

“Vaccine Preventable Diseases and Immunization Programs”

Paul K. Drain, MD, MPH
Massachusetts General Hospital and
Brigham and Women’s Hospital

pdrain@partners.org

Created: April 2007

Revised: May 2012

Prepared as part of an education project of the Global Health
Education Consortium and collaborating partners

Medical Student Reviewers

- Jonathan Abelson, MD
 - University of Virginia School of Medicine
 - jonathanabelson@gmail.com
- Mary MacLennan, MSc
 - World Health Organization
 - Mary.maclennan@gmail.com
- Nilofer Khan Habibullah, MD
 - American International Medical University
 - Nilofer.habibullah@gmail.com

Learning objectives

1. Understand major vaccine-preventable diseases recommended in developing countries.
2. Understand other available vaccines and candidate vaccines.
3. Understand major challenges for national immunization programs in developing countries.

Presentation Outline

- **Immunization Background and Epidemiology**
- Major Vaccine-Preventable Diseases
- Other Vaccine-Preventable Diseases
- Candidate Vaccines
- Immunization Programs
- Summary
- Self-assessment Quiz

Immunization Background and Epidemiology

- Vaccine-preventable diseases responsible for nearly 20% of the 8.8 million deaths/year among children <5 years
- In 1974, <5% of children were immunized in their first year against 6 targeted diseases
- World Health Organization launched Expanded Programme on Immunization (EPI) in 1974 to develop and expand immunization programs around the world
 - As a result, by 2005, 80% of children immunized in their first year against 6 targeted diseases
 - EPI efforts prevent an estimated 3 million deaths/year

Notes on: Immunization Background and Epidemiology

Resources: The Expanded Programme on Immunization (EPI) was established in 1974 through a World Health Assembly resolution (resolution WHA27.57) to build on the success of the global smallpox eradication programme, and to ensure that all children in all countries benefited from life-saving vaccines.

-The first diseases targeted by the EPI were diphtheria, whooping cough, tetanus, measles, poliomyelitis and tuberculosis.

-- The Expanded Programme on Immunization remains committed to its goal of universal access to all relevant vaccines for all at risk. The programme aims to expand the targeted groups to include older children, adolescents and adults and work in synergy with other public health programmes in order to control disease and achieve better health for all populations, particularly the underserved populations.

-References:

Global Immunization Data - March 2012 -- http://www.who.int/immunization_delivery/en/
Keja K et al. Expanded programme on immunization. [World Health Stat Q.](#) 1988;41(2):59-63.

Immunization Background and Epidemiology

- Vaccinations are one the most successful and cost-effective public health investments
 - 1980, global smallpox eradication achieved.
 - 1988, polio targeted for global eradication with infections falling by 99%
- Original six basic EPI vaccines for developing countries
 - Bacille Calmette Guerin (BCG), Polio, Diphtheria, Pertussis, Tetanus, Measles
- Coverage levels of measles vaccine is an indicator for one of the Millennium Development Goals.

Notes to: Immunization Background and Epidemiology

Resources: [Smallpox](#): An immunization campaign carried out by the World Health Organization (WHO) from 1967 to 1977 resulted in the eradication of smallpox. When the programme began, the disease still threatened 60% of the world's population and killed every fourth victim

[Polio: http://www.ted.com/talks/bruce_aylward_how_we_ll_stop_polio.html](http://www.ted.com/talks/bruce_aylward_how_we_ll_stop_polio.html)

Also on polio: Since the launch by WHO and its partners of the Global Polio Eradication Initiative in 1988, infections have fallen by 99%, and some five million people have escaped paralysis.

Only four countries remain endemic – Afghanistan, India, Nigeria and Pakistan – down from more than 125 countries in 1988.

-Millennium Development Goals / MDGs:

Goal 1: Eradicate extreme poverty and hunger; Target Halve, between 1990 and 2015, the proportion of people whose income is less than \$1 a day

Goal 2: Achieve universal primary education; Target Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary Schooling

Goal 3: Promote gender equality and empower women: Target Eliminate gender disparity in primary and secondary education, preferably by 2005, and in all levels of education no later than 2015

Goal 4: Reduce child Mortality: Target Reduce by two thirds, between 1990 and 2015, the underfive mortality rate

Goal 5: Improve maternal Health: Target Reduce by three quarters, between 1990 and 2015, the maternal mortality ratio

Goal 6: Combat HIV/AIDS, malaria and other Diseases: Target Have halted by 2015 and begun to reverse the spread of HIV/AIDS

Goal 7: Ensure environmental Sustainability: Target Integrate the principles of sustainable development into country policies and programmes and reverse the loss of environmental resources

Goal 8: Develop a global partnership for development

- Launched in 2006 as a ten-year framework to control morbidity/mortality from vaccine-preventable diseases
- Primary aims:
 - Immunize more people against more diseases
 - Introduce a range of newly available vaccines
 - Integrate vaccinations with basic health interventions
 - Manage vaccination programmes within the context of global interdependence
- Estimates saving more than 5.5 million future deaths

References: GAVI alliance. The recent launch of the advance market commitment, through the GAVI Alliance, has accelerated the introduction of the pneumococcal conjugate vaccine in the poorest countries. The vaccine has been introduced in five low-income countries and another 11 countries are planning to introduce it in 2011. Countries are expected to introduce rotavirus vaccines in increasing numbers, starting in 2011. Large-scale immunization campaigns with a meningococcal A conjugate vaccine, produced in India through technology transfer facilitated by the Program for Alternative Health Technologies and WHO and with financial support from the Bill & Melinda Gates Foundation, was initiated in Burkina Faso, Mali and Niger in September 2010. Financial support for procuring this vaccine, which was made available at a price of less than US\$ 0.50 per dose for the preventive campaigns, was provided by the GAVI Alliance. SIXTY-FOURTH WORLD HEALTH ASSEMBLY

Presentation Outline

- Immunization Background and Epidemiology
- **Major Vaccine-Preventable Diseases**
- Other Vaccine-Preventable Diseases
- Candidate Vaccines
- Immunization Programs
- Summary
- Self-assessment Quiz

Major Vaccine-preventable diseases

- Tuberculosis - Bacille Calmette Guerin (BCG) vaccine
- Diphtheria
- Hepatitis B
- Measles
- Pertussis
- Polio
- Tetanus
- Yellow Fever

BCG vaccine: Uses and Benefits

- First used in 1921 as freeze-dried (“lyophilized”) live attenuated vaccine of *Mycobacterium bovis*
- In areas with high TB burden, all newborns should receive single dose at birth
- In areas with low TB burden, countries may choose to limit vaccination to high risk groups
- Most effective in preventing TB meningitis and military TB (disseminated) in infants
- Good evidence for also protecting against *Mycobacterium leprae* (leprosy)

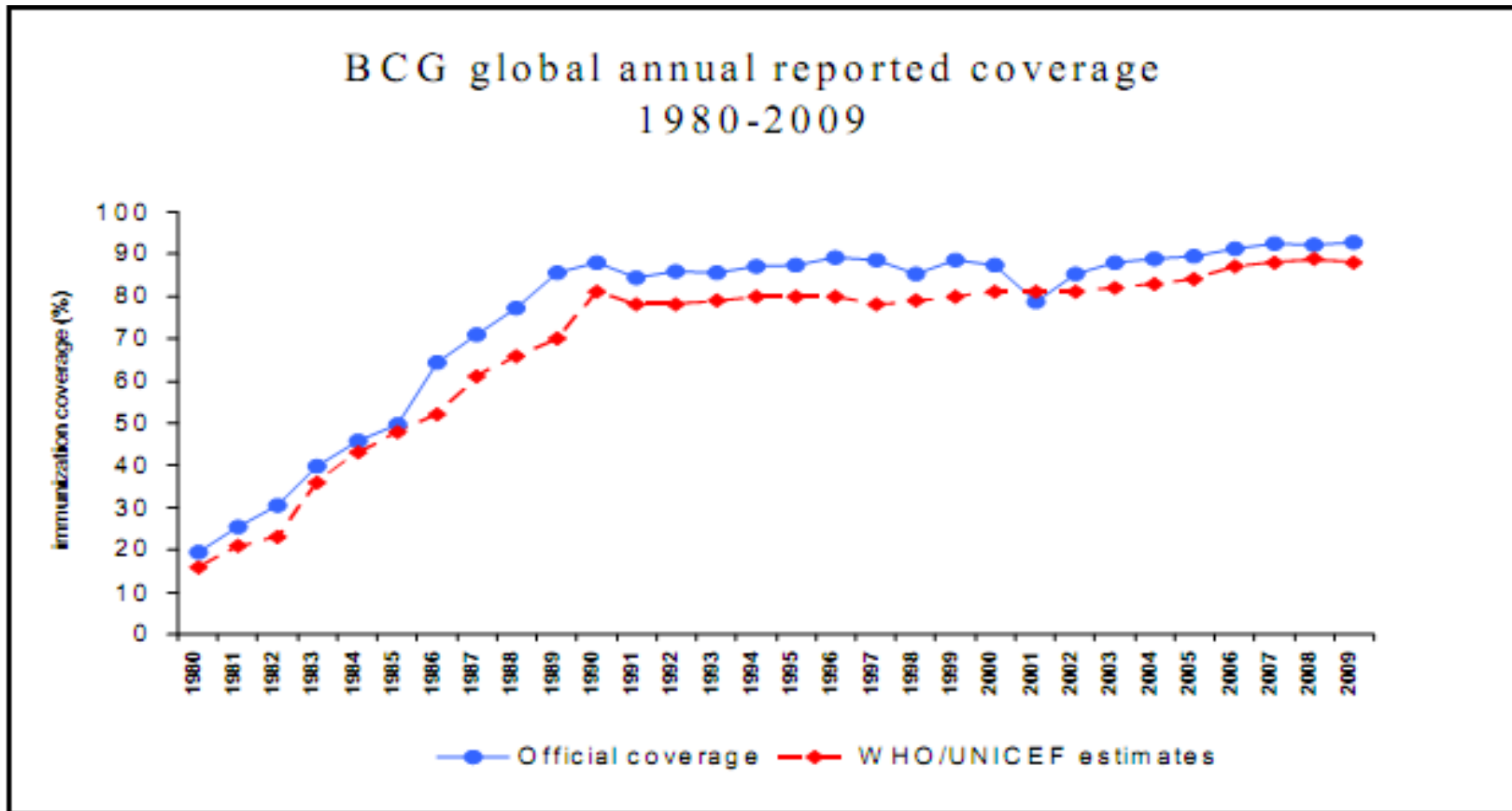
World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

BCG vaccine: Limitations and Concerns

- Does NOT prevent primary infection with TB or reactivation of latent pulmonary infection
- Some developed countries, such as the United States, do NOT vaccinate with BCG
- Often causes a scar at the injection site
- May distort reading tuberculin skin test (PPD), one of the primary methods for screening for latent TB
- Concern for use in immune compromised people (HIV/AIDS) since live attenuated vaccine could reactivate and cause infection

Tuberculosis is contagious and airborne. <http://www.who.int/wer/2004/en/wer7904.pdf>

BCG coverage among 160 countries



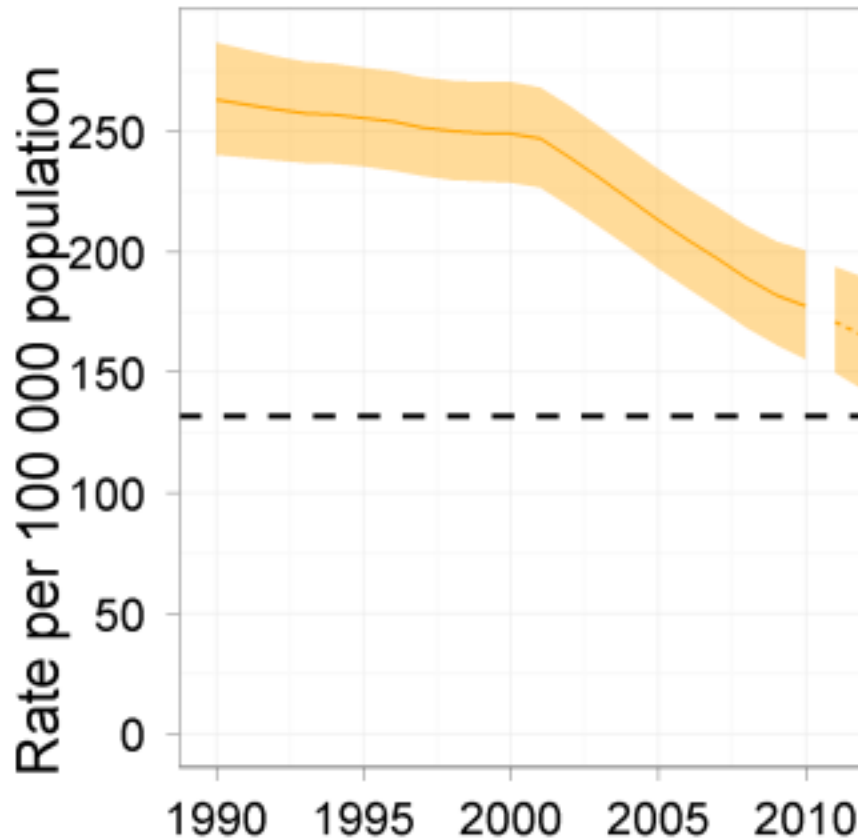
World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.

Notes to BCG coverage among 160 countries

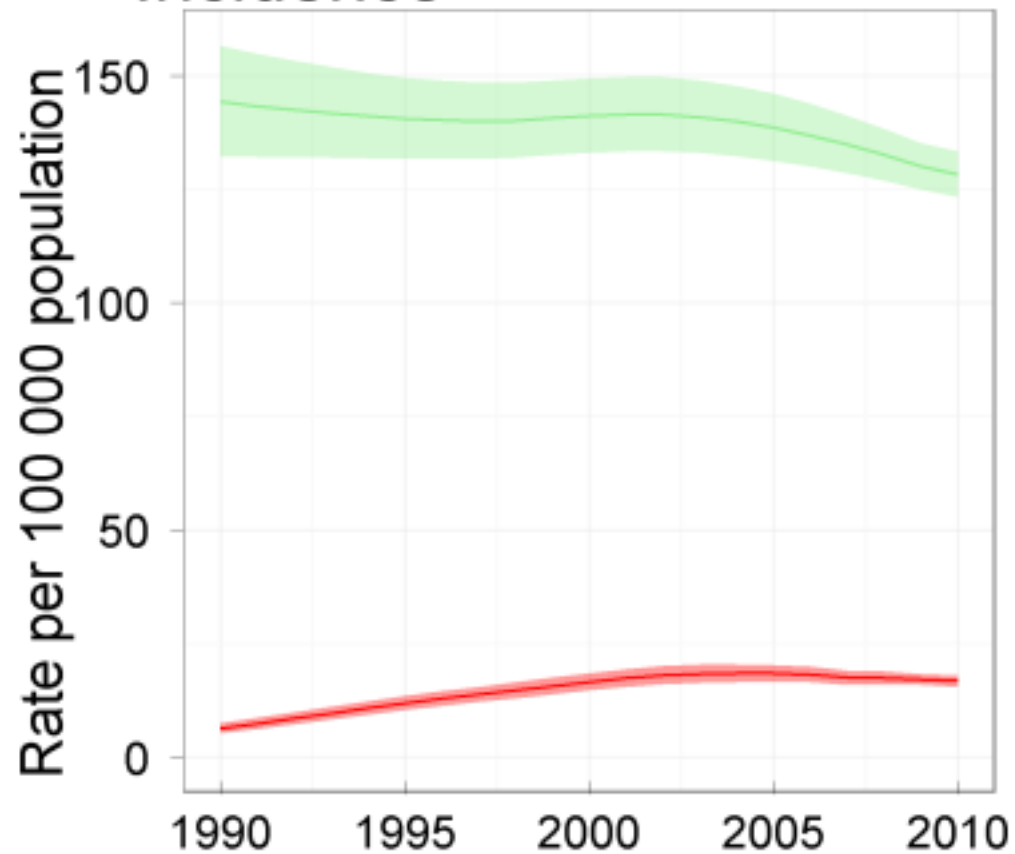
REFERENCES: BCG coverage increased during the 1980s due to increasing numbers of Member States establishing national immunization services and increasing BCG coverage in these Member States. BCG coverage peaked in 1990 as a result of the push to achieve the goals for Universal Childhood Immunization through routine immunization services, and campaigns focusing on unreached children. Reported coverage remained high throughout the 1990s. The drop at global level observed from 2000 to 2001 was mainly the result of a change in the methodology used to produce official national estimates in two Member States, China and India which, because of the size of their infant populations, had a significant impact on the global figure. The decline was less pronounced in the WHO/UNICEF estimates and the two figures converged. The reported figures and the WHO/UNICEF estimates differ again from 2002. This is again mainly because of China and India where the official estimates are higher. In many Member States BCG is administered at or shortly after birth. For births occurring in hospital settings, the BCG is often given by hospital staff, with the dose not being reported through the regular immunization reporting. If so, this can lead to underreporting of the number of BCG doses administered, as can be demonstrated through surveys. BCG is often used to reflect the proportion of children who are protected against the severe forms of tuberculosis during the first year of life, and also as an indicator of access to health services. WHO

Global Tuberculosis Control Report

Prevalence



Incidence



BCG Vaccine: Challenges

- Global annual TB mortality is approximately 3 million people, of which 95% reside in developing countries
- 83% of target population vaccinated among developing countries in 2005*
- BCG vaccine has limited ability to reduce transmission of TB, so controlling spread of TB will rely on diagnosis and treatment
- Current challenges for TB lie in treatment of multidrug-resistant TB, with just 16% of patients receiving correct treatment

*In 2010, estimated prevalence of 650,000 cases of multidrug-resistant TB (MDR-TB), with just 16% receiving treatment 12% of newly diagnosed TB patients in 2009 were HIV positive --

<http://www.who.int/mediacentre/factsheets/fs104/en/index.html> SUMMARY

WHO Global Tuberculosis Control Report 2010 (www.who.int/tb/publications/2010/factsheet_tb_2010.pdf)

Diphtheria Toxoid: Uses and Benefits

- Protects against *Corynebacterium diphtheriae*
- Vaccine consists of diphtheria toxoid proteins that induce immunity
- Usually combined with tetanus toxoid and whole cell or acellular pertussis vaccines (DTP or DTaP) for children
- Intramuscular injection in outer mid-thigh for infants and outer upper arm for children and adults
- Combined with tetanus vaccine (Td) as booster depending on national immunization programs

REFERENCES: 5'000 estimated deaths (in 2004)

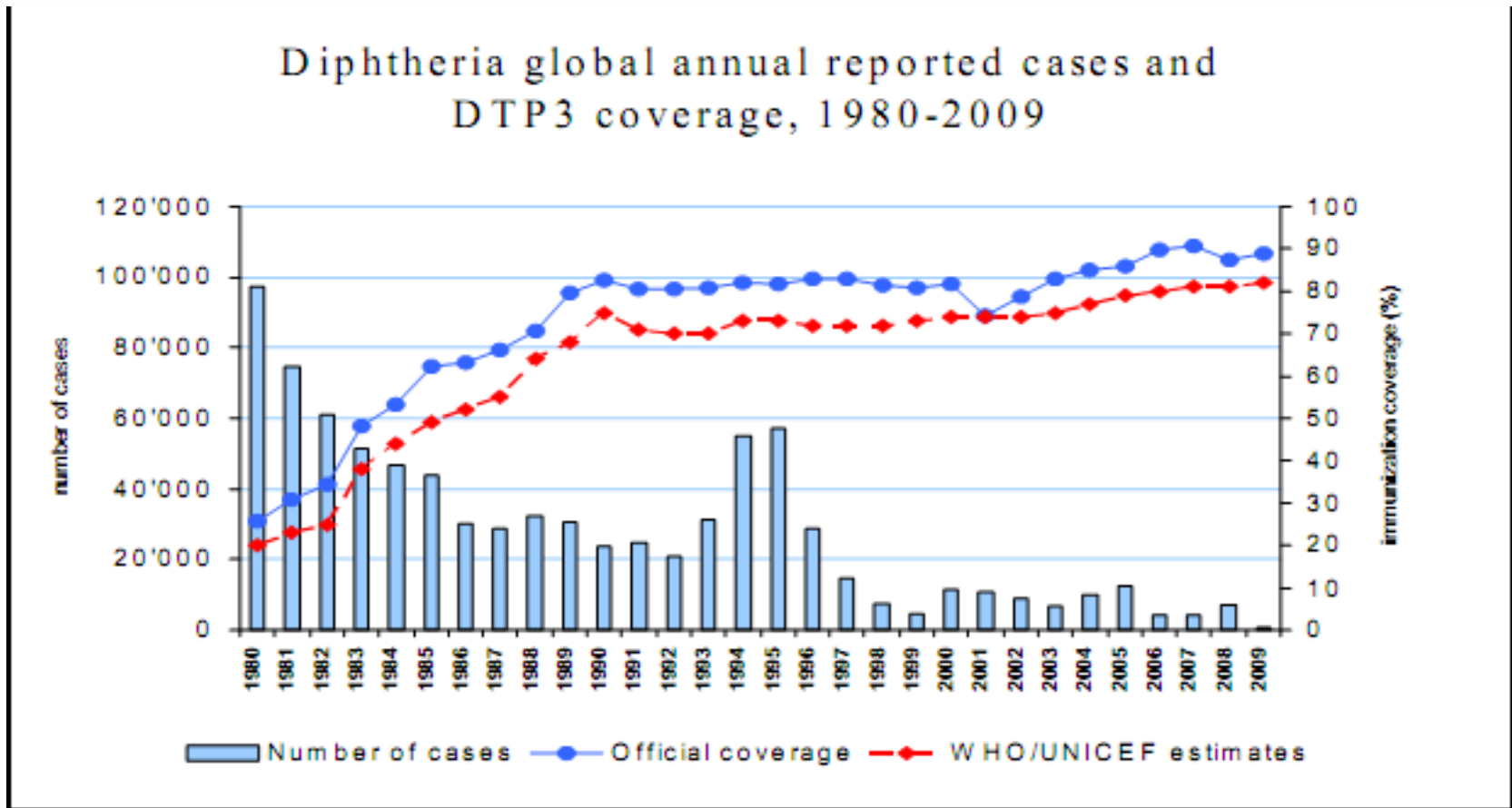
http://www.who.int/immunization_monitoring/diseases/diphtheria/en/

Diphtheria Toxoid: Limitations and Concerns

- Dosing schedule requires follow-up, which decreases compliance
 - Administer three primary DTP doses (usually at 6, 10, 14 weeks) and one DTP booster (18 months to 6 years)
- Vaccine must NOT be frozen; store at 2-8 degrees Celsius
- Up to 50% of children receiving vaccine may develop local reaction at site of injection

REFERENCE: Diphtheria vaccine, WHO position paper

Diphtheria cases/coverage among 160 countries



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.

Notes to: Diphtheria cases/coverage among 160 countries

Resources: An estimated 19.3 million children under the age of one did not receive DTP3 vaccine in 2010. Seventy percent of these children live in ten countries, including Afghanistan, Democratic Republic of the Congo, Ethiopia, India, Indonesia, Iraq, Nigeria, Pakistan, South Africa and Uganda. Global Immunization Data (www.who.int/entity/immunization.../Global_Immunization_Data.pdf) – March 2012

REFERENCES: DTP3 coverage increased during the 1980s because increasing numbers of Member States established national immunization services and also increased coverage. It peaked in 1990 as a result of the push to achieve Universal Childhood Immunization through routine services and through campaigns. Reported coverage remained high during the 1990s. The drop at global level observed from 2000 to 2001 was mainly the result of a change in the methodology used to produce official national estimates in two Member States, China and India which, because of the size of their infant populations, had a significant impact on the global figure. The decline was less pronounced in the WHO/UNICEF estimates and the two figures converged. The reported figures and the WHO/UNICEF estimates differ again from 2002. This is mainly because of China and India where the official estimates are higher. DTP3 coverage data are used to reflect the proportion of children protected against diphtheria, pertussis and tetanus, and to indicate performance of immunization services and the health system in general. DTP3 figures are also compared with DTP1 to assess "drop-out" rates — an indicator of the quality of services and managerial capacity. The Member State profiles also show district achievements (percentage of districts achieving various levels of DTP3 coverage). Diphtheria incidence is affected by DTP3 coverage and booster doses using DT and Td (see immunization schedules in the Member State profiles). The decline in reported diphtheria cases in the 1980s is consistent with the reported increasing DTP3 coverage. **The sudden increase in incidence during the 1990s is due to an epidemic in Member States of the former Soviet Union. Since 1990, outbreaks were also reported from Algeria, Iraq, the Lao People's Republic, Mongolia, Papua New Guinea, the Sudan, and Thailand.** Reported data on diphtheria incidence should be interpreted with caution due to variations in case definitions used and performance of surveillance systems. The decrease in the number of cases from 2008 is mainly due to India not reporting incidence data in 2009. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.1

Diphtheria Toxoid: Challenges

- About 23 million children <1 year do not receive the 3rd dose of the DTP vaccine (DTP-3)
 - 70% of these children live in 10 countries, and >50% live in India and Nigeria.
- Incidence affected by DTP-3 coverage and booster doses using DT and Td; decline in reported diphtheria cases in the 1980s consistent with increasing coverage
- 87% and 75% of target population vaccinated with first and third doses, respectively, among developing countries in 2005.¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006. -- 89% of population vaccinated with third doses globally in 2009 (WHO Vaccine Preventable Diseases: monitoring system, 2010 global summary)

Hepatitis B vaccine: Uses and Benefits

- Protects against Hepatitis B virus (HBV)
- Recombinant DNA or plasma-derived antigen vaccine
- All infants should receive 1st dose of hepatitis B vaccine within 24 hours after birth, since perinatal is an important cause of chronic infections globally
- Routine childhood immunization in 177 countries
- The primary 3-dose vaccine series induces protective antibody concentrations in >95% of healthy infants, children, and young adults

Hepatitis B vaccine: Limitations and Concerns

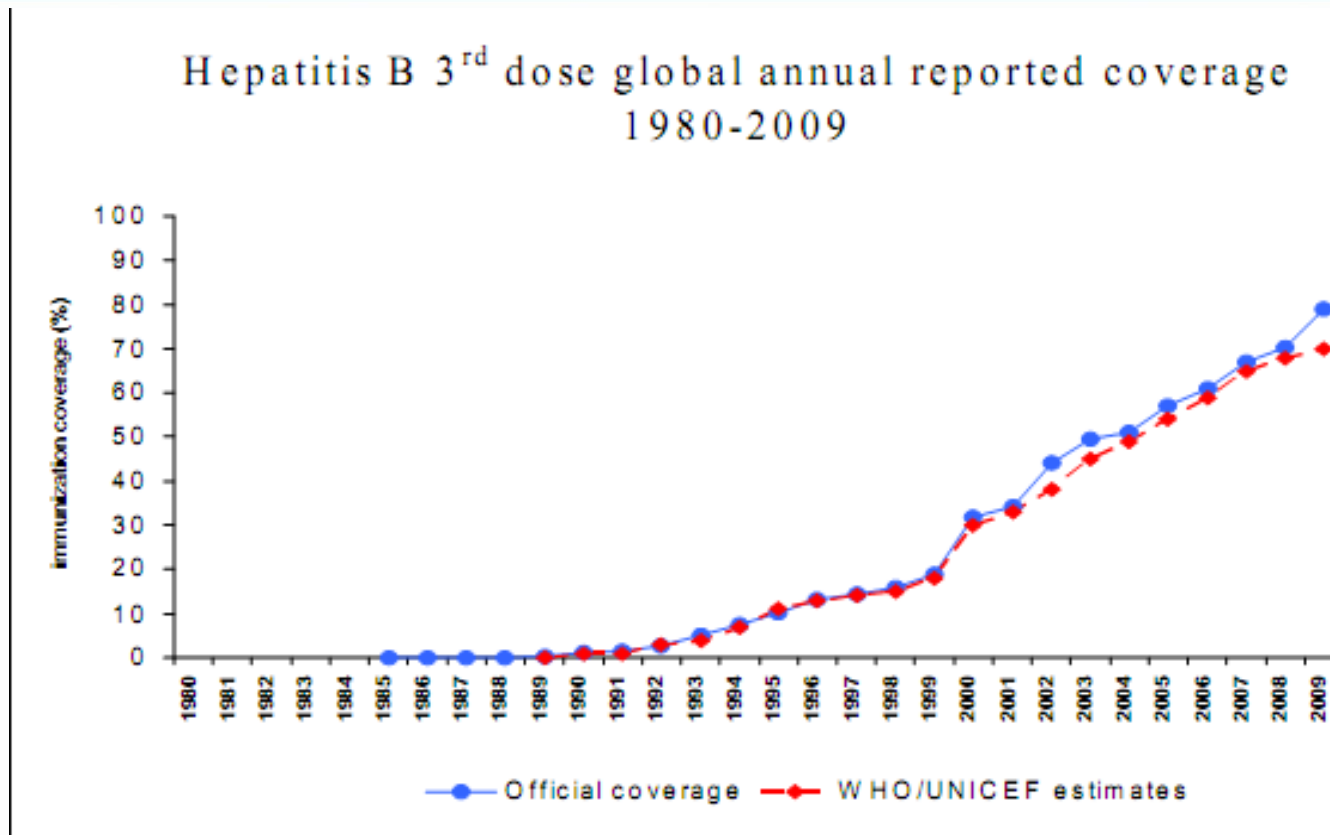
- Dosing schedule requires three doses over 6 months
- Must NOT be frozen, store between 2-8 degrees Celsius
- 1-6% may develop a fever within 24 hours, but considered a very safe vaccine
- Contraindicated only in patients with history of allergic reaction to vaccine components

As of 2008, 177 countries had incorporated hepatitis B vaccine as an integral part of their national infant immunization programmes, and an estimated 69% of the 2008 birth cohort received 3 doses of hepatitis B vaccine.⁷ In 2006, the last year for which such data are available, approximately 27% of newborns worldwide received a birth dose of hepatitis B vaccine.

Weekly epidemiological record, Relevé épidémiologique hebdomadaire

2 October 2009, 84th year / 2 octobre 2009, 84e année

No. 40, 2009, 84, 405–420. <http://www.who.int/wer>. <http://www.who.int/wer/2009/wer8440.pdf>



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.

REFERENCES: HepB3 coverage has steadily increased since 1990 due to the increasing numbers of Member States introducing hepatitis B vaccine into their routine immunization services, as well as increasing coverage in these Member States. Since 2008, in South-East Asia Region, there was an increase in the reported national coverage estimates. This is mainly due to phased introduction of the vaccine in India. HepB3 coverage data are critical to estimate the impact of the vaccine on chronic infection with hepatitis B and its deadly sequelae (hepatoma and cirrhosis). World-wide annual deaths from hepatitis B infection (2002) were estimated by WHO at 600'000.

Hepatitis B vaccine: Challenges

- In 2006, approximately 27% of newborns worldwide received a birth dose of hepatitis B vaccine
- 57% of target population vaccinated with third dose among developing countries in 2005¹
- Worldwide mortality rate from Hep B estimated (2002) at 600,000/year
- Catch-up strategies to vaccinate older age groups or high-risk groups may be needed in countries with endemicity to hasten population-based immunity

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006. Also: <http://www.who.int/wer/2009/wer8440.pdf>

Measles vaccine

- Globally, estimated 30-40 million cases occur annually
 - Immunization peaked in 1990 due to Universal Childhood Immunization programs
 - Estimated measles mortality was 873,000 in 1999
 - Estimated global mortality rates was 164,000 in 2008
- 90% of deaths occur among children <5 years of age
- Represents about 50% of deaths attributable to vaccine-preventable diseases in childhood
- 75% of target population vaccinated among developing countries in 2005¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Measles vaccine: Uses and Benefits

- Freeze-dried preparation of live attenuated virus
- Single dose administered by sub-cutaneous injection at 9 months of age
- In most developed countries, measles is combined with mumps and rubella (MMR) and is administered around 12-15 months. Second dose at 4-6 years of age.
- In 2005, MMR combined with Varicella (chickenpox) MMRV was licensed¹
- By 2009, 136 of 193 member states recommended 2nd dose for measles in routine immunization schedules.

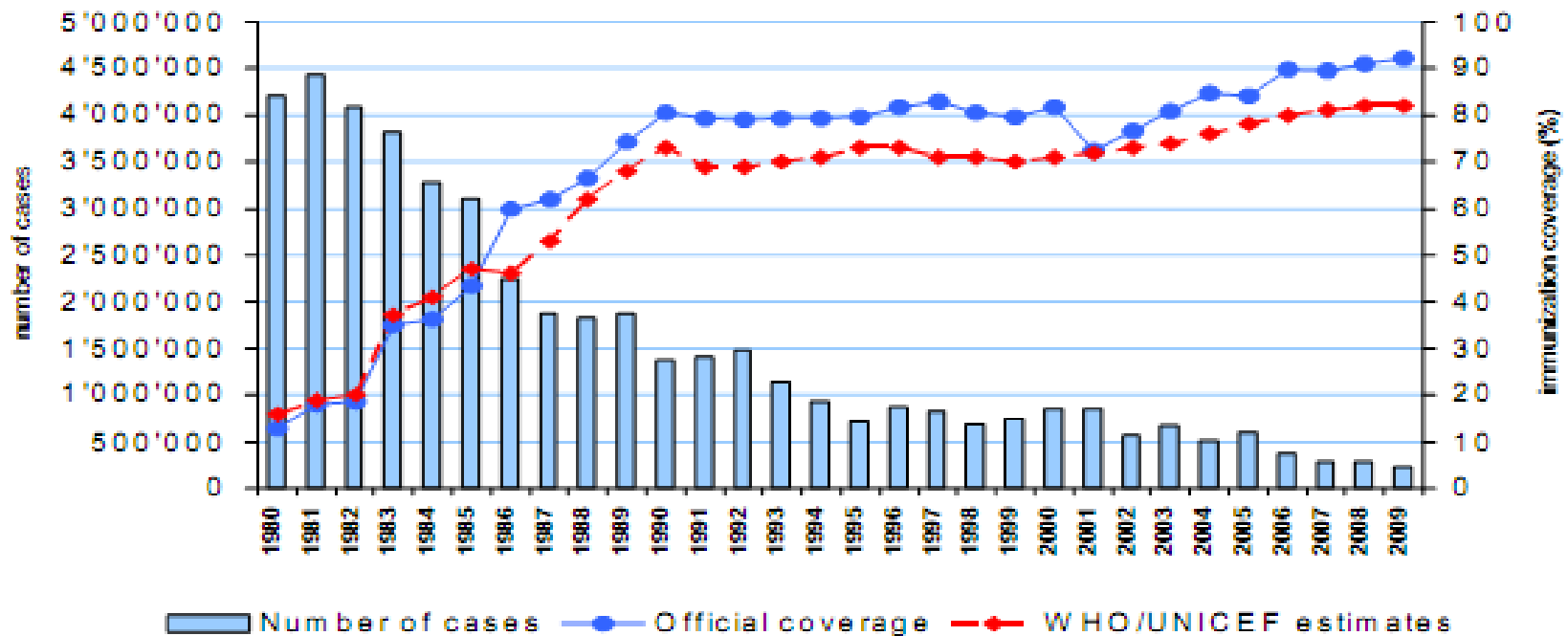
1. Vaccines and Preventable Diseases: Measles Vaccination. Centers for Disease Control and Prevention (CDC) <http://www.cdc.gov/vaccines/vpd-vac/measles/default.htm#concerns>

Measles vaccine: Limitations and Concerns

- Febrile seizures occur, but are very rare
- Early findings from an ongoing CDC study show that children who get an MMRV vaccine may be twice as likely to have a febrile seizure 7-10 days than children who get MMR and varicella vaccines (2 shots)¹

1. MMRV Vaccine Safety: Febrile Seizures and MMRV http://www.cdc.gov/vaccinesafety/Vaccines/MMRV/MMRV_qa.html#3

Measles global annual reported cases and MCV coverage, 1980-2009



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.

Drop in 2000-02 was due to change in methodology used for national reporting at China and India. Decrease in 2005-06 is due to control in WHO Africa region. Decrease in 2007 in the WHO European region is due to member states not reporting.

Pertussis vaccine

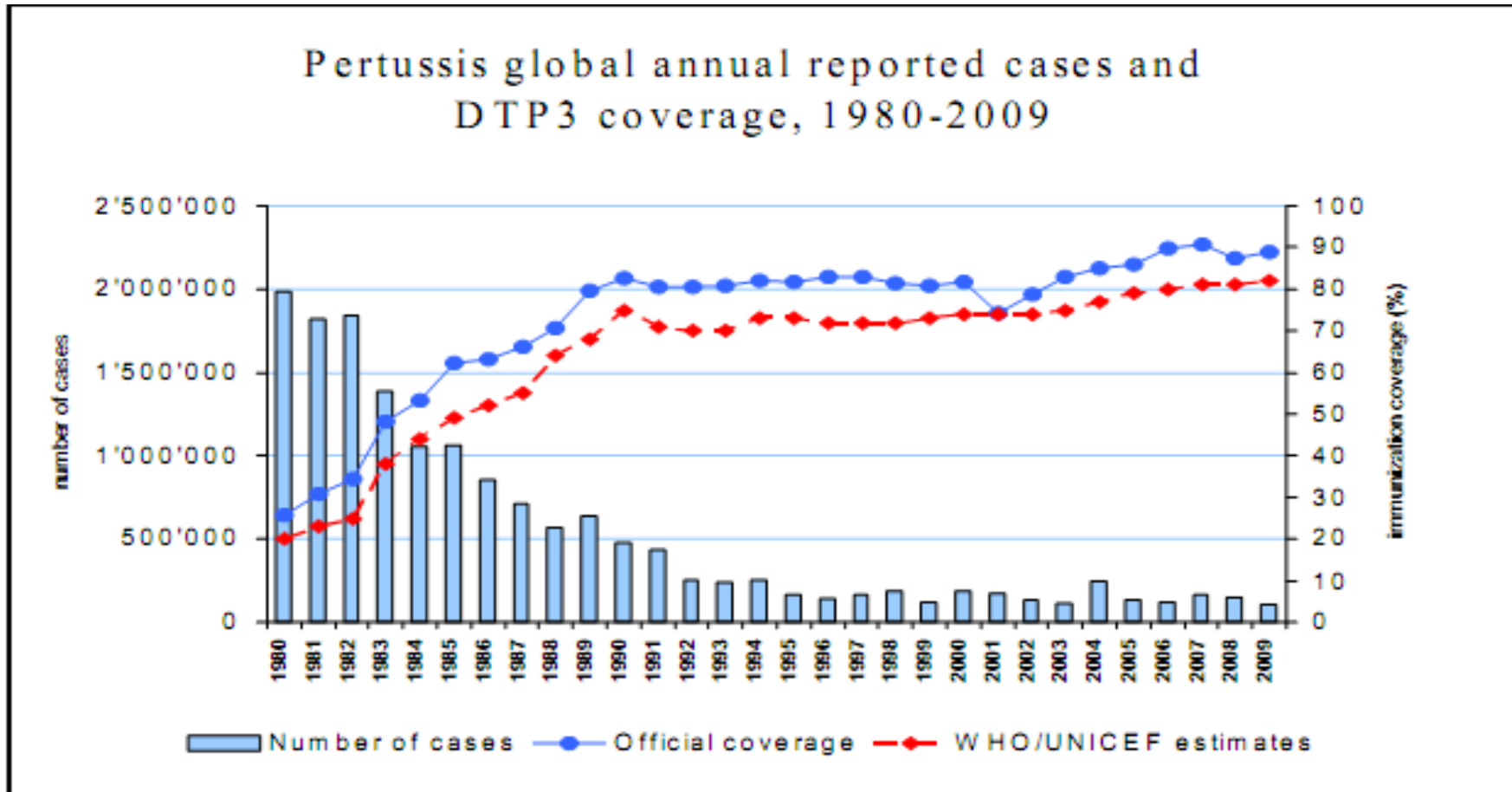
- Global annual mortality estimated at 195,000 people in 2008, by WHO. Nearly all deaths were among children <5 years
- Acellular pertussis used in minority of developing countries (as of 2009, 53 member states used acellular vaccine)
- Reporting variations are due to outbreaks (e.g., Switzerland 1994-95) and decreased uptake of vaccine due to concerns of side-effects (e.g., Japan)
- Epidemiology shifting to older age groups in U.S. and Canada
- 87% and 75% of target population vaccinated with first and third doses, respectively, among developing countries in 2005.¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Pertussis vaccine: Uses and Benefits

- Vaccine available in two forms:
 - Whole-cell killed pertussis bacteria (greater risk for neurological complications)
 - Acellular purified immunogenic components of the bacteria (more recent, reduced risk for neurological complications)
- Either vaccine requires three doses to elicit strong immune response.

Pertussis cases/coverage among 193 countries



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010. Global decline during 1980s is due to increased immunizations coverage.

Polio virus

- Eradication campaign launched in 1988
- By January 2012, only 3 countries remained endemic (Pakistan, Afghanistan, Nigeria)
- India marked polio eradication on 13th January 2012
- 2,033 reported cases in 2005
- 76% of target population vaccinated with third dose among developing countries in 2005¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Polio vaccine: Uses and Benefits

- Vaccine available in two forms:
 - Live attenuated virus given by mouth (Sabin)
 - Killed virus given by injection (Salk)
- Each vaccine contains strains of three different types of poliovirus (types 1, 2 and 3)
- Three doses to infants at 6, 10, and 14 weeks of age
- Live attenuated vaccine used in developing countries to allow for transmission and herd immunity

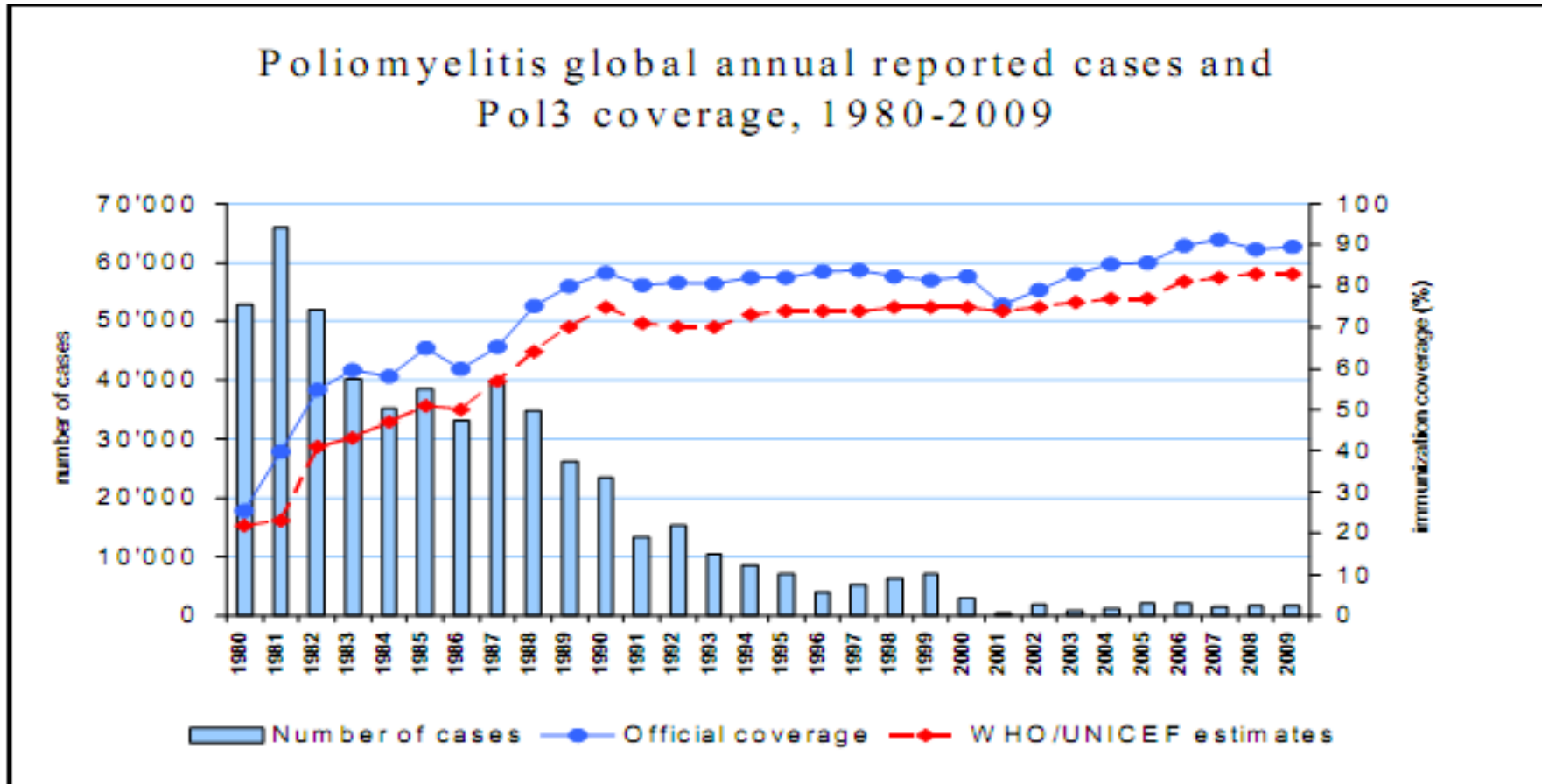
Polio eradication program+ <http://www.polioeradication.org/>

Polio vaccine: Salk and Sabine

- The Salk vaccine, made in 1952, constitutes killed poliovirus given as a shot.
- The second polio vaccine licensed, created by Albert Sabin, was an oral polio vaccine, which was made by using a weakened version of the poliovirus.
- By 1963, a formulation of this vaccine which prevented three strains or types of polio was available — like the Salk vaccine before it

Vaccines and Preventable Diseases: Polio-The Unprotected Story
<http://www.cdc.gov/vaccines/vpd-vac/polio/unprotected-story.htm>

Polio cases/coverage among 193 countries



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.

Polio coverage peaked in 1990s due to Universal Childhood Immunization Programs. Steep drop observed between 2000-01 is due to change in estimating methodology of China and India.

Tetanus toxoid vaccine

- Protects against *Clostridium tetanus*.
- Formaldehyde-inactivated preparation of tetanus toxin absorbed into aluminum salts.

Tetanus toxoid vaccine: Uses and Benefits

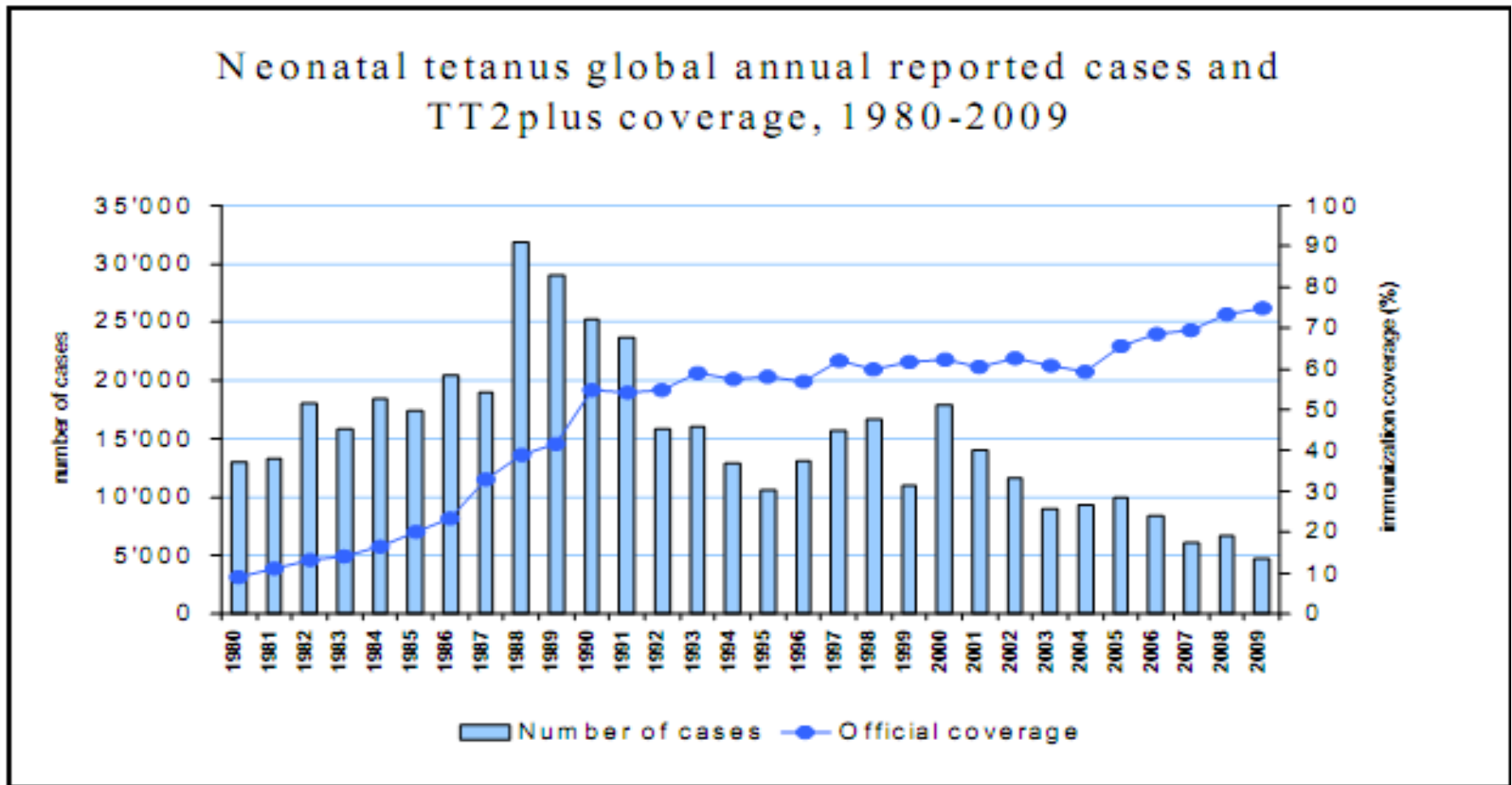
- Administered by intramuscular injection
- Three doses to infants at 6, 10, and 14 weeks of age.
- Normally given to infants in combination with diphtheria and pertussis vaccines (TDP), but can be given with diphtheria alone (TD).

Neonatal Tetanus

- Prevent with toxoid vaccine administered to pregnant mothers (≥ 2 doses) and infant (3 doses)
- Estimated 10,000 cases/year in 2005
- 56% of target population of pregnant women vaccinated with at least two doses among developing countries in 2005¹
- 87% and 75% of target population vaccinated with first and third doses, respectively, among developing countries in 2005¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Neonatal Tetanus cases/coverage among 110 countries*



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.

Adult Tetanus

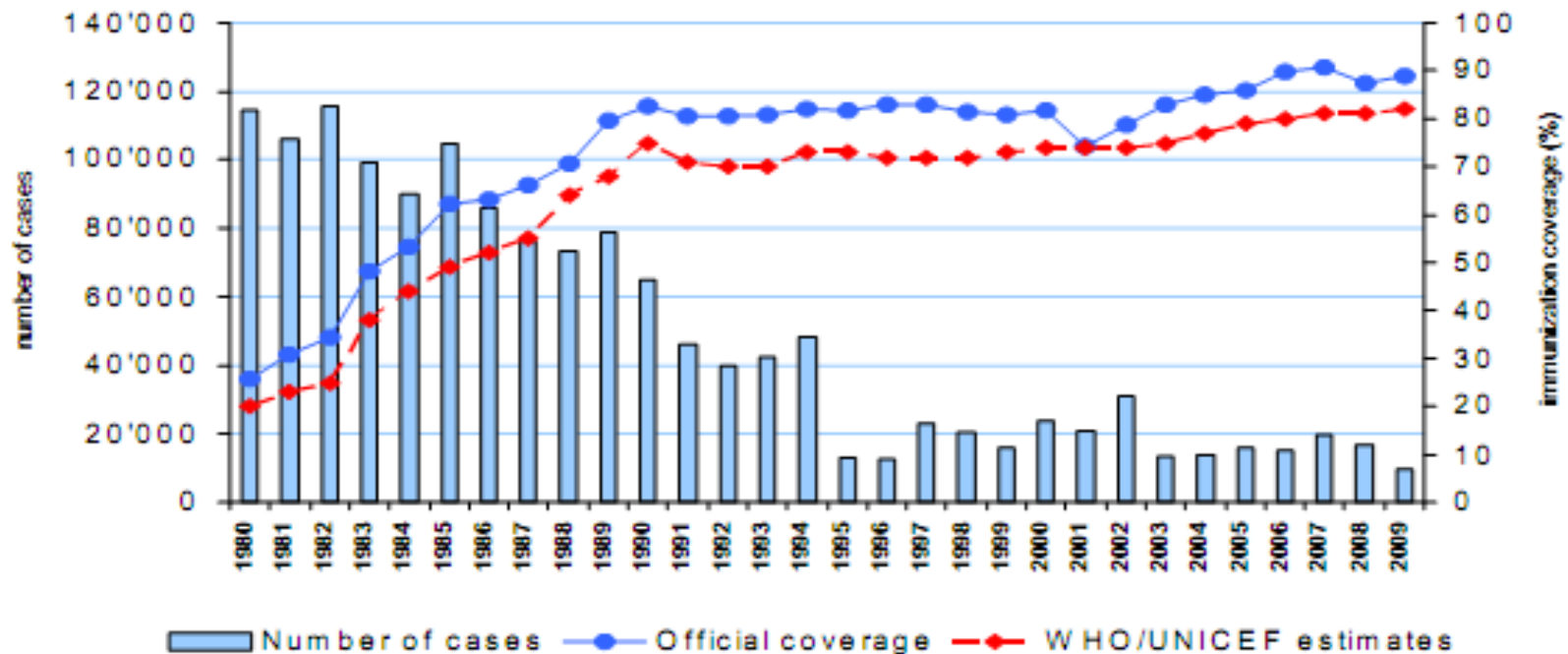
- Global mortality in 2002 estimated at 213,000, 93% were age <5 (including neonatal tetanus)
- Global mortality in 2008 estimated at 61,000 (including neonatal tetanus)
- Administered as tetanus toxoid, either with (DT) or without (TT) diphtheria
- Booster doses every 10 years
- Primary course of immunizations can be given to adults who did not receive childhood course

Tetanus toxoid vaccine

- Given to pregnant woman inducted anti-toxin antibodies that cross placenta to prevent neonatal tetanus
- Schedule for pregnant women
 - TT-1 at first contact or as early as possible
 - TT-2 at least 4 weeks after TT-1
 - TT-3 at least 6 months after TT-2
 - TT-4 at least 1 year after TT-3 or during subsequent pregnancy
 - TT-5 at least 1 year after TT-4 or during subsequent pregnancy
- Complete 5 doses will protect woman and infants during all childbearing years

Adult Tetanus cases and coverage

Total tetanus global annual reported cases and DTP3 coverage, 1980-2009



World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010

Step drop in 1995-96 occurred due to absence of reported figures from India. Reporting from India recommenced in 1997 at a much lower incidence rate.

Yellow Fever

- 45 countries considered at risk
 - (31 Africa, 2 Eastern-Mediterranean, 12 America)
 - 35 of 45 have introduced vaccine in routine schedule
- Two countries out of the high-risk group - Paraguay & Seychelles - have included vaccine in routine schedule
- Global annual mortality estimated at 30,000, 50% occurred among age <5 years, in 2002
- 9% of target population vaccinated among developing countries in 2005¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Yellow Fever vaccine

- Freeze-dried preparation of live attenuated virus (17D strain) grown in egg embryos
- Administered as sub-cutaneous injection
- Immunologic protection lasts for at least 10 years

Presentation Outline

- Immunization Background and Epidemiology
- Major Vaccine-Preventable Diseases
- **Other Vaccine-Preventable Diseases**
- Candidate Vaccines
- Immunization Programs
- Summary
- Self-assessment Quiz

Other Vaccines-Preventable Diseases

- *Haemophilus influenzae type b* (Hib)
- Hepatitis A virus
- Human Papillomavirus
- Influenza virus
- Japanese encephalitis
- *N. meningitidis* (Meningococcal vaccine)
- Mumps
- *S. pneumoniae* (Pneumococcal vaccine)
- Rabies
- Rubella
- *S. typhi* (Typhoid vaccine)

Haemophilus influenzae type b (Hib) vaccine

Uses and Benefits	Challenges
<ul style="list-style-type: none">- Hib polysaccharides conjugated with either diphtheria or tetanus toxoids.- Administered by injection.- Three doses during infancy, normally with DTP.- Risk of serious infection falls sharply after age 4, so only recommended for those at high risk in this age group.	<ul style="list-style-type: none">- 17% of target population vaccinated with third dose among developing countries in 2005.¹

1. World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006. Tetanus – 4190 DALYs (Global Burden of Disease, World Health Organization, 2008).

Hepatitis A vaccine

Uses and Benefits	Challenges
<ul style="list-style-type: none">- Formaldehyde-inactivated preparation of hepatitis A virus grown in human diploid cells.- Administered by injection.	<ul style="list-style-type: none">- Single booster recommended at 12 months.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Influenza A vaccine

Uses and Benefits	Limitations	Challenges
<ul style="list-style-type: none">- Inactivated influenza virus that has been grown in eggs.- Administered by injection.	<ul style="list-style-type: none">- Virus continually alter haemagglutinin and neuraminidase surface proteins, so new vaccine strain developed each year.	<ul style="list-style-type: none">- Recommended for people at higher risk, particularly the elderly.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Japanese encephalitis vaccine

Uses and Benefits	Challenges
<ul style="list-style-type: none">- Formalin-inactivated preparation of virus grown in tissue.- Administered by sub-cutaneous injection.- Widely used in Asia countries where Japanese Encephalitis is considered epidemic	<ul style="list-style-type: none">- Two doses given 1-2 weeks apart, additional dose given 4 weeks later, and boosters every 1-4 years.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006. 790 DALYs (Global Burden of Disease, World Health Organization, 2008).

Meningococcal vaccine

Uses and Benefits	Limitations	Challenges
<ul style="list-style-type: none"> - Capsular polysaccharide purified from various subgroups (A, C, W-135, Y) of <i>N. meningitidis</i>. - Monovalent A group vaccine administered by injection to people >2 years of age. 	<ul style="list-style-type: none"> - Monovalent C group vaccine is effective in adults, but not children. 	<ul style="list-style-type: none"> - Vaccine is not available for B group, which is responsible for most meningococcal deaths in Africa.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006. 8823 DALYs (Global Burden of Disease, World Health Organization, 2008).

Mumps vaccine

Uses and Benefits	Limitations
<ul style="list-style-type: none">- Live attenuated strain of virus grown in tissue culture.- Normally administered as injection with measles and rubella vaccine (MMR) at 12-15 months and again at 3-5 years.	<ul style="list-style-type: none">- 2 doses are needed for long-term protection.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Pneumococcal vaccine

Uses and Benefits	Limitations
<ul style="list-style-type: none">- Capsular polysaccharide antigens from different subtypes of <i>S. pneumoniae</i>.- Administered by injection.- Recommended for people >2 years of age with high risk of severe infection.	<ul style="list-style-type: none">- Does not induce immunity in children <2 years of age, which is one of the groups with the highest attack rate.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Rabies vaccine

Uses and Benefits	Limitations	Challenges
<ul style="list-style-type: none">- Freeze-dried inactivated preparation of virus grown in culture.	<ul style="list-style-type: none">- Older vaccine associated with high rates of post-vaccination severe neurological complications (~1:1,000).	<ul style="list-style-type: none">- New ways of delivering this vaccine are being developed, and its use is increasing across the world.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Rubella vaccine

Uses and Benefits	Challenges
<ul style="list-style-type: none">- Preparation of Wistar strain of the virus.- Administered as injection, usually in combination with measles and mumps (MMR).	<ul style="list-style-type: none">- Often administered to girls between ages 10-14 to reduce likelihood of primary infection in pregnant women, which could cause congenital rubella syndrome in offspring.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

Uses and Benefits	Limitations	Challenges
<ul style="list-style-type: none"> - Three forms : A) Killed-whole cell suspension for injection. B) Purified form of capsular polysaccharide for injection. C) Oral live attenuated preparation of the bacteria. - All elicit protective immunity in adults and children >2 years of age. 	<ul style="list-style-type: none"> - Residents of endemic regions who are frequently exposed to <i>S. typhi</i> require boosters every 3 years. 	<ul style="list-style-type: none"> - The changing epidemiology of typhoid and paratyphoid presents challenges for typhoid control as there is not a parathyroid vaccine(Experience from Thailand & China)¹

World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006.

¹Typhoid vaccine use in countries – progress and challenges: Feedback from the regions and countries on the implementation of SAGE recommendations on typhoid vaccines, World Health Organization

Presentation Outline

- Immunization Background and Epidemiology
- Major Vaccine-Preventable Diseases
- Other Vaccine-Preventable Diseases
- **Candidate Vaccines**
- Immunization Programs
- Summary
- Self-assessment Quiz

Candidate Vaccines

- Cholera
- Dengue
- Enterotoxigenic *E. coli*
- Human Immunodeficiency Virus (HIV)*
- Malaria*
- Parainfluenza Virus
- Respiratory Syncytial Virus
- Rotavirus
- Schistosomiasis

*HIV -

<http://communications.uwo.ca/media/hivvaccine/>

*Malaria - <http://www.bbc.co.uk/news/health-15358554>, <http://www.bbc.co.uk/news/health-16253364>

DALY Global Burden of Disease (WHO, 2008)

Dengue - 420 DALYs; HIV - 64 662 DALYs;
malaria - 32 342 DALYs; schisto – 1457 DALYs

Presentation Outline

- Immunization Background and Epidemiology
- Major Vaccine-Preventable Diseases
- Other Vaccine-Preventable Diseases
- Candidate Vaccines
- **Immunization Programs**
- Summary
- Self-assessment Quiz

Immunization Programs

- Syringes
- Medical waste
- Vaccines supply and distribution
- Cold chain transport
- Global efforts
 - Meningococcal Disease
 - Polio
 - Malaria

Syringes

- Type of syringes for immunization usage
 - Sterilizable - risk of contaminated reuse.
 - Reusable Disposable - risk of contaminated reuse, higher cost, and more medical waste.
 - Non-reusable Disposable (“auto-disable”) - higher cost and more medical waste, but eliminates reuse.
 - Currently recommended by WHO for national immunization programs
 - Prefilled injection devices - combine vaccine and syringe in single non-reusable unit.

Medical waste

- Syringes pose a significant problem of medical waste when not disposed of properly.
- Sharps containers should be supplied at each vaccination site.
- Non-reusable syringes reduce reuse, but expand sharps waste.
- Syringes can be incinerated or a needle-remover can be used to remove needles from syringes to reduce quantity of sharps waste.

Vaccine Supply and Distribution

- Vaccines typically received at major port or capital city and must be distributed to smallest health centers.
- Maintaining their supply within expiration limits has been a significant logistical challenge.
- In addition, many vaccines are inactivated if not kept at proper cold temperature or become frozen.

Cold Chain Supply

- System derived to maintain cold temperature for vaccines during distribution and until delivery to recipient.
- If vaccine not kept at appropriate temperatures, recipient may receive ineffective vaccine.
- ‘Vaccine vial monitors’ are simple stickers on vials that identify vaccines vials exposed to warm temperatures.
- Mass immunization campaign conducted outside health centers pose additional challenges for maintaining proper vaccine temperatures.

- **Meningitis Vaccine Project**

- Partnership between WHO & PATH has developed affordable (<\$0.50 per dose) serogroup A conjugate vaccine called MenAfriVac
- it includes a north-to-south transfer of technology and capacity
- WHO and UNICEF leading an effort to immunize between 250 – 300 million Africans in high-risk areas
- The GAVI Alliance approved US\$100 million for the introduction of MenAfriVac™ in Cameroon, Chad, and Nigeria.

- **Global Meningococcal Initiative (GMI)**

- Independent group established in 2009 by international collaboration of scientists, clinicians, and public health officials
- Primary goal is the promotion of global prevention of invasive meningococcal disease through education and research

The Global Meningococcal Initiative: Recommendations for reducing the global burden of meningococcal disease. Vaccine 29 (2011) 3363–3371. Meningococcal vaccines: WHO position paper, November 2011.

<http://www.meningvax.org/>

Global Efforts - Polio

- **Polio Eradication Programme**
 - Public-private partnership led by national governments and spearheaded by the WHO, Rotary International, the CDC, and UNICEF (In 1988, the World Health Assembly resolved to eradicate polio)
 - **1. Routine immunization; 2. Supplementary immunization; 3. Surveillance; 4. Targeted “mop-up” campaigns**
 - The number of cases dropped from 350,000 in 1988 to less than 2,000 in 2009; and the number of endemic countries decreased from over 125 to four by the end of 2006 (Afghanistan, India, Nigeria and Pakistan)

<http://www.polioeradication.org/>

Global Efforts - Malaria

- **Malaria Vaccine Initiative**

- PATH initiative to identify promising malaria vaccine approaches and bring them to development, including clinical evaluation.
- Also addresses issues of access in countries where it is most needed, such as laying the foundation for a competitive market and considering vaccine financing.
- Aspires to have a vaccine by 2015 with a protective efficacy of over 30% against clinical disease, and that lasts longer than a year; and, by 2025, a vaccine with 80% efficacy that lasts up to four years.

<http://www.malariavaccine.org/>

Presentation Outline

- Immunization Background and Epidemiology
- Major Vaccine-Preventable Diseases
- Other Vaccine-Preventable Diseases
- Candidate Vaccines
- Immunization Programs
- **Summary**
- Self-assessment Quiz

Summary

- Vaccinations are one the most successful and cost-effective public health investments available.
- There are many global efforts to increase usage, improve existing vaccines, and to develop new vaccines.
- Although effective in preventing TB meningitis and miliary TB, BCG vaccine has limited ability to reduce TB transmission.
- Vaccine for diphtheria toxoid is effective, but sequential dosing limits compliance.
- Similarly, HepB vaccine is effective, but routine adoption of the vaccine worldwide must be expanded.

Summary

- Measles represents 50% of deaths attributable to vaccine-preventable deaths in children.
- Whole-killed Pertussis vaccines carries higher neurological risks compared to acellular purified version.
- Neonatal tetanus coverage increased from early 1980s due to increased number of member states providing Tetanus toxoid vaccine through antenatal care services.
- Yellow Fever still remains to be included in routine immunization schedules of all countries at risk (35 of 45 countries at risk have included in routine schedules)

Summary

- New vaccines are needed to address current epidemics.
- National immunization programs face several challenges in effectively and safely administering vaccines, such as the proper use of syringes, adequate vaccine supply and distribution (including cold chain transport), managing the proper disposal of medical waste.
- There is a great deal of global effort to develop vaccines through innovative mechanisms (e.g., the Meningitis Vaccine Project) and to lessen the burden of disease, even aiming for eradication of diseases such as polio.
- Polio is now endemic in only 3 countries: Afghanistan, Pakistan, Nigeria.

Presentation Outline

- Immunization Background and Epidemiology
- Major Vaccine-Preventable Diseases
- Other Vaccine-Preventable Diseases
- Candidate Vaccines
- Immunization Programs
- Summary
- **Self-assessment Quiz**

Self-assessment Quiz

Write down the answer codes for the 10 questions and then compare your answers with those listed at the end of the module

Question #1

Which one of these statements is false?

- A. The pneumococcal vaccine induces immunity in children under the age of two
- B. The rubella vaccine is often administered to girls to reduce the risk of primary infection during pregnancy
- C. The rabies vaccine is associated with relatively high rates of neurological complications
- D. Two doses of the mumps vaccine are needed for long-term protection

Question #2

Which is not a form of the typhoid vaccine?

- A. Purified capsular polysaccharide
- B. Toxoid
- C. Killed whole suspension
- D. Live attenuated

Question #3

Which statement regarding immunization programs is false?

- A. The WHO is involved in the Meningitis Vaccines Project
- B. Syringes can be incinerated
- C. Vaccine vial monitors measure the amount of vaccine in the vial
- D. Auto-disable syringes are recommended by the WHO

Question #4

Which one of the following statements about the BCG vaccine is false?

- A. The BCG vaccine is effective at preventing primary infection with TB
- B. Since the vaccine is live-attenuated, caution should be taken in immune-compromised patients
- C. In countries with high burden of TB, all newborns should receive the vaccine at birth
- D. Patients may develop a scar where they received the BCG vaccine

Question #5

Which statement regarding the diphtheria toxoid vaccine is false?

- A. The vaccine provides protection against *Corynebacterium diphtheriae*
- B. It is usually combined with tetanus toxoid and pertussis vaccines for children
- C. Immunity is induced with a single dose
- D. It is considered one of the major vaccine-preventable disease

Question #6

A 28-year old health woman gives birth to a baby boy at 40 weeks gestational age in a country with a "high burden" of TB. What vaccination(s) should the baby receive in the first 24 hours?

- A. Polio
- B. Hepatitis B
- C. BCG
- D. B and C

Question #7

A mother brings her 6-week old baby girl to the clinic. When the clinician tells her that her daughter should receive DTP (diphtheria, tetanus, and pertussis), she gets nervous because she heard from a friend that the vaccine may harm her baby. Which of the following responses is most accurate?

- A. The vaccine is completely safe and she has nothing to worry about
- B. Up to 50% of children receiving the vaccine may develop fever within 24 hours, but it is usually not life threatening
- C. All children will have at least a mild adverse reaction to the vaccine, with some children having fatal reactions
- D. The first dose is usually completely safe, but each successive dose presents more risk for the child

Question #8

Which of the following statements is false regarding the Pertussis vaccine?

- A. Current trends show an epidemiological shift into older age groups in U.S. and Canada, thus requiring a change in immunization policies.
- B. Whole–cell killed version carries higher neurological risks compared to acellular purified versions.
- C. Adults should not receive a vaccine if they were vaccinated during childhood.
- D. Acellular pertussis form is used only in a few developing countries.

Question #9

Sabin vaccine is:

- A. Live attenuated virus given by mouth
- B. Live purified virus given by injection
- C. Killed virus given by injection
- D. Killed whole-celled virus given by mouth

Question #10

Which of the following is false regarding Measles vaccine?

- A. 90% of deaths occur among children <5 years of age.
- B. Coverage peaked in 1990 due to Universal Childhood Immunization program.
- C. Vaccine medium is a freeze-dried preparation of killed virus
- D. Measles represents largest cause of death in vaccine preventable diseases in children.

Answers

1. A
2. B
3. C
4. A
5. C
6. D
7. B
8. C
9. A
10. C

References

- World Health Organization. WHO vaccine-preventable diseases: monitoring system. WHO/IVB/2006
- World Health Organization. WHO vaccine-preventable diseases: Monitoring system, 2010 global summary. 2010.
- Global Burden of Disease, World Health Organization, 2008
- WHO Global Tuberculosis, Control Report 2010 (www.who.int/tb/publications/2010/factsheet_tb_2010.pdf)
- Global Immunization Data - March 2012, http://www.who.int/immunization_delivery/en/
- Keja K et al. Expanded programme on immunization. World Health Stat Q. 1988;41(2):59-63.
- Vaccines and Preventable Diseases: Measles Vaccination. Centers for Disease Control and Prevention (CDC) <http://www.cdc.gov/vaccines/vpd-vac/measles/default.htm#concerns>

References

- MMRV Vaccine Safety: Febrile Seizures and MMRV
http://www.cdc.gov/vaccinesafety/Vaccines/MMRV/MMRV_qa.html#3
- MMRV Vaccine Safety: Febrile Seizures and MMRV
http://www.cdc.gov/vaccinesafety/Vaccines/MMRV/MMRV_qa.html#3
- Vaccines and Preventable Diseases: Polio-The Unprotected Story,
<http://www.cdc.gov/vaccines/vpd-vac/polio/unprotected-story.htm>
- Typhoid vaccine use in countries – progress and challenges: Feedback from the regions and countries on the implementation of SAGE recommendations on typhoid vaccines, World Health Organization
- Weekly epidemiological record, Relevé épidémiologique hebdomadaire, 2 October 2009, 84th year / 2 octobre 2009, 84e année, No. 40, 2009, 84, 405–420, <http://www.who.int/wer>, <http://www.who.int/wer/2009/wer8440.pdf>
- The Global Meningococcal Initiative: Recommendations for reducing the global burden of meningococcal disease. Vaccine 29 (2011) 3363–3371.

Additional Resources

- International AIDS Vaccine Initiative
 - www.iavi.org
- AERAS Global TB Vaccine Foundation
 - www.aeras.org
- Malaria Vaccine Initiative
 - www.mvi.org
- Global Alliance for Vaccines and Immunizations
 - www.gavialliance.org

WHO Immunization: <http://www.who.int/topics/immunization/en/>

MSF also does a bit on vaccines: <http://www.msfaccess.org/our-work/vaccines>

Credits

The author would like to thank student reviews Jonathan Abelson, Mary MacLennan, and Nilofer Khan Habibullah for reviewing drafts of this teaching module.

The Global Health Education Consortium and the Consortium of Universities for Global Health gratefully acknowledge the support provided for developing teaching modules from the:

Margaret Kendrick Blodgett Foundation

The Josiah Macy, Jr. Foundation

Arnold P. Gold Foundation



This work is licensed under a [Creative Commons Attribution-Noncommercial-No Derivative Works 3.0 United States License](https://creativecommons.org/licenses/by-nc-nd/3.0/us/).