

# VACCINATION

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September 2021

# Outline

- Basics of vaccination.
- General rules in vaccination
- Vaccines in common use (routine childhood vaccines and vaccination)
- Expanding the vaccination schedule
- Recent COVID vaccines
- Vaccination schedules
- Vaccines in use in Jordan

# Basics of immunization




## IMMUNIZATION SAVES LIVES

- Immunization saves up to 3 million lives annually
- Vaccines are available to protect against the following 26 infectious diseases, with many more in development






*Cholera • Dengue • Diphtheria • Hepatitis A • Hepatitis B • Hepatitis E • Haemophilus influenzae type b (Hib) • Human papillomavirus • Influenza • Japanese encephalitis • Malaria • Measles • Meningococcal meningitis • Mumps • Pertussis (whooping cough) • Pneumococcal disease • Poliomyelitis • Rabies • Rotavirus • Rubella • Tetanus • Tick-borne encephalitis • Tuberculosis • Typhoid • Varicella (chickenpox) • Yellow Fever*  
**RECENTLY ADDED COVID vaccines**

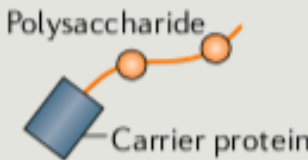
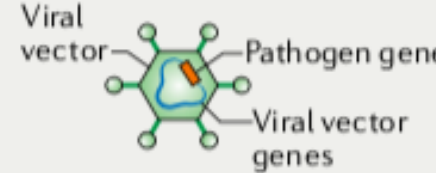

# Vaccines are not new! The history

Type of vaccine		Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)		Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism		Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid		Diphtheria, tetanus	1923 (diphtheria)


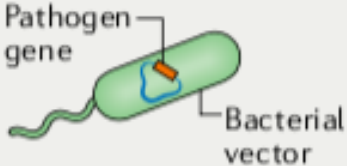
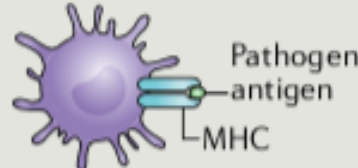
# New and old ways of making vaccines

<b>Subunit (purified protein, recombinant protein, polysaccharide, peptide)</b>		Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
<b>Virus-like particle</b>		Human papillomavirus	1986 (hepatitis B)
<b>Outer membrane vesicle</b>		Group B meningococcal	1987 (group B meningococcal)

# Other modes of making vaccines

<b>Protein-polysaccharide conjugate</b>	 <p>Polysaccharide Carrier protein</p>	<i>Haemophilus influenzae</i> type B, pneumococcal, meningococcal, typhoid	1987 ( <i>H. influenzae</i> type b)
<b>Viral vectored</b>	 <p>Viral vector Pathogen gene Viral vector genes</p>	Ebola	2019 (Ebola)
<b>Nucleic acid vaccine</b>	 <p>DNA RNA Lipid coat</p>	SARS-CoV-2	2020 (SARS-CoV-2)

# New ways of making vaccines

<b>Nucleic acid vaccine</b>	 <p>DNA</p> <p>RNA</p> <p>Lipid coat</p>	SARS-CoV-2	2020 (SARS-CoV-2)
<b>Bacterial vectored</b>	 <p>Pathogen gene</p> <p>Bacterial vector</p>	Experimental	–
<b>Antigen-presenting cell</b>	 <p>Pathogen antigen</p> <p>MHC</p>	Experimental	–

# Vaccination NOT vaccines (by themselves) SAVE LIVES AND KEEPS PEOPLE HEALTHY

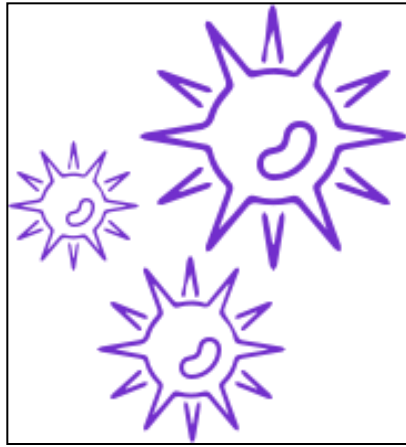
- Immunization saves up to 3 million lives annually
- Vaccines are available to protect against the following 26 infectious diseases, with many more in development
- The challenge is to make sure that all members of society have access to needed vaccines



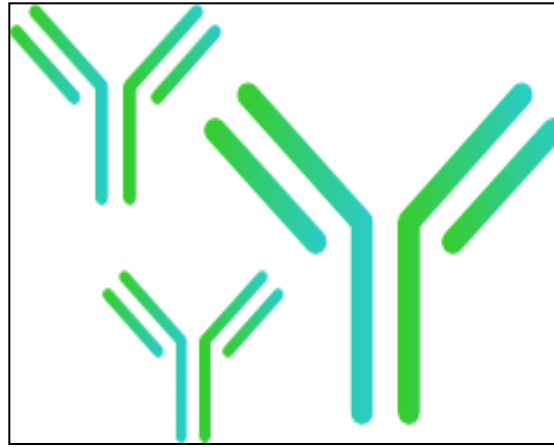
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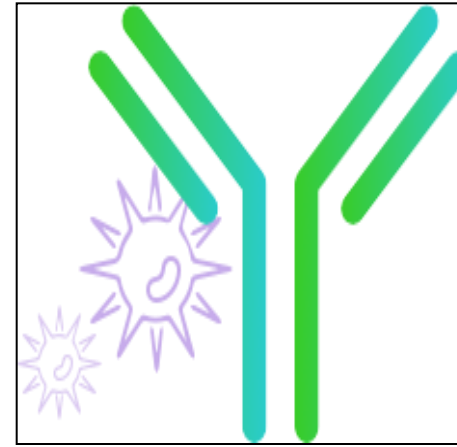
# HOW VACCINES WORK



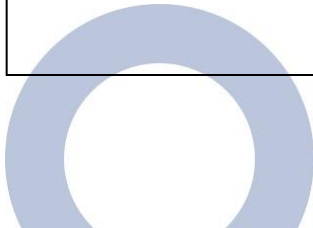
The body is exposed to a weakened or dead pathogen



The body's immune cells make antibodies to attack the pathogen



If the body is exposed to the pathogen again, the body will be prepared with antibodies



However vaccines by themselves do not prevent disease, vaccination should be strengthened to deliver vaccines

- Vaccination prevents disease
- The wider the coverage the greater the protection
- Vaccination should be viewed as a human right and all those who need vaccines should be provided vaccines
- Prioritization is acceptable in case of limited supply only if the health condition warrants this
- Vaccines and vaccine adoption in a country is based on availability for all who need it

# General rules for vaccination

- Vaccination is a **process** and all steps have to be taken care of and delivered appropriately. The vaccine and the host have to be appropriately matched for vaccine dose and schedule
- These include host related issues including, age, sex, health status, previous number of doses, health status
- The antigen should be well kept at all steps before delivery including in transportation and in controlled temperature before administration in order to assure that this is effective

## General rules in delivering vaccines to a host

- Minimum age at vaccination for the vaccine
- Minimum interval between vaccine doses
- Appropriate Dosing of vaccines, adult versus children content and amount of antigen
- Vaccination in special situations such as mass vaccination
- Vaccination of special hosts
- Planning for vaccination is different
- However routine scheduled vaccines are most important

## Types of immunity against an infectious disease agent

**Active Immunity = Antigen**

**Passive Immunity = Antibody**

# Types of antigens

- Live attenuated organisms
  - Viral
  - Bacterial
- Inactivated
  - Whole organisms
    - Viral
    - bacterial
  - Fractional
    - Protein
    - Polysaccharides
    - Conjugate polysaccharide vaccines
    - New types of vaccines, mRNA, mDNA,

# Viral Vaccines

- Live attenuated
  - OPV
  - MMR
  - Chickenpox\*
  - Live attenuated influenza vaccine\*
  - Rotavirus vaccines\*
- Inactivated
  - IPV
  - Hepatitis a vaccine\*
  - Influenza vaccine\*
- Component
  - Hepatitis b vaccine
  - Subunit influenza vaccines
  - HPV vaccines\*

# Live viral and bacterial vaccines

- BCG
- OPV
- MMR
- Rotavirus
- Chickenpox
- Intranasal influenza vaccine
- Oral typhoid vaccine



# Killed or fractional vaccines

- IPV
- Hepatitis a vaccine
- DTP
- Injectable influenza vaccine
- DTaP
- HB
- HIB

- Pneumo
- Meningo
- HPV

# Modern vaccines using new technology

- mRNA
- mDNA
- Viral Vector Vaccines
- Protein subunit
- These types of vaccines were Recently used for COVID 19

# VACCINES PROTECT THE COMMUNITY

## COMMUNITY IMMUNITY

When a sufficient proportion of a population is immune to an infectious disease to make its spread from person to person unlikely.

## COVERAGE THRESHOLD

The minimum percentage of individuals immune to a disease needed to prevent an outbreak.

These may differ according to disease, however as a general rule the more uptake of vaccines the greater is the protection

Only  
**6**

countries in the EU/EEA achieved the 95% coverage threshold needed to prevent measles outbreaks in 2017

# Vaccines in use for children

## Vaccines in use in Jordan

- Diphtheria
- Tetanus
- Pertussis
- Polio both IPV and OPV
- Measles,
- Mumps
- Rubella
- Hemophilus influenza b
- Hepatitis b
- Hepatitis a
- BCG
- Rotavirus vaccine

## Recently introduced Vaccines some not yet adopted in Jordan

- Chickenpox
- Pneumococcal vaccine
- VZV vaccine (zoster)
- Influenza vaccine
- Acellular pertussis vaccine for adolescents and adults
- Meningococcal vaccine
- HPV vaccine



## Vaccination schedule Jordan 2008 upgrade is needed

Age	Vaccine
1 <sup>st</sup> contact	BCG
2 months	DTaP + HepB <sub>1</sub> + Hib <sub>1</sub> + IPV
3 months	DTaP + HepB <sub>2</sub> + Hib <sub>2</sub> + IPV, OPV
4 months	DTaP + HepB <sub>3</sub> + Hib <sub>3</sub> + OPV
9 months	Measles + OPV
18 Months	MMR + DTP <sub>booster1</sub> + OPV <sub>booster1</sub>
<b>1<sup>st</sup> &amp; 10<sup>th</sup> class</b>	<b>Td (OPV for 1<sup>st</sup> class)</b>

# Vaccination to school age children

- 1st elementary class

Td +OPV booster2

Validation MMR

- 10th class Td Second dose of MMR
- Recent additions to be added such as HAV and COVID 19

# Diphtheria, *Corynebacterium diphtheriae*

- Greek *diphtheria* (leather hide)

Gram positive rod, a human pathogen that is transmitted by droplets, both asymptomatic and symptomatic individuals may transmit infection

There are four biotypes (*mitis*, *intermedius*, *belfanti*, and *gravis*). All biotypes of *C diphtheriae* may be either toxigenic or nontoxigenic.

Diphtheria is caused by toxigenic strains of *Corynebacterium diphtheriae*

# Diphtheria pathogenesis

- Toxigenic strains produce exotoxin. This is phage induced and is the cause of the serious complications of the infection
- The toxin inhibits protein synthesis in all cells, including myocardial, renal, and peripheral nerve cells
- Since the disease is toxin mediated the vaccine is made up of the inactivated toxin only, this is diphtheria toxoid



# Diphtheria vaccine

- Formalin-inactivated diphtheria toxin
- Protein antigen
- Must administer by deep IM
- Do not freeze
- Efficacy      Approximately 95%
- Duration      Approximately 10 years
- Amount of antigen higher in children
- Should be administered with tetanus toxoid as DTP. DTaP, DT, Td, or Tdap

# DTP, DTaP, DT, and Td

	<u>Diphtheria</u>	<u>Tetanus</u>
DTP,DTaP, DT	7-8 Lf units	5-12.5 Lf units
Td, Tdap (adult)	2-2.5 Lf units	5 Lf units

**(D)** Designated the formula used for children which has more antigen given to children <7 yrs.

**(d)** Designated formulation with lesser toxin found in Tdap which is used for older individuals

10-18 years (Boostrix)

11-64 years (Adacel)

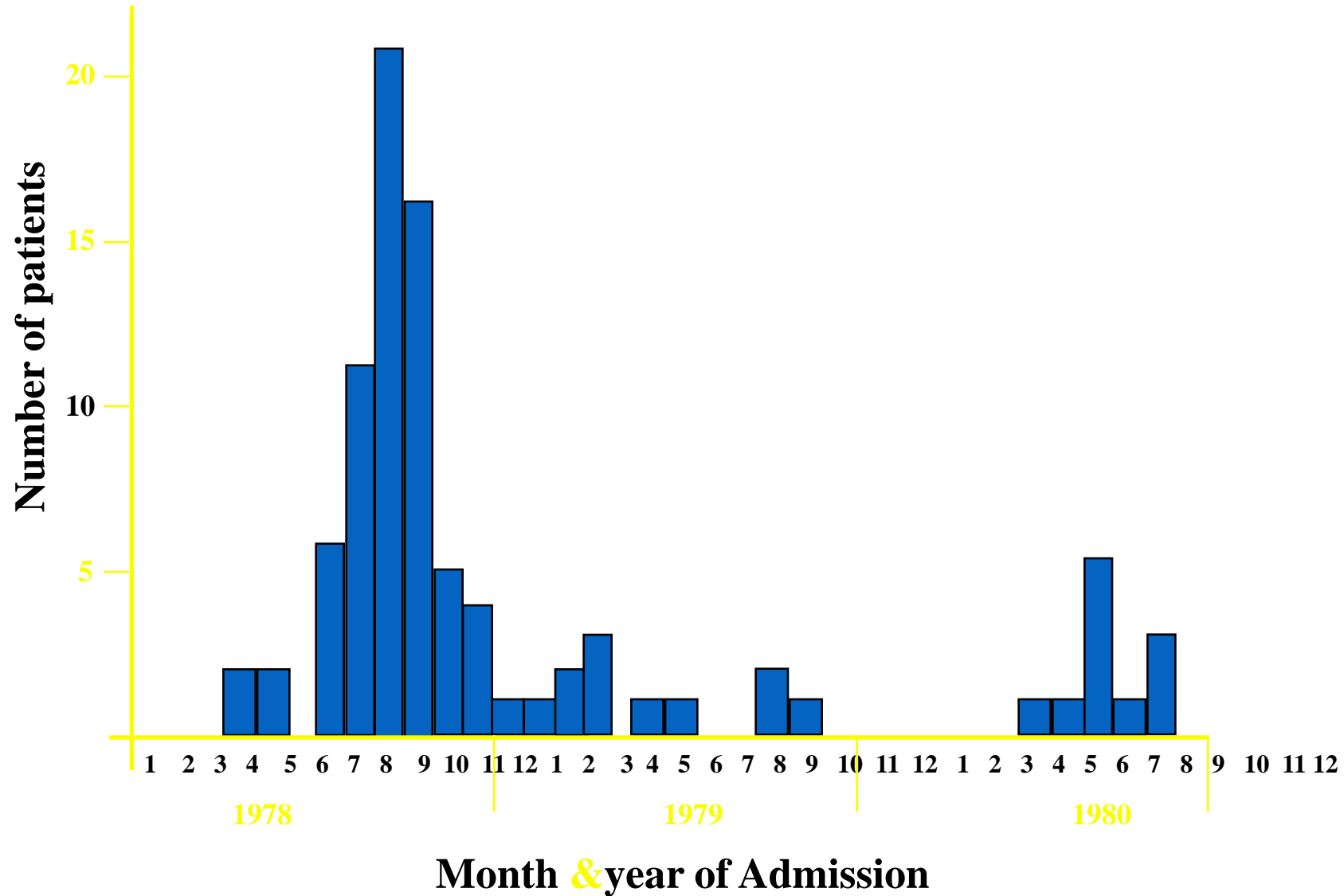
# Diphtheria and Tetanus Toxoids Adverse Reactions

- Local reactions (erythema, induration)
- Exaggerated local reactions (Arthus-type)
- Fever and systemic symptoms not common
- Severe systemic reactions rare





# Number of admissions of cases of paralytic disease to the Jordan University Hospital each month from January 1978- December 1980.





## Diphtheria and Tetanus Toxoids Contraindications and Precautions

Severe allergic reaction to vaccine component or following a prior dose

Moderate or severe acute illness, Hx of seizures

Note that If diphtheria vaccination is interrupted outbreaks occur since some people carry the bacterium but are asymptomatic and immunity may decrease with time. Hence diphtheria vaccine should continue inspite of control of the disease

Natural infection does not lead to immunity and even patients who recover from diphtheria should be vaccinated



# Tetanus

- First described by Hippocrates
- *Clostridium tetani* is an Anaerobic gram-positive, spore-forming bacteria
- Spores are found in soil, animal feces etc; may persist for months to years, hence any dirty wound may get infected with the bacterium and if there are anaerobic conditions, an exotoxin maybe released
- The exotoxin also called Tetanospasmin is very lethal, estimated human lethal dose = 2.5 ng/kg

# Tetanus Epidemiology

- |                    |   |
|--------------------|---|
| • Reservoir        | Soil and intestine of animals<br>and humans |
| • Transmission     | Contaminated wounds<br>Tissue injury        |
| • Temporal pattern | Peak in summer or<br>wet season             |
| • Communicability  | Not contagious                              |

# Pathogenesis of tetanus

- Anaerobic conditions allow germination of spores in wounds
- The vegetative form of *C tetani* produces a potent plasmid-encoded exotoxin (tetanospasmin)
- This binds to gangliosides at the myoneural junction of skeletal muscle and on neuronal membranes in the spinal cord, blocking inhibitory impulses to motor neurons.
- This Leads to unopposed muscle contraction and spasm which are the cornerstone of the disease
- NOTE that *C tetani* is in the environment and soil, every dirty wound has the potential to lead to tetanus unless the host is vaccinated or receives antitoxin

# Tetanus Toxoid (inactivated toxin)

- Formalin-inactivated tetanus toxin
- Schedule Three or four doses + booster  
Booster every 10 years
- Efficacy Approximately 100%
- Duration Approximately 10 years
- Vaccine content same for children and adults
- Should be administered with diphtheria toxoid as DTP, DTaP, DT, Td, or Tdap

# Tetanus Wound Management

	Clean, minor wounds	All other wounds
Vaccination History		
<b>Unknown or &lt;3 doses</b>	<b>Td</b> <b>TIG</b> Yes    No	<b>Td</b> <b>TIG</b> Yes    Yes
<b>3+ doses</b> Yes, if >10 years since last dose Yes, if >5 years since last dose Dose of TIG is 250 units regardless of age and weight	<b>No*</b> <b>No</b>	<b>No**</b> <b>No</b>

# Pertussis

- Highly contagious respiratory infection caused by *Bordetella pertussis* a fastidious gram negative bacterium
- Outbreaks first described in 16th century
- *Bordetella pertussis* isolated in 1906
- Estimated 285,000 deaths worldwide in 2001

# Pertussis Epidemiology

- Reservoir            Human  
                                 Adolescents and adults
- Transmission            Respiratory droplets
- Communicability            Maximum in catarrhal stage  
                                 Secondary attack rate  
                                 up to 80%

# Pertussis Pathogenesis

- Attachment to cilia of ciliated epithelial cells in respiratory tract
- Pertussis antigens allow evasion of host defenses (lymphocytosis promoted but impaired chemotaxis)
- Local tissue damage in respiratory tract
- Systemic disease may be toxin mediated
- Antigenic and biologically active components:
  - pertussis toxin (PT)
  - filamentous hemagglutinin (FHA)
  - agglutinogens
  - adenylate cyclase
  - pertactin
  - tracheal cytotoxin
- NO Bacteremia



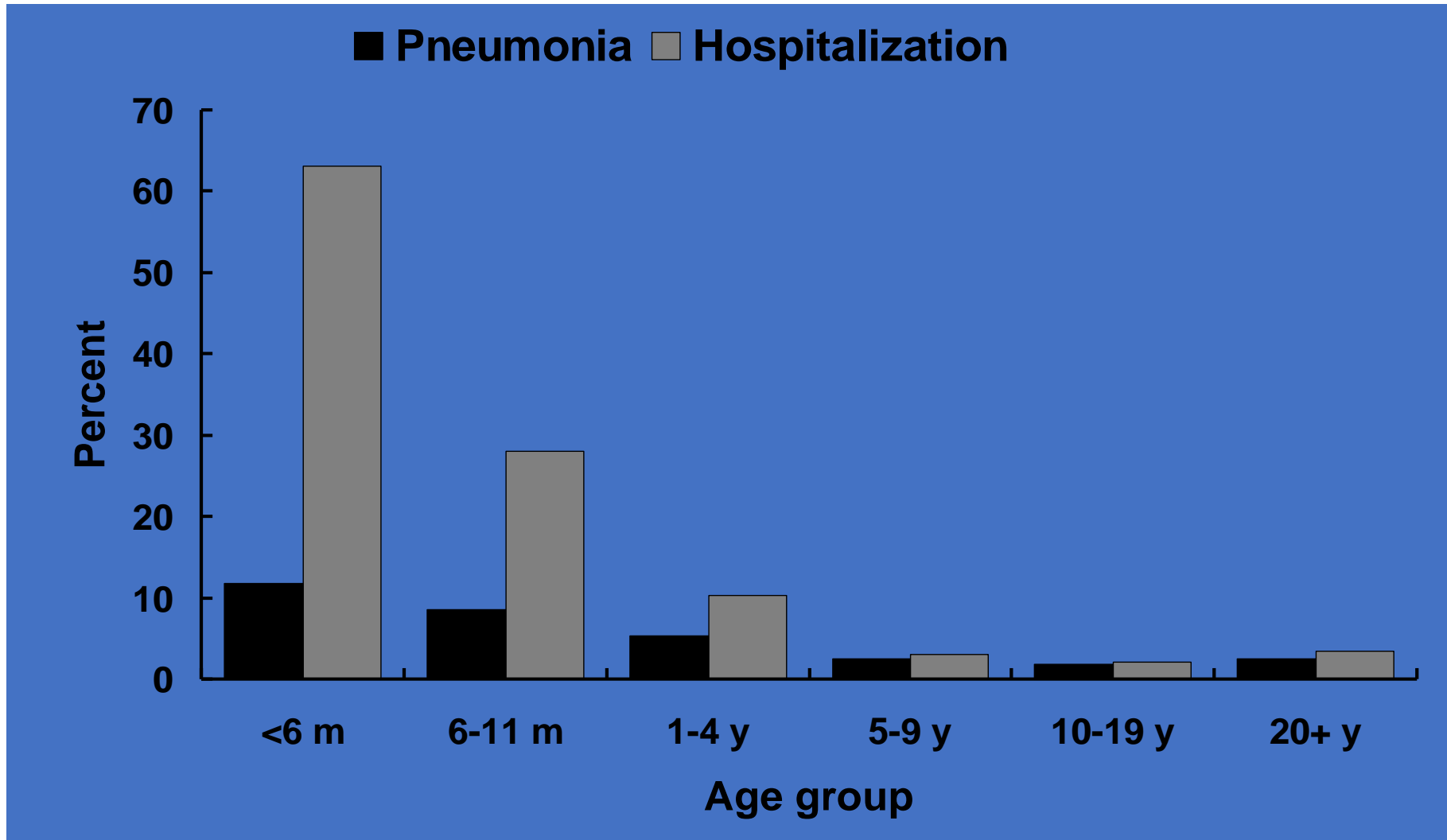
# Pertussis Clinical Features

- Incubation period 7-10 days (range 4-21 days)
- Insidious onset, similar to minor upper respiratory infection with nonspecific cough
  - Catarrhal stage                      1-2 weeks
  - Paroxysmal cough stage              1-6 weeks
  - Convalescence                      Weeks to months
- Fever usually minimal throughout course of illness

# Pertussis Among Adolescents and Adults

- Disease often milder than in infants and children
- Infection may be asymptomatic, or may present as classic pertussis or chronic irritative cough
- Adolescents and adults account for more than half of reported cases
- Older persons often source of infection for children
- Infants less than six months of age are at increased risk since maternal antibodies are not sufficient to prevent infection unless mother is immunized in pregnancy

# Pertussis Complications by Age



# Pertussis vaccines

- Whole cell inactivated vaccine or acellular pertussis
- WC Should not be administered after the age of 6 years
- Immunity decreases with time and hence re vaccination in older individuals is needed
- Acellular vaccines are available for adolescents and for older individuals as well.
- Different antigen content

## Pertussis vaccines in use

- DTwP made of whole cell vaccine
- DTaP acellular pertussis vaccine
- Tdap Made of acellular vaccine for use in adolescence and adults

# Whole-Cell Pertussis Vaccine

- Developed in mid-1930s and combined as DTP in mid-1940s
- 70%-90% efficacy after 3 doses
- Protection for 5-10 years
- Local adverse reactions common

# Acellular Pertussis Vaccines

- Purified "subunit" vaccines
- Pediatric formulations (DTaP) licensed for full series in 1996
- Adolescent and adult formulations (Tdap)

## Composition\* of Acellular Pertussis Vaccines

<b><u>Product</u></b>	<b><u>PT</u></b>	<b><u>FHA</u></b>	<b><u>PERT</u></b>	<b><u>FIM</u></b>
<b>Daptacel</b>	<b>10</b>	<b>5</b>	<b>3</b>	<b>5</b>
<b>Infanrix</b>	<b>25</b>	<b>25</b>	<b>8</b>	<b>--</b>
<b>Tripedia</b>	<b>23</b>	<b>23</b>	<b>--</b>	<b>--</b>
<b>Boostrix</b>	<b>8</b>	<b>8</b>	<b>2.5</b>	<b>--</b>
<b>Adacel</b>	<b>2.5</b>	<b>5</b>	<b>3</b>	<b>5</b>

mcg per dose



# DTP whole cell reactions

• Fever	40%
• Local reactions	35%
• Seizures	1/1750
• HHE	1/1750
• Encephalopathy	1/110,000

# DTaP Adverse Reactions

- Local reactions (pain, redness, or swelling at the site of injection)
- Local reactions more common following 4<sup>th</sup> and 5<sup>th</sup> doses
- Reports of swelling of entire limb
- Extensive swelling after 4th dose NOT a contraindication to 5th dose
- Low-grade fever

# DTP/DTaP Contraindications

- Severe allergic reaction to vaccine component or following a prior dose
- Encephalopathy not due to another identifiable cause occurring within 7 days after vaccination
- Progressive CNS disease

## DTP/DTaP Precautions\*

- Moderate or severe acute illness
- Temperature  $\geq 105^{\circ}$  F ( $40.5^{\circ}$  C) or higher within 48 hours with no other identifiable cause
- Collapse or shock-like state (hypotonic hyporesponsive episode) within 48 hours
- Persistent, inconsolable crying lasting  $\geq 3$  hours, occurring within 48 hours
- Convulsions with or without fever occurring within 3 days