Global Health Policy: Vaccines

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Department of Pediatrics
Children’s Hospital Colorado
Conflict of Interest

• Financial
  – Presiding a DSMB for sanofi-Pasteur
  – Conducted research studies sponsored by SP and Crucell vaccines (public health protocols)

• Potential membership biases
  – Member of the Global Advisory Committee on Vaccine Safety
  – Latin American Society for Infectious Diseases and the Committee for Future of Vaccines
Outline

• From protective technology to preventive policy
• Past, who, how, when?
• Drivers, partners and goals
• What are the challenges and barriers?
History of a Preventive Technology: Vaccines

- **Heroic era** (1891 => 1930s)

- **National public health**: Growth and divergence (1930 - 1990)

- **Global vaccination programs** (1960s - 2000s)

- **Biotechnology, partnerships and market** (>1990)
# Environments for Vaccine Policy

<table>
<thead>
<tr>
<th></th>
<th>TECHNOLOGY</th>
<th>ECONOMICS</th>
<th>POLITICS</th>
<th>REGULATION</th>
<th>LEGAL AND INTELLECTUAL PROPERTY</th>
<th>TECHNOLOGY TRANSFER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HEROIC</strong></td>
<td>Low</td>
<td>Low cost</td>
<td>Colonial policy plus altruism</td>
<td>Nearly absent</td>
<td>Absent</td>
<td>Institut Pasteur</td>
</tr>
<tr>
<td><strong>MID-CENTURY</strong></td>
<td>Moving</td>
<td>Increasing cost</td>
<td>National health programs</td>
<td>Strengthening from a low base</td>
<td>Absent</td>
<td>WHO, national institutes, meetings, education?</td>
</tr>
<tr>
<td><strong>ERADICATION PROGRAMS</strong></td>
<td>Moving</td>
<td>Pressure by buyers</td>
<td>Altruism, global budget issues</td>
<td>Strengthening WHO preQ</td>
<td>Nearly absent</td>
<td>WHO, expert groups, donor funding</td>
</tr>
<tr>
<td><strong>CURRENT</strong></td>
<td>High</td>
<td>High cost/low margin, economies of scale</td>
<td>Self-sufficiency, biotechnology, donor politics, market</td>
<td>High domestic and parallel WHO preQ</td>
<td>Strengthening but mainly on intermediates and processes</td>
<td>WHO DCVMN, biotech programs, corporate strategic</td>
</tr>
</tbody>
</table>

Adapted from jbarton@stanford.edu
Global Vaccination Programs

- Eradication campaigns
  - PAHO & smallpox – 1950-67
  - WHO - Global smallpox – 1967-77
  - WHO - Polio – 1985-200?

- EPI – 1974

- CVI – 1990

- GAVI – 2000

- Emergence of UNICEF/Rotary purchase system with tiered pricing
Smallpox Eradication

The success of global collaboration and programs

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Annual Count of Wild Poliovirus cases reported worldwide 1980-2010

No. of Poliomyelitis Cases, thousands

No. of Cases, thousands

Year

1293
1961 – 1st Schedule Published by WHO

TABLE 2. SUGGESTED SCHEDULE OF IMMUNIZATION IN AREAS WITH INADEQUATE MEDICAL SERVICES; TO BE MODIFIED AS REQUIRED TO SUIT LOCAL CONDITIONS

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccination</th>
<th>Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 weeks</td>
<td>(1) BCG vaccination</td>
<td>1st</td>
</tr>
<tr>
<td>3-9 months</td>
<td>(2) Smallpox vaccination</td>
<td>2nd and 3rd</td>
</tr>
<tr>
<td></td>
<td>(3) Diphtheria-pertussis-tetanus (triple vaccine with alum): 2 doses at an interval of one month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>The first injection could be given at the time of smallpox vaccination. Smallpox vaccination is verified at the second visit. Failures of smallpox vaccination are revaccinated.</td>
<td></td>
</tr>
<tr>
<td>School entry or soon thereafter</td>
<td>(4) Diphtheria/tetanus booster (plain or with alum)</td>
<td>4th and 5th</td>
</tr>
<tr>
<td></td>
<td>(5) TAB vaccination (where necessary): 2 doses at an interval of one month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(6) Smallpox revaccination: at the time of second TAB injection</td>
<td></td>
</tr>
<tr>
<td>10-14 years</td>
<td>(7) BCG revaccination (in tuberculin-negative reactors)</td>
<td>6th and 7th</td>
</tr>
<tr>
<td></td>
<td>(8) Smallpox revaccination</td>
<td></td>
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<tr>
<td></td>
<td>(9) TAB booster</td>
<td></td>
</tr>
</tbody>
</table>

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Courtesy of P. Duclos, WHO
About WHO

- WHO is the directing and coordinating authority for health within the United Nations system.
- It is responsible for providing leadership on global health matters
- Shaping the health research agenda
- Setting norms and standards
- Articulating evidence-based policy options
- Providing technical support to countries
- Monitoring and assessing health trends.
Vaccines for Used in Developing Country EPI Programs

1984
1. BCG
2. Diphtheria
3. Tetanus
4. Pertussis
5. Polio - OPV
6. Measles
7. (Yellow Fever)

Added/Adding
1. Hepatitis B
2. *H. influenzae* type b (Hib)
3. Mumps
4. Rubella
5. Rotavirus
6. Pneumococcal
7. *N. meningitidis*
8. HPV
9. Malaria
# EPI program success around the world

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>7,088</td>
<td>5,000</td>
<td>82%</td>
<td>92.8%</td>
<td>26%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>16,628</td>
<td>163,000</td>
<td>82%</td>
<td>85.8%</td>
<td>26%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>151,568</td>
<td>254,000</td>
<td>82%</td>
<td>92.4%</td>
<td>26%</td>
</tr>
<tr>
<td>Polio</td>
<td>1,731</td>
<td>&lt;1000</td>
<td>83%</td>
<td>96.3%</td>
<td>&gt;75%</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td></td>
<td>600,000</td>
<td>69%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Measles</td>
<td>281,972</td>
<td>*164,000</td>
<td>83%</td>
<td>93.6%</td>
<td>§ 58%</td>
</tr>
</tbody>
</table>

*2008, §>90% coverage

http://www.who.int/immunization_monitoring/diseases/en/
Economic Benefits of Immunization

Pre-Vaccine Era

Costs of treating more than 10 million cases of various diseases annually

Vaccine Era

Costs of vaccinating 3.8 million children each year against those same diseases

Direct costs

Indirect costs

Billions of dollars

12.65

44.96

1.99

2.43

If there were no immunization in the United States, 33,494 deaths and 10,541,569 cases of diphtheria, tetanus, pertussis, polio, measles, mumps, rubella, congenital rubella syndrome, Hib and hepatitis B infection could be expected each year.
U.S.A. Immunization Schedule

Recommended Immunization Schedule for Persons Aged 0 Through 6 Years—United States • 2011

For those who fall behind or start late, see the catch-up schedule

<table>
<thead>
<tr>
<th>Vaccine ▼</th>
<th>Age ▼</th>
<th>Birth</th>
<th>1 month</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
<th>12 months</th>
<th>15 months</th>
<th>18 months</th>
<th>19–23 months</th>
<th>2–3 years</th>
<th>4–6 years</th>
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<tbody>
<tr>
<td>Hepatitis B¹</td>
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<tr>
<td>Rotavirus²</td>
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<tr>
<td>Diphtheria, Tetanus, Pertussis³</td>
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<tr>
<td>Haemophilus influenzae type b⁴</td>
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<tr>
<td>Pneumococcal⁵</td>
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<tr>
<td>Inactivated Poliovirus⁶</td>
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<tr>
<td>Influenza⁷</td>
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<tr>
<td>Measles, Mumps, Rubella⁸</td>
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<tr>
<td>Varicella⁹</td>
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<tr>
<td>Hepatitis A¹⁰</td>
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<td>HepA (2 doses)</td>
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<tr>
<td>Meningococcal¹¹</td>
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This schedule includes recommendations in effect as of December 21, 2010. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Considerations should include provider assessment, patient preference, and the potential for adverse events. Providers should consult the relevant Advisory Committee on Immunization Practices statement for detailed recommendations: http://www.cdc.gov/vaccines/pubs/acip-list.htm. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS) at http://www.vaers.hhs.gov or by telephone, 800-822-7967. Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.
Measles Cases United States, 1962 - 2007

- 1963 Vaccine Licensed 1st Dose Recommendation
- 1989 2nd Dose Recommendation
- 2000 Elimination Declared

- 1-dose preschool coverage
- 2-dose adolescent coverage

- 1989-91 Resurgence

Measles Cases

% Measles Vax Coverage

Year

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Rapid communications

Measles is still a cause for concern in Europe

M. Muscat, H. Bang, S. Gittamann

1. EURACENET Hub, Department of Epidemiology, Statens Serum Institut, Copenhagen, Denmark

131 cases
17 importations
21 virologic evidence
D4 (10), D5 (9), H1 (2)

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Estimated Measles Cases in Africa, 2000-2010

>98% reduction deaths since 2000

Cost per death averted: $184

Source: MMWR 2011
Supported by a $37 million 4-year grant from GAVI/GVF

- *Haemophilus influenzae* type b (**Hib**) is a bacterium which can cause meningitis and severe pneumonia
- 3 million cases of serious illness and 400,000 deaths each year in children under 5 years of age from Hib
- In 2006, only 26% of children worldwide received **Hib vaccine**
- 1/3 of the countries eligible for funding from the GAVI Alliance (i.e., Gross national income/capita <$1000 per year) are using Hib vaccines
- The Hib Initiative focuses on coordination, communication and research.
Countries having introduced Hib vaccine in 1997 and 2009

1997
- 29 countries introduced
- 2 countries partially introduced

2009
- 158 countries introduced
- 2 countries partially introduced

Source: WHO/IVB database, July 2010
193 WHO Member States. Date of slide: 29 July 2010
Immunization Policy Advisory Framework

- Safety
- Standards
- Practice
- Burden assessment/modeling

Other WHO Technical Advisory Committees

Strategic Advisory Group of Experts (SAGE)

- Global policy recommendations & strategies
- Support regional/national challenges

Regional Technical Advisory Group

- Regional policies & strategies
- Identify & set regional priorities
- Monitor regional progress

Countries

National Technical Advisory Group on Immunization

• National Policies & Strategies
• Prioritize problems & define optimal solutions
• Implement national programme & monitor impact
Strategic Advisory Group of Experts (SAGE)

- Meetings and operational procedures
  - Two meetings a year (April and Nov)
  - Two preparatory teleconferences for each meeting
  - Only plenary sessions – transparent process
  - Extensive representation from key partner organizations
  - Experts invited as needed
  - Evidence-based
  - Background documents web and Yellow Book
  - Tracking sheet for follow-up on implementation of recommendations
  - Working groups
  - Agenda setting

- Strong links with Regional Technical Advisory Groups
- Report and communications

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

Contents
1. Meeting of the Immunization Strategic Advisory Group of Experts, November 2007 – conclusions and recommendations
15. Compendium

Meeting of the immunization Strategic Advisory Group of Experts, November 2007 – conclusions and recommendations

The Strategic Advisory Group of Experts (SAGE) on immunization met in Geneva, Switzerland, on 6-7 November 2007 to discuss issues ranging from vaccine research and development, to immunization delivery. Its purview extends beyond childhood immunization to all vaccine-preventable diseases. SAGE met on 6-7 November 2007 in Geneva, Switzerland.

Reunion du Groupe stratégique consultatif d’experts sur la vaccination, novembre 2007 – conclusions et recommandations

Le Groupe stratégique consultatif d’experts (SAGE) a tenu compte au Directeur général de l’OMS sur des questions allant de la recherche et développement à l’administration des vaccins. Son domaine de compétence s’étend au-delà de la vaccination des enfants à toutes les maladies épidémiques liées à la vaccination. Le SAGE s’est réuni du 6 au 7 novembre 2007 à Genève (Suisse).
Is SAGE delivering on Access, Equity & Ethics?

- Transparent, public appointment process
- Declaration of interests
- Regional representation on SAGE & Regional viewpoints
- Open plenaries & transparent decision making
- Public access to decisions
- Best evidence-based recommendations
- Impact based
- Guided by equity, ethics and access
GAVI
Global Alliance for Vaccines and Immunization
GAVI: Five Strategic Objectives

- Improve access to sustainable immunization services
- Expand use of all existing cost-effective vaccines
- Accelerate introduction of new vaccines
- Accelerate R&D on vaccines for developing countries, (HIV/AIDS, malaria and tuberculosis)
- Make immunization coverage a centrepiece in international development efforts
The Global Fund For Children’s Vaccines

GAVI Board
Establishes Principles recommendations on fund allocation

Contributors
Gates Foundation USA, UK, Norway, Netherlands, ...

The Fund
- Independent Board for fundraising & management
- Working Capital Account (at UNICEF) for vaccine procurement and resource disbursement
- Three Sub-accounts:
  - Immunization services
  - Vaccines & Safe injection materials
  - R & D (not yet active)

Financial Tools: Shares, matching grants
Vaccine procurement

Strengthened Immunization Services and New Vaccines Delivered in Countries

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What will the GAVI FUND Finance?

Basic Conditions
- GNP/capita < US$ 1000
- ICC or equivalent
- Immunization assessment in last 3 years
- Multi-year plan for immunization

DTP3 coverage
- <50% → Support for immunization services
- 50% - 80% → Support for immunization services and new and under-used vaccines
- >80% → Support for new and under-used vaccines
Coverage of DTP3 Hepatitis B and Hib immunisation in GAVI-eligible countries

Projections

Estimated costs & financing gaps for immunisation, 2006-15

- **Campaign** ($2.2 Bn, 6%)
- **Vaccines** ($11.5 Bn, 33%)
- **Systems** ($20.8 Bn, 61%)
- **Funding Gap** ($12.9 Bn, 40%)
- **GAVI / IFFIm** ($4.9 Bn, 15%)
- **Govt** ($8.7 Bn, 27%)
- **External Donor** ($5.7 Bn, 18%)

Cost per Capita: $1.0
Funding Gap per Capita: $0.32

Source: Global Immunisation Vision and Strategy – WHO costing
Estimated Global Distribution of Rotavirus-related Deaths (from Parashar, 2006)

- Africa: 229,701
- Asia: 289,354
- Latin America: 18,981
- Europe and Canada: 125
- United States: 11,838
Forecasted Rotavirus Demand—Doses—All Regions

Forecasted Demand, Doses (1000x Doses)

Approximately 160 million doses in peak year 2021—for 64 GAVI-eligible countries
UNICEF is the world’s largest **purchaser of vaccines** for developing countries and a key partner in global immunisation efforts.

Its supply division, based in Copenhagen, is responsible for global purchasing, including some **$100 million per year spent on vaccines and safe injection equipment**.
Who produces the vaccines of the world?

6.3 Billion Dose Global Market

- Sanofi Pasteur: 14%
- GSK: 20%
- Merck: 1%
- Wyeth: 1%
- Chiron: 7%
- Others: 57%

Source: WMA 2004, SP Internal
Note: SP MSD sales split by origin

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Who shares the market from the vaccines of the world? (2008)

- Novartis: 8.0%
- Wyeth: 12.3%
- GSK: 21.2%
- Pfizer: 12.3%
- Merck: 21.6%
- Sanofi Aventis: 21.8%
- Others: 15.0%

€15 B Global Market

(1) Based on reported FY2008 results and sanofi-aventis internal estimates for “Others”
(2) Includes 50% of Sanofi Pasteur MSD joint venture sales
The free market has given rise to tiered pricing

Figure 21: Tiered pricing: vaccine prices in different markets

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>UNICEF/GAVI Market</th>
<th>US Public Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monovalent* (HepB)</td>
<td>0.21</td>
<td>8.65</td>
</tr>
<tr>
<td>Tetravalent* (DTP3-HepB)</td>
<td>0.88</td>
<td>27.19</td>
</tr>
<tr>
<td>Pentavalent* (DTP3-HepB-Hib)</td>
<td>3.52</td>
<td>29.70</td>
</tr>
<tr>
<td>Pneumococcal**</td>
<td>7.00</td>
<td>70.29</td>
</tr>
<tr>
<td>Rotavirus***</td>
<td>?</td>
<td>55.73</td>
</tr>
</tbody>
</table>

* Average price per dose for 3-dose vaccines between 2006-2009
** 2010 price for 7-valent vaccines (US public market) and price for AMC vaccines (UNICEF/GAVI market)
*** 2010 average price per dose assuming 3-dose equivalence among available products (US public market)

Source: UNICEF Supply Division, CDC Vaccine Price List
Social Problems for the 21\textsuperscript{st} Century

- Safety and Acceptance
- Cost and Availability
- Sufficient Production
We still could reduce 1/5 of childhood deaths with current or upcoming vaccines.

**Causes of Death for Children Under Age 5**

- **42%** Neonatal
- **8%** Malaria
- **10%** Diarrhea (rotavirus)
- **5%** Diarrhea (non-rotavirus)
- **5%** Pneumonia (Pneumococcus)
- **8%** Pneumonia (non-Pneumococcus)
- **19%** Other

Total under-5 deaths in 2008 = 8.8 million

2% AIDS

1% Measles

Preliminary estimates by the Child Health Epidemiology Reference Group of WHO and UNICEF.
Global Immunization Vision and Strategy (GIVS) for the period 2006-2015

- UNICEF/WHO initiative
- Reduce mortality due to vaccine-preventable diseases by 2/3 by 2015
- Reach 90% coverage by 2015
- Introduce new vaccines (which?)
- Can we afford GIVS? Wolfson et al. (2008) try to answer this!
• Investment in vaccines by governments and the private sector
• Vaccines the number-one priority at the Gates Foundation
• Prevent the deaths of some 7.6 million children under 5 from 2010-2019
• 1.1 million children could be saved with the rapid introduction of a malaria vaccine beginning in 2014
Final Remarks on Vaccine Policy

• One of the most effective and equitable health preventive technologies
• Global Policy requires sound epidemiology, science, commitment and partnership
• Use of vaccines is key to their preventive success
• Addressing the safety and societal concerns is a priority