Prospects for measles eradication

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Measles remains one of the 10 most important causes of death due to infectious diseases
Faroe Islands measles outbreak in 1846 was the first in \( >60 \) years

Peter Panum, a Danish physician observed:

- The disease is contagious
- There is a 14 day incubation period
- 100% attack rate for susceptibles
- Life long immunity
$R_0$ for some important human viruses

<table>
<thead>
<tr>
<th>Virus</th>
<th>$R_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>12-18</td>
</tr>
<tr>
<td>Mumps</td>
<td>10-12</td>
</tr>
<tr>
<td>Polio</td>
<td>10-15</td>
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<tr>
<td>Rubella</td>
<td>7-8</td>
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<tr>
<td>Smallpox</td>
<td>5-7</td>
</tr>
<tr>
<td>Influenza</td>
<td>3-4</td>
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</tbody>
</table>
Infection with wild type measles virus induces protective levels of antibody that are life-long.
Ongoing maturation of the measles virus-specific immune response over months after WT infection results in life-long immunity.

- IgM
- IgG
- NAb
- ASCs
- Avidity

Viral RNA

LN RNA+

< 4 weeks | 1 month | 2-3 months | 3-5 months | > 5 months

Tfh
Viral strategies for population-level persistence of human viruses

Acute (most RNA viruses)

Latent (e.g. herpesviruses)

Persistent (e.g. HIV, HCV)
Characteristics of measles that affect eradication

- Man - the only host
- Virus spread begins prior to onset of rash
- Permanent immunity after recovery
- Spread of virus by the respiratory route
- Transmission stops spontaneously in remote areas
- Vaccine provides long-term protection
Isolation of measles virus in culture paved the way for vaccine development.

John Franklin Enders
1897–1985
Measles vaccine passage history

Edmonston → Edmonston wild-type

Edmonston-Enders

Zagreb

Edmonston Seed ‘A’

CE (am)/22
DK/15
WI-38/19*

Edmonston Seed ‘B’

CE (am)/6
CEF/13

CEF/5
CEF (32 C)/85

CEF/3
CEF (32 C)/40

CEF (36 C)/3

HK/7
Vero/6

HK/24
HA/28

HA/12
SK (33 C)/17*
CEF (33 C)/22*

AIK-C

CEF (36 C)/8
CEF (32 C)/40

CEF (36 C)/3

Schwarz

Moraten

Edmonston B (Rubeovax)
Amino acid differences from Edmonston “WT” shared by all vaccine strains

<table>
<thead>
<tr>
<th>Prot</th>
<th>aa</th>
<th>Mor</th>
<th>EZ</th>
<th>WT</th>
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<tbody>
<tr>
<td>N</td>
<td>148</td>
<td>G</td>
<td>E</td>
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<tr>
<td></td>
<td>479</td>
<td>T/A</td>
<td>S</td>
<td>S</td>
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<tr>
<td>P/V</td>
<td>225</td>
<td>G</td>
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<td>M</td>
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<td>S</td>
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<td>K</td>
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<td></td>
<td>142</td>
<td>N</td>
<td>S</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>285</td>
<td>M</td>
<td>I</td>
<td>M</td>
</tr>
</tbody>
</table>

|      | F   | 163 | T   | A   | A  |
|      |     | 263 | G   | R   | R  |
| H    |     | 362 | Y/A | S   | S  |
|      |     | 117 | L   | F   | F  |
|      | 211 | G   | G   | S  |
|      | 280 | V   | A   | V  |
|      |     | 481 | Y   | Y   | N  |
|      |     | 484 | T   | N   | T  |
|      |     | 546 | S   | G   | G  |
| L    |     | 331 | T   | I   | I  |
|      |     | 1409 | A  | T   | A  |
|      |     | 1649 | M  | R   | R  |
|      |     | 1887 | D  | N   | N  |

- Nucleocapsid protein (N)
- Phosphoprotein (P)
- Matrix protein (M)
- Fusion protein (F)
- Attachment protein (H)
- Polymerase (L)
Current measles vaccine

- Live attenuated virus derived from the Edmonston strain of MeV
- Requires cold chain
- Given s.c. or i.m. at 12-15 months of age
- Requires 2nd dose to assure high levels of population immunity
- Safe and efficacious
Vaccine-induced immunity is not as durable as natural immunity.
Antibody responses are better after wild type MeV than vaccine MeV lung infection.

Lin et al, unpublished
Similar biphasic induction of MeV-specific IFN-γ-producing T cells after infection with wild type and vaccine MeV

**Wild type**

![Wild type IFN-γ SFCs](image)

**Vaccine**

![Vaccine IFN-γ SFCs](image)

Lin et al, unpublished
In macaques vaccine MeV replication in lymphoid tissue and PBMCs is restricted compared to WT.

Vaccine at 7 days

PBMCs
WT and vaccine

Lin et al unpublished
Measles Eradication

“Participants agreed that measles eradication is technically feasible with available vaccines and recommended the adoption of the goal of global eradication with a target date during 2005-2010.”

WHO, Pan American Health Organization and CDC
MMWR June 1997
Measles cases in the United States

Number of cases/year

Elimination from the US declared

Centers for Disease Control
Measles: WHO European region 2010-2018
Swiss measles cases were primarily in unvaccinated persons.
Failure of measles control

• Need for very high coverage to interrupt transmission (>95%)
• Problems with vaccine delivery in developing countries
  • Health infrastructure for routine infant immunization
  • Second dose/need for mass vaccination campaigns
  • Cold chain
  • Needles and syringes/need for skilled health workers
• Problems with vaccine acceptance in developed countries
  • Safety worries/sins of omission vs commission
  • Individual rights vs public health
• Secondary vaccine failure?
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