The Certification of Smallpox Eradication and Implications for Other Diseases: Confirming and Maintaining a Negative

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SEC2010 Smallpox Eradication after 30 Years: Lessons, Legacies and Innovations
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### Away All Disease!

#### DEFINITIONS

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CONTROL:</strong></td>
<td>Reduction of disease incidence, prevalence, morbidity, mortality, and disability to a locally acceptable level</td>
</tr>
<tr>
<td><strong>ELIMINATION:</strong></td>
<td>Reduction of infection and disease to zero in a defined area. Surveillance crucial. Continued efforts required.</td>
</tr>
<tr>
<td><strong>ERADICATION:</strong></td>
<td>Permanent reduction of worldwide incidence to zero as a result of deliberate interventions. Surveillance crucial. Continued efforts may not be required.</td>
</tr>
<tr>
<td><strong>DESTRUCTION:</strong></td>
<td>Destruction of all isolates of microbial agent.</td>
</tr>
</tbody>
</table>
Eradication Programs

Human
- Hookworm, 1909
- Yellow fever, 1915
- *Aedes aegypti*, 1934-42
- *Anopheles gambiae*, 1939-68
- Malaria, 1955-1973
- Yaws, 1950
- Smallpox, 1958, 1966-80
- Poliomyelitis, 1985
- Dracunculiasis, 1987

“Guinea Worm”

Animal
- Bovine contagious pleuropneumonia (cows), 1884
- Glanders (horses, mules)
- Piroplasmosis (cattle)
  “Texas fever”
- Dourine (STD of horses)
- Rinderpest
- Sheep pox
<table>
<thead>
<tr>
<th>Feature</th>
<th>Smallpox</th>
<th>Guinea Worm</th>
<th>Poliomyelitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation Period</td>
<td>14-17 days</td>
<td>9-12 months</td>
<td>7-21 days</td>
</tr>
<tr>
<td>Syndrome visible</td>
<td>Yes (eruption)</td>
<td>Yes (worm)</td>
<td>Sometimes (paralysis)</td>
</tr>
<tr>
<td>Recognized by public</td>
<td>Yes (eruption)</td>
<td>Yes (worm)</td>
<td>Sometimes (paralysis)</td>
</tr>
<tr>
<td>Asymptomatic carriers</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Transmission mode</td>
<td>Respiratory</td>
<td>Water</td>
<td>Fecal-oral</td>
</tr>
<tr>
<td>Vector/Reservoir</td>
<td>Human</td>
<td>Cyclops/Human</td>
<td>Human</td>
</tr>
<tr>
<td>Secondary attack rate among</td>
<td>Intermediate (20%-40%)</td>
<td>?Low</td>
<td>High (10%-90%)</td>
</tr>
<tr>
<td>susceptibles</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Survey Considerations for Certification of Eradication: Smallpox, Guinea Worm and Poliomyelitis (2)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Smallpox</th>
<th>Guinea Worm</th>
<th>Poliomyelitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveys</td>
<td>“Fever and rash” Facial pock marks</td>
<td>“Hanging worms” Blisters on legs</td>
<td>Acute flaccid paralysis (AFP)</td>
</tr>
<tr>
<td>Target Group</td>
<td>School children</td>
<td>Villages at risk</td>
<td>Children &lt;15yrs</td>
</tr>
<tr>
<td>Diagnostic Dilemma</td>
<td>Chickenpox, monkeypox</td>
<td>Trauma, infection (bacterial)</td>
<td>Vaccine-associated AFP, Guillan –Barre Syndrome</td>
</tr>
<tr>
<td>Environmental surveys for microbe</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Laboratory Confirmation</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Rumor Registers</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Reward</td>
<td>Yes</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td>Interval before Certification</td>
<td>2 years</td>
<td>3 years</td>
<td>3 years</td>
</tr>
<tr>
<td>Continuing research</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Summary of Smallpox Manifestations, Pathogenesis and Immunity

- Infection
- Incubation
- Prodrome
- Eruption
- Papules
- Vesicles
- Pustules
- Crusts
- Desquamation

Temperature:
- 7-17 Days
- 2-3 Days
- 1-2 Days
- 1-2 Days
- 2-3 Days
- 5-8 Days
- 5-7 Days
- Weeks

Immune response:
- Infected macrophages, activated T and B cells

HI and neutralizing antibody
CF antibody

Infectiousness:
- Oropharyngeal secretions

Infection:
- Incubation period:
- Day of rash:
- 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

- Nose, mouth, pharyngeal mucosa
- Regional lymph nodes
- Viremia: Spleen, liver, reticuloendothelial system
- Viremia: Dermis

Intraepidermal multilocular vesicles with ballooning degeneration, cell necrosis, and serous exudation

Pathogenesis:
- Nose, mouth, pharyngeal mucosa
- Regional lymph nodes
- Viremia
- Immune response
- Infectiousness
Rahima Banu, Bangladesh
Last Case with Variola major

Age 3, 1975

Age 31, 2002
Reward Posters
Active Search for Smallpox, Somalia, 1977-1978
Certification of Smallpox Eradication in Africa, 1976-1979
Smallpox Certification Activities, Sudan
International Commission Visits, 1976
# Smallpox Certification Activities, India

## Pockmark Surveys, 1977

<table>
<thead>
<tr>
<th>Age group</th>
<th>Survey</th>
<th>Number of persons examined</th>
<th>Total</th>
<th>With facial pockmarks*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preschool children</td>
<td>National International Commission</td>
<td>271 897 3 139</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>School-age children</td>
<td>National International Commission</td>
<td>224 297 26 665</td>
<td>38</td>
<td>18</td>
</tr>
<tr>
<td>Adults</td>
<td>National International Commission</td>
<td>1 451 125 14 307</td>
<td>650</td>
<td>94</td>
</tr>
</tbody>
</table>

* Due to smallpox contracted before 1972.
# Smallpox Certification by the Numbers 1973-1980

<table>
<thead>
<tr>
<th>Countries</th>
<th>Number</th>
<th>Population (billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countries</td>
<td>200</td>
<td>4.5</td>
</tr>
<tr>
<td>Submitting statements</td>
<td>121</td>
<td>1.5</td>
</tr>
<tr>
<td>Visited by Commissions</td>
<td>79</td>
<td>3.0</td>
</tr>
<tr>
<td>At special risk</td>
<td>44</td>
<td>1.8</td>
</tr>
<tr>
<td>Endemic during SEP</td>
<td>35</td>
<td>1.2</td>
</tr>
<tr>
<td>Specimens Collected</td>
<td>17,000</td>
<td></td>
</tr>
</tbody>
</table>
Recommendations of the Global Commission, 1979

- Vaccination policy
- Reserve vaccine stocks
- Investigation of suspected cases
- Laboratories retaining variola viruses
- Human monkeypox
- Laboratory investigations
- Documentation and dissemination
- Committee on orthopoxviruses
- Vaccinia virus as a vector for foreign genes
Villages reported dracunculiasis cases in Sudan and Ethiopia during 2009.
Villages reported dracunculiasis cases in West Africa during 2009.
Wild Poliovirus infected districts*, 28 Jan 2010 – 27 Jul 2010

**Table:**

<table>
<thead>
<tr>
<th>Status</th>
<th>Country</th>
<th>Date of most recent type 1</th>
<th>Date of most recent type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endemic</td>
<td>Pakistan</td>
<td>18-Jun-10</td>
<td>24-Jun-10</td>
</tr>
<tr>
<td></td>
<td>Nigeria</td>
<td>18-Jun-10</td>
<td>15-Jun-10</td>
</tr>
<tr>
<td></td>
<td>India</td>
<td>12-Jun-10</td>
<td>14-Jun-10</td>
</tr>
<tr>
<td></td>
<td>Afghanistan</td>
<td>23-May-10</td>
<td>11-Apr-10</td>
</tr>
<tr>
<td>Re-established transmission</td>
<td>Angola</td>
<td>15-Jun-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Chad</td>
<td>NA</td>
<td>22-May-10</td>
</tr>
<tr>
<td>Active outbreak</td>
<td>Tajikistan</td>
<td>04-Jul-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>DR Congo</td>
<td>25-Jun-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nepal</td>
<td>05-Jun-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Mali</td>
<td>01-May-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>20-Apr-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Mauritania</td>
<td>20-Apr-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Niger</td>
<td>NA</td>
<td>01-Apr-10</td>
</tr>
<tr>
<td></td>
<td>Liberia</td>
<td>05-Mar-10</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Sierra Leone</td>
<td>29-Feb-10</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Excludes viruses detected from environmental surveillance and vaccine-derived polioviruses. WPV1 in Jammu and Kashmir, date of onset of 07 Feb 2010, does not appear on the map.

*Data in WHO HQ as of 27 July 2010*

- Wild virus type 1
- Wild virus type 3
- Wild virus type 1/3

Endemic countries
Case or outbreak following importation (0 - 6 months)
Case or outbreak following importation (6 - 12 months)

Data in WHO HQ as of 10 Aug 2010

*Excludes viruses detected from environmental surveillance and vaccine derived polioviruses. 1 WPV1 in Jammu and Kashmir, date of onset of 07 Feb 2010, does not appear on the map.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2010. All rights reserved
Eradication, Certification, and the Final Inch

“The rule of the final inch consists in this: not to shirk this critical work, not to postpone it.... One’s purpose lies not in completing things faster, but in the attainment of perfection.”

Alexander Solzhenitsyn
The First Circle, 1968
Lessons Applicable to Other Programs

• Clear objectives known to all

• Scientifically justifiable
  * No animal reservoir
  * Clinically manifest
  * Two-week incubation period
  * Virus did not survive in environment
Lessons Applicable to Other Programs (2)

- Operationally feasible but difficult
  - Effective, heat-stable vaccine
  - Vaccine protection of long duration
  - Vertical programs supported nationally and internationally
  - All programs started together
  - Field staff needs are top priority
Lessons Applicable to Other Programs (3)

- Research and evaluation is crucial
  * Diagnosis
  * Active surveillance for cases
  * Coverage surveys for vaccination
  * Epidemiology to define groups at risk
  * Vaccine delivery systems
  * Adverse events from vaccination
  * Monkeypox and other orthopoxviruses
  * Poxviruses as vaccine vectors
  * Therapeutics
Lessons Applicable to Other Programs (4)

- Confirmation of eradication
  - Independent commissions
  - Certification format
  - Credibility and confidence
Lessons Applicable to Other Programs (5)

- **Exchange of experiences**
  * Routine disease surveillance
  * Special communications (research, outbreaks)
  * Cross-notification of importations
  * Transparency

- **Political, administrative, and economic**
  * Commitment of high-level leadership
  * Use political/administrative infrastructure
  * Sustaining interest is difficult at the end
  * Show medical and economic improvements
  * Use staff who have been successful in one program in others
  * Achieve altruistic goal
Impact of Smallpox Eradication on Global Health

- Expanded program on immunization
- Onchocerciasis Control Program
- Polio Eradication Initiative
- Dracunculiasis Eradication Program
- Epidemic outbreaks: detection and control (IDs: ex. Ebola; Environmental: ex. Bhopal, environmental catastrophes)
- Global Outbreak and Response Network (SARS, Influenza)
- Public health leadership and administration