;34
Invasive Pneumococcal Disease in Hospitalised Malaysian Children

- Children with IPD & isolation of Strept. Pneumo. in sterile sites recruited (blood, CSF, pleural fluid, joint, peritoneal & pericardial) between 1 Jan 2007-31 Dec 2009
- 13 participating hospitals nationwide
- Pneumococcal isolates send to IMR for serotyping.
- Quellung reaction for serotyping
Participating Hospitals (N=13)

- HKL
- HIP
- HPP
- HKB
- HTJ
- UMMC
- HKT
- HTAA
- HTAR
- HSB Alor Setar
- HSelayang
- HUS Kuching
- HLikas KK

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Results (1) - Demographics

- Total patients with IPD =164 (2008:88 ; 2009:76)
- Gender distribution : Males 56.7%(N=93) ; Females 43.3%(N=71)(M:F = 1.3 : 1)
- Racial distribution : Malays 66.7% , Chinese 7.3% , Indians 1.8% , Ibans 1.8% , Bidayuh(0.6%) , Kadazan 0.6% , Others 21.2%

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Results(2) - Demographics

- Mean age = 25.7 mths
- Median age = 15.0 months
- Range = 0-144 months
- Age < 2 yrs = 68.3% (N=112)
- Age < 5 yrs = 86.6%(N=142)
Results(3) – Blood, CSF, Pleural fluid

- Blood culture +ve = 85.6% (N=160)
- CSF culture +ve = 39.6% (N=56)
- CSF antigen +ve (latex) = 55.6% (N=20)
- Pleural fluid culture +ve = 64.3% (N=28)

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Results(4) - Pneumococcal Serotypes (N=79)

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Serotypic Coverage

- 7-valent = 37.9% (30/79)
- 10-valent = 43.0% (34/79)
- 13-valent = 51.8% (41/79)
Outcome

- Alive: 76%
- Dead: 19%
- Transferred: 4%
- AOR: 1%

13% (N=21) has neurological sequelae at discharge

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Ventilatory Support

- 44% (N=72) required ventilatory support
- Median duration = 4 days
- Range = 1-43 days

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Penicillin Susceptibility

- Blood isolates: S 84.5% I 2.3% R 13.2%
- CSF isolates: S 89.5% I 10.5% R 0%

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
Study Limitations

- Mild cases may not be captured
- Private hospital cases not included
- Culture method limited by prior antibiotics
- Molecular methods during study not available
Summary of findings

- IPD is severe in Malaysian children
- Significant mortality
- Serotypic coverage moderate
- Penicillin resistance moderate
Conclusions

• Invasive pneumococcal disease is a serious cause of morbidity & mortality in Malaysian children
• Different spectrum of pneumococcal infection seen
• Mortality does occur in spite of appropriate therapy
• Penicillin resistance moderate
• Preventive measure by vaccination needs urgent consideration

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)
**Perubahan Jadual Imunisasi MMR**

**Jadual Lama:**

<table>
<thead>
<tr>
<th>IMUNISASI</th>
<th>Umur (Bulan)</th>
<th>(Tahun)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 5 6 9 12 18 21 7 13 15</td>
<td></td>
</tr>
<tr>
<td>BCG</td>
<td>Dos 1 Dos 2</td>
<td>Tiada perlu</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>DTaP</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>Hib</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>Measles</td>
<td>Sabah sahaja</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>Dos 1</td>
<td>Booster</td>
</tr>
<tr>
<td>MR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td></td>
<td>Booster</td>
</tr>
</tbody>
</table>

**Jadual Baru:**

<table>
<thead>
<tr>
<th>IMUNISASI</th>
<th>Umur (Bulan)</th>
<th>(Tahun)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 5 6 9 12 18 21 7 13 15</td>
<td></td>
</tr>
<tr>
<td>BCG</td>
<td>Dos 1</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>DTaP</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>Hib</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>Dos 1 Dos 2 Dos 3</td>
<td>Booster</td>
</tr>
<tr>
<td>Measles</td>
<td>Sabah sahaja</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>Dos 1 Dos 2</td>
<td>Booster</td>
</tr>
<tr>
<td>MR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td></td>
<td>Booster</td>
</tr>
<tr>
<td>JE (Sarawak)</td>
<td>Dos 1 Dos 2</td>
<td></td>
</tr>
</tbody>
</table>

**Jadual baru Imunisasi MMR digunakan bermula tahun 2016**
Some concerns of parents
Common questions about vaccines

• Do I need to vaccinate my child against diseases that aren’t common anymore?\textsuperscript{15}
• Are vaccines safe?\textsuperscript{16}
• Do vaccines cause autism?\textsuperscript{16}
• Are preservatives found in vaccines?\textsuperscript{16}
• Can my child get a disease from a vaccine?\textsuperscript{16}
• My child is allergic to eggs
• Are vaccines halal?

Ref 15: CDC, p 8
Ref 16: IOM, p 1, 4
Some vaccine side effects

• Common side effects\textsuperscript{5}
  – Redness, swelling, and pain at injection site
  – Low-grade fever

• Uncommon, serious side effects\textsuperscript{5}
  – Allergic reaction

Ref 5: AAP, p 38, 46
Advice on vaccination of those with egg allergy

- Influenza vaccines (containing <1 μg of ovalbumin per dose) can be given to most people with egg allergy, including anaphylaxis
  - Those with severe allergy should be vaccinated in settings where anaphylaxis can be recognised/treated

- MMR vaccines can be given to any egg allergic person
“Natural Immunity”
(Getting Immunity By Getting Sick)

• What is it? Does it work? What are the costs?

• Some people believe that it’s better to get a disease naturally than to be vaccinated against it.

• One theory is that chickenpox, for example, helps mature the immune system.

• And a mature immune system should be better able to fight infection from diseases, right?

• What are the facts about natural immunity?
Choosing Natural Immunity Is Risky!

• Chickenpox kills children in the United States every year.
• Before a chickenpox vaccine was licensed, almost 7,000 children per year were hospitalized for serious complications of chickenpox like encephalitis, hepatitis, flesh eating-strep, and toxic shock syndrome.
Choosing Natural Immunity Can Be Risky To Others.

- A parent who is not immune to chickenpox can easily catch the disease from an infected child. 1 in 5 adults who get chickenpox develops pneumonia, which can be deadly.
- If a “routine” disease like chickenpox can have these results, natural immunity is a risky alternative to vaccination.
Childhood Diseases Carry Serious Risks.

• **Hib or pneumococcal disease** can cause bacterial meningitis, leading to brain damage or death.

• **Pertussis (whooping cough)** can cause coughing spells so bad that it is hard for infants to eat, drink, or breathe. These spells can last for weeks. Pertussis can lead to pneumonia, seizures, brain damage, and death.

• **Polio** may lead to paralysis and death. Polio used to be very common in the United States, killing and paralyzing thousands of people a year.

• **Tetanus (lockjaw)** infection can cause painful tightening of the muscles. It can lead to "locking" of the jaw so the victim cannot open his mouth or swallow. Tetanus results in death in about 10% of cases.
HERD IMMUNITY

• Children who are immunised are protected from the disease. They cannot get the disease and they cannot give the disease.
• If enough children are vaccinated against a disease then the disease cannot spread into the community.
• This is called “herd immunity”
A prickly problem

Diphtheria, a deadly disease that was wiped out in Malaysia, is back and there has been a huge spike in the number of measles cases - all because parents believe in myths and rumour-mongering about vaccination. The Health Ministry, the Education Ministry and even the state religious authorities are working to ensure children get immunised for their own good.

>See reports on Page 4
Anti Immunization Movement

MMR and Autism

- The original paper (now RETRACTED) – Lancet, 1998

2. Time trends in autism and in MMR immunization coverage in California - JAMA, 2001
3. A population-based study of measles, mumps, and rubella vaccination and autism - NEJM, 2002
5. MMR vaccination and pervasive developmental disorders: a case-control study - Lancet, 2004
7. Vaccines for measles, mumps and rubella in children - Cochrane Collaboration, 2005
9. How the case against the MMR vaccine was fixed by Brian Deer, BMJ, 2011
10. Wakefield’s article linking MMR vaccine and autism was fraudulent - BMJ Editorial, 2011
The Cold Chain
Store in Freezer
5°F (-15°C) or colder
- MMR^x
- Varicella^x
- Zoster^x
- MMR^x.*

Store in Refrigerator
35°F–46°F (2°C–8°C)
- MMR^x.*
- Inactivated Combination Vaccines
- Vaccines containing Diphtheria, Tetanus, and/or acellular Pertussis
- Hepatitis A  Hepatitis B
- Hib^x
- HPV
- Influenza (LAIV & TIV)
- IPV
- Meningococcal (MCV & MPSV)
- Pneumococcal (PCV & PPV)
- Rotavirus

* Do not expose to light.
+ Unreconstituted lyophilized (freeze-dried) MMR may be frozen or refrigerated.
Dengvaxia (Sanofi)
Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial

Maria Rosario Capeling, Ngoc Hau Tran, Sri Rezeki S Hadinegoro, Hussain Imam HJ Mohammad Iqmal, Tawee Chatpitayasunondh, Mary Norreen Chuo, Chien Quang Luong, Kusnadi Rusmil, Dews Nyoman Wirawan, Revathy Nallusamy, Punnee Pitsuttithum, Usa Thisyakorn, In-Kyu Yoon, Diane van der Vliet, Edith Langevin, Theima Laot, Yanee Hutagalung, Carina Frago, Mark Boaz, T Anh Wartel, Nadia G Torniseporth, Melanie Saville, Alain Bouckenooghe, and the CYD 14 Study Group

Summary

Background An estimated 100 million people have symptomatic dengue infection every year. This is the first report of a phase 3 vaccine efficacy trial of a candidate dengue vaccine. We aimed to assess the efficacy of the CYD dengue vaccine against symptomatic, virologically confirmed dengue in children.
Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease


ABSTRACT

BACKGROUND
A candidate tetravalent dengue vaccine is being assessed in three clinical trials involving more than 35,000 children between the ages of 2 and 16 years in Asian-Pacific and Latin American countries. We report the results of long-term follow-up interim analyses and integrated efficacy analyses.

METHODS
We are assessing the incidence of hospitalization for virologically confirmed dengue as a surrogate safety end point during follow-up in years 3 to 6 of two phase 3 trials, CYD14 and CYD15, and a phase 2b trial, CYD23/57. We estimated vaccine efficacy using pooled data from the first 25 months of CYD14 and CYD15.

The authors’ full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Saville at Sanofi Pasteur, 2 Ave. Pont Pasteur, 69367 Lyon CEDEX 07, France, or at melanie.saville@sanofipasteur.com.

A complete list of investigators in the CYD-TDV Dengue Vaccine Working Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on July 27, 2015, at NEJM.org.