MONASH University

Medicine, Nursing and Health Sciences

Introduction to Immunisation

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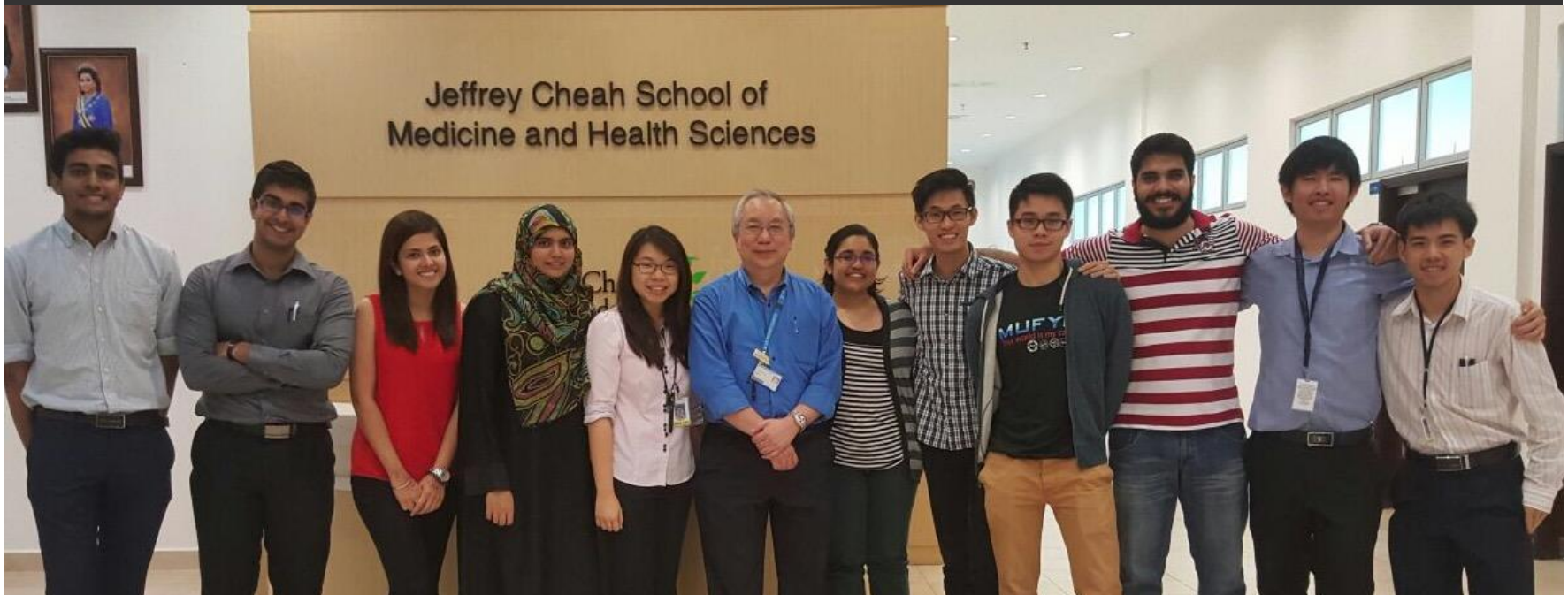
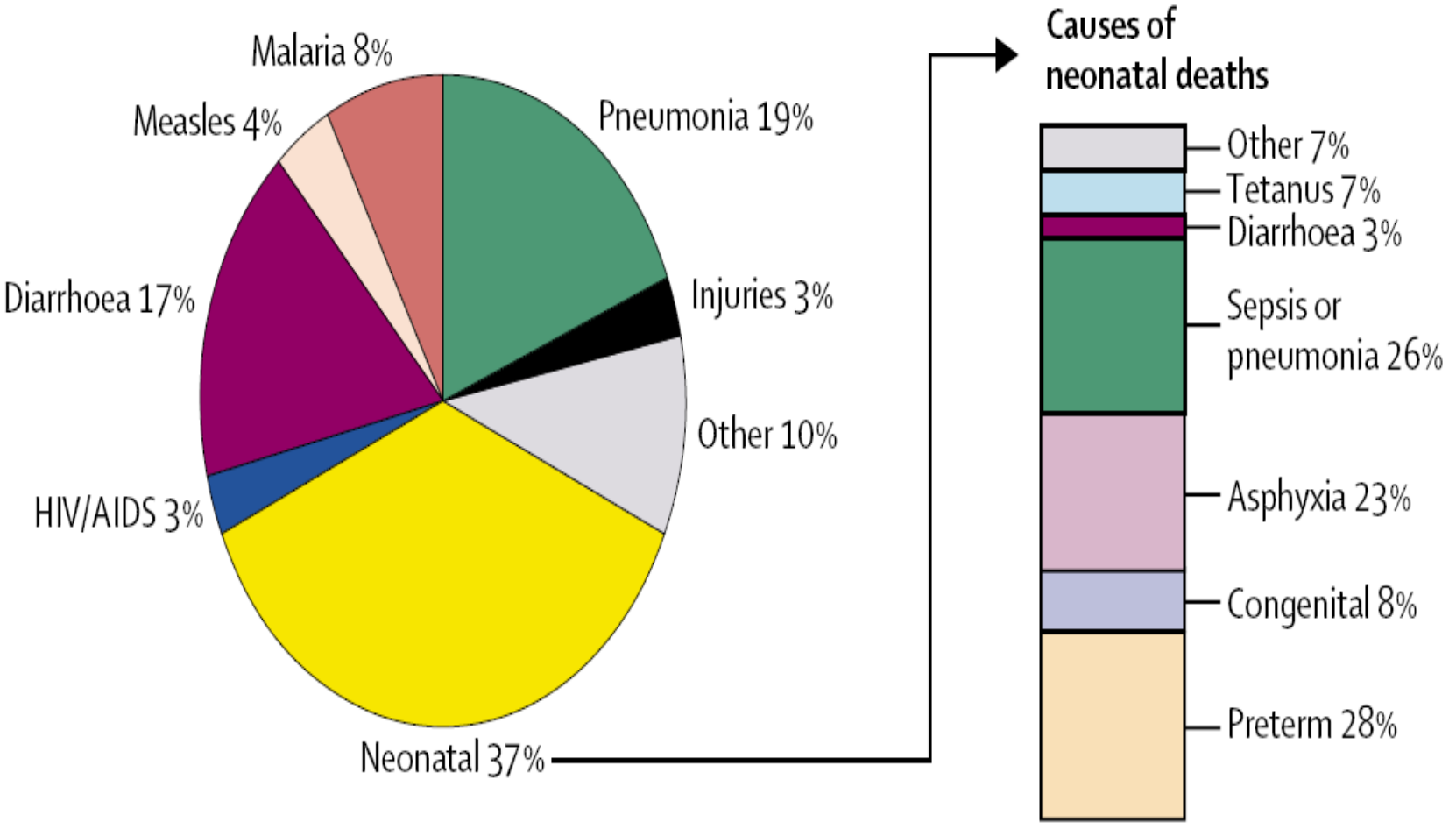


Objective

- Overview of the immunisation schedules
- Basis of immunisation
- Infections
- Concerns of parents
- The cold chain

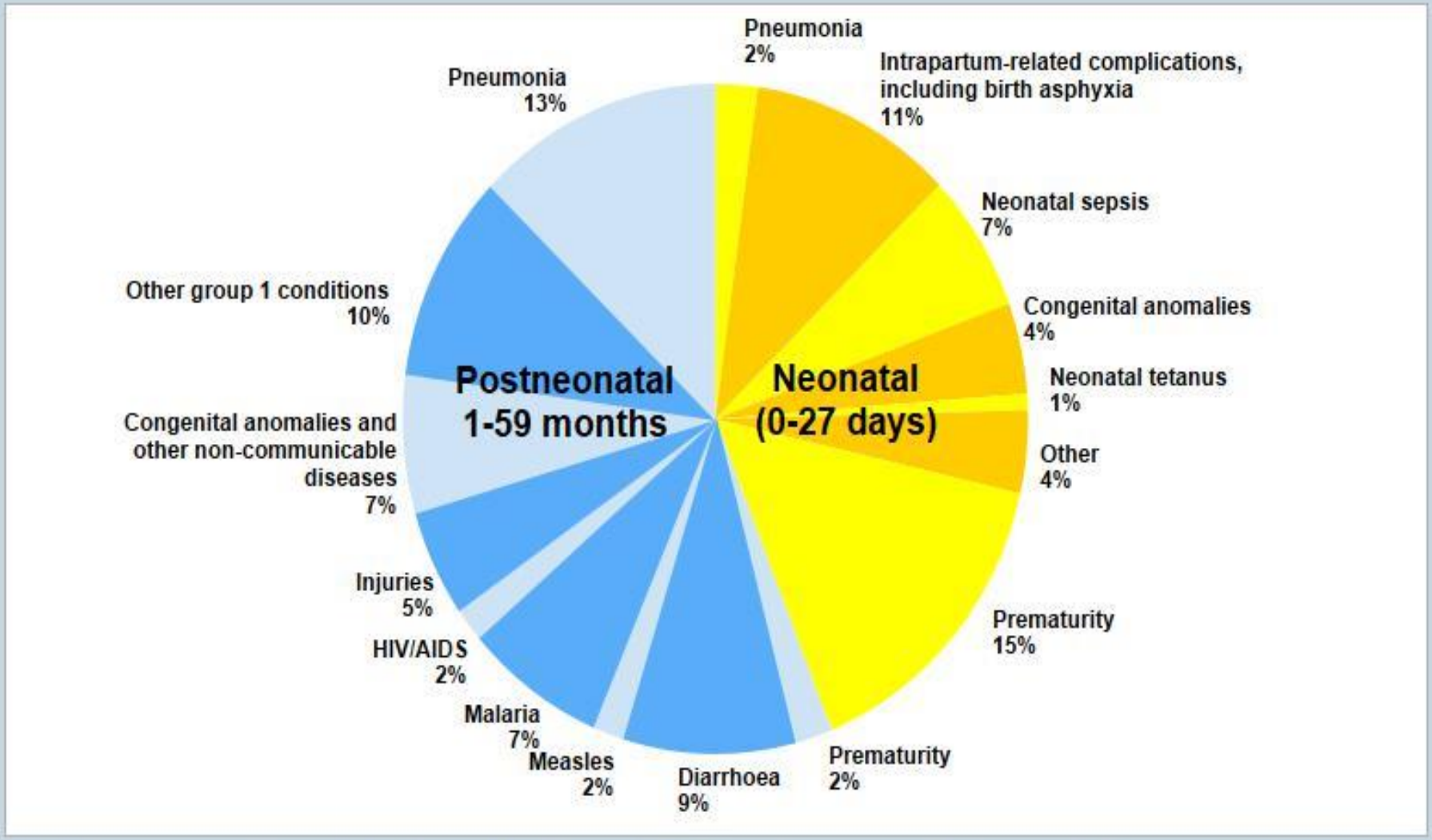
WHO: Major causes of death in children younger than age 5 years and in neonates



Lancet 2005; 365: 1147–52

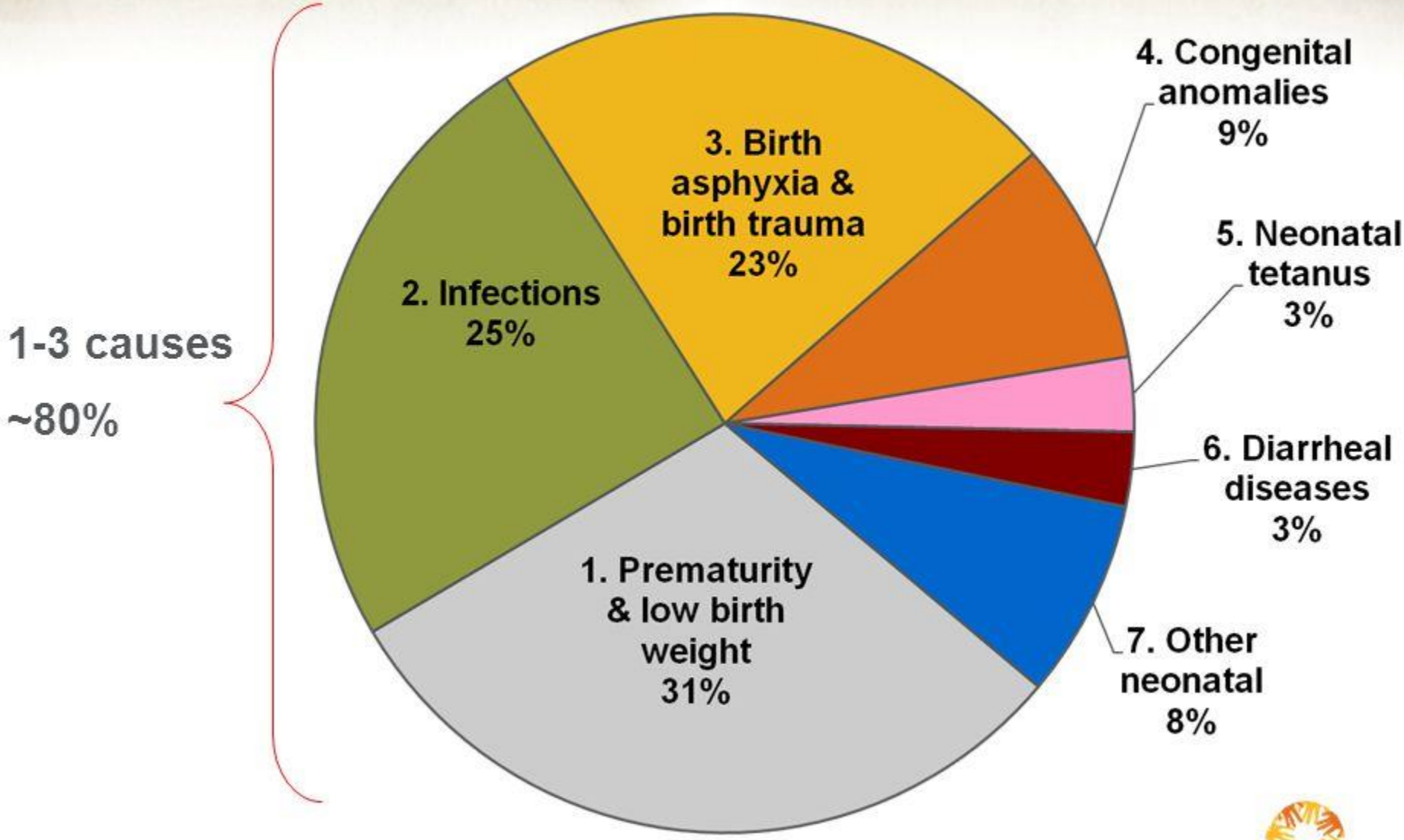
Causes of deaths among children under 5 years, 2013

World Health Organization



Source: CHERG-WHO methods and data sources for child causes of death 2000-2013 (Global Health Estimates Technical Paper WHO/HIS/HSI/GHE/2014.6.2)

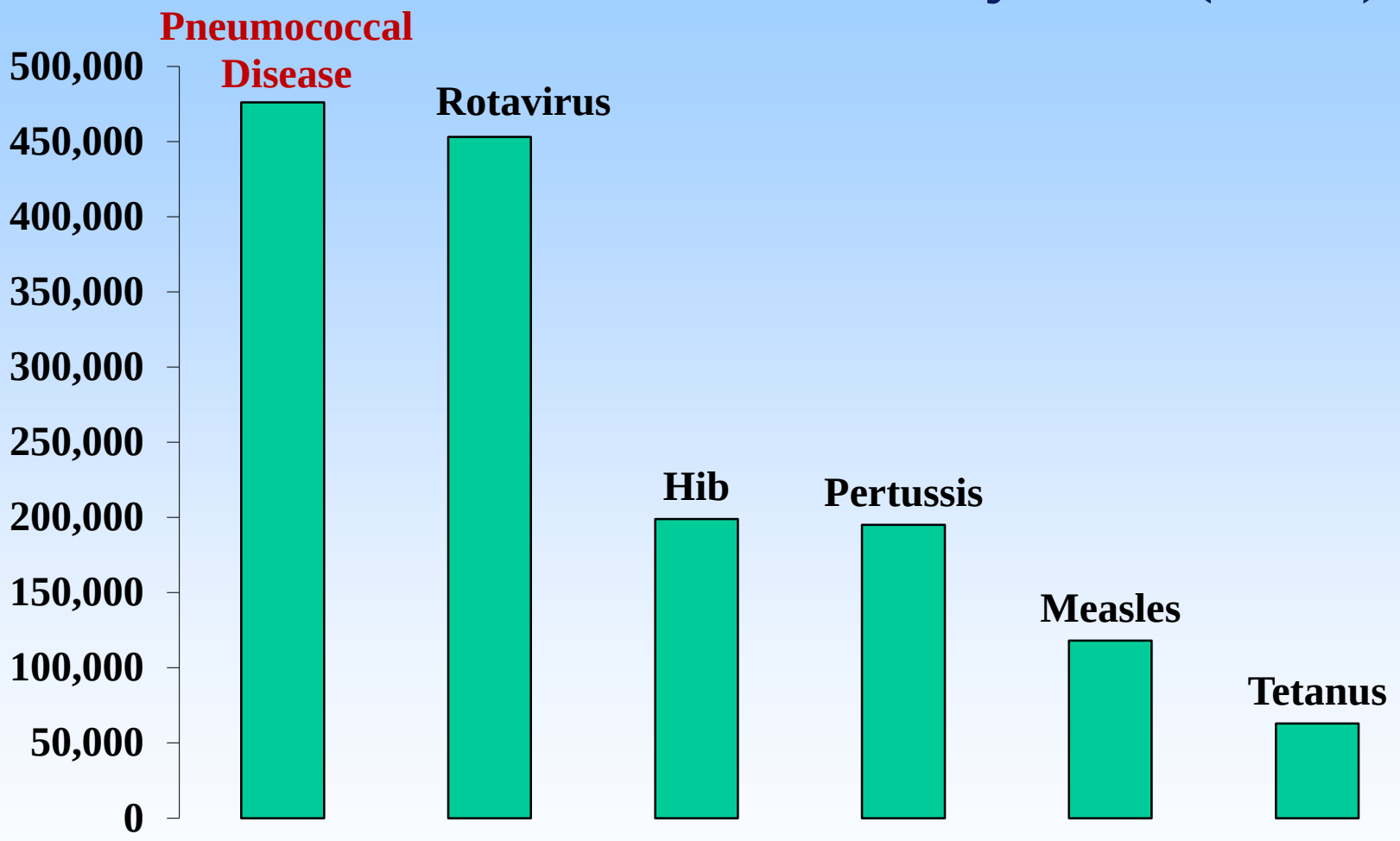
Major Causes of Neonatal Deaths



Source: *World Health Organization. The Global Burden of Disease: 2004 update. WHO, Geneva, 2008.*

care

Global Leading Causes of Vaccine-Preventable Death in Children < 5 yrs old(2008)



Source : http://www.who.int/immunization/monitoring_surveillance/burden/estimates/en/

Vaccination schedule

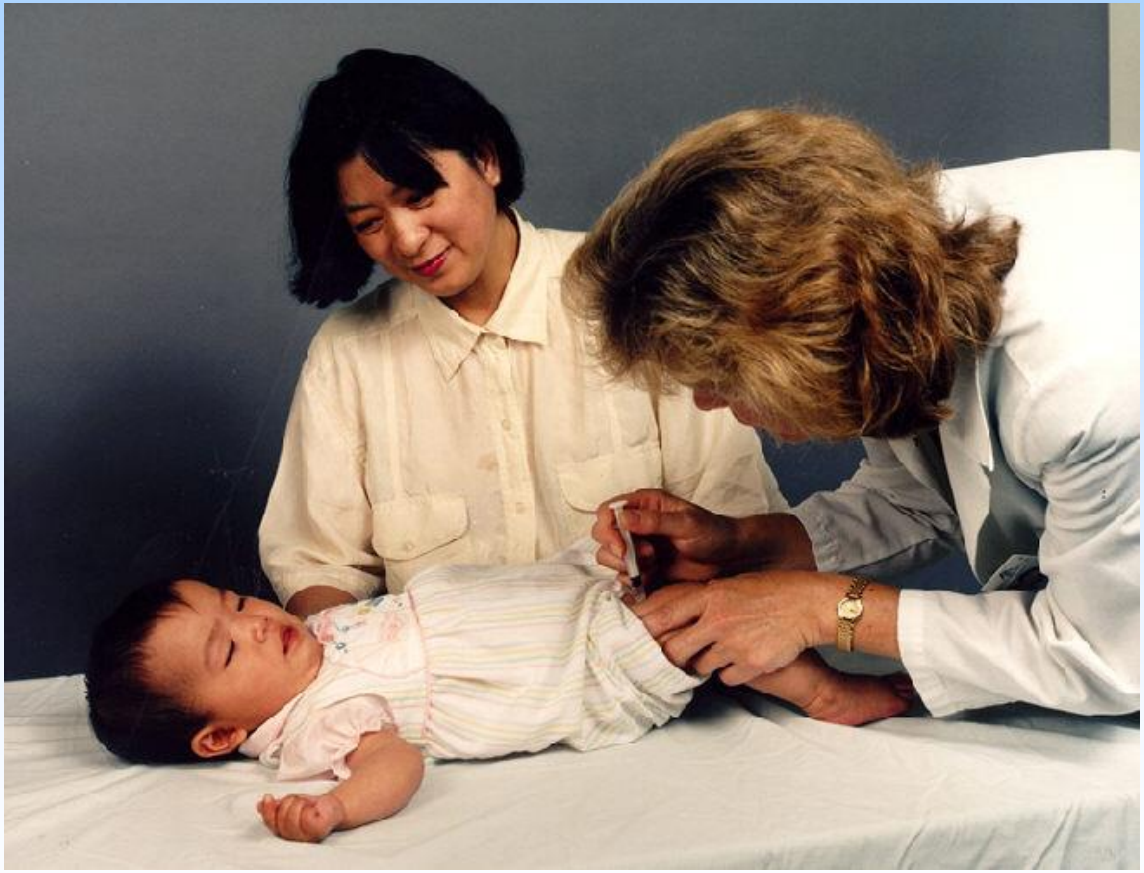


Photo from Centers for Disease Control and Prevention. *Childhood immunization* (1999) Public Health Image Library (PHIL) 982.

Immunisation Schedule in Malaysia

IMUNISASI	Umur (Bulan)										(Tahun)		
	0	1	2	3	5	6	9	12	18	21	7	13	15
BCG	Dos 1										Tiada parut		
Hepatitis B	Dos 1	Dos 2				Dos 3							
DTaP			Dos 1	Dos 2	Dos 3				Booster				
Hib			Dos 1	Dos 2	Dos 3				Booster				
Polio (IPV)			Dos 1	Dos 2	Dos 3				Booster				
Measles						Sabah sahaja							
MMR								Dos 1					
MR											Booster		
DT											Booster		
OPV													
HPV												Perempuan sahaja	
Tetanus													Booster

Perubahan Jadual Imunisasi MMR

Jadual Lama :

IMUNISASI	Umur (Bulan)										(Tahun)		
	0	1	2	3	5	6	9	12	18	21	7	13	15
BCG	Dos 1										Tiada parut		
Hepatitis B	Dos 1	Dos 2				Dos 3							
DTaP			Dos 1	Dos 2	Dos 3				Booster				
Hib			Dos 1	Dos 2	Dos 3				Booster				
Polio (IPV)			Dos 1	Dos 2	Dos 3				Booster				
Measles						Sabah sahaja							
MMR								Dos 1					
MR											Booster		
DT											Booster		
OPV													
HPV												Perempuan sahaja	
Tetanus													Booster

Jadual Baru :

IMUNISASI	Umur (Bulan)										(Tahun)		
	0	1	2	3	5	6	9	12	18	21	7	13	15
BCG	Dos 1												
Hepatitis B	Dos 1	Dos 2				Dos 3							
DTaP			Dos 1	Dos 2	Dos 3				Booster				
Hib			Dos 1	Dos 2	Dos 3				Booster				
Polio (IPV)			Dos 1	Dos 2	Dos 3				Booster				
Measles						Sabah sahaja							
MMR							Dos 1	Dos 2					
MR											Booster		
DT											Booster		
OPV													
HPV												Perempuan sahaja	
Tetanus													Booster
JE (Sarawak)							Dos 1			Dos 2			

Jadual baru Imunisasi MMR digunakan bermula tahun 2016

Diterbitkan oleh :
Bahagian Pendidikan Kesihatan
Kementerian Kesihatan Malaysia
www.infosihat.gov.my I www.myhealth.gov.my

Optional Vaccines in Malaysia

Vaccine	Month								
	0	1	2	3	4	5	6	12	15
Pneumococcal Vaccine									
Chickenpox Vaccine									
Hepatitis A Vaccine									
Rotavirus									

National Childhood and Adolescent Immunisation Schedule, Singapore
For persons aged 0 to <18 years

Vaccination against	Birth	1 month	3 months	4 months	5 months	6 months	12 months	15 months	18 months	6-7 years^	10-11 years^^
Tuberculosis	BCG										
Hepatitis B*	HepB (D1)	HepB (D2)			HepB (D3)#						
Diphtheria, Tetanus, Pertussis			DTaP (D1)	DTaP (D2)	DTaP (D3)				DTaP (B1)		Tdap (B2)
Poliovirus			OPV (D1)	OPV (D2)	OPV (D3)				OPV (B1)	OPV (B2)	OPV (B3)
Measles, Mumps, Rubella							MMR (D1)	MMR (D2)##			
Pneumococcal Disease**			PCV (D1)		PCV (D2)		PCV (B1)				
Human Papillomavirus		*Recommended for females 9 to 26 years; three doses are required at intervals of 0, 2, 6 months*									
Influenza		*Recommended annually for all children aged 6 months to <5 years and children aged 6 months to <18 years in high-risk groups****									

National Immunisation Registry, Health promotion Board, Singapore, update 23/06/2011

Australian Government Department of Health and Ageing National Immunisation Program Schedule (1 Feb 2013-30 June 2013)

Birth	Hepatitis B (hepB)
2 months	• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV) • Pneumococcal conjugate (13vPCV) • Rotavirus
4 months	• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV) • Pneumococcal conjugate (13vPCV) • Rotavirus
6 months	• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV) • Pneumococcal conjugate (13vPCV) • Rotavirus
12 months	•*Haemophilus influenzae* type b (Hib) • Meningococcal C (MenCCV) • Measles, mumps and rubella (MMR)
18 months	• Varicella (chickenpox)
4 years	• Diphtheria, tetanus, acellular pertussis (whooping cough) and inactivated poliomyelitis (polio) (DTPa-IPV) • Measles, mumps and rubella (MMR)

Australian Government Department of Health and Ageing National Immunisation Program Schedule (From July 2013)

Birth	Hepatitis B (hepB)
2 months	• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV) • Pneumococcal conjugate (13vPCV) • Rotavirus
4 months	• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV) • Pneumococcal conjugate (13vPCV) • Rotavirus
6 months	• Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV) • Pneumococcal conjugate (13vPCV) • Rotavirus
12 months	•*Haemophilus influenzae* type b (Hib) • Meningococcal C (MenCCV) • Measles, mumps and rubella (MMR)
18 months	•Measles, mumps, rubella and varicella (chickenpox) (MMRV)
4 years	• Diphtheria, tetanus, acellular pertussis (whooping cough) and inactivated poliomyelitis (polio) (DTPa-IPV) • Measles, mumps and rubella (MMR)

2016 Recommended Immunizations for Children from Birth Through 6 Years Old

Vaccine	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
HepB	HepB				HepB						
RV			RV	RV	RV						
DTaP			DTaP	DTaP	DTaP		DTaP				DTaP
Hib			Hib	Hib	Hib	Hib					
PCV			PCV	PCV	PCV	PCV					
IPV			IPV	IPV	IPV						IPV
Influenza (Yearly)*					Influenza (Yearly)*						
MMR						MMR					MMR
Varicella						Varicella					Varicella
HepA§						HepA§					

Is your family growing? To protect your new baby and yourself against whooping cough, get a Tdap vaccine in the third trimester of each pregnancy. Talk to your doctor for more details.

Shaded boxes indicate the vaccine can be given during shown age range.

NOTE: If your child misses a shot, you don't need to start over, just go back to your child's doctor for the next shot. Talk with your child's doctor if you have questions about vaccines.

FOOTNOTES:

* Two doses given at least four weeks apart are recommended for children aged 6 months through 8 years of age who are getting an influenza (flu) vaccine for the first time and for some other children in this age group.

§ Two doses of HepA vaccine are needed for lasting protection. The first dose of HepA vaccine should be given between 12 months and 23 months of age. The second dose should be given 6 to 18 months later. HepA vaccination may be given to any child 12 months and older to protect against HepA. Children and adolescents who did not receive the HepA vaccine and are at high-risk, should be vaccinated against HepA.

If your child has any medical conditions that put him at risk for infection or is traveling outside the United States, talk to your child's doctor about additional vaccines that he may need.

SEE BACK PAGE FOR MORE INFORMATION ON VACCINE-PREVENTABLE DISEASES AND THE VACCINES THAT PREVENT THEM.

For more information, call toll free
1-800-CDC-INFO (1-800-232-4636)
or visit
http://www.cdc.gov/vaccines

CDC

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

AMERICAN ACADEMY OF FAMILY PHYSICIANS
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American Academy of Pediatrics
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2015 Recommended Immunizations for Children from 7 Through 18 Years Old

These shaded boxes indicate when the vaccine is recommended for all children unless your doctor tells you that your child cannot safely receive the vaccine.

These shaded boxes indicate the vaccine should be given if a child is catching-up on missed vaccines.

These shaded boxes indicate the vaccine is recommended for children with certain health conditions that put them at high risk for serious diseases. Note that healthy children **can** get the HepA series[6]. See vaccine-specific recommendations at www.cdc.gov/vaccines/pubs/ACIP-list.htm.

FOOTNOTES

[1] Tdap vaccine is recommended at age 11 or 12 to protect against tetanus, diphtheria and pertussis. If your child has not received any or all of the DTaP vaccine series, or if you don't know if your child has received these shots, your child needs a single dose of Tdap when they are 7 -10 years old. Talk to your child's health care provider to find out if they need additional catch-up vaccines.

[2] All 11 or 12 year olds – both girls *and* boys – should receive 3 doses of HPV vaccine to protect against HPV-related disease. The full HPV vaccine series should be given as recommended for best protection.

[3] Meningococcal conjugate vaccine (MCV) is recommended at age 11 or 12. A booster shot is recommended at age 16. Teens who received MCV for the first time at age 13 through 15 years will need a one-time booster dose between the ages of 16 and 18 years. If your teenager missed getting the vaccine altogether, ask their health care provider about getting it now, especially if your teenager is about to move into a college dorm or military barracks.

[4] Everyone 6 months of age and older—including preteens and teens—should get a flu vaccine every year. Children under the age of 9 years may require more than one dose. Talk to your child's health care provider to find out if they need more than one dose.

[5] Pneumococcal Conjugate Vaccine (PCV13) and Pneumococcal Polysaccharide Vaccine (PPSV23) are recommended for some children 6 through 18 years old with certain medical conditions that place them at high risk. Talk to your healthcare provider about pneumococcal vaccines and what factors may place your child at high risk for pneumococcal disease.

[6] Hepatitis A vaccination is recommended for older children with certain medical conditions that place them at high risk. HepA vaccine is licensed, safe, and effective for all children of all ages. Even if your child is not at high risk, you may decide you want your child protected against HepA. Talk to your healthcare provider about HepA vaccine and what factors may place your child at high risk for HepA.

For more information, call toll free 1-800-CDC-INFO (1-800-232-4636) or visit http://www.cdc.gov/vaccines/teens

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Your Ref :

Our Ref :

Date :

Recommended Immunisation Schedule

Age (month)	Immunisation	
1	• General checkup. No injection 普检。无注射	
2	• Triple antigen+polio+Hep B+ Hib (6 in 1) 三种并合针, 小兒麻痺症, 乙型肝炎及脑膜炎疫苗（6 合 1） • Rotavirus 轮状病毒口服疫苗	
3	• Pneumococcal (PncV) 肺炎链球菌疫苗	
4	• Triple antigen+polio+Hep B+ Hib (6 in 1) 三种并合针, 小兒麻痺症, 乙型肝炎及脑膜炎疫苗（6 合 1） • Rotavirus 轮状病毒口服疫苗	
5	• Pneumococcal (PncV) 肺炎链球菌疫苗	
6	• Triple antigen+polio+Hep B+ Hib (6 in 1) 三种并合针, 小兒麻痺症, 乙型肝炎及脑膜炎疫苗（6 合 1） • ±Rotavirus 轮状病毒口服疫苗	
7	• ±Pneumococcal (PncV) 肺炎链球菌疫苗	
9	• MMR 麻疹，腮腺炎及風疹	
12	• MMR-Chickenpox/MMR 麻疹，腮腺炎及風疹 /水痘	
13	• ±Chickenpox 水痘 (see above)	
15	• Booster Pneumococcal (PncV) 肺炎链球菌疫苗	
18	• Booster Double antigen+polio+ Hib 二種并合針, 小兒麻痺症及脑膜炎疫苗	

Years		
6	• Booster Double antigen+polio 二種并合針及小兒麻痺症 • MMR 麻疹，腮腺炎及風疹	
9-13	• HPV (for girls) 人类乳头状瘤病毒疫苗	
15	• Tetanus 破伤风	

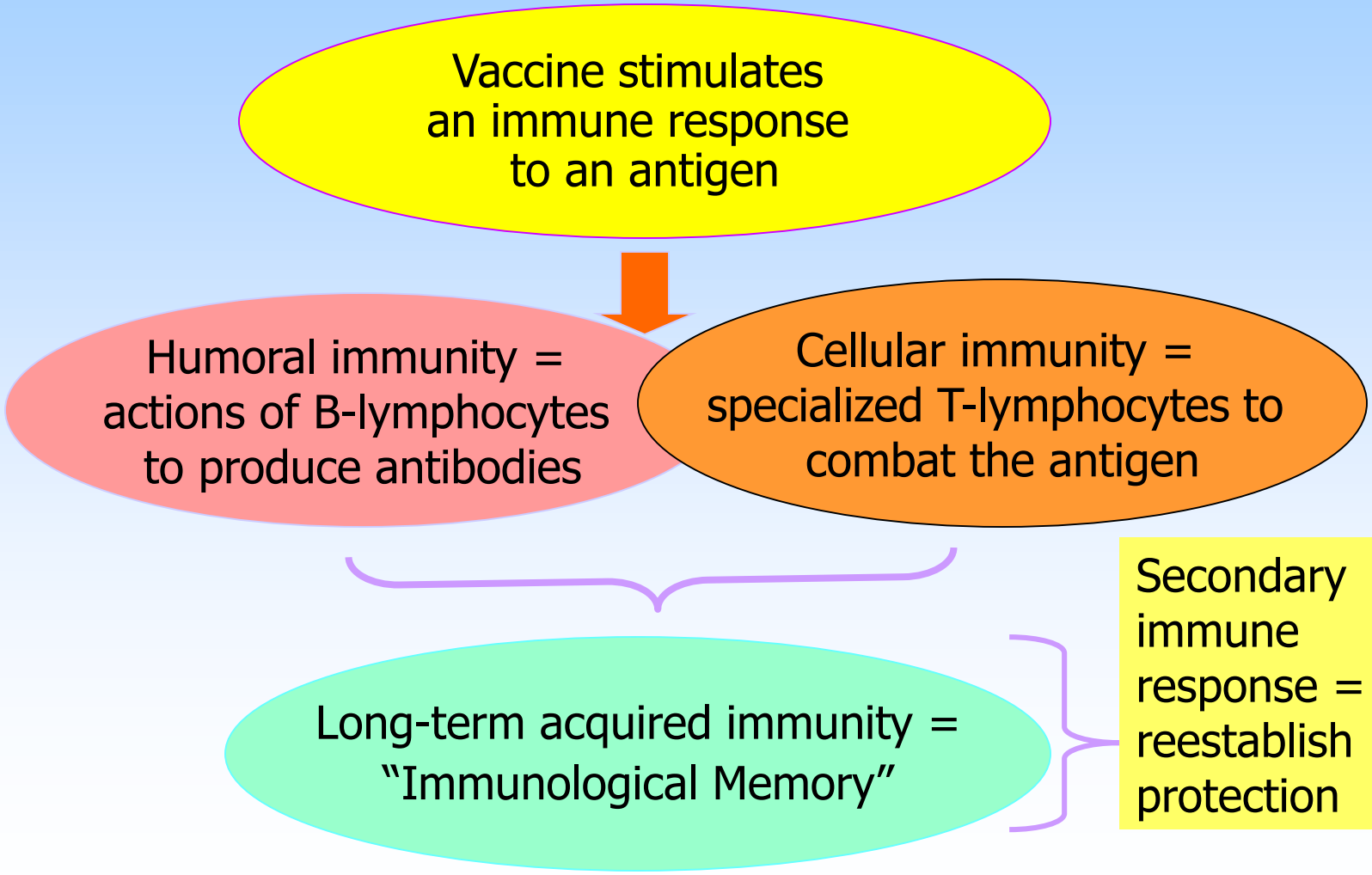
(updated Jan 2016)

Vaccination successes

- Vaccination has:
  - Eradicated smallpox[5]
  - Nearly eradicated polio[8]
  - Controlled many major diseases[3]

Ref 3: Plotkin, p 1
Ref 5: AAP, p 554
Ref 8: CDC, p 721

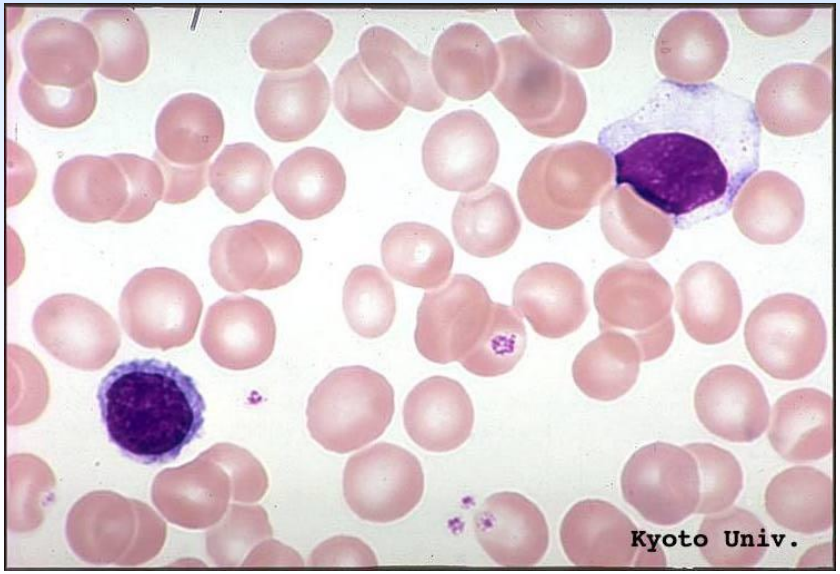
Immunological Memory



The Main Cell Types in the Immune Response

Phagocytes
- Monocytes
- Macrophages
- Polymorphonuclear neutrophils (PMNs)

Lymphocytes
- B cells
- T cells
  - Helper
  - Killer
- Natural Killer cells



Indirect Effect of Vaccination

Vaccines help to reduce the spread of disease through indirect effect, sometimes called “herd immunity” or “community immunity.”

- Once a person is vaccinated against a disease, they are less likely to develop it as well as pass it on to someone who is not immunized.

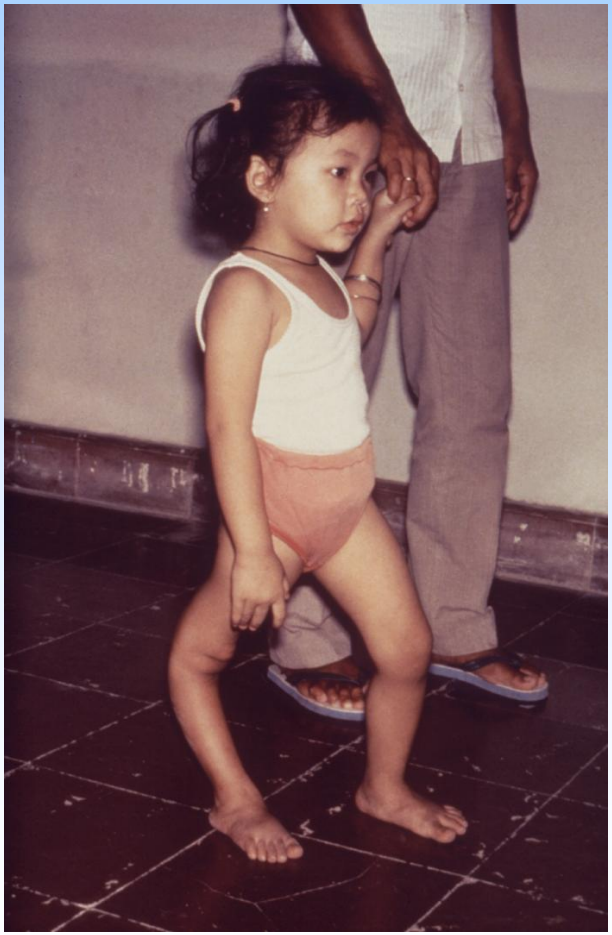
Vaccine-Preventable Diseases and the Vaccines that Prevent Them

Disease	Vaccine	Disease spread by	Disease symptoms	Disease complications
Chickenpox	Varicella vaccine protects against chickenpox.	Air, direct contact	Rash, tiredness, headache, fever	Infected blisters, bleeding disorders, encephalitis (brain swelling), pneumonia (infection in the lungs)
Diphtheria	DTaP* vaccine protects against diphtheria.	Air, direct contact	Sore throat, mild fever, weakness, swollen glands in neck	Swelling of the heart muscle, heart failure, coma, paralysis, death
Hib	Hib vaccine protects against *Haemophilus influenzae* type b.	Air, direct contact	May be no symptoms unless bacteria enter the blood	Meningitis (infection of the covering around the brain and spinal cord), intellectual disability, epiglottitis (life-threatening infection that can block the windpipe and lead to serious breathing problems), pneumonia (infection in the lungs), death
Hepatitis A	HepA vaccine protects against hepatitis A.	Direct contact, contaminated food or water	May be no symptoms, fever, stomach pain, loss of appetite, fatigue, vomiting, jaundice (yellowing of skin and eyes), dark urine	Liver failure, arthralgia (joint pain), kidney, pancreatic, and blood disorders
Hepatitis B	HepB vaccine protects against hepatitis B.	Contact with blood or body fluids	May be no symptoms, fever, headache, weakness, vomiting, jaundice (yellowing of skin and eyes), joint pain	Chronic liver infection, liver failure, liver cancer
Influenza (Flu)	Flu vaccine protects against influenza.	Air, direct contact	Fever, muscle pain, sore throat, cough, extreme fatigue	Pneumonia (infection in the lungs)
Measles	MMR** vaccine protects against measles.	Air, direct contact	Rash, fever, cough, runny nose, pinkeye	Encephalitis (brain swelling), pneumonia (infection in the lungs), death
Mumps	MMR**vaccine protects against mumps.	Air, direct contact	Swollen salivary glands (under the jaw), fever, headache, tiredness, muscle pain	Meningitis (infection of the covering around the brain and spinal cord) , encephalitis (brain swelling), inflammation of testicles or ovaries, deafness
Pertussis	DTaP* vaccine protects against pertussis (whooping cough).	Air, direct contact	Severe cough, runny nose, apnea (a pause in breathing in infants)	Pneumonia (infection in the lungs), death
Polio	IPV vaccine protects against polio.	Air, direct contact, through the mouth	May be no symptoms, sore throat, fever, nausea, headache	Paralysis, death
Pneumococcal	PCV vaccine protects against pneumococcus.	Air, direct contact	May be no symptoms, pneumonia (infection in the lungs)	Bacteremia (blood infection), meningitis (infection of the covering around the brain and spinal cord), death
Rotavirus	RV vaccine protects against rotavirus.	Through the mouth	Diarrhea, fever, vomiting	Severe diarrhea, dehydration
Rubella	MMR** vaccine protects against rubella.	Air, direct contact	Children infected with rubella virus sometimes have a rash, fever, swollen lymph nodes	Very serious in pregnant women—can lead to miscarriage, stillbirth, premature delivery, birth defects
Tetanus	DTaP* vaccine protects against tetanus.	Exposure through cuts in skin	Stiffness in neck and abdominal muscles, difficulty swallowing, muscle spasms, fever	Broken bones, breathing difficulty, death

* DTaP combines protection against diphtheria, tetanus, and pertussis.
** MMR combines protection against measles, mumps, and rubella.

Last updated January 2016 • CS261834-D •

Polio



CDC

- Affects the nervous system and spinal cord, causing paralysis
- ≈1/200 infections lead to paralysis
- Two types of vaccine
- In 1994, wild polio transmission was interrupted in the Americas

POLIO IN MALAYSIA

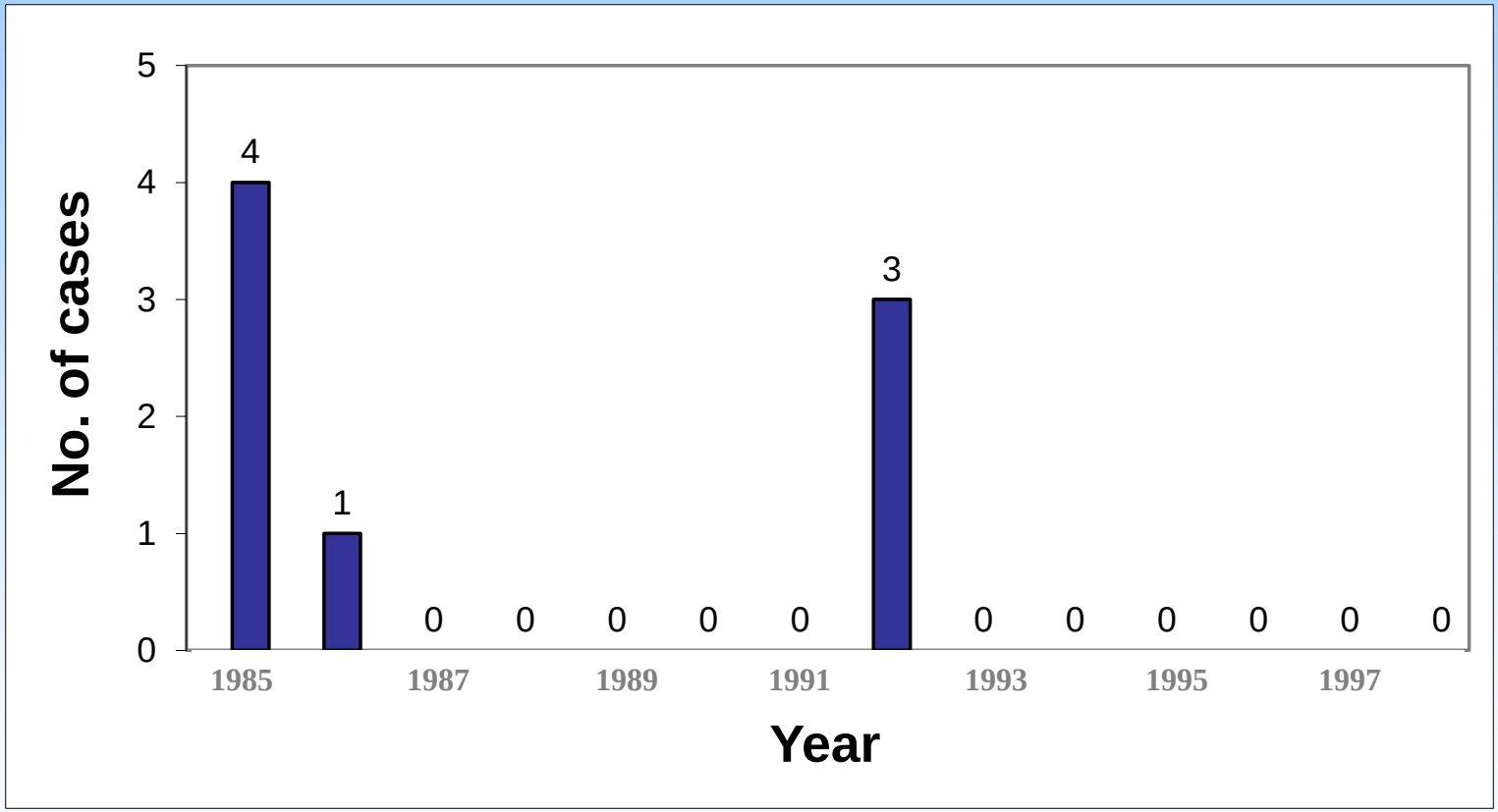
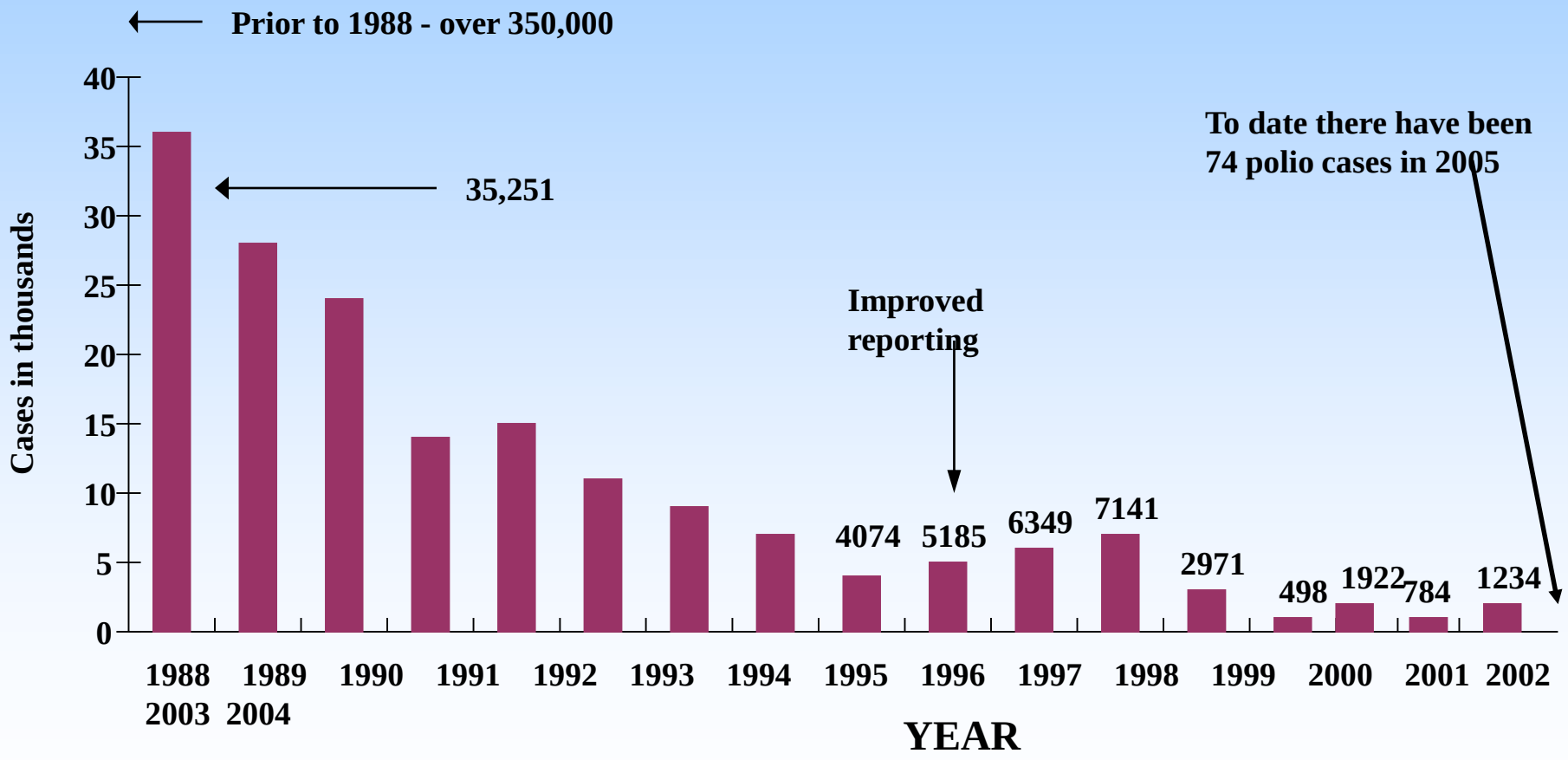


Figure 1: Incidence of paralytic poliomyelitis in Malaysia (Ministry Of Health)

GLOBAL INCIDENCE OF POLIO

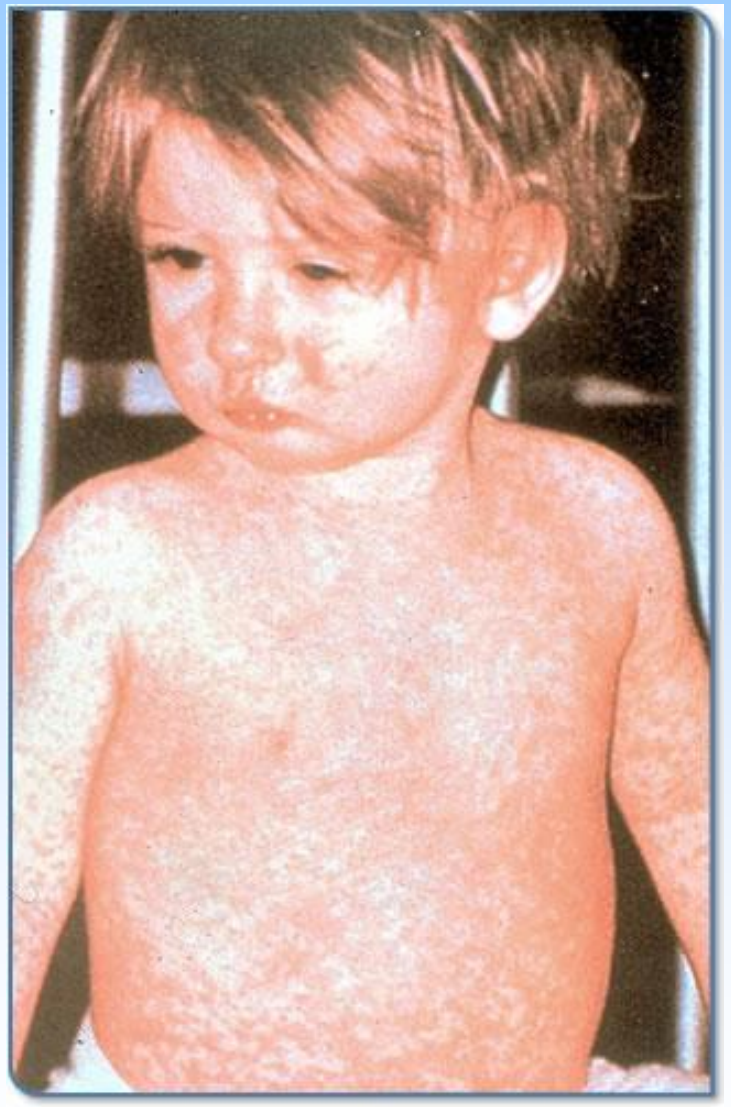
Reported cases of acute poliomyelitis per year



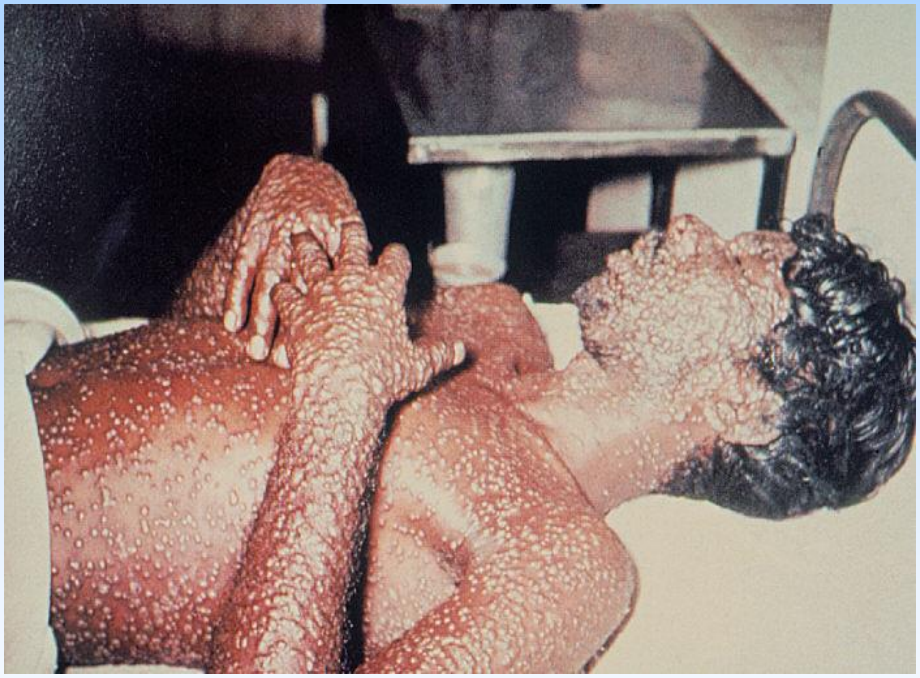
http://www.who.int/vaccines/casecount/afpextractnew.cfm

MMR – THE FACTS

- Measles, Mumps & Rubella
- Short memories of deadly Measles epidemic
- 1990 – 45 million Measles; 1 million dead
- 32.8/100,000 (1987) – 2.6/100,000 (1997)
- National epidemic 1999-2000; 10 deaths
- 2004 – PI 270 cases in 6 mths.
- 2 deaths, 45 pneumonia, 8 bro. obliterans



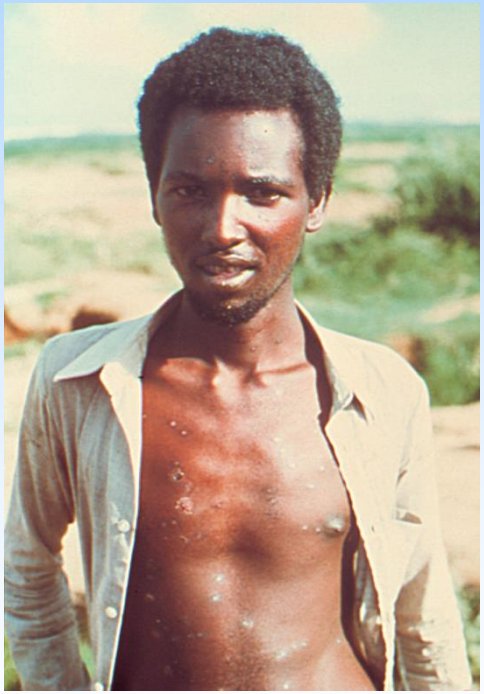
Smallpox



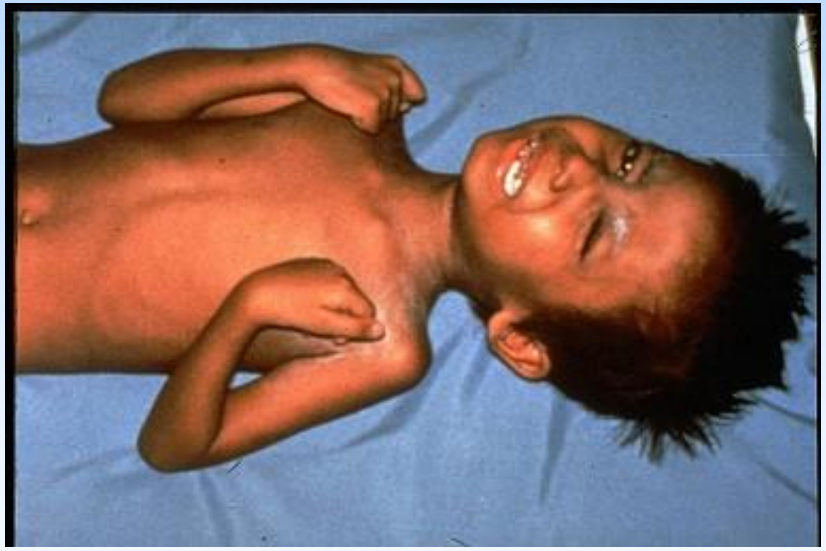
CDC/Barbara Rice

- Caused by variola virus
- A deadly disease
- Most survivors scarred with residual facial marks, some left blind

Last Person Infected with Naturally Occurring Smallpox in Somalia in 1977



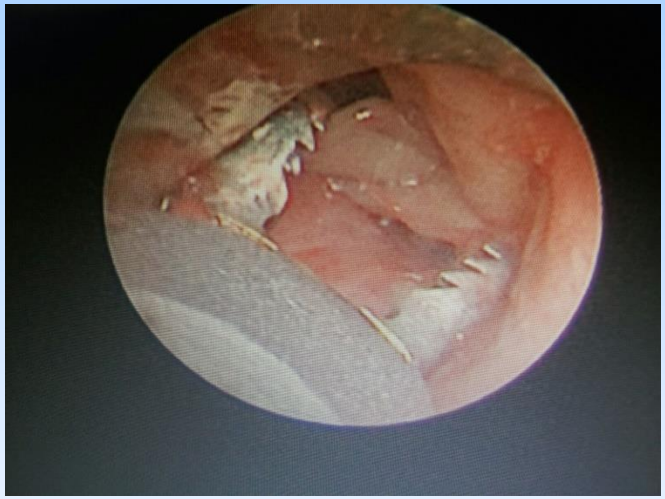
Tetanus

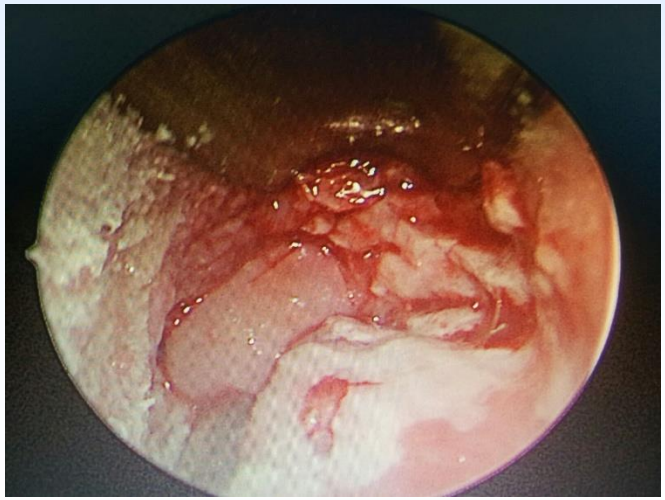


CDC

- Known as lockjaw
- Caused by *Clostridium tetani*
  - Releases a toxin causing muscle spasms
  - May lead to death by suffocation
- Neonatal tetanus occurs most often in developing countries

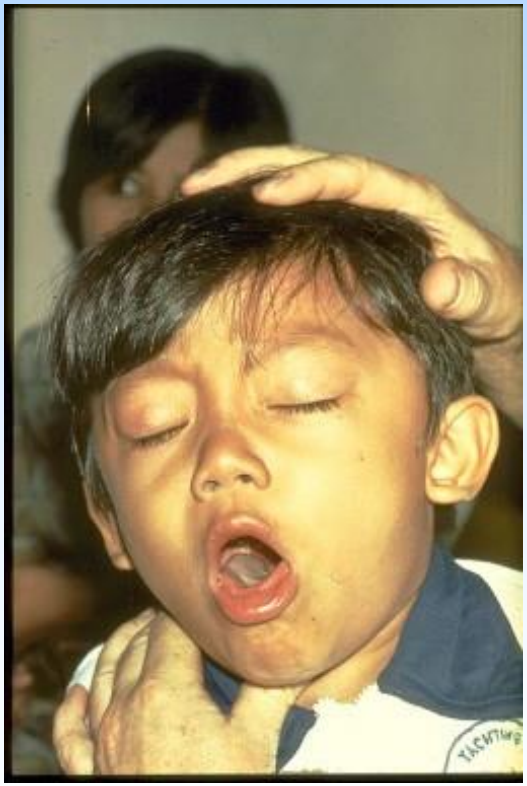
Diphtheria





- Caused by *Corynebacterium diphtheriae*
- Affects upper respiratory tract, also other organs
- Mortality rate 5-10 percent
  - If early treatment, < 1 percent

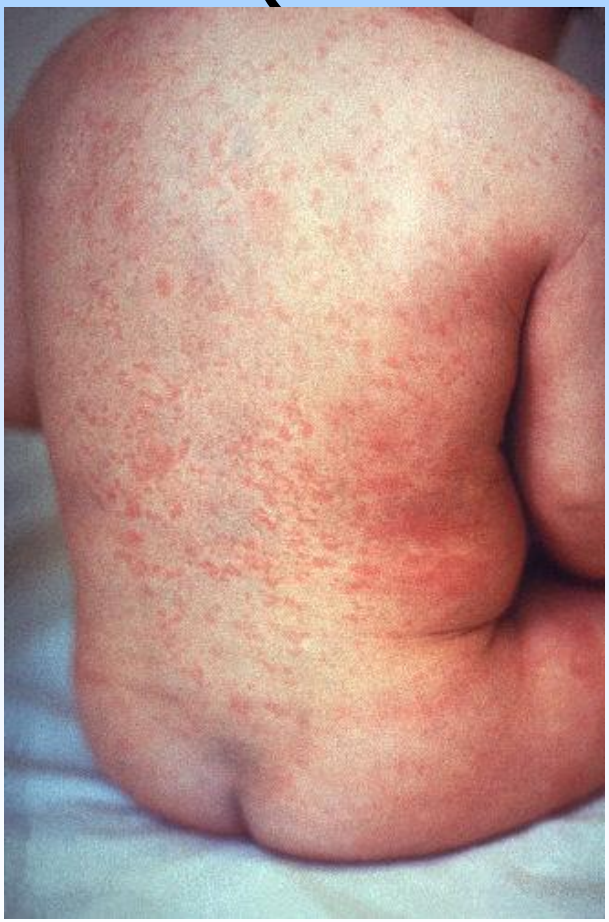
Pertussis ("Whooping Cough")



CDC

- Caused by *Bordetella pertussis*
- Characteristic cough
- Three phases
  - Catartrhal phase
  - Paroxysmal phase
  - Convalescent phase
- Greatest risk in infants and young children

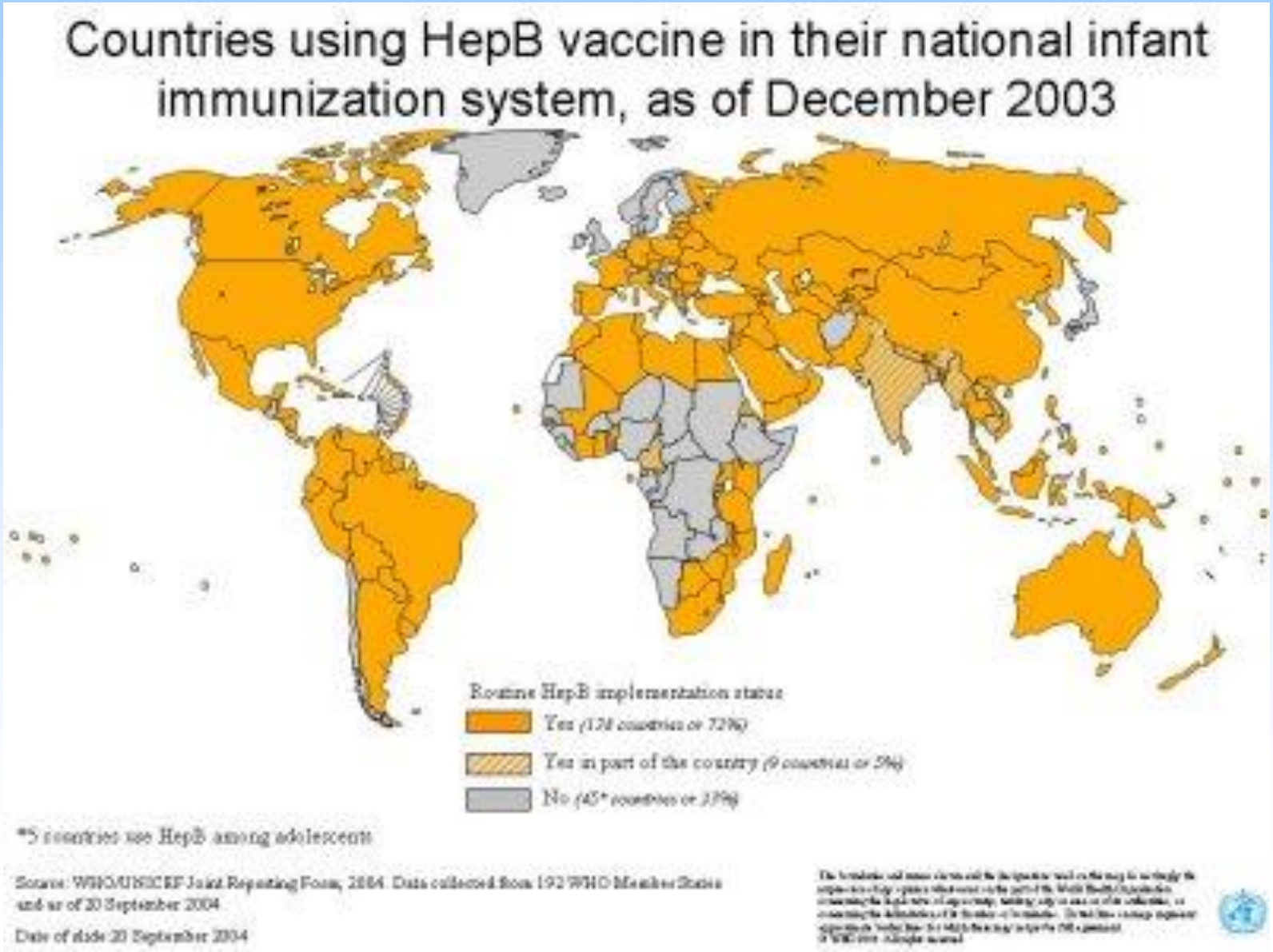
Rubella ("German Measles")

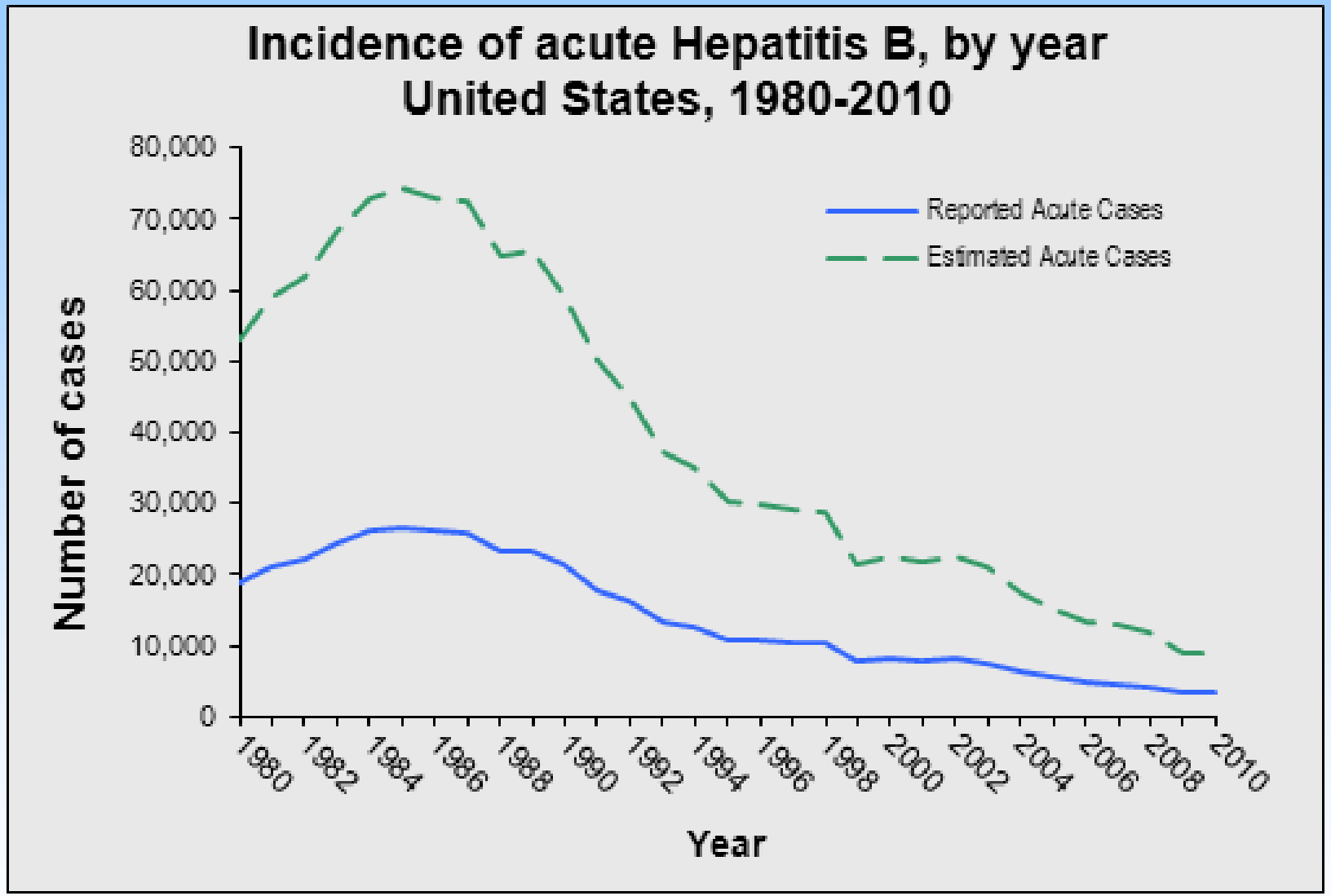


CDC

- A generally mild childhood disease caused by a virus
- Infection during pregnancy may result in fetal infection (congenital rubella syndrome)
  - Multiple defects in infants
    - Brain, Heart, Hearing, Liver

Hepatitis B

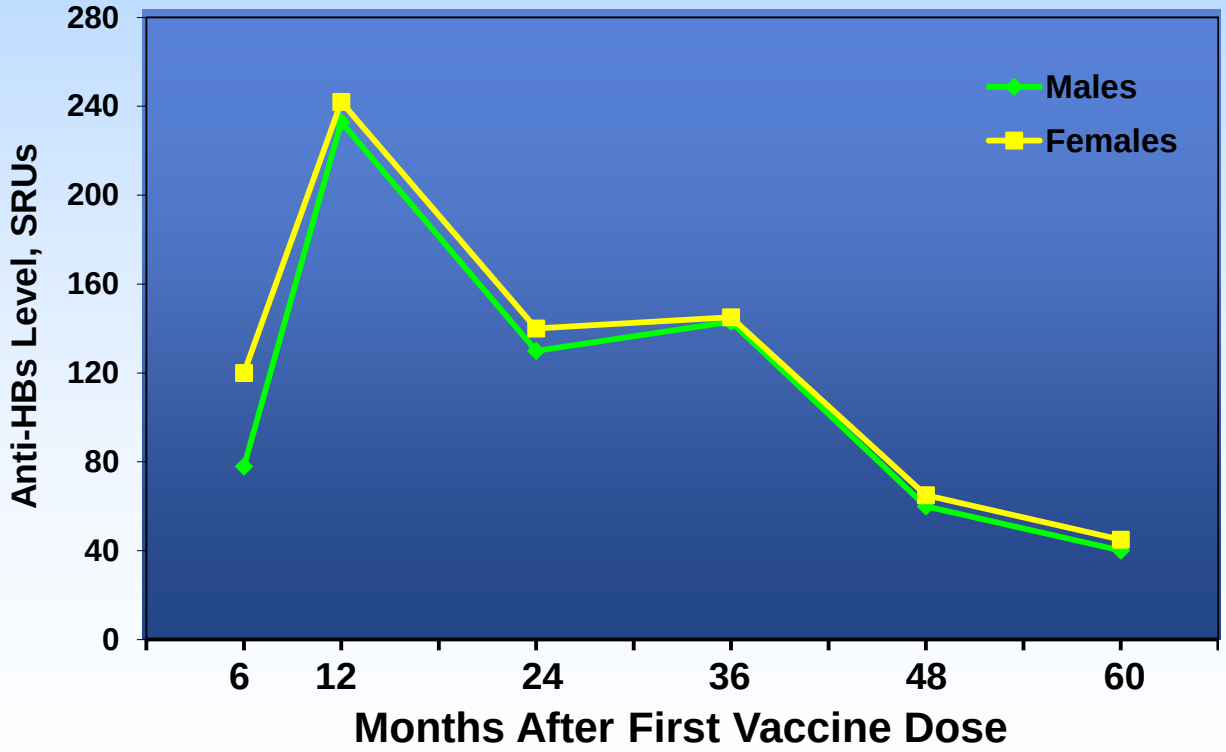

Countries using HepB vaccine in their national infant immunization system, as of December 2003
Routine HepB implementation status
Yes (138 countries or 72%)
Yes in part of the country (9 countries or 5%)
No (45* countries or 23%)
*5 countries use HepB among adolescents
Source: WHO/UNICEF Joint Reporting Form, 2004. Data collected from 192 WHO Member States as of 20 September 2004
Date of slide: 20 September 2004



http://www.cdc.gov/hepatitis/statistic.html (accessed 20 Oct 2011)

Hepatitis B Immune Response Level Through 5 Years Post-Vaccination[1]

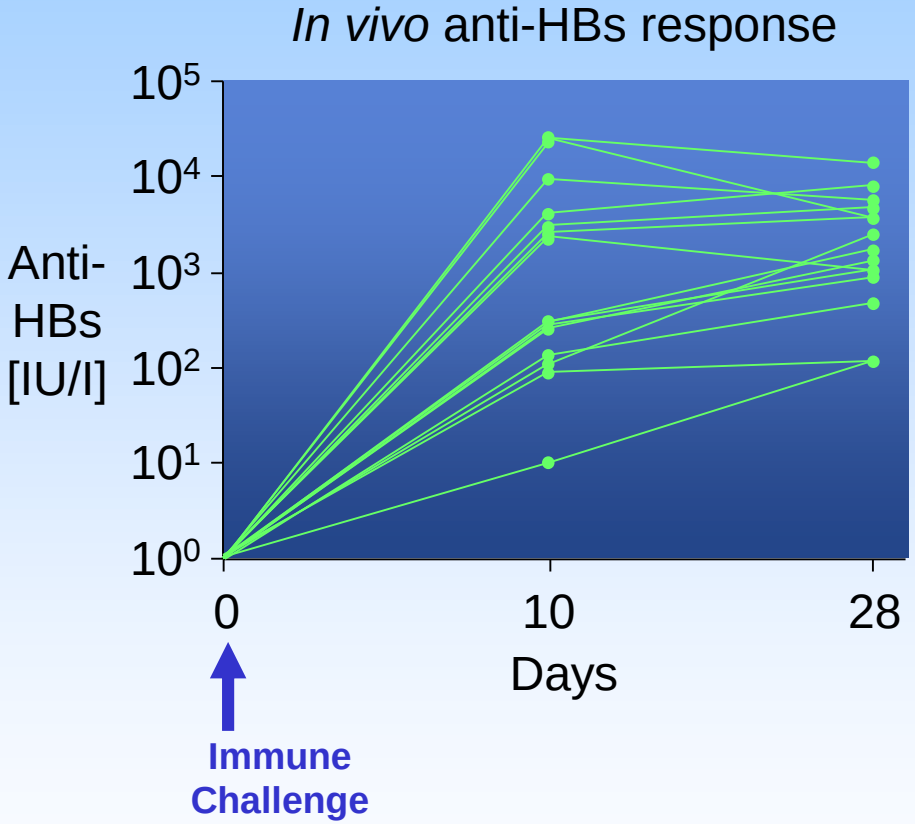
- Protection against hepatitis B virus (HBV) is based on the presence of specific antibodies against anti-HBs antigen.[2]
  - Anti-HBs levels disappear in 10-50% of vaccinees after a few years.[2]
  - No booster has been recommended to date.[3]



1. Wainwright RB, McMahon BJ, Bulkow LR, et al. *JAMA*. 1989;261:2362–2366. 2. Bauer T and Jilg W. *Vaccine*. 2006;24:572-577. 3. Mast E, Mahoney F, Kane M, Margolis H. Hepatitis B vaccine. In: Vaccine, 4th Ed. Plotkin SA, Orenstein WA editors. Elsevier Inc. USA publisher; 2004.

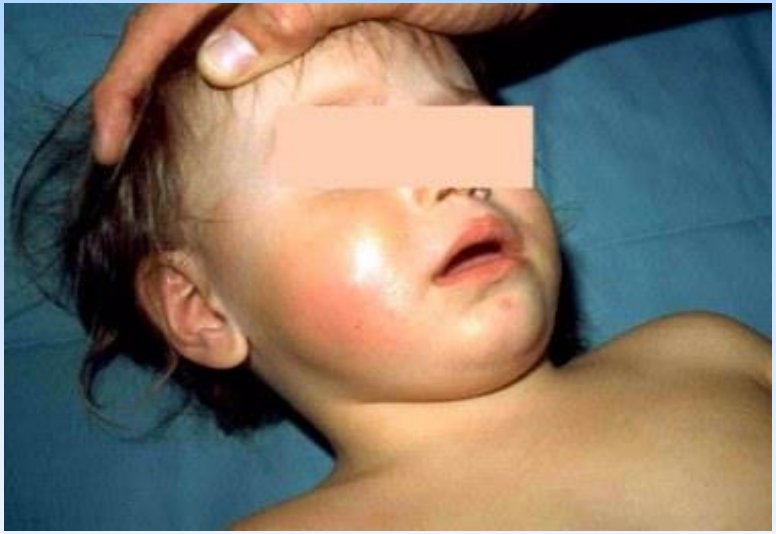
Anti-HBs After Immune Challenge[1]

- Immune memory persists beyond the time at which anti-HBs levels may no longer be detectable.
- Immune memory leads to a rapid anamnestic response after exposure to HBV, which prevents acute infection (and disease).



1. Bauer T, Jilg W. *Vaccine*. 2006;24:572–577.

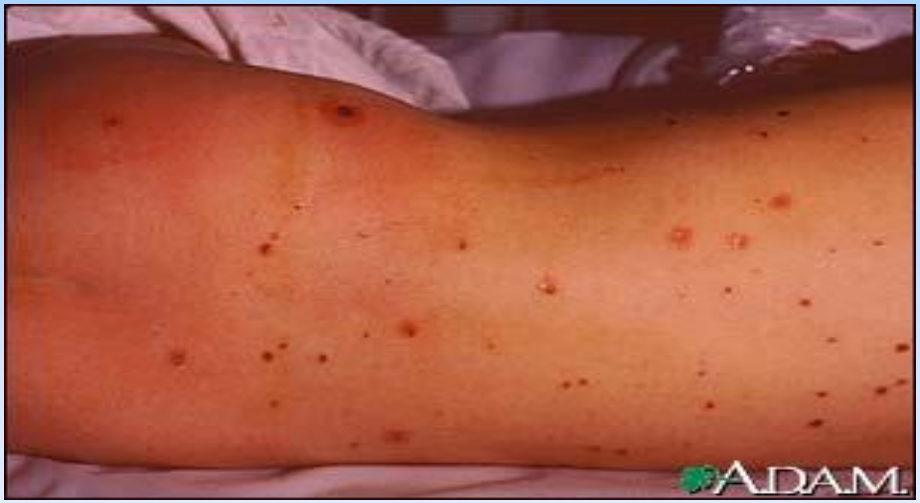
Haemophilus influenzae type b (Hib)



AAP

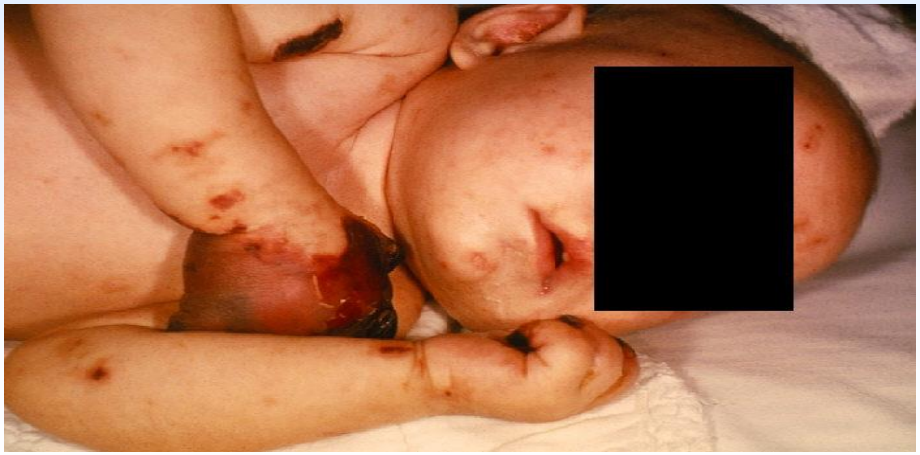
- Causes severe infection in many organs
- Before routine use of effective vaccines, Hib was the leading cause of bacterial meningitis in young children

Neisseria Meningitidis



National Library of Medicine

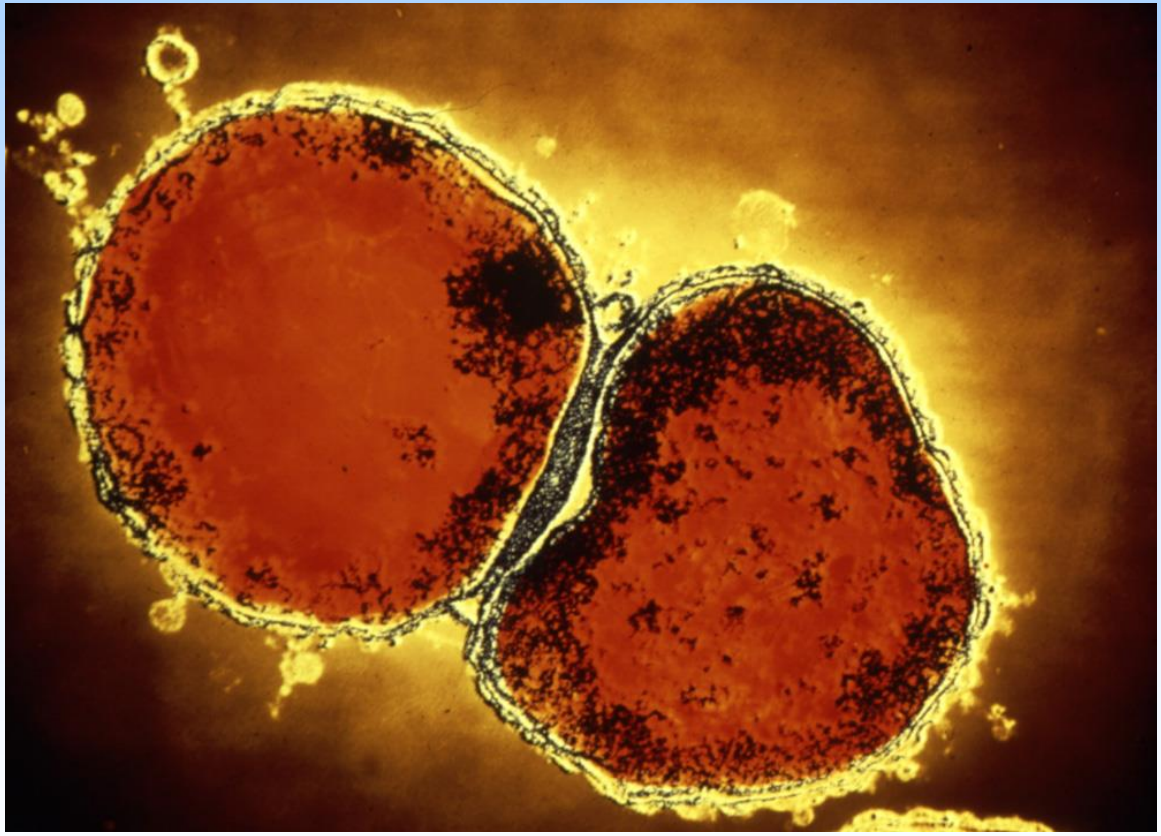
Typical rash of meningococcal septicemia



CDC/Mr. Gust

In this picture, confluent purpuric areas have formed with blistering and necrosis

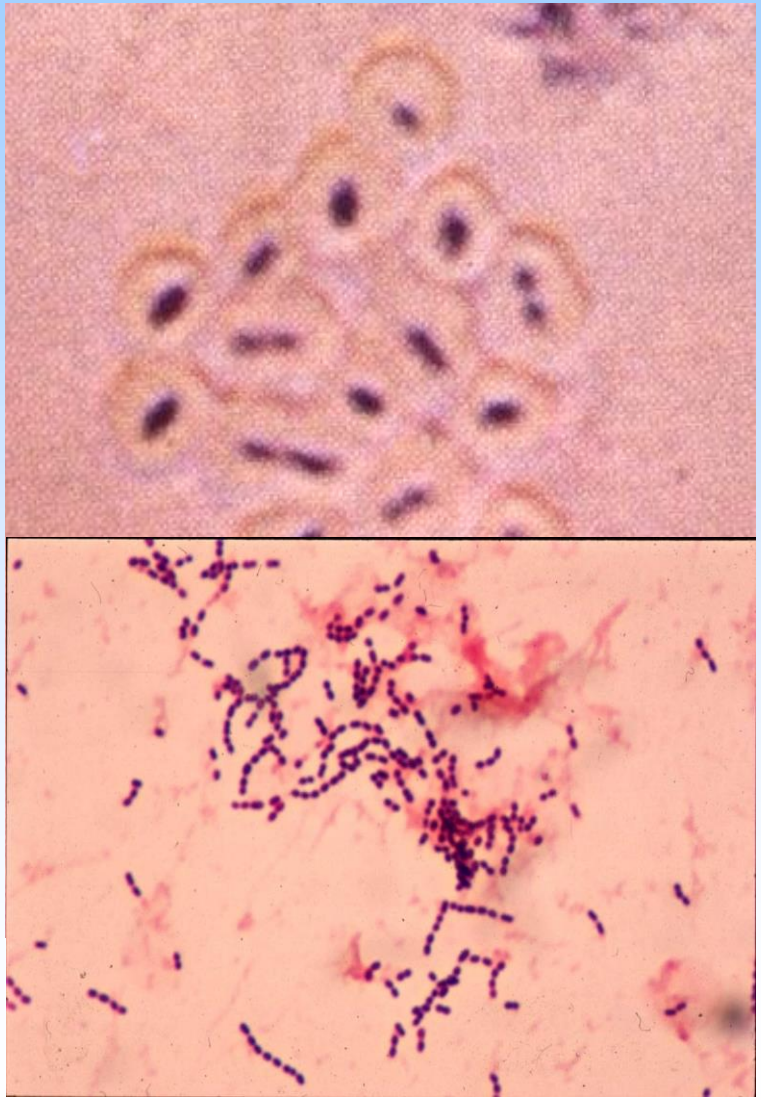
N. meningitidis[63]



Custom Medical Stock Photo, 2003

Streptococcus pneumoniae

- Gram-positive, facultative, encapsulated
- Capsular polysaccharides form the basis of serogroup and serotype classifications
- 90 serotypes
- Leading cause of vaccine-preventable bacterial disease in children
- The most common bacterial cause of
  - Community-acquired pneumonia (17-28%)
  - AOM (２５－５０%)
  - Sinusitis



Pediatr Infect Dis J 1992;11:S7--11

S. pneumoniae Disease Classification

Mucosal Disease	Invasive Disease
Pneumonia	Pneumonia*
Acute otitis media (AOM)	Bacteremia/sepsis
Sinusitis	Meningitis
Conjunctivitis	Other focal, sterile-site infections from hematogenous dissemination

***S. pneumoniae* disease may be classified as mucosal or invasive**

*Pneumonia may be classified as mucosal or invasive disease.
It is invasive if accompanied by bacteremia, pleural effusion, or other invasive complication.

CDC. *Morb Mortal Wkly Rep.* 1997;46(RR-8):1-24.

Impact of Pneumococcal Disease on Children

- Pneumococcal disease can result in[1-5]:
  - Death
  - Paralysis
  - Mental retardation
  - Seizures
  - Learning disabilities
  - Hearing loss
  - Other sequalae

1. Kornelisse RF, et al. *Clin Infect Dis*. 1995;21:1390-1397.
2. CDC. *Morb Mortal Wkly Rep*. 1997;46(RR-8):1-24.
3. Klein JO, et al. *Textbook of Pediatric Infectious Diseases.* 5th ed.; 2004:215-235.
4. Pikis A, et al. *Clin Pediatr (Phila).* 1996;35:72-78.
5. Dodge PR, et al. *N Engl J Med.* 1984;311:869-874.

Risk Factors for IPD

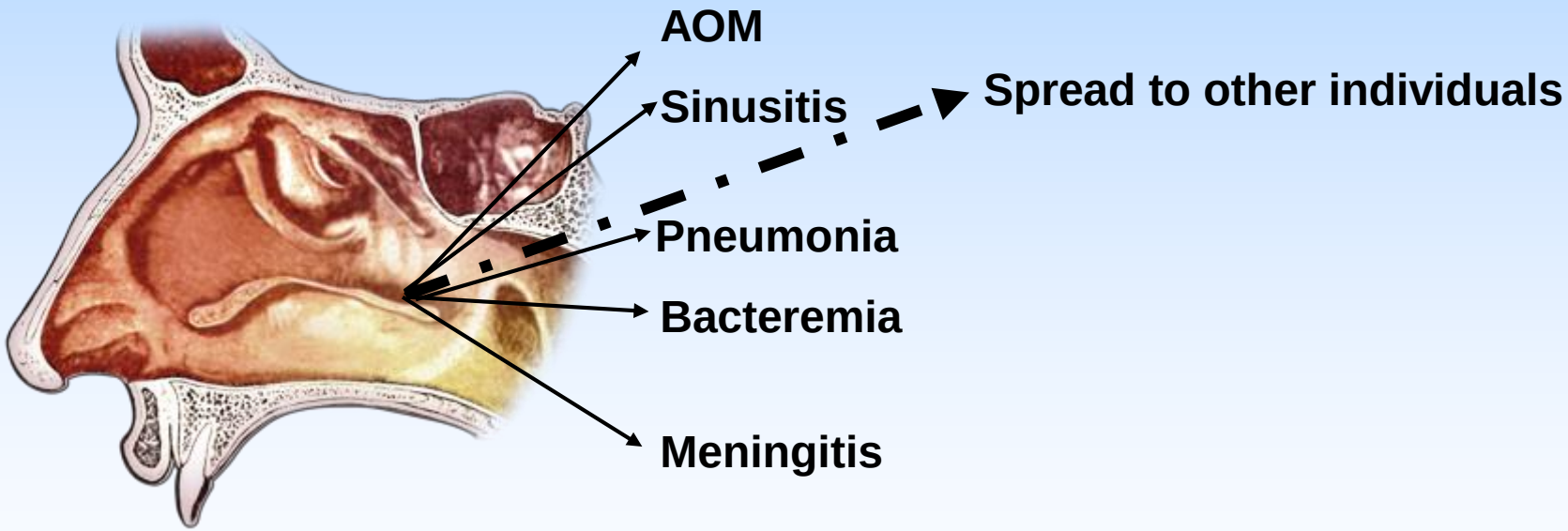
Age[1]	Underlying Medical Conditions[2,3]	Demographic Features[3,4]
• Children ≤2 years of age • Adults ≥65 years of age	• Congenital or acquired immunodeficiency • Sickle cell disease, asplenia, HIV • Pulmonary disease • Chronic heart disease • Chronic renal insufficiency, nephrotic syndrome • Diabetes • Cerebrospinal fistula • Existing or cochlear implants	• Day care attendance • Ethnicity

- **Age is the most important risk factor for pneumococcal disease[1]**

1. CDC. *Morb Mortal Wkly Rep*. 1997;46(RR-8):1-24.
2. Pickering LK. *Red Book.* 26th ed; 2003.
3. CDC. *Morb Mortal Wkly Rep*. 2000;49(RR-9):1-35.
4. Levine OS, et al. *Pediatrics.* 1999;103:1-5.

Nasopharyngeal Colonization

- ***S. pneumoniae*** **can be a normal inhabitant of the nasopharynx[1]**
- **Global nasopharyngeal (NP) colonization/carriage ranges:**
  - **10% to 85% in children <5 years of age[2,3]**
  - **4% to 45% in adults[2-4]**

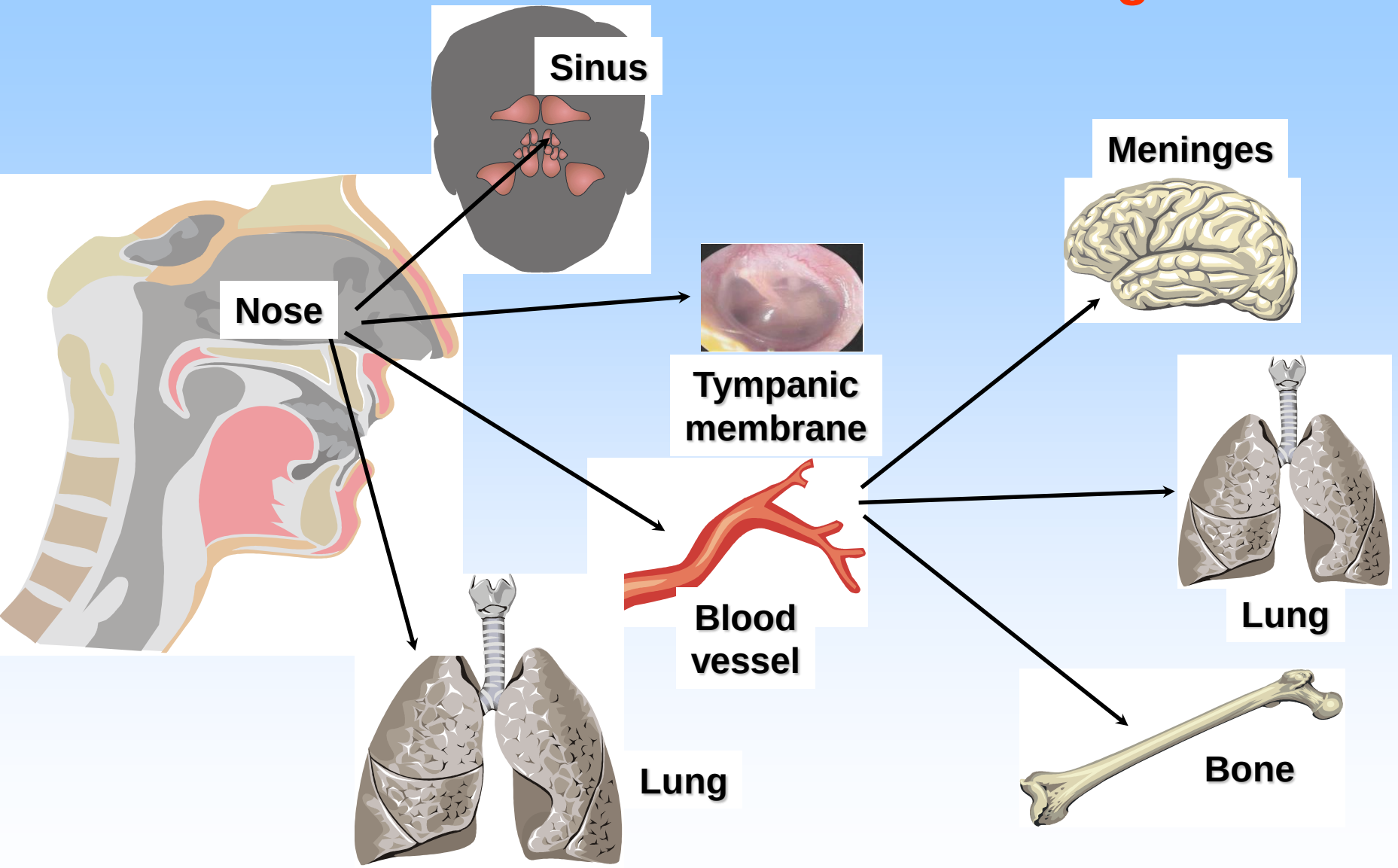


NP colonization is generally a prerequisite for mucosal and invasive pneumococcal disease[2,4]

Image adapted from: http://www.1911encyclopedia.org/images/f/f4/Olfactorysystem-2.jpg.

1. Hull MW, et al. *Infect Dis Clin North Am*. 2007;21:265-282.
2. Cardozo DM, et al. *Braz J Infect Dis*. 2006;10:293-303.
3. Regev-Yochay G, et al. *Clin Infect Dis*. 2004;38:632-639.
4.Chi DH, et al. *Am J Rhinol*. 2003;17:209-214.

Infection Pathogenesis



Invasive Pneumococcal Diseases among Malaysian Children

Tan Kah Kee MD
Pediatric Infectious Disease Consultant
Hospital Tuanku Ja'afar
70300 Seremban

Presented at National Pneumococcal workshop 28 March 2015

Pneumococcal Infections

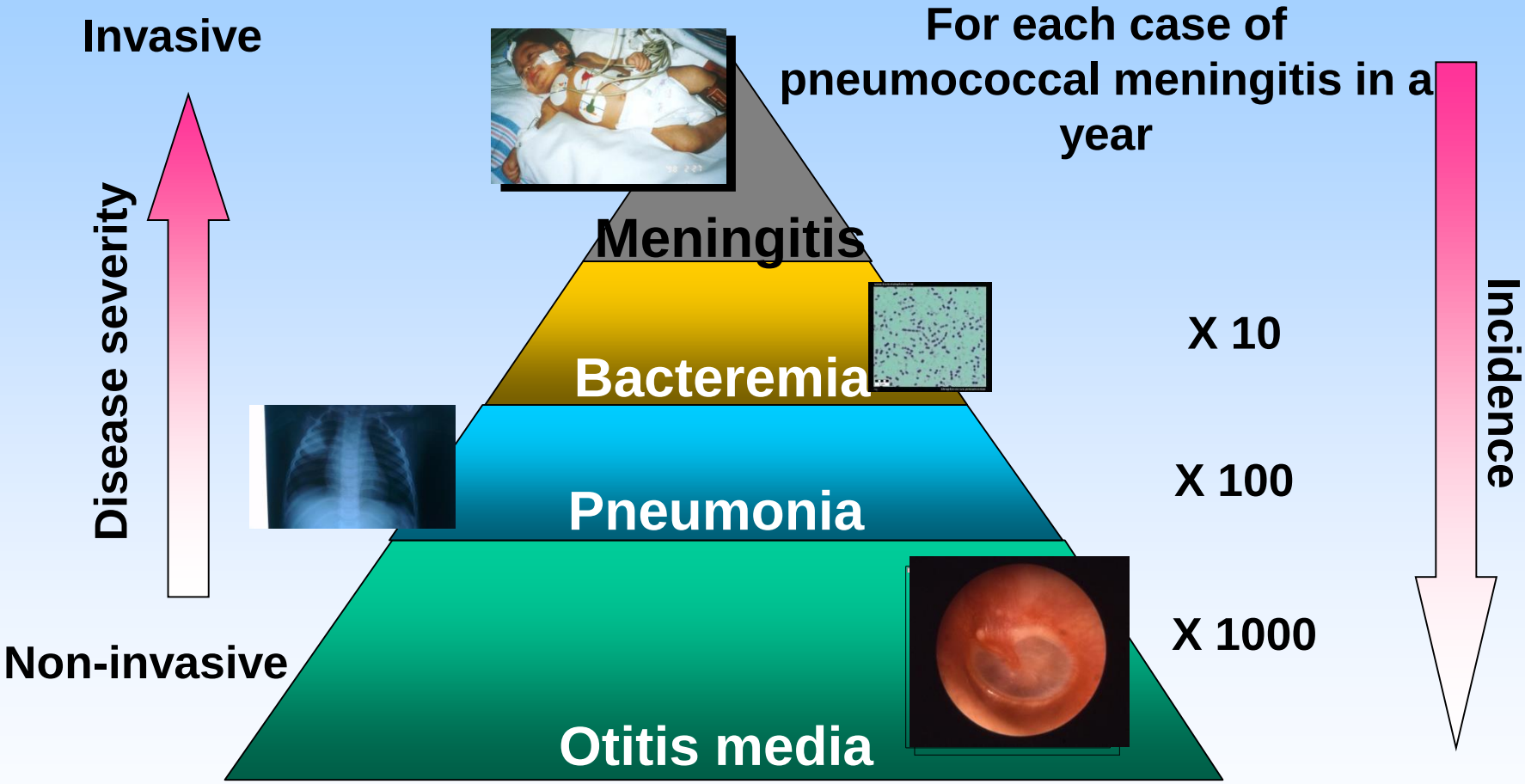
- Burden of disease highest in youngest & oldest sections of population
- Annual deaths : 1 million < 5 years old
- High case fatality rates in meningitis(20-50%)
- 30-60 % of survivors with long-term sequalae
- Treatment complicated by worldwide emergence of penicillin-resistance (IMR 2011: 36.9% penicillin-nonsusceptible)

Streptococcus Pneumoniae

- Common inhabitants of respiratory tract
- > 90 known serotypes
- 6-11 most common serotypes account for >70% of invasive disease worldwide.
- Polysaccharide capsule important virulence factor
- Type-specific antibody is protective

Weekly Epidemiol Record 2012 ; 87:129-144
Johnson HL et al;PLoS Med 2010

S. pneumoniae Disease Burden in Children



Annual incidence of invasive pneumococcal disease in <2 year olds ~150/100,00, United States

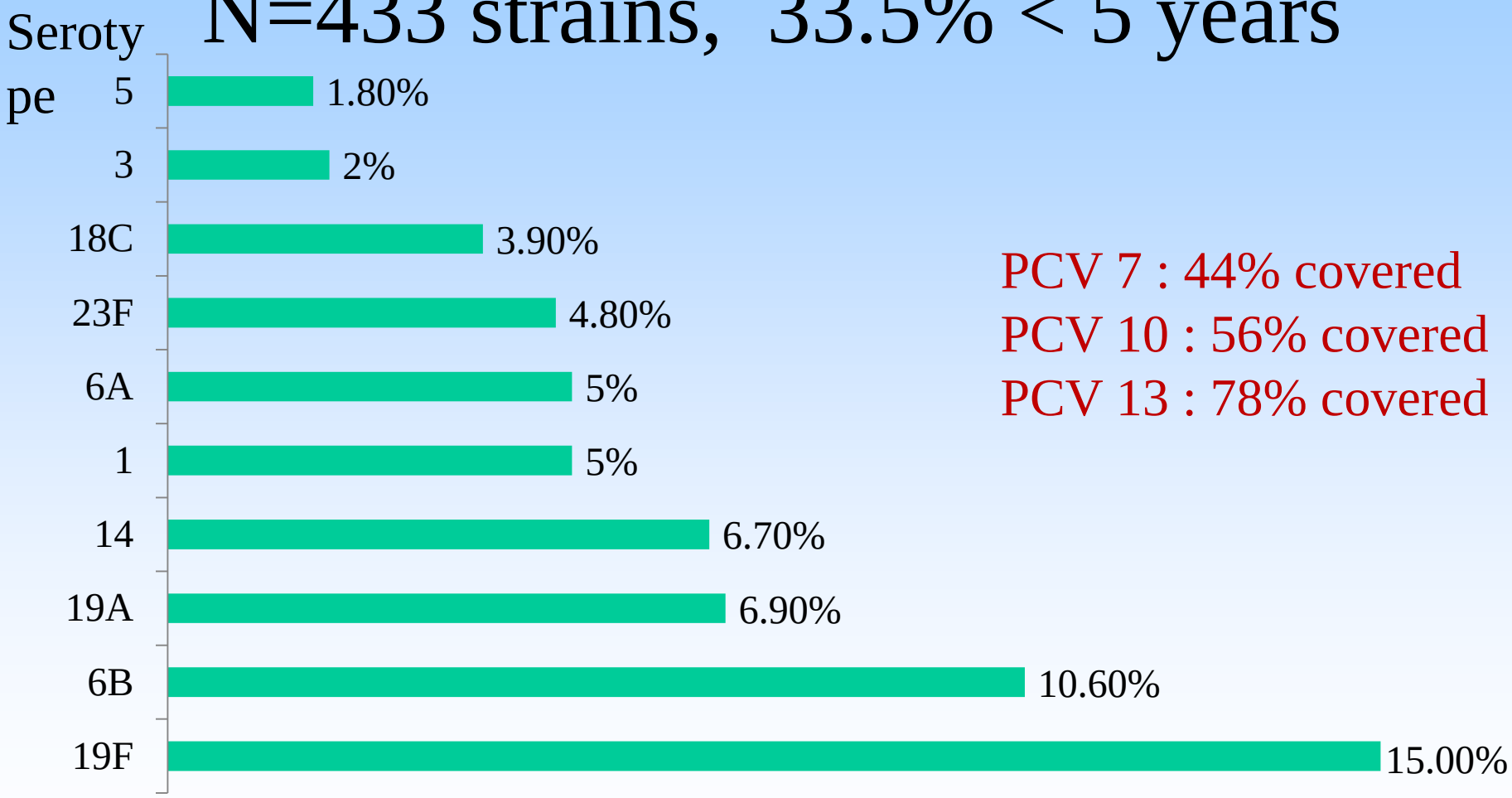
Pediatrics. 2000;106:367-376 & MMWR. 1997;46:1-24

Invasive Pneumococcal Disease Syndromes

- Bacteremia
- Meningitis
- Pneumonia
- Septic arthritis
- Hemolytic uremic syndrome

Copelovitch L et al;Pediatrics 2010 ; 125

Pneumococcal serotypes in Malaysia N=433 strains, 33.5% < 5 years



PCV 7 : 44% covered
PCV 10 : 56% covered
PCV 13 : 78% covered

Yasin MR et al;Vaccine 2011;34

Invasive Pneumococcal Disease in Hospitalised Malaysian Children

- Children with IPD & isolation of Strept. Pneumo. in sterile sites recruited (blood,CSF,pleural fluid, joint,peritoneal & pericardial) between 1 Jan 2007-31 Dec 2009
- 13 participating hospitals nationwide
- Pneumococcal isolates send to IMR for serotyping.
- Quellung reaction for serotyping

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Participating Hospitals (N=13)

- HKL
- HIP
- HPP
- HKB
- HTJ
- UMMC
- HKT
- HTAA
- HTAR
- HSB Alor Setar
- HSelayang
- HUS Kuching
- HLikas KK

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Results (1) - Demographics

- Total patients with IPD =164 (2008:88 ; 2009:76)
- Gender distribution : Males 56.7%(N=93) ; Females 43.3%(N=71)(M:F = 1.3 : 1)
- Racial distribution : Malays 66.7% , Chinese 7.3% , Indians 1.8% , Ibans 1.8% , Bidayuh(0.6%) , Kadazan 0.6% , Others 21.2%

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Results(2) - Demographics

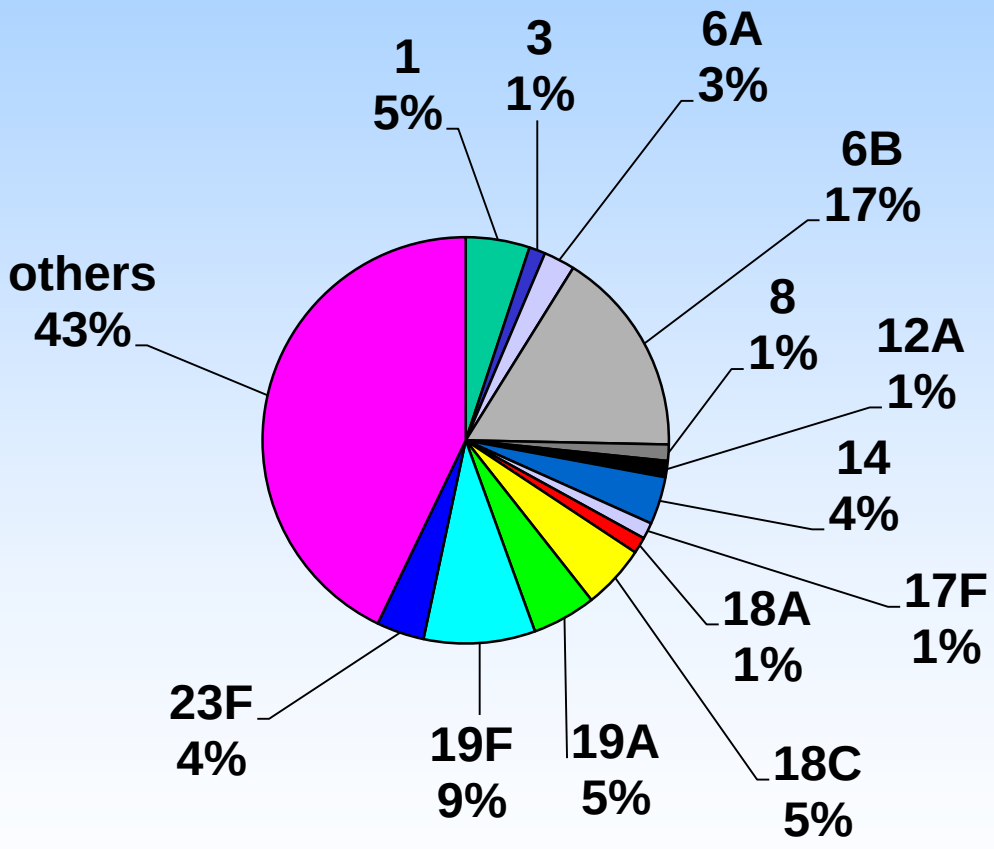
- Mean age = 25.7 mths
- Median age = 15.0 months
- Range = 0-144 months
- Age < 2 yrs = 68.3% (N=112)
- Age < 5 yrs = 86.6%(N=142)

Results(3) – Blood , CSF , Pleural fluid

- Blood culture +ve = 85.6% (N=160)
- CSF culture +ve = 39.6% (N=56)
- CSF antigen +ve(latex) = 55.6%(N=20)
- Pleural fluid culture +ve = 64.3%(N=28)

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Results(4)- Pneumococcal Serotypes (N=79)



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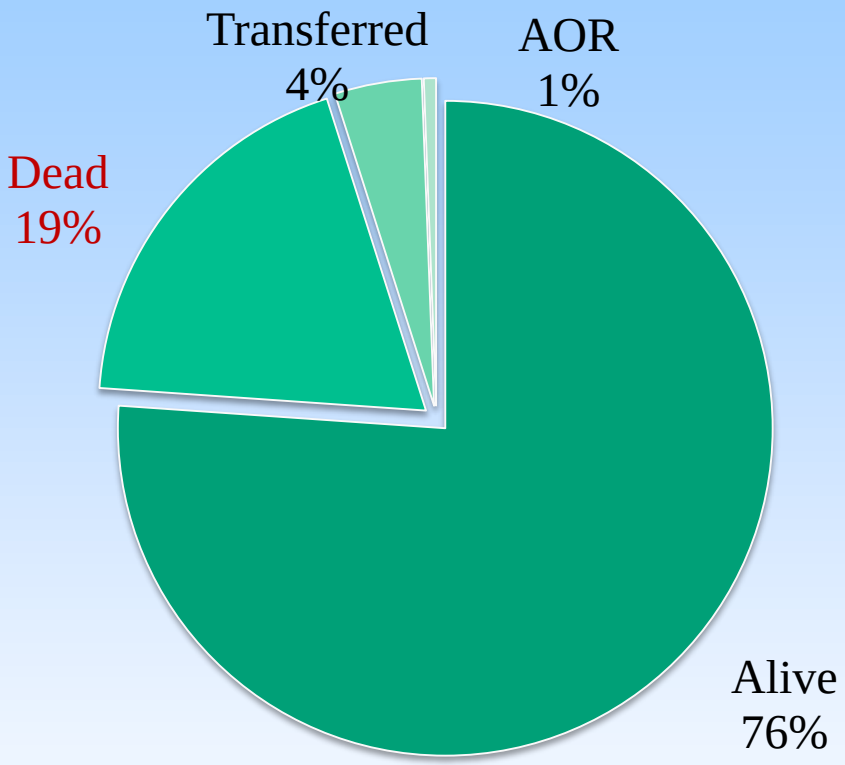
Serotypic Coverage

- 7-valent = 37.9% (30/79)
- 10-valent = 43.0% (34/79)
- 13-valent = 51.8% (41/79)

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Outcome



13%(N=21) has neurological sequalae at discharge

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Ventilatory Support

- 44%(N=72) required ventilatory support
- Median duration = 4 days
- Range = 1-43 days

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Penicillin Susceptibility

- Blood isolates : S 84.5% I 2.3% R 13.2%
- CSF isolates : S 89.5% I 10.5% R 0%

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Study Limitations

- Mild cases may not be captured
- Private hospital cases not included
- Culture method limited by prior antibiotics
- Molecular methods during study not available

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Summary of findings

- IPD is severe in Malaysian children
- Significant mortality
- Serotypic coverage moderate
- Penicillin resistance moderate

Dr Tan Kah Kee, Paediatric Infectious Disease Specialist (used with permission)

Conclusions

- Invasive pneumococcal disease is a serious cause of morbidity & mortality in Malaysian children
- Different spectrum of pneumococcal infection seen
- Mortality does occur in spite of appropriate therapy
- Penicillin resistance moderate
- Preventive measure by vaccination needs urgent consideration

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Perubahan Jadual Imunisasi MMR

Jadual Lama :

IMUNISASI	Umur (Bulan)										(Tahun)		
	0	1	2	3	5	6	9	12	18	21	7	13	15
BCG	Dos 1										Tiada parut		
Hepatitis B	Dos 1	Dos 2				Dos 3							
DTaP			Dos 1	Dos 2	Dos 3				Booster				
Hib			Dos 1	Dos 2	Dos 3				Booster				
Polio (IPV)			Dos 1	Dos 2	Dos 3				Booster				
Measles						Sabah sahaja							
MMR								Dos 1					
MR											Booster		
DT											Booster		
OPV													
HPV												Perempuan sahaja	
Tetanus													Booster

Jadual Baru :

IMUNISASI	Umur (Bulan)										(Tahun)		
	0	1	2	3	5	6	9	12	18	21	7	13	15
BCG	Dos 1												
Hepatitis B	Dos 1	Dos 2				Dos 3							
DTaP			Dos 1	Dos 2	Dos 3				Booster				
Hib			Dos 1	Dos 2	Dos 3				Booster				
Polio (IPV)			Dos 1	Dos 2	Dos 3				Booster				
Measles						Sabah sahaja							
MMR							Dos 1	Dos 2					
MR											Booster		
DT											Booster		
OPV													
HPV												Perempuan sahaja	
Tetanus													Booster
JE (Sarawak)							Dos 1			Dos 2			

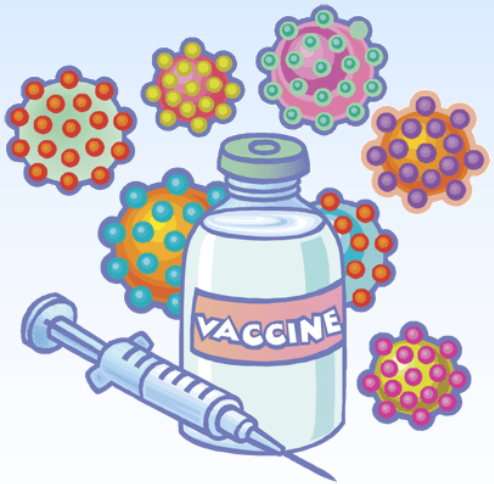
Jadual baru Imunisasi MMR digunakan bermula tahun 2016

Diterbitkan oleh :
Bahagian Pendidikan Kesihatan
Kementerian Kesihatan Malaysia
www.infosihat.gov.my I www.myhealth.gov.my

Some concerns of parents

Common questions about vaccines

- Do I need to vaccinate my child against diseases that aren't common anymore?[15]
- Are vaccines safe?[16]
- Do vaccines cause autism?[16]
- Are preservatives found in vaccines?[16]
- Can my child get a disease from a vaccine?[16]
- My child is allergic to eggs
- Are vaccines halal?



Ref 15: CDC, p 8

Ref 16: IOM, p 1, 4

Some vaccine side effects

- Common side effects[5]
  - Redness, swelling, and pain at injection site
  - Low-grade fever
- Uncommon, serious side effects[5]
  - Allergic reaction

Ref 5: AAP, p 38, 46

Advice on vaccination of those with egg allergy

- Influenza vaccines (containing <1 μg of ovalbumin per dose) can be given to most people with egg allergy, including anaphylaxis
  - Those with severe allergy should be vaccinated in settings where anaphylaxis can be recognised/treated
- MMR vaccines can be given to any egg allergic person

“Natural Immunity” (Getting Immunity By Getting Sick)

- What is it? Does it work? What are the costs?
- Some people believe that it’s better to get a disease naturally than to be vaccinated against it.
- One theory is that chickenpox, for example, helps mature the immune system.
- And a mature immune system should be better able to fight infection from diseases, right?
- What are the facts about natural immunity?

Choosing Natural Immunity Is Risky!

- Chickenpox kills children in the United States every year.
- Before a chickenpox vaccine was licensed, almost 7,000 children per year were hospitalized for serious complications of chickenpox like encephalitis, hepatitis, flesh eating-strep, and toxic shock syndrome.

Choosing Natural Immunity Can Be Risky To Others.

- A parent who is not immune to chickenpox can easily catch the disease from an infected child. 1 in 5 adults who get chickenpox develops pneumonia, which can be deadly.
- If a “routine” disease like chickenpox can have these results, natural immunity is a risky alternative to vaccination.

Childhood Diseases Carry Serious Risks.

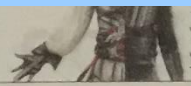
- Hib or pneumococcal disease can cause bacterial meningitis, leading to brain damage or death.
- Pertussis (whooping cough) can cause coughing spells so bad that it is hard for infants to eat, drink, or breathe. These spells can last for weeks. Pertussis can lead to pneumonia, seizures, brain damage, and death.
- Polio may lead to paralysis and death. Polio used to be very common in the United States, killing and paralyzing thousands of people a year.
- Tetanus (lockjaw) infection can cause painful tightening of the muscles. It can lead to "locking" of the jaw so the victim cannot open his mouth or swallow. Tetanus results in death in about 10% of cases.

HERD IMMUNITY

- Children who are immunised are protected from the disease. They cannot get the disease and they cannot give the disease
- If enough children are vaccinated against a disease then the disease cannot spread into the community.
- This is called “herd immunity”

seas are part of the day's routine for navy men. >8

Rights of non-Muslims in Islamic countries are protected, says mufti. >12



videogames into movies for years, with limited success. >2

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THE Star

the people's paper

world

QUICKIE DIVORCE

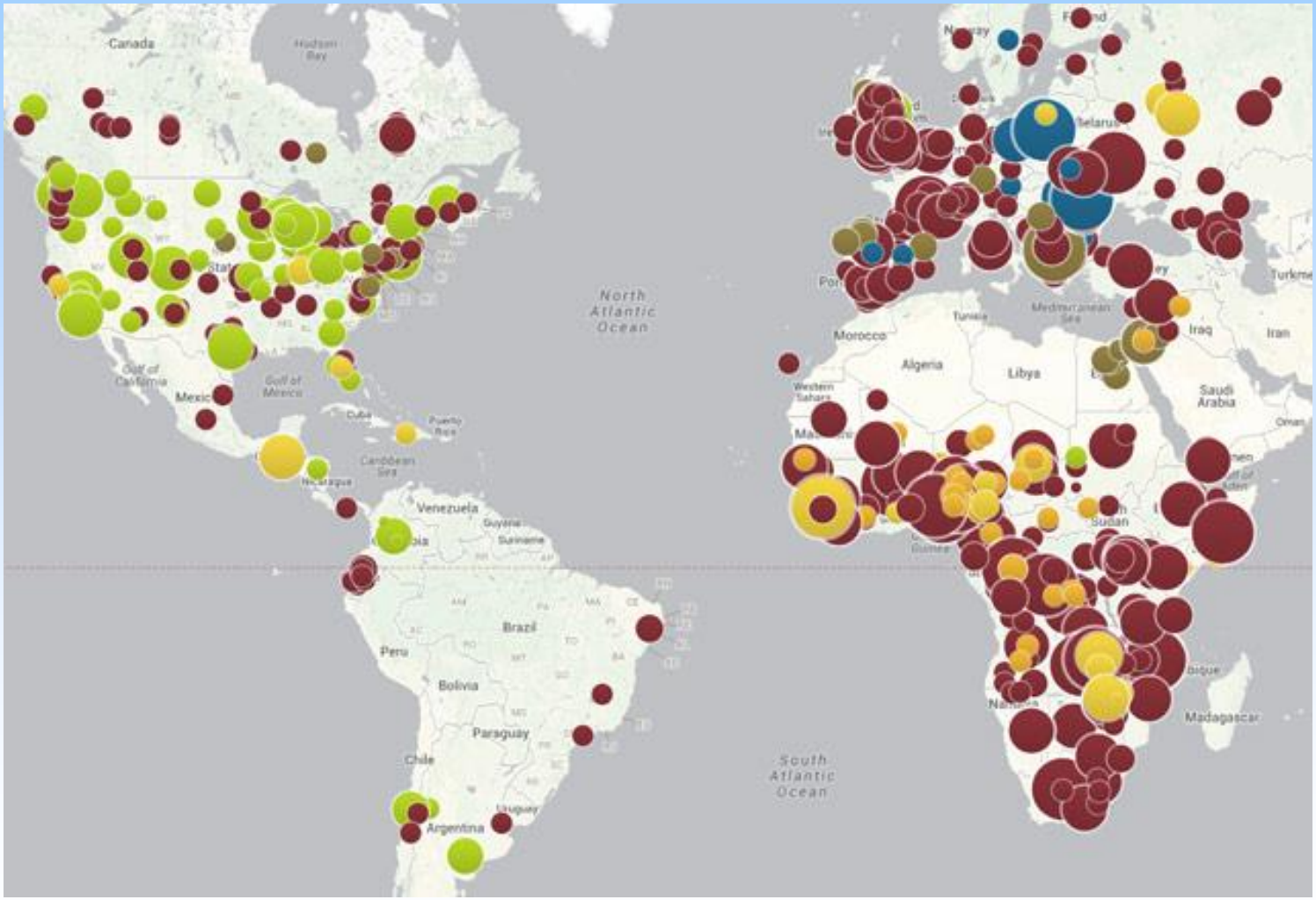
EU wants Britain to make a quick exit but German chancellor calls for a sober separation. >20

A prickly problem

Diphtheria, a deadly disease that was wiped out in Malaysia, is back and there has been a huge spike in the number of measles cases – all because parents believe in myths and rumour-mongering about vaccination. The Health Ministry, the Education Ministry and even the state religious authorities are working to ensure children get immunised for their own good.

>See reports on Page 4

Anti Immunization Movement



Measles outbreaks (purple) worldwide and whooping cough (green) in the U.S. 2008-2014 (Council on Foreign Relations),

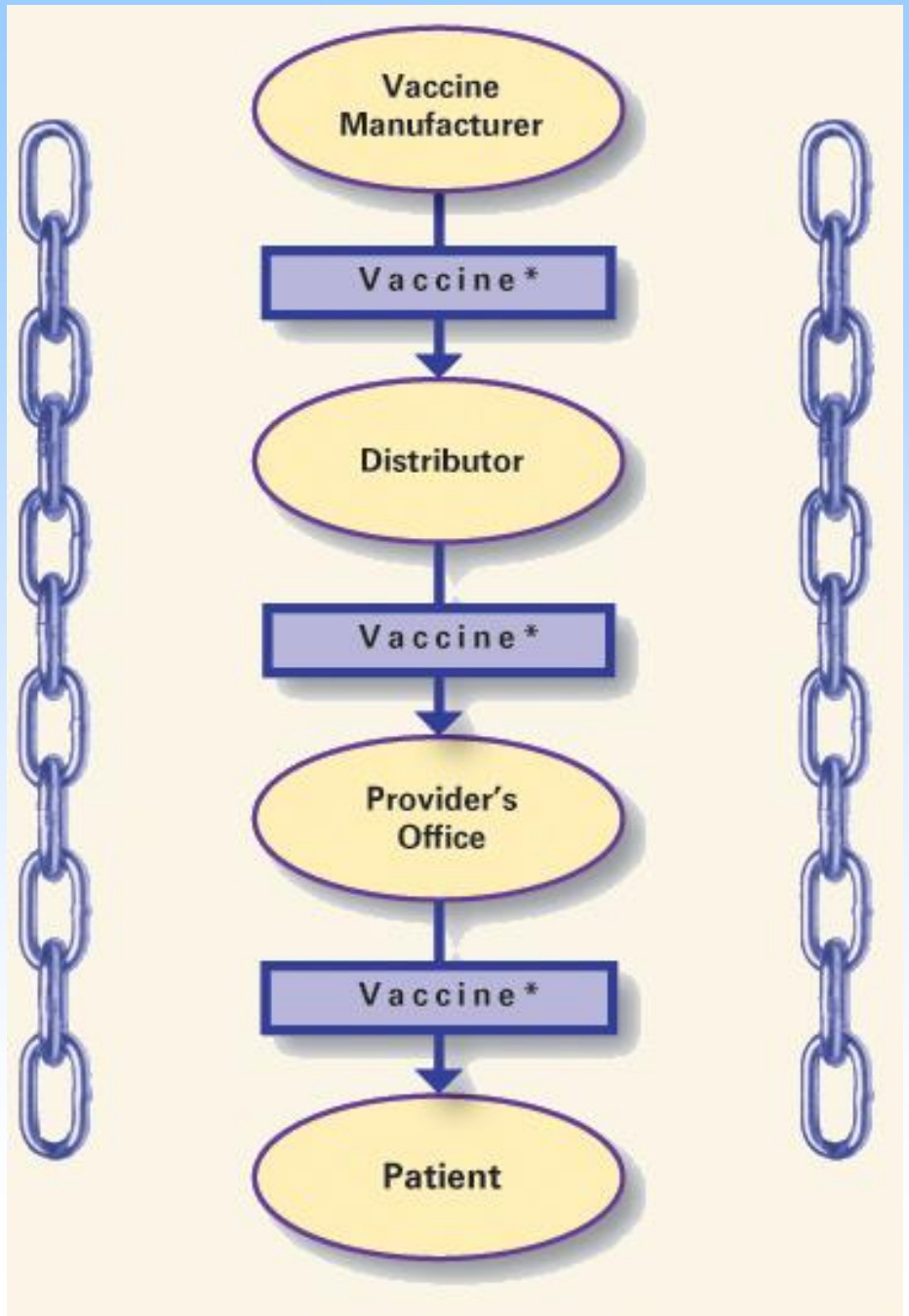
Accessed 23 Jan 2014. http://www.latimes.com/business/hiltzik/la-fi-mh-antivaccination-movement-20140120,0,5576371.story#ixzz2rHqM1Aec

MMR and Autism

- The original paper (now RETRACTED) – Lancet, 1998

1. *Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association* - Lancet, 1999
2. *Time trends in autism and in MMR immunization coverage in California* - JAMA, 2001
3. *A population-based study of measles, mumps, and rubella vaccination and autism* - NEJM, 2002
4. *Neurologic disorders after measles-mumps-rubella vaccination* - Pediatrics, 2002
5. *MMR vaccination and pervasive developmental disorders: a case-control study* - Lancet, 2004
6. *Age at first measles-mumps-rubella vaccination in children with autism and school-matched control subjects: a population-based study in metropolitan Atlanta* - Pediatrics, 2004
7. *Vaccines for measles, mumps and rubella in children* - Cochrane Collaboration, 2005
8. *Vaccines for measles, mumps and rubella in children* - Cochrane Collaboration, 2012
9. *How the case against the MMR vaccine was fixed by Brian Deer*, BMJ, 2011
10. *Wakefield's article linking MMR vaccine and autism was fraudulent* - BMJ Editorial, 2011

The Cold Chain


Vaccine Manufacturer
Vaccine*
Distributor
Vaccine*
Provider's Office
Vaccine*
Patient


VACCINE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Store in Freezer
5°F (-15°C) or colder
MMRV*
Varicella*
Zoster*
MMR*,+
Store in Refrigerator
35°F–46°F (2°–8°C)
MMR*,+
Inactivated Combination Vaccines
Vaccines containing Diphtheria, Tetanus, and/or acellular Pertussis
Hepatitis A
Hepatitis B
Hib
HPV*
Influenza (LAIV & TIV)
IPV
Meningococcal (MCV & MPSV)
Pneumococcal (PCV & PPV)
Rotavirus
* Do not expose to light.
+ Unreconstituted lyophilized (freeze-dried) MMR may be frozen or refrigerated.

Dengvaxia (Sanofi)

Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial

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Summary

Background An estimated 100 million people have symptomatic dengue infection every year. This is the first report of a phase 3 vaccine efficacy trial of a candidate dengue vaccine. We aimed to assess the efficacy of the CYD dengue vaccine against symptomatic, virologically confirmed dengue in children.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease

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ABSTRACT

BACKGROUND

A candidate tetravalent dengue vaccine is being assessed in three clinical trials involving more than 35,000 children between the ages of 2 and 16 years in Asian–Pacific and Latin American countries. We report the results of long-term follow-up interim analyses and integrated efficacy analyses.

METHODS

We are assessing the incidence of hospitalization for virologically confirmed dengue as a surrogate safety end point during follow-up in years 3 to 6 of two phase 3 trials, CYD14 and CYD15, and a phase 2b trial, CYD23/57. We estimated vaccine efficacy using pooled data from the first 25 months of CYD14 and CYD15.

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*A complete list of investigators in the CYD-TDV Dengue Vaccine Working Group is provided in the Supplementary Appendix, available at NEJM.org.

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