Outbreak Response Vaccination for Measles

Rebecca Freeman Grais
April 1, 2009
Outline

- Measles background
- Recommendations for measles vaccination in emergencies
- MSF Experience
  - Niamey, Niger Case Study
- Barriers to intervention
- Evaluating the capacity to respond
- Conclusions and Recommendations
Measles Overview

- A leading cause of vaccine-preventable death among children.
- ~410,000 children < 5 ys die globally
- Can cause severe health complications
  - Pneumonia
  - Diarrhea
  - Encephalitis
  - Corneal scarring, which can lead to blindness.
- Primary reason for deaths is the failure to deliver at least one dose of measles vaccine.
- Case Fatality Ratio (CFR)
  - Developing countries: CFR: 1-5%
  - Refugee/Displaced settings and among malnourished children: CFR may reach 10-30%.
Measles Overview: Dynamics

- Seasonal disease
- Multi-year epidemic cycle
- Infectious period begins before rash
- Directly transmitted
- Herd immunity requires 90 - 95% population immunity
Characteristics of Measles Vaccine

- Attenuated, live, injectable vaccine

- Antibodies to measles
  - appear 12-15 days after vaccination
  - peak 20-28 days after vaccination

- Vaccine Efficacy
  - 85% 9 mo
  - 95% 12-15 mo

- Vaccination within 72 hours of exposure may decrease severity of disease and transmission potential
Recent Global Evolution of Measles Control

- **1990s**: Urban campaigns targeting 9m-5y in Africa

- **2000**: UNICEF/WHO Measles Mortality Reduction and Regional Elimination Strategic Plan 2001-2005 (WHO/V&B/01.13)
  - Strengthen routine immunization
  - Second opportunity for measles immunization
  - Enhanced surveillance
  - Improved case management

- **2000**: Measles Initiative
  - Reduce measles deaths by 90% worldwide by 2010 (compared to 2000).
Implications

- Highly-endemic measles confined to most challenging settings
- Political will to improve current situation
- Great success in global measles control, BUT pockets remain which may (or may not) be considered “emergencies”
Current Recommendations for Emergencies

- Médecins sans Frontières (MSF)
  “Outbreak control.....The main control measure is to accelerate the immunization as measles transmission is not rapid enough to infect all susceptible individuals before they can be vaccinated...”

Refugee Health, MSF, 1997
Current Recommendations, cont.

- UNHCR

  ".. Immunization against measles for young children is the only essential immunization in the early stages of an emergency...."

UNHCR Handbook for Emergencies, 2007
Definition of an Emergency

- Crude mortality of 1/10,000 adults/day or 2/10,000 children/day?
- Doubling of baseline crude mortality?
- Situation where life or well-being threatened unless immediate and appropriate action is taken?
Pockets of highly endemic measles

- Precarious situation
- Insufficient vaccination coverage
- Poor surveillance
- Limited access to care
- High birth-rates
MSF Experience

- Interventions in more than 20 outbreaks in open contexts in last 10 years
- MSF interventions during outbreaks
  - Reinforcement of surveillance
  - Case management
  - Vaccination
## Recent MSF Experience

<table>
<thead>
<tr>
<th>Place</th>
<th>Year</th>
<th>Length (months)</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kinshasa, DRC</td>
<td>2002</td>
<td>1</td>
<td>17,624</td>
</tr>
<tr>
<td>Kinshasa, DRC</td>
<td>2005</td>
<td>6</td>
<td>40,857</td>
</tr>
<tr>
<td>Niamey, Niger</td>
<td>2003</td>
<td>12+</td>
<td>10,880</td>
</tr>
<tr>
<td>Adamawa, Nigeria</td>
<td>2004</td>
<td>12+</td>
<td>2,505</td>
</tr>
<tr>
<td>Ndjamen, Chad</td>
<td>2005</td>
<td>12+</td>
<td>8,015</td>
</tr>
</tbody>
</table>
Background, Niamey, Niger 2003-4

- Although surveillance system in place, no alert given
- Epidemic never officially declared
- Estimated vaccine coverage: 70%
- Intervention occurred late in the epidemic
- Asked to intervene to cover 100%, but only 50% of all children 6-59m targeted
- Polio Immunization Day occurring at the same time
Reported measles cases in Niamey, Niger (2003-2004) (10880 cases)

- **Intervention**
- **Beginning of outbreak**

![Graph showing reported measles cases in Niamey, Niger (2003-2004) with peaks and intervention marked.]
Reported Cases by Health Center, Niamey, Niger 2003-2004
What would have happened if…?

1. Measure the impact of vaccination intervention
2. Examine:
   - Timing of interventions in course of epidemic
   - Age range to vaccinate
   - Intervention vaccination coverage
3. Learn for the future
Recreating an epidemic, Niamey, Niger 2003-2004: Key Assumptions

- **Constant**
  - 15 day delay between decision and delivery
  - 10 day intervention
  - Vaccine efficiency = 85%

- **Variable**
  - 2 age ranges for vaccination (standard):
    - 6m to 59m
    - 6m to <15y
  - Interventions:
    - 2, 3 or 4 months after epidemic starts
    - Vaccination coverage: 30% – 100%
Model Overview: Niamey
Model Overview: Niamey, Niger

Probability of infection:
- age
- immune status
- vaccination status
- location in the city
- status of other children
- contact decreases with distance
- time
Model Overview: Niamey, Niger

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- time

\[ P_{i,t,a} = 1 - \exp \left\{ - \left( \frac{\beta_{\text{quartier}} I_{\text{quartier}}}{N_{\text{quartier}}} + \frac{\beta_{\text{CSI}} I_{\text{CSI}}}{N_{\text{CSI}}} + \frac{\beta_{\text{commune}} I_{\text{commune}}}{N_{\text{commune}}} + \frac{\beta_{\text{city}} I_{\text{city}}}{N_{\text{city}}} \right) \right\} \]

8.1% [4.9, 8.9] averted with intervention on day 161
Proportion cases prevented by intervention coverage and time: 6 to 59m, Niamey, Niger
Proportion cases prevented by intervention coverage and time: 6 to 15y, Niamey, Niger
Lessons Learned

- More time than we thought to intervene
- 3 Key Factors
  - Timing
  - Age range for vaccination
  - Vaccination coverage objective
- Benefit of intervening
- But, barriers to intervention remain
Major Barriers to Intervention: What happens in reality

1. Different outbreak definitions
2. “Always too late” argument
3. “Catch-up” campaign planned
4. Perception
   • Logistical Difficulties
   • Cost
   • Common disease
5. Current WHO guidelines do not recommend mass vaccination
1. Different outbreak definitions

- Definition using different criteria
  - Number of cases (ex, 1 case in a camp, 2 or 3 cases at health center over 14 days)
  - Comparison with previous years (ex, increase over 2-3 weeks at district level compared to same time last year)
  - Evolution over weeks (ex, doubling over 3 weeks)
- Simultaneously always and never an epidemic
- Lack of definition mean no declaration and … no action or long delay
2. “Always too late”
Examples of outbreaks (2002-05)
Reported Measles Cases, N’Djamena, Chad (2004-2005) (8015 cases)

No more data available
Reported measles cases, Kinshasa, DRC, 2002-2003
Spatial-temporal diffusion  Kinshasa, DRC 2002-2003
Estimating the Effective Reproductive Ratio (R)

- Niamey, Niger (2003-2004): 2.8
- Kinshasa, DRC (2005-6): 1.9
- Ndjamen, Chad (2005): 2.5

$R =$ avg number secondary cases generated by one case in a partially immune population
3. Catch-up campaign planned

- **Objective of catch-up campaign**
  To raise vaccine coverage to reduce morbidity and mortality and PREVENT future outbreaks

- **Objective of vaccination during outbreak**
  To reduce quickly morbidity and subsequent mortality

- **Soroti, Uganda, 2003**
  - displaced arrive June/August
  - Catch-up campaign planned for October (refusal)
  - Retrospective survey:
    - 6.0 deaths/10,000/day (under 5) with measles as principal reason
4. Perceptions

- Logistics
  - MSF: 15 days from decision to 1st dose delivered
  - Experienced groups capable of intervening

- Cost per child vaccinated is low (<1$)

- Burden and severity underestimated
### 4. Retrospective Surveys: Cases and Attack Rates

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Niamey (Boukoki)</th>
<th>N’Djamena (Moursal)</th>
<th>Adamawa State (Dong District)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (n)</td>
<td>AR</td>
<td>Cases (n)</td>
</tr>
<tr>
<td>Under 5</td>
<td>884</td>
<td>18.0</td>
<td>542</td>
</tr>
<tr>
<td>5-14</td>
<td>108</td>
<td>1.7</td>
<td>191</td>
</tr>
<tr>
<td>15 and above</td>
<td>108</td>
<td>0.7</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>1,100</td>
<td>4.1</td>
<td>767</td>
</tr>
</tbody>
</table>
4. Retrospective Surveys: Case Fatality Ratios

- Niamey (Boukoki)
  - CFR: 3.9% (n = 30/771)

- N’Djamena (Moursal)
  - CFR: 2.8% (n = 20/706)

- Adamawa (Dong District)
  - CFR: 7.0% (n = 80/1142)
5. Current WHO Guidelines

- “The immunization response in most outbreaks occurs too late to affect the impact of the outbreak… Supplementary vaccination activities in the course of an outbreak are NOT recommended unless there is substantial political or community pressure…”
  
  WHO/CDS/CSR/ISR/99.1

- Regional WHO policies may differ

- WHO reconsidering recommendations

- May prohibit early comprehensive vaccination intervention
- Restricts the possibility of funding outbreak response
- No clear definition of intervention
So now what?

- Research shows there is benefit to interventions
- Political barriers to intervention can be overcome
- Evaluate capacity to respond BEFORE an outbreak
Measles Vaccination Campaigns

1. **PLANNING** - Coordination among the core partners to determine target populations, resource needs, and logistics
2. **THE COLD CHAIN** (supply) - getting the vaccine and all needed supplies to vaccination posts
3. **SOCIAL MOBILIZATION** (demand) - spreading the word
4. **FOLLOW-UP** - Processing the results of the campaign to determine the successes based on coverage, weak points, and future plans
Evaluating Capacity to Respond

- Must be able to respond **well**
- Evaluate epidemiologic capacity
  - Timely surveillance system
  - Identification of risk groups
  - Identification of areas at risk
Evaluating Capacity to Respond

Resources
(internal/external)

- Vaccinators
- Vaccine, syringes, safe disposal
- Operational costs
- Training
- Supervision
- Timing of supply availability
Other Considerations

- Ethical imperative
- Political costs of non-intervention
- Competing resource demands/ opportunity costs
- Local decision making necessary
Conclusions

- Consensus on vaccination in “emergencies”
- Range and number of variables limit formulation of recommendations for all situations; local decision making necessary
- Confusion in between vaccination for
  - Prevention
  - Outbreak response
Recommendations

- Ensure Surveillance System is functioning
- Declare Outbreak
- Provisional WHO Guidelines
  - Immediate selective vaccination (6m to 5y)
  - District level outbreak management team
    - decision about whether mass campaign needed
- Coordinate with other actors
- Ask for help! (WHO, MSF)
Acknowledgements

- Ministries of Health, Niger, Nigeria, Chad, DRC
- MSF-F and MSF-B in field and Paris
- WHO
- Survey teams
- Study participants
- Center for Infectious Disease Dynamics
- CERMES
- EPIET
- Lisa Cairns
Estimating R

We model the time course of an epidemic as a chain of binomial infection events from the pool of susceptible (S) individuals such that the probability of I infected individuals at time $t$ is given by:

$$P(I_{t+1} = I) = \binom{S_t}{I} (1 - e^{\beta S_t I_t})^I (e^{\beta S_t I_t})^{S_t - I}$$

$$S_t = S_0 - \sum_{j=1}^{t} I_j$$

$S_0$ is the initial number of susceptible individuals, we can write a likelihood for the time series of case counts, $I_t$, in terms of the transmission rate, $\beta$, and the initial number of susceptibles, $S_0$. 
## Interventions

<table>
<thead>
<tr>
<th></th>
<th>Niamey 2004</th>
<th>N’Djamena 2005</th>
<th>Adamawa State 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>EPI reinforcement</td>
<td>Mass campaign</td>
<td>Not formal</td>
</tr>
<tr>
<td><strong>Age Group (months)</strong></td>
<td>6-59</td>
<td>6-59</td>
<td></td>
</tr>
<tr>
<td><strong>Objectives (% children to be vaccinated)</strong></td>
<td>50%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td><strong>Delay</strong>*</td>
<td>+15 weeks</td>
<td>+15 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>Vaccination Coverage</strong></td>
<td>70% Before 85% After</td>
<td>30% Before 85% After</td>
<td></td>
</tr>
</tbody>
</table>

*Weeks after outbreak identified

**Epicentre LQAS surveys
Reported measles cases, Kinshasa, DRC 2005
What impact is worthwhile?