Prospects for measles eradication

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Disclosures

• nil
Contents

• Severity of measles – Sudan, Fiji
• Complications of measles – eyes, post-measles syndrome
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• Control – Americas, WPRO, AFRO, Europe
• What have we learned about measles?
• Current control strategy – 2 doses of MCVs plus SIAs
• 2015 situation
• The polio legacy
• Prospects for eradication
Lessons from History

• Measles in Africa –
  • Prior to the 1980s child mortality in sub-Saharan Africa close to 50%

• Measles in Fiji –
  • 1875 infected ship docks in Suva
  • Grand Council of Chiefs meeting underway
  • Massive mortality – one third of 150,000 population

• Measles most severe with –
  • Unexposed communities
  • Crowding
  • Malnutrition
  • Poor management
Measles and magic – stories from Ethiopia

• Measles seen as a form of possession

• “Possessed” children:
  • Do not like the shadows of grown-ups to cross them
  • Do not like injections
  • Do not like to be spoken to as if a child
  • Like pop-corn and candy
Severe measles

• 10th century Iranian physician – Zakariya al-Razi (865-925)
  • Distinguished between measles and small pox
  • Described the rash of fatal measles
Measles.....

• As a cause of death
  • Immediate
  • Delayed
• As a cause of blindness (with Vitamin A deficiency)
• As a cause of malnutrition
• As a cause of immune suppression
After 5 days Vitamin A

The true mortality burden of measles

• Early studies showed greater mortality benefit than could be explained on the basis of measles prevention alone

• Two explanations:
  • Long term effects of measles increase mortality
    • Post measles syndrome – malnutrition, depression, persistent diarrhoea, pneumonia
  • Non-specific mortality benefit attributable to the vaccine
    • Many observational studies by P Aaby and colleagues in Guinea Bissau showed beneficial effect of measles vaccine on mortality
    • Definitive trial underway in Guinea Bissau and Burkina Faso
Immunological recovery after measles

ANNE WESLEY, H. M. COOVADIA & LINDA HENDERSON Department of Paediatrics and Child Health
University of Natal

(Received 4 January 1978)

SUMMARY

Twenty-two children with measles were studied at the stage of the rash and 6 weeks later, and results compared with matched controls.
<table>
<thead>
<tr>
<th>Group</th>
<th>Absolute lymphocyte counts (per cm³)</th>
<th>T cells (per cm³)</th>
<th>B cells (per cm³)</th>
<th>Null cells (per cm³)</th>
<th>FT cells (per cm³)</th>
<th>Lymphocyte transformation (d/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>4209 ± 654</td>
<td>2989 ± 455</td>
<td>987 ± 116</td>
<td>234 ± 63</td>
<td>81 ± 22</td>
<td>9100 ± 1784</td>
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<tr>
<td>6 weeks</td>
<td>6918 ± 430</td>
<td>4364 ± 302</td>
<td>1270 ± 151</td>
<td>284 ± 47</td>
<td>162 ± 31</td>
<td>7970 ± 1751</td>
</tr>
<tr>
<td>Controls</td>
<td>7603 ± 742</td>
<td>4746 ± 453</td>
<td>2051 ± 247</td>
<td>805 ± 128</td>
<td>140 ± 40</td>
<td>31745 ± 5249</td>
</tr>
</tbody>
</table>
Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality

Michael J. Mina, 1,2* C. Jessica E. Metcalf, 1,3 Rik L. de Swart, 4 A. D. M. E. Osterhaus, 4 Bryan T. Grenfell 1,3

Immunosuppression after measles is known to predispose people to opportunistic infections for a period of several weeks to months. Using population-level data, we show that measles has a more prolonged effect on host resistance, extending over 2 to 3 years. We find that nonmeasles infectious disease mortality in high-income countries is tightly coupled to measles incidence at this lag, in both the pre- and post-vaccine eras. We conclude that long-term immunologic sequelae of measles drive interannual fluctuations in nonmeasles deaths. This is consistent with recent experimental work that attributes the immunosuppressive effects of measles to depletion of B and T lymphocytes. Our data provide an explanation for the long-term benefits of measles vaccination in preventing all-cause infectious disease. By preventing measles-associated immune memory loss, vaccination protects polymicrobial herd immunity.
Decline in non-measles infectious diseases deaths following measles vaccine introduction
Strategies for measles control

• Isolation of cases – useless

• Effective treatment
  • Vitamin A and antibiotics can reduce morbidity and mortality, but not transmission

• Vaccination and immunity
  • Maternally derived immunity 6-9 months, declining
  • Shwartz live-attenuated vaccine

• During 90s plans developed for eradication of measles based on polio strategy
  • Routine immunization + regular campaigns
Epidemiologic Basis for Eradication of Measles (1967)

- Virtually universal infection
- Reservoir is humans, no non-human reservoirs
- Chronic carriers do not exist
- Transmission dependent on balance between immunes and susceptibles
- Transmission dies off before all susceptibles exhausted

Reported Measles Incidence, United States, 1950-2001

- Vaccine licensed
- One dose school immunization laws started in all states
- Improved first dose preschool coverage
- Second dose strategy and school laws

From: Hinman AR et al. JID 2004; 189 (Suppl 1): S17-S22
Polio – the model for disease eradication

- By the late 1980s,
  - True burden of polio established
  - Experience in Latin America shows polio can be eliminated
    - NIDs, SNIDs, mopping up, etc.
  - Strong drive from civil society (Rotary International)
- From 1990 WHO adopts polio eradication as a global goal
WHO-EPI Staff Strength
African Region, 1992-1999

Health Technology and Pharmaceuticals
Africa
immunization coverage 1980-98
2000 – the polio awakening

• Around March 2000 WHO Director General Bruntland informed that polio would *not* be eradicated in 2000
  • Explosive response with diversion of funds to polio
• “Eradicationists” badly burned
• New strategy –
  • Don’t mention measles until polio is finished
2000 – The measles burden dilemma

• Measles mortality estimates ranged from 770,000 deaths (WHO) to 55,000 (M Garenne)
• All estimates based on models
  • Assume 10% primary vaccine failure
  • Assume all non-immunes will get measles
  • Derive case fatality rate from reports (mainly outbreaks)
• WHO locked into high estimates
  • Deaths $\propto$ money for measles control
• High throughput hospitals in Africa not reporting many cases
Global estimated measles mortality and measles deaths averted, 2000 - 2013

- Estimated measles deaths in absence of vaccination
  (numbers give the cumulative number of deaths prevented in millions)
- Estimated measles deaths with vaccination
- 95% CI of estimated measles deaths with vaccination
- Deaths averted by measles vaccination

75% drop in est. mortality

15.6 million deaths averted
Reported measles cases by WHO Region, 2000-2014

71% drop in incidence
2014: 42 per million

Data as of 27 May 2015. 148 / 194 Member States reporting data for 2014
Progress in measles reduction since 2008

• In Africa, 172,000 reported cases in 2010 (from 37,000 in 2008)
  • Declining funding
  • Problems with some religious groups

• Many cases in Europe (esp. France)

• Major outbreak in UK in 2013
  • Areas with poor coverage
  • Related to spurious, but ongoing argument about autism

• Outbreaks in countries certified measles free
  • Brazil
  • Mongolia

• Many groups in UK and US choosing not to be vaccinated
WHO Measles Targets

**Global milestones** by 2015:

1. Measles dose 1 coverage ≥ 90% national and ≥ 80% in every district
2. Measles reported incidence <5 cases per million
3. Measles mortality reduction of 95% vs. 2000

**Regional targets:**

**Measles** Elimination goals:

- 2000  PAHO
- 2012  WPRO
- 2015  EURO, EMRO
- 2020  AFRO, SEARO
Measles vaccine coverage in Europe, 2014
Measles in Africa
Measles vaccine coverage, Kenya 2002
Does modelling help?

• If >X% of individuals are non-immune then there is a risk of an epidemic

• But:
  • Non-immunes are rarely evenly distributed in any society
    • Marginalized groups not connected with health services
    • Religious groups opposed to immunization
    • Anti-vaccine communities
  • Even apparently highly vaccinated communities can support outbreaks

• Vaccination schedules
  • Timing of 1st dose
Waning maternal immunity and timing of doses

• Vaccine derived and no natural boosting
• In theory children should be vaccinated early
• Does it work? Guinea Bissau study
  • RCT: 892 infants MV at 9 mths vs 441 infants MV at 4&9 months
  • Measles cases 77 cases 8 cases
  • Deaths 12 1
  • Vaccine effectiveness 94%

• So countries with mature vaccination programs with measles well controlled should be vaccinated earlier, *right*?
Mongolia

- Territory – 1.6 million square kilometers
- Population – 3.1 million
- Population living in poverty 32%
- Extremely isolated
- Extreme climate
- Very significant indoor and outdoor air pollution, especially in winter
Measles in Mongolia

• Political upheaval 1991 – breakdown of public health
• High vaccine coverage since early 90s
• Declared measles free by WHO 2014
• March – October 2015
  • Over 20,000 suspected measles cases, many 15-24 years
  • 1,434 lab confirmed
  • 50% under 5 years old, half under 9 months
• 2 main groups
  • Young adults
  • Young infants
Measles in the Americas 2015

Outbreaks

Brazil (Pernambuco and Ceará, 19 March 2013 – 15 January 2015)

USA - 648 confirmed cases in 2014, 169 cases in 2015
Measles in the Americas 2015
Barriers to measles eradication

• The global political situation is worse than 20 years ago
  • Large areas of the middle-east now no-go areas
  • Polio workers targeted thanks to US military activities
• Global travel much more accessible
• Stepwise country by country; region by region will not work
• Global control in all areas with high coverage of MCV2 needed, followed by co-ordinated “final push”
  • Perhaps this will be achieved by 2020, what then?
  • Proportion of non-immunes will steadily increase...
"After consulting with their respective Regional Technical Advisory Group, every region establish a regional verification commission, and after consulting with their respective National Immunization Technical Advisory Group, every country explore options for establishing a national verification commission, to scrutinize and monitor progress towards the measles and rubella elimination targets."

**Progress:**

- Global Verification Framework published in 2013
  - Definitions
  - Criteria for elimination
  - 5 lines of evidence
- 4 Regions have developed their verification guidelines
- AMR, EUR, WPR have fully functional Regional Commissions
- Differences in definitions and surveillance indicators
Issues - regional

• Africa –
  • More input into SIAs and routine activities
  • Marginalized communities

• Europe –
  • Countries like Austria and UK need to step up
  • Anti-vaccination lobby groups

• Americas and Asia
  • Need to re-establish control
Issues - global

• Do complex regional and national targets really help?
• Are new vaccines needed?
• Dogmatic approach to schedules seems outdated
• Models help, but most conclusions are self evident
• New research, fresh thinking needed
Conclusions

• Regional experiences have shown that measles can be eliminated
• Global political will and cooperation is needed
• The slow progress of polio stands as a barrier
• Eradication push should not start until all countries have adequate control and a final push is adequately resourced