The next candidate for eradication: Is measles on your list?

Kevin Brown
National Infection Service

6 June 2019
Measles - Key Facts

- A leading cause of death among young children, despite an effective vaccine for > 50 years.

- In 2016, an estimated 7M people infected with measles
  89,780 measles deaths globally
  i.e. 245 deaths every day
  or 10 deaths every hour

- Immunization prevents suffering, complications
  and death caused by measles.

- Vaccination has had a major impact on measles deaths
  between 2000 and 2016, global measles mortality decreased by 84%.
  in Africa measles cases and deaths fell by >90%

Measles eradication?
Measles infection

Respiratory transmission
droplets spread by close contact, coughing and sneezing

Highly infectious
one of the most contagious agents known
$R_0$ (reproductive number) $\sim 15 - 20$
Potential for major epidemics in pops with low immunity
Pop needs $>95\%$ immunity to prevent outbreaks

Virus is a –ve stranded non enveloped RNA virus
*Morbillovirus* of Paramyxovirus family

Cell targets
lymphocytes/dendritic cells - SLAM or CD 150
epithelial cells - nectin
Clinical features of Measles

Incubation period - 8-10 days
Prodromal illness:
  - fever
  - cough
  - coryza
  - conjunctivitis
    (cranky child)
    (4 Cs)
Rash – maculopapular rash d14
Complications:
  - otitis media
  - bronchitis
  - pneumonia/pneumonitis
  - neurological disease
Measles Virus Genotyping

N and H genes: ~ 7% variability
450bp COOH-terminus of N 12% variation

Estimate of 1.8x10^{-3} substitutions/site/year

1) Amplify and sequence 450 nt. encoding hypervariable COOH-terminal 150 amino acids of N protein
   1 PCR product -

2) Amplify and sequence entire coding region H gene (for new genotypes)
Sequences are compared to sequences of WHO reference strains to make a genotype assignment

N P/C/V M F H L

Standardisation of the nomenclature for describing genetic characterisation of wild type measles viruses. WER 1998:73; 265-72
Named and reference sequences
Could measles be eradicated?

For eradication:

- Disease only in humans
  - no pocket of infection in wild-life
- Acute infection, with no persistent infection
- Most disease is symptomatic
- Diagnostic assays readily available
- Highly effective vaccine for measles is available

Currently no measles and rubella plan but 70th World Health Assembly (31/5/2017) requested that -

Director-General to report through the Executive Board to the 73rd World Health Assembly in 2020

“on the epidemiological aspects and feasibility of, and potential resource requirements for, measles and rubella eradication, taking into account the assessment of the Strategic Advisory Group of Experts on immunization.”
Measles case definition
‘Case with fever of 38C, maculopapular rash, either cough, coryza or conjunctivitis, or any case which a physician thinks is measles’
Only ~20% notified cases true measles

Measles eradication?
Could measles be eradicated

For eradication:

- Disease only in humans
  - no pocket of infection in wild-life
- Acute infection, with no persistent infection
- Most disease is symptomatic – unlike polio
- Diagnostic assays available – needed for confirming true cases/discarding non-cases
- Highly effective vaccine for measles is available – cold chain/needle phobia/anti-vax

BUT

- Highly infectious BEFORE symptomatic
What about elimination?

Measles elimination is one of the steps on the way to eradication

No endemic transmission within a region or country for more than 36 months

Endemic transmission is defined as the same measles genotype or strain for more than 12 months within an area/country/region.

Countries that have ‘eliminated measles’ may still have cases, but any imported cases should not lead to on-going transmission chains

Need > 90% population immunity to prevent on-going transmission in a community
UK measles vaccination coverage and measles notifications from 1950 to 2016

Measles vaccine introduced

MMR vaccine introduced

MR campaign

MMR2 + OF testing

MMR1 (routine)

MMR2 (routine)

Catch-Up Cohort

Catch-Up Campaign

Notifications (000s)

Vaccine coverage (%)

Year


100 80 60 40 20 0

600 400 200 0

800 600 400 200 0

Measles eradication?
Confirmed measles by month, Jan 2011 – Jul 2017, England
UK 'eliminates measles' for first time

The elimination of measles has been achieved in the UK for the first time, the World Health Organization says.
Confirmed measles by month, Jan 2011 – Mar 2019, England
Measles Incidence Rate per Million (12M period) <5 cases/million

### Top 10**

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madagascar</td>
<td>84804</td>
<td>3406.53</td>
</tr>
<tr>
<td>Ukraine</td>
<td>78659</td>
<td>1770.06</td>
</tr>
<tr>
<td>India</td>
<td>53170</td>
<td>40.15</td>
</tr>
<tr>
<td>Pakistan</td>
<td>22693</td>
<td>117.46</td>
</tr>
<tr>
<td>Philippines</td>
<td>16898</td>
<td>163.55</td>
</tr>
<tr>
<td>Yemen</td>
<td>13639</td>
<td>494.45</td>
</tr>
<tr>
<td>Nigeria</td>
<td>12745</td>
<td>68.53</td>
</tr>
<tr>
<td>Brazil</td>
<td>10316</td>
<td>49.68</td>
</tr>
<tr>
<td>Thailand</td>
<td>6914</td>
<td>100.4</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>5908</td>
<td>328.45</td>
</tr>
</tbody>
</table>

### Other countries with high incidence rates***

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>4678</td>
<td>1191.72</td>
</tr>
<tr>
<td>Liberia</td>
<td>2367</td>
<td>513.02</td>
</tr>
<tr>
<td>Israel</td>
<td>3755</td>
<td>458.38</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>2534</td>
<td>425.47</td>
</tr>
<tr>
<td>The Republic of</td>
<td>885</td>
<td>425.23</td>
</tr>
<tr>
<td>North Macedonia</td>
<td>1169</td>
<td>399.47</td>
</tr>
</tbody>
</table>

### Measles cases from countries with known discrepancies between case-based and aggregate surveillance, as reported by country

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Cases in Case-based</th>
<th>Cases in Aggregate</th>
<th>Data Source for aggregate #s</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR Congo</td>
<td>2018</td>
<td>5621</td>
<td>67072</td>
<td>SITUATION EPIDEMIOLOGIQUE DE LA ROUGEOLE EN RDC, Week of 07/05/2019</td>
</tr>
<tr>
<td></td>
<td>2019</td>
<td>1414</td>
<td>76107</td>
<td></td>
</tr>
<tr>
<td>Somalia</td>
<td>2018</td>
<td>131</td>
<td>9135</td>
<td>Somali EPI/POL Weekly Update Week 17</td>
</tr>
<tr>
<td></td>
<td>2019</td>
<td>6</td>
<td>1432</td>
<td></td>
</tr>
</tbody>
</table>

Notes: Based on data received 2019-05 and covering the period between 2018-04 and 2019-03 - Incidence: Number of cases / population* * 100,000 - * World population prospects, 2017 revision - ** Countries with the highest number of cases for the period - *** Countries with the highest incidence rates (excluding those already listed in the table above)
WHO Regions with measles and rubella elimination goals

Elimination:
The interruption of indigenous transmission in a defined geographical area for at least 36 months in the presence of a well-performing surveillance system.
Verification of measles and rubella elimination – national level

Measles and rubella data

**Surveillance:**
*Epidemiological data*
*Laboratory data*

**Immunization:**
*Coverage data*
*Performance data*

Annual Status Update report

Status of Measles and Rubella Elimination
Update for the year 2019
COUNTRY NAME
Genotype disappearance?

24 genotypes originally recognised in 8 different clades, but:

### Table

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>B2</td>
<td>1</td>
<td>12</td>
<td>52</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B3</td>
<td>17</td>
<td>94</td>
<td>387</td>
<td>336</td>
<td>1082</td>
<td>596</td>
<td>1494</td>
<td>566</td>
<td>721</td>
<td>2673</td>
<td>2778</td>
<td>93</td>
</tr>
<tr>
<td>D4</td>
<td>425</td>
<td>338</td>
<td>666</td>
<td>2026</td>
<td>927</td>
<td>134</td>
<td>41</td>
<td>66</td>
<td>53</td>
<td>15</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>D5</td>
<td>114</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D8</td>
<td>76</td>
<td>37</td>
<td>96</td>
<td>246</td>
<td>832</td>
<td>1700</td>
<td>1223</td>
<td>1301</td>
<td>1552</td>
<td>2552</td>
<td>3284</td>
<td>314</td>
</tr>
<tr>
<td>D9</td>
<td>26</td>
<td>28</td>
<td>41</td>
<td>225</td>
<td>91</td>
<td>79</td>
<td>91</td>
<td>33</td>
<td>96</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D11</td>
<td>0</td>
<td>6</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3</td>
<td>0</td>
<td>0</td>
<td>25</td>
<td>51</td>
<td>1</td>
<td>15</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H1</td>
<td>157</td>
<td>144</td>
<td>158</td>
<td>29</td>
<td>66</td>
<td>181</td>
<td>4850</td>
<td>3167</td>
<td>2599</td>
<td>544</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>
Distribution of measles genotypes (last 12 months)

- Notes: Data Source: MeaNS database (Genotypes) and IVB Database (Incidence) as of 2019-05-08 and covering the period 2018-04-01 to 2019-03-31 - Pie charts proportional to the number of sequenced viruses
Measles case distribution by month and WHO Region (2015-2019)
Is it theoretically possible to eradicate measles?
Yes

Will it be easy to eradicate measles?
No

Are there any tools becoming available to make elimination easier?
Yes – rapid diagnostic tests (IgM and IgG)
patch vaccination (no needles/cold chain)

Will it be the next virus to be eliminated?
?? .... But I think we could do rubella if we really wanted to
Acknowledgments

UK data
Immunisation team
Mary Ramsay, Jamie Lopez, Antoaneta Bukasa

Virus Reference Department
Li Jin, Heather Lawson, Ana Penedos

MeaNS
David Williams

WHO data
Global Labnet
Mick Mulders, Paul Rota, Myriam Ben Mamou

Global data from Global Measles and Rubella Update May 2019

Please note for all global data that this is provisional data based on monthly data reported to WHO (Geneva) as of May 2019