Act Locally, Think Globally: The Role of Immunization in Georgia to our Community and to the World

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Op-Ed from Steven Weinreb, an internist certified in oncology and hematology

• “I have chronic lymphocytic leukemia. Three months ago, I underwent an allogeneic stem-cell transplant ....” For the next seven months or so ... I have a newborn’s immunity; I am prey to illnesses like chickenpox, the measles, and the flu.”

• “The truth is, we should not get vaccinated for ourselves alone; we should do it for one another.”

US National Vaccine Plan 2010

• In the era of global pandemics and mass travel, the public health of U.S. citizens is closely related to diseases occurring in other countries. Even though many VPDs such as polio, measles, and rubella have been eliminated in this country, the U.S. remains vulnerable to importations as long as these diseases continue to persist elsewhere. Support for overseas (pre-departure) vaccination of mobile populations, including refugees and immigrants migrating to the U.S., will reduce the likelihood of importation. Support for developing and introducing new vaccines to address diseases in other countries and assisting with strengthening and enhancing capacity of their immunization programs contributes toward providing an “umbrella of protection” for the U.S. and fulfilling the U.S. government’s broader commitment to global public health.  
http://www.hhs.gov/nvpo/vacc_plan/
Topics to be covered

• Basic background on herd immunity
• Disease eradication as the ultimate goal (smallpox, polio, measles)
• Global burden of vaccine-preventable diseases
• Measles as an “indicator disease” for problems
• Global Immunization Structure
• What healthcare providers can do
• Not covered – new vaccines and new technologies that would help
Community Immunity - #1

- Sustained transmission:
  - Transmitting case ➔ Susceptible ➔ Transmitting case ➔ Susceptible

- Transmission terminated:
  - Transmitting case ➔ Immune
Community Immunity - #2

Transmitting case

- Immune
- Immune
- Immune
- Immune
- Immune (Indirectly Protected)
- Susceptible (Indirectly Protected)
<table>
<thead>
<tr>
<th>Infection</th>
<th>Basic Reproduction Number ($R_0$)</th>
<th>Crude Herd Immunity Threshold, $H$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>6-7</td>
<td>85</td>
</tr>
<tr>
<td>Influenza$^+$</td>
<td>1.4-4</td>
<td>30-75</td>
</tr>
<tr>
<td>Measles$^+$</td>
<td>12-18</td>
<td>92-94</td>
</tr>
<tr>
<td>Mumps</td>
<td>4-7</td>
<td>75-86</td>
</tr>
<tr>
<td>Pertussis</td>
<td>12-17</td>
<td>92-94</td>
</tr>
<tr>
<td>Polio$^+$</td>
<td>2-15</td>
<td>50-93</td>
</tr>
<tr>
<td>Rubella</td>
<td>6-7</td>
<td>83-85</td>
</tr>
<tr>
<td>Smallpox</td>
<td>5-7</td>
<td>80-85</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Tuberculosis$^+$</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Varicella$^+$</td>
<td>8-10?</td>
<td>?</td>
</tr>
</tbody>
</table>

*It should be emphasized that the values given in this table are approximate, and that they do not properly reflect the tremendous range and diversity among populations. Nor do they reflect the full immunologic complexity underlying the epidemiology and persistence of these infections. See text for further discussion.

$^+$ $R_0$ of influenza viruses probably varies greatly between subtypes.

$^+$ Herd immunity thresholds as low as 55% have been published.

$^+$ Complicated by uncertainties over immunity to infection and variation related to hygiene standards.

$^+$ Protective immunity not defined.

$^+$ Immunity not sterile, herd immunity threshold not defined.

Smallpox
Benefits of Smallpox Eradication to the US

• Sencer and Axnick documented in the United States during 1968:
  • 14.2 million persons were vaccinated of whom 5.6 million were primary vaccinations and 8.6 million were revaccinations.
  • Because of vaccine complications, 238 required hospitalization
  • 9 died, and 4 were permanently disabled.
  • The total costs to the country, including the costs of quarantine services, were estimated to be US$150 million.

Global U5 Mortality: Role of Vaccine Preventable Diseases (2008 data)

8.8 million under five deaths

17% (1.5 million) from vaccine preventable diseases

- Pneumonia other: 12%
- Pneumococcal diseases*: 6%
- Pertussis: 2%
- Hib*: 2%
- Tetanus: 1%
- Measles: 1%
- Rotavirus*: 5%
- Diarrhoea other: 10%
- HIV: 2%
- Malaria: 9%
- Other: 18%
- Perinatal: 32%


* WHO/IVB estimates

Provided by Thomas Cherian via email 3/7/12
1.5 million Vaccine preventable deaths, children under age of 5, 2008

- Pneumococcal diseases* 476 000
- Rotavirus* 453 000
- Hib* 199 000
- Pertussis 195 000
- Measles 118 000
- Tetanus 63 000

* WHO/IVB estimates
1.5 million deaths among children from vaccine preventable disease by WHO regions, 2008

* WHO/IVB estimates

Provided by Thomas Cherian via email 3/7/12
Measles

Selected Complications:

Pneumonia
Diarrhea
Otitis Media
Encephalitis
SSPE
Keratitis
Death
Measles Elimination, the Americas, 1980-2011*.  

A total of 3.2 million measles cases and 16,000 deaths would have occurred between 2000-2020 if PAHO strategies were not implemented. This resulted in a savings of US$ 208 million in treatment costs.1

Source: Country reports to PAHO/WHO.
*Data until EW 35/2011; coverage data not available for 2010.
1 Ibidem Acharya et. al.

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
Measles, United States, 1996-Present

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
Measles, United States, 2011
Geographic Distribution of Cases (n=222)

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
## Measles, United States, 2011
### Source of Importations, n=72

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Total no. of cases</th>
<th>Countries</th>
<th>Genotype identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>4</td>
<td>Ethiopia (1), Kenya (2), Nigeria (1)</td>
<td>B3 (4)</td>
</tr>
<tr>
<td>Eastern</td>
<td>3</td>
<td>Jordan (1), Pakistan (2)</td>
<td>D4 (1)</td>
</tr>
<tr>
<td>Mediterranean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>33</td>
<td>Bulgaria (1), <strong>France (13)</strong>, Italy (4), Poland (1), Romania (1), Spain (1), United Kingdom (5), France/Germany/Italy/Spain (1), France/Germany/Spain (1), France/Italy (1), France/Spain/United Kingdom (1), France/United Kingdom (1), Hungary/Romania (2)</td>
<td>D4 (16), G3 (1)</td>
</tr>
<tr>
<td>Americas</td>
<td>2</td>
<td>Canada (1), Dominican Republic† (1)</td>
<td>D4 (1)</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>19</td>
<td>Bangladesh (1), <strong>India (16)</strong>, Indonesia (2)</td>
<td>D8 (5), D4 (1)</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>11</td>
<td>China (2), Malaysia (2), Philippines (6), Malaysia/Philippines/Singapore/Vietnam (1)</td>
<td>H1 (1), D9 (6)</td>
</tr>
</tbody>
</table>

72% of importations were among U.S. residents traveling abroad

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
2009 Imported Measles, U.S., as of 12/31/2009

71 cases
21 importations
12 imported virus cases

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
Measles Outbreaks*
United States, 2011

• 112/222 (50%) annual cases were outbreak-associated
• 17 total outbreaks
• Median outbreak size was 6 (range: 3 – 21)
• 44% of outbreak-associated cases were unvaccinated philosophical belief exemptions

*Outbreak = 3 or more epidemiologically linked cases

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
Impact of Selected Measles Importations Into the US in 2011

• Minnesota – 22 cases started by an unvaccinated child of Somali heritage, infected in Kenya, returned to the US and attended drop in child care

• Measles developed in 3 contacts at the center (including the first case, the infant living at the homeless shelter)

• Subsequent cases occurred in 2 homeless shelters, 2 health care facilities, 2 households, and 1 other child care center. Fourteen children were hospitalized
Impact of Selected Measles Importations Into the US in 2011 II

• Indiana – 14 cases started by a 24 year old unvaccinated US resident exposed in Indonesia, hospitalized with diagnosis of “Dengue Fever”

• Of the additional patients who were infected, 10 exposed others in health care facilities.

• An investigation identified more than 780 persons who came in contact with infected individuals, including exposures in a church, factory, and school bus.

From Hampton T, JAMA 2011;306:2440-2442
Impact of Selected Measles Importations Into the US in 2011

• Measles Salt Lake County, Utah - 9 cases traced back to an unvaccinated high school student who traveled to Europe
• Public health authorities investigated 49 confirmed or suspected cases, quarantined 184 individuals, and notified approximately 12 000 contacts.
• The Utah Department of Health, Salt Lake Valley Health Department, and Primary Children’s Medical Center estimated that the direct cost of health department and PCMC physician and staff time was $250 000 and the cost of vaccines, immunoglobulin, and blood work was approximately $41 700.
• Direct costs for controlling this outbreak conservatively totaled nearly $300 000.

From Hampton T, JAMA 2011;306:2440-2442
Keys to Maintaining Measles Elimination in the U.S.

- High 2-dose MMR vaccination coverage
- High quality surveillance system
- Rapid identification of and response to measles cases
- Measles is reportable within 24 hours per Council of State and Territorial Epidemiologists guidelines
- Aggressive outbreak control measures
- Access to reliable laboratory testing capabilities
- Genotyping can give clues to source in some instances
- Information sharing tools (Epi-X, HAN)

Thinking beyond our borders

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
Vaccination of U.S.-Bound Refugees

- 70,000 refugees resettled (70 nationalities from 100 countries) to 49 states annually
- Refugees not legally required to get vaccinations before U.S. resettlement
  - ~ 1/3 of refugees arrive in U.S. with no documented vaccinations
- > 40 VPD outbreaks in last 5 years
  - 1 recent imported measles case in Burmese refugee from Malaysia led to 8 cases in U.S., costly state/local PH response, and delayed resettlement of refugees
- Missed opportunity to vaccinate refugees between required overseas health assessment & arrival in U.S. (4-6 months)

Provided by Anne Schuchat, Presentation to NVAC 2/8/12
Major cause of mortality among children under 5 years, 2000-2010

2000  9.6 million

- Diarrhoea 11%
- Measles 5%
- Injury 4%
- Malaria 6%
- AIDS 3%
- Meningitis 3%
- Other disorders 15%
- Pneumonia 15%
- Other neonatal 33%
- Pneumonia (neonatal) 4%

2010  7.6 million

- Diarrhoea 10%
- Measles 2%
- Injury 5%
- Malaria 7%
- AIDS 2%
- Meningitis 2%
- Other disorders 18%
- Pneumonia 14%
- Other neonatal 35%
- Pneumonia (neonatal) 4%

Measles accounts 18% of total reduction

Resurgence in Africa

• 4-fold increase since 2008
• Large outbreaks in Burkina Faso (2009), S. Africa (2010), and DRC (2011)
• Outbreaks in drought affected Horn of Africa
  – High case-fatality

Weak Immunization Systems

- **1\(^{st}\) dose:**
  - 71 Countries have MCV1 coverage <90%

- **2\(^{nd}\) dose (routine):**
  - 53 countries do not have routine 2\(^{nd}\) dose

- **Campaigns:**
  - Variable quality
  - Delayed

Measles 1\(^{st}\) dose coverage among infants, 2011

Provided by Peter Strebel via email 3/8/12
#1: India

14 states with MCV1 <80% are implementing measles SIAs

17 states with MCV1 coverage ≥80% introduced a routine second dose by August 2011.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Target pop (millions)</th>
<th>Vaccinated (millions)</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase-1</td>
<td>13.8</td>
<td>12.1</td>
<td>88%</td>
</tr>
<tr>
<td>Phase-2</td>
<td>42.9</td>
<td>28.6</td>
<td>67%*</td>
</tr>
<tr>
<td>Phase-3</td>
<td>72.7</td>
<td>Planned</td>
<td>--</td>
</tr>
<tr>
<td>Total</td>
<td>129.4</td>
<td>40.7*</td>
<td>--</td>
</tr>
</tbody>
</table>

* Phase-2 campaigns ongoing; data as on 23 Jan 2012.

Source: Based on target population available with GoI

Provided by Peter Strebel, via email 3/8/12

* Excludes all country contributions and direct social mobilization funding from partners

Provided by Peter Strebel via email 3/8/12

In October 2003, the Pennsylvania Dept of Health and CDC were notified of a suspected case of respiratory diphtheria in a previously healthy Pennsylvania man aged 63 years who reported that he had never been vaccinated against diphtheria. He and seven other men from NY, PA, and W. VA. had returned from a week-long trip to rural Haiti, where they helped build a church.

Source: MMWR, January 9, 2004 / 52(53);1285-1286
Polio – a paralysing disease for life
## Milestones on the way to Polio Eradication

<table>
<thead>
<tr>
<th>Year</th>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1985</td>
<td>Pan American Health Organization launches initiative to eradicate polio in the Americas by 1990</td>
</tr>
<tr>
<td>1988</td>
<td>World Health Assembly passes a resolution to eradicate polio by the year 2000</td>
</tr>
<tr>
<td>1994</td>
<td>Americas certified as polio-free. Last case indigenous case 1991</td>
</tr>
<tr>
<td>1999</td>
<td>Last outbreak of wild poliovirus type 2, Aligarh, India</td>
</tr>
<tr>
<td>2000</td>
<td>Western Pacific region certified polio free</td>
</tr>
<tr>
<td>2002</td>
<td>Europe certified polio free</td>
</tr>
<tr>
<td>2012</td>
<td>India without wild viruses detected for 1 year – Last case with onset 13 Jan 2011</td>
</tr>
</tbody>
</table>
1988

- 350,000 cases
- 125 endemic countries
- World Health Assembly voted to eradicate polio

2011

650 cases reported (as of 20 March 2012)

4 endemic countries

3 countries with re-established transmission
  (sustained > 12 mos)

9 additional countries with transmission
Selected Challenges

- Political commitment
- Management of human resources and accountability
- Inaccessible areas in endemic countries
- Continued quality SIAs with monitoring
- Area-specific gaps in surveillance quality
- Continuing outbreaks
- Funding

Source: Modified from Martin R, WHO, *Polio, It’s everyone’s problem*, NVAC February 8
GPEI Financing 2012-2013: $1.14 billion contributions*

2012-13 Funding Gap:
US$1.09 B of $2.23 B budget

Source: Martin R, WHO, Polio, It’s everyone’s problem, NVAC February 8
Selected Key Organizations Involved in Global Immunization

• WHO
• UNICEF
• GAVI Alliance
• Bill & Melinda Gates Foundation
• US Organizations
  – CDC
  – USAID
  – FDA
  – NIH
• Polio Eradication – Rotary International
WHO Mandate: Immunization Vaccines & Biologicals

• Housing scientific expertise and disseminating global immunization intelligence

• Convening the world's leading expertise in Immunization, Vaccines and Biologicals

• Facilitating technical cooperation with member states*, technical institutions, academia and public/private partnerships

• Coordinating technical assistance to member states
  • *194 Member States across Six Regional Offices

Source: McKinney S, USAID, Immunization: Global Architecture, NVAC February 8
UNICEF: Immunization Program Division

• UNICEF supports a wide array of activities at country, regional and global levels

• UNICEF works in support of governments and in collaboration with partners (e.g. GAVI)

• Focus on:
  – Demand creation and social mobilisation
  – Supply, logistics and cold chain systems
  – Reaching the Unreached (reduce inequities by focusing on immunizing the “Fifth Child”)

Bill and Melinda Gates Foundation (BMGF)

- Investing billions in Global Health
- Vaccines & Immunization – a focus of their global health strategy
  - Discovery
  - Development
  - Delivery
  - Advocacy
- Multi pronged approach and a very engaged partner in many areas of vaccine development and immunization
- Positioned to take risks and do so gladly

USAID’s role

• USAID’s vaccines and immunization programs serve two functions:

  – Donor agency – provide funds to areas that help to achieve our mission of reducing child mortality through immunization, (global, regional, country levels)
  – Policy development - engage in policy dialogue and development (global and country level), and
  – Technical support – engage in technical dialogue and development and to provide technical support (global and country level).

GAVI: Four strategic goals
Strategic plan 2011-2015

- Accelerate the uptake of underused and new vaccines
- Contribute to strengthening the capacity of integrated health systems to deliver immunisation
- Improve the sustainability of national financing for immunisation and increase predictability of global financing
- Shape vaccine markets to provide appropriate vaccines at sustainable prices

New vaccines and tiered pricing

** Pentavalent*  
(DTP3-HepB-Hib)  
2.58  

** Pneumococcal**  
3.50  

*** Rotavirus***  
(2.50)  

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>UNICEF/GAVI market</th>
<th>US public market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentavalent* (DTP3-HepB-Hib)</td>
<td>2.58</td>
<td>29.70</td>
</tr>
<tr>
<td>Pneumococcal**</td>
<td>3.50</td>
<td>91.75</td>
</tr>
<tr>
<td>Rotavirus***</td>
<td>(2.50)</td>
<td>55.73</td>
</tr>
</tbody>
</table>

* Average price per dose for 3-dose vaccines between 2006–2009.

** 2010 price for 13-valent vaccines (US public market) and price for AMC vaccines (UNICEF/GAVI market). Under the AMC, companies will receive an additional payment of US$ 3.50 per dose for approximately 20% of the total number of doses they provide. This additional payment is funded by donor commitments.

*** 2010 average price per dose assuming 3-dose equivalence among available products (US public market). Price through UNICEF not yet available.

Source: UNICEF Supply Division; CDC
GAVI: Children immunised with pneumococcal and rotavirus vaccines

Goal 5 of the National Vaccine Plan 2010

• *Increase global prevention of death and disease through safe and effective vaccination*

• *Lists 6 objectives and strategies for achieving the goal*

http://www.hhs.gov/nvpo/vacc_plan/
What Can Healthcare Providers Do? I

• Assure their patients are fully immunized for vaccines currently recommended in the US
• Assure their patients who are traveling receive all recommended vaccines for international travel (wwwnc.cdc.gov/travel/page/vaccinations.htm)
• Particularly important for measles for young infants – can vaccinate as young as 6 months (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6013a1.htm?s_cid=mm6013a1_w)
What Can Healthcare Providers Do? II

• Help make polio eradication a reality by working with local Rotary Clubs in their area
• Help in advocating with government officials about the importance of US government financial support and technical assistance for global immunization
• Volunteer for UNICEF
• A resource available from the American Academy of Pediatrics can be found at: [www2.aap.org/immunization/about/globalpartnerships.html](http://www2.aap.org/immunization/about/globalpartnerships.html)
Acknowledgments

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