Epidemiology Of Diphtheria

- Diphtheria is an acute infectious disease caused by the bacterium *Corynebacterium diphtheriae*.
- The bacterium produces an exotoxin that is carried in the bloodstream

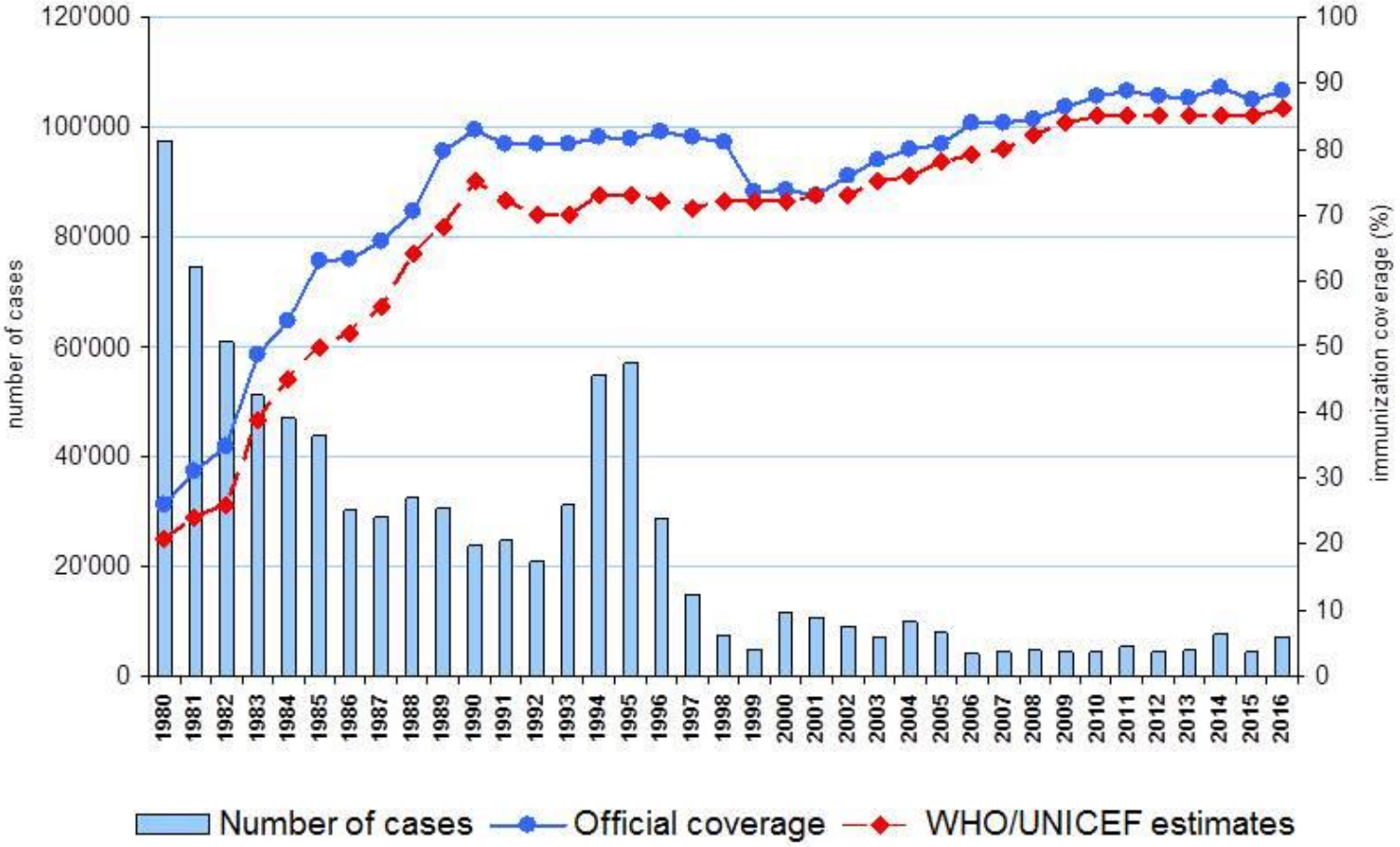
Problem statement

WORLD

- Outbreak reported in Russian Federation, Ukraine in 1990 and Thailand and Laos in 1996.
- These outbreaks highlight the need for booster vaccinations.
- Shift in the affected age group.
- In developing countries disease continue to be endemic
- Incomplete reporting

Date of chart: 02 August 2017

Diphtheria global annual reported cases and DTP3 coverage, 1980-2016

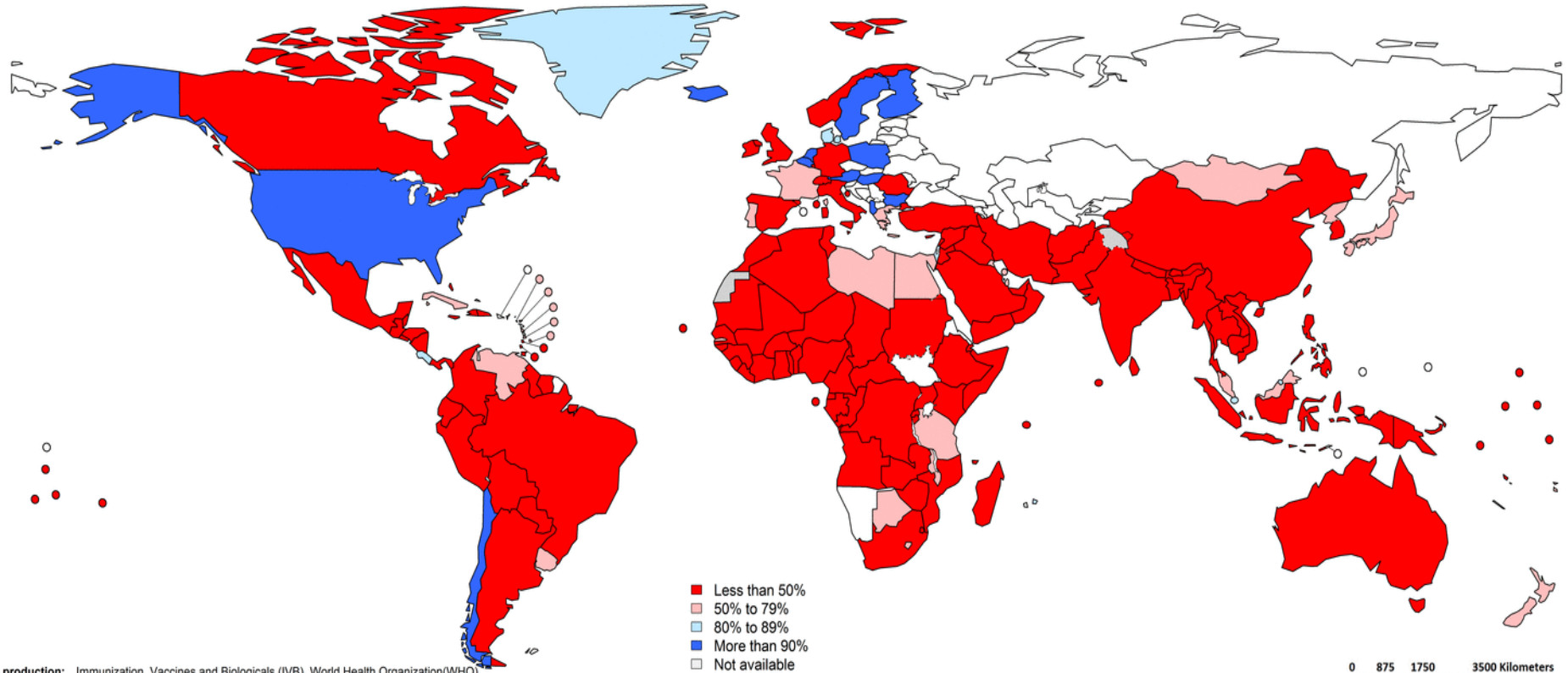


Source: WHO/IVB database, 2017
194 WHO Member States.
Data as of 19 July 2017

WHO

Immunization coverage with 3rd dose of diphteria and tetanus toxoid and pertussis containing vaccines

1980

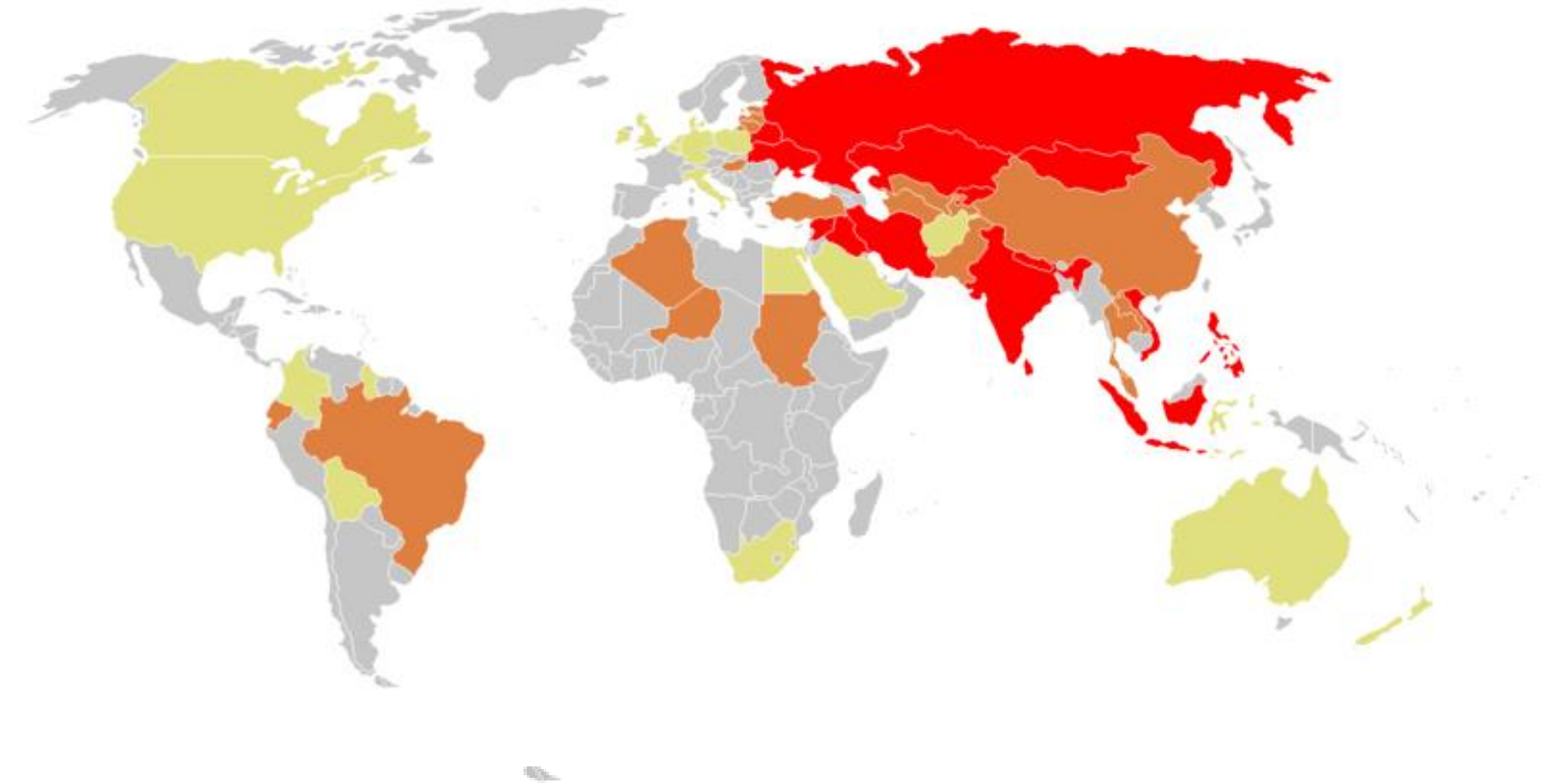


Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization(WHO)
Data source: WHO/UNICEF estimates 2016 revision, March 2018.
194 WHO Member states.

Disclaimer:

The boundaries and names shown and the designations used on this map do notimply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area nor of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

World Health Organization



WHO- Year 2002

- 185,000 DALYs
- 5000 death

Global and regional immunization profile

Data received as of 2018-Feb-28

South-East Asia Region

Next overall update June 2018
Next WHO UNICEF estimates July 2018

Population data in thousands [1]

	2016	2015	2014	2013	2012	2000	1990	1980
Total population	1'947'631	1'926'539	1'905'197	1'883'602	1'861'731	1'572'403	1'312'853	1'055'065
Live births	36'197	36'327	36'503	36'740	37'042	39'754	39'612	37'600
Surviving infants	35'008	35'093	35'219	35'400	35'639	37'353	36'332	33'572
Pop. less than 5 years	174'760	176'129	177'464	179'156	180'986	182'971	177'709	157'112
Pop. less than 15 years	539'684	542'063	544'165	546'046	547'550	530'862	493'113	421'340
Female 15-49 years	510'111	504'181	498'343	492'290	486'085	400'597	316'950	246'816

Number of reported cases

Diphtheria	4'016	2'504	7'666	4'080	3'953	5'470	11'582	47'354
Japanese encephalitis	3'500	2'831	3'320	1'356	282	-	-	-
Measles	27'530	48'888	42'899	24'564	31'582	78'558	224'925	199'535
Mumps	31'739	42'937	38'327	36'352	47'086	9'395	-	-
Pertussis	43'141	29'813	54'953	37'602	45'847	38'510	156'028	399'310
Polio	0	2	0	0	0	591	11'313	20'089
Rubella	10'361	6'515	9'690	10'434	6'877	1'165	-	-
Rubella (CRS)	319	183	86	23	14	26	-	-
Tetanus (neonatal)	399	983	658	721	872	4'322	11'725	3'149
Tetanus (total)	5'771	3'806	7'099	4'153	3'681	11'554	35'452	62'176
Yellow fever	0	0	0	0	0	0	-	-

Percentage of target population vaccinated, by antigen

based on WHO-UNICEF estimates
TT2plus is based on reported coverage

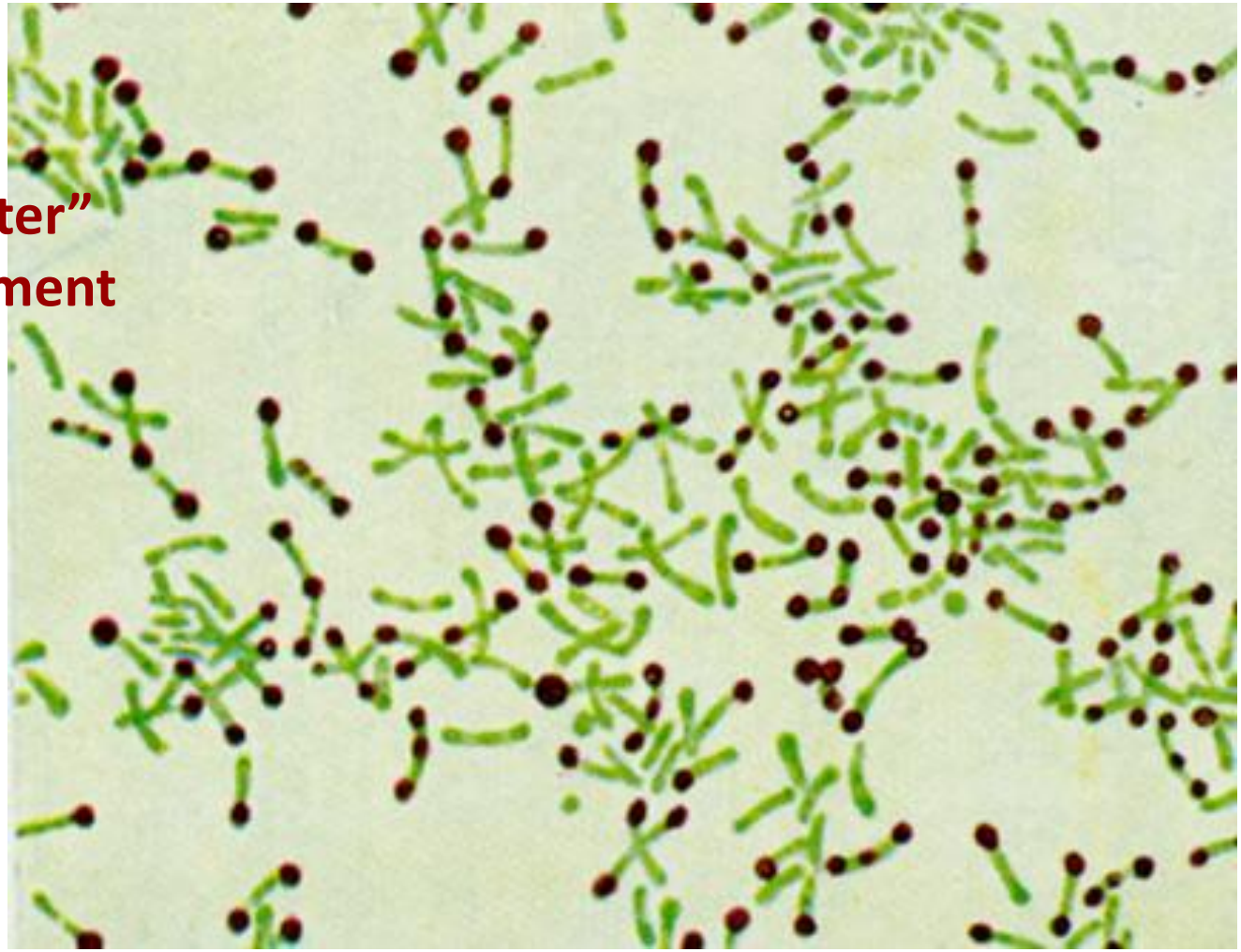
BCG	89	88	90	91	91	78	71	12
DTP1	93	92	92	92	91	78	87	22
DTP3	88	87	86	85	84	65	70	7
HepB_BD	34	32	29	27	17	0	-	-
HepB3	88	87	82	76	77	10	0	-
Hib3	80	56	32	28	11	0	0	-
IPV1	37	6	-	-	-	-	-	-
MCV1	87	86	85	84	84	63	59	0
MCV2	75	65	59	58	42	3	-	-
PCV3	9	4	0	0	0	-	-	-
Pol3	87	87	85	84	82	64	67	3
RCV1	15	15	13	12	5	3	0	0
RotaC	3	0	0	0	0	-	-	-
TT2plus	77	78	71	67	88	81	74	17

Most countries have standard recommendations regarding which vaccines should be offered and at what ages they should be given. In general, vaccines are recommend for the youngest age group at risk for developing the disease whose members are known to respond to the immunization without adverse effects.

- **INDIA**
  →endemic, but a declining trend
- 1987 (before vaccination) was 12952
  while during 2000 it was 265 cases
  showing a decline of about **99.06%**

- **BUT NOW……. Resurgence?????**

"**Chinese-letter"**
arrangement



- Gram positive, Non motile, Non capsulaed, club-shaped bacillus. No invasive power

Toxigenic strain

- Toxigenic strains are infected by a bacteriophage that contains the gene for toxin production & Produces a powerful exotoxin
- sensitive to penicillin
- Killed by chemical and heat
- May survive for short periods in dust and fomites

Agent

- **Bio type-** gravis, intermedius and mitis.
- Gravis infection is more severe.
- Non toxic strain may turn toxic- when expose to bacteriophase– Beta phase

Source of infection

- Case- clinical, subclinical
- Carriers- 95 carrier per 5 clinical cases

Incidence- 0.5% to 1%

-Temporary or chronic

- Nasal or throat

Nasal carrier is most dangerous

Immunization does not prevent the carrier stage

Infective material

-Nasopharyngeal secretions

- Dust

- Droplet

-Contaminated fomites

-Discharges from skin lesion

- CFR- 10% in Untreated

5% in properly treated

- **Incubation period** – 2-6 days
- **Infective Period-**
  - 2-4 weeks from the onset of he disease in untreated
  - Carriers– Longer period– > 6 months
  - When treated with antibiotics, the contagious period can be reduced to less than 2 days.

Non communicable

2 negative cultures 24 hrs. apart

HOST FACTORS

AGE:

- 1 to 5 years (80 % cases < 15 years age group)
- Shift in age affected from preschool to school age
- Females = males

NUTRITION:

- Malnutrition– More in children < 60% of expected weight

SES:

- Poverty

Immunity

- Natural Infection - long-lasting immunity to the typical clinical manifestations.
- People with acquired immunity (vaccine) may become infected with an atypical strain.
- Protection from maternal antibodies for first few weeks or months of life
- Herd immunity- 70% to prevent epidemic spread

Environment

- All seasons but more in winter
- Over crowded conditions
- Poor sanitation.

Spread

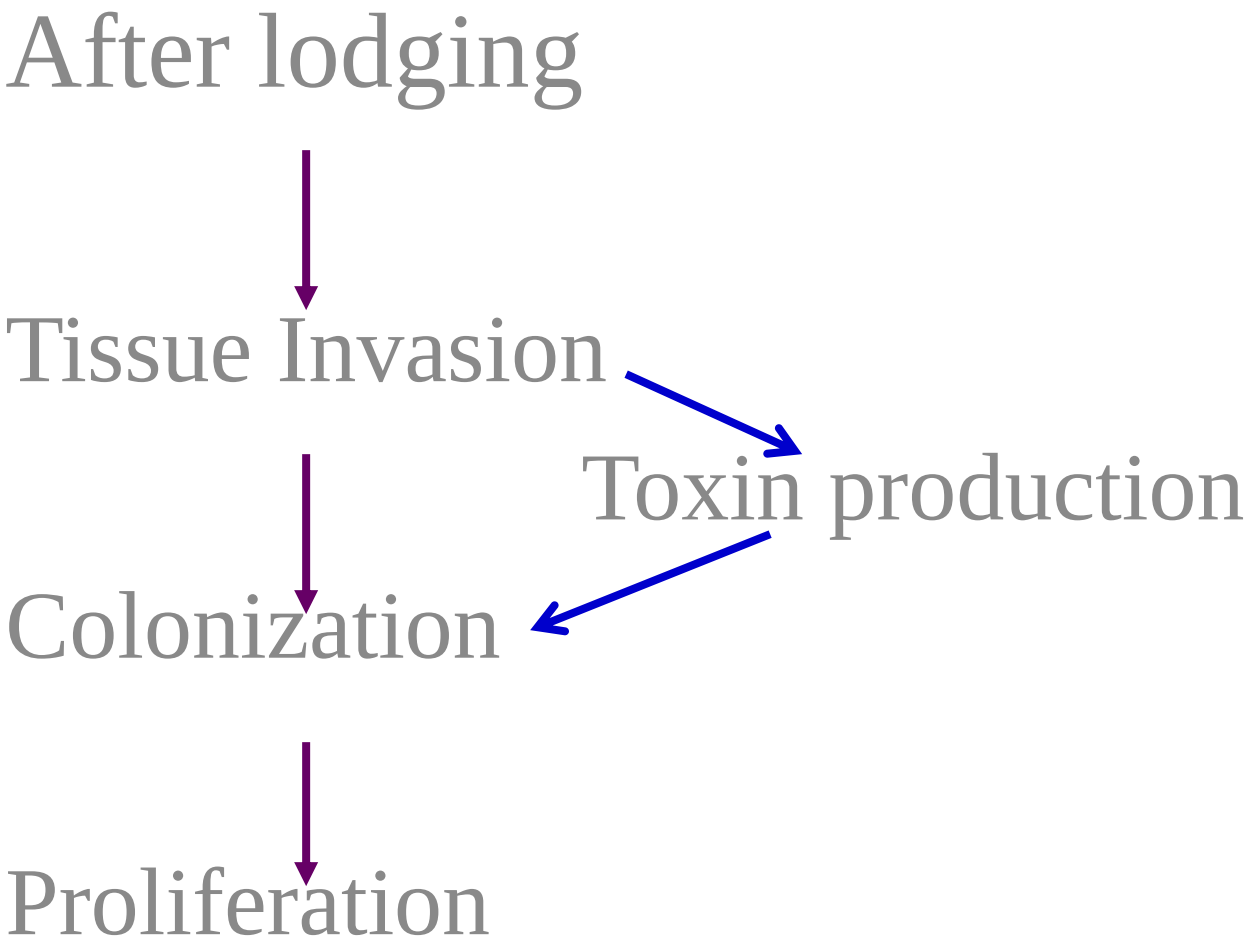
- Person to person by respiratory droplets from the throat through coughing and sneezing.
- By close face to face contact with an infected person.
- Close contact- Infected cutaneous lesion
- From objects which have been contaminated by the droplet secretions.
- From contaminated raw milk.

Portal of entry

- Respiratory route
- Umbilicus in new born.
- Eye, genitalia, middle ear
- Ulcerated skin

Pathogenicity

1. **Invasion** -of the local tissues of the throat, which requires colonization and subsequent bacterial proliferation. the bacteria produce several types of pili. The diphtheria toxin, as well, may be involved in colonization of the throat.
2. **Toxigenesis**: bacterial production of the toxin. The diphtheria toxin causes the death of cells and tissues by inhibition protein synthesis in the cells. Although the toxin is responsible for the lethal symptoms of the disease, the virulence of *C. diphtheriae* cannot be attributed to toxigenicity alone, since a distinct invasive phase apparently precedes toxigenesis. However, it has not been ruled out that the diphtheria toxin plays an essential role in the colonization process due to short-range effects at the colonization site.


After lodging
Tissue Invasion
Toxin production
Colonization
Proliferation

Proliferate and liberate exotoxin

↓

Inhibit protein synthesis of cell

↓

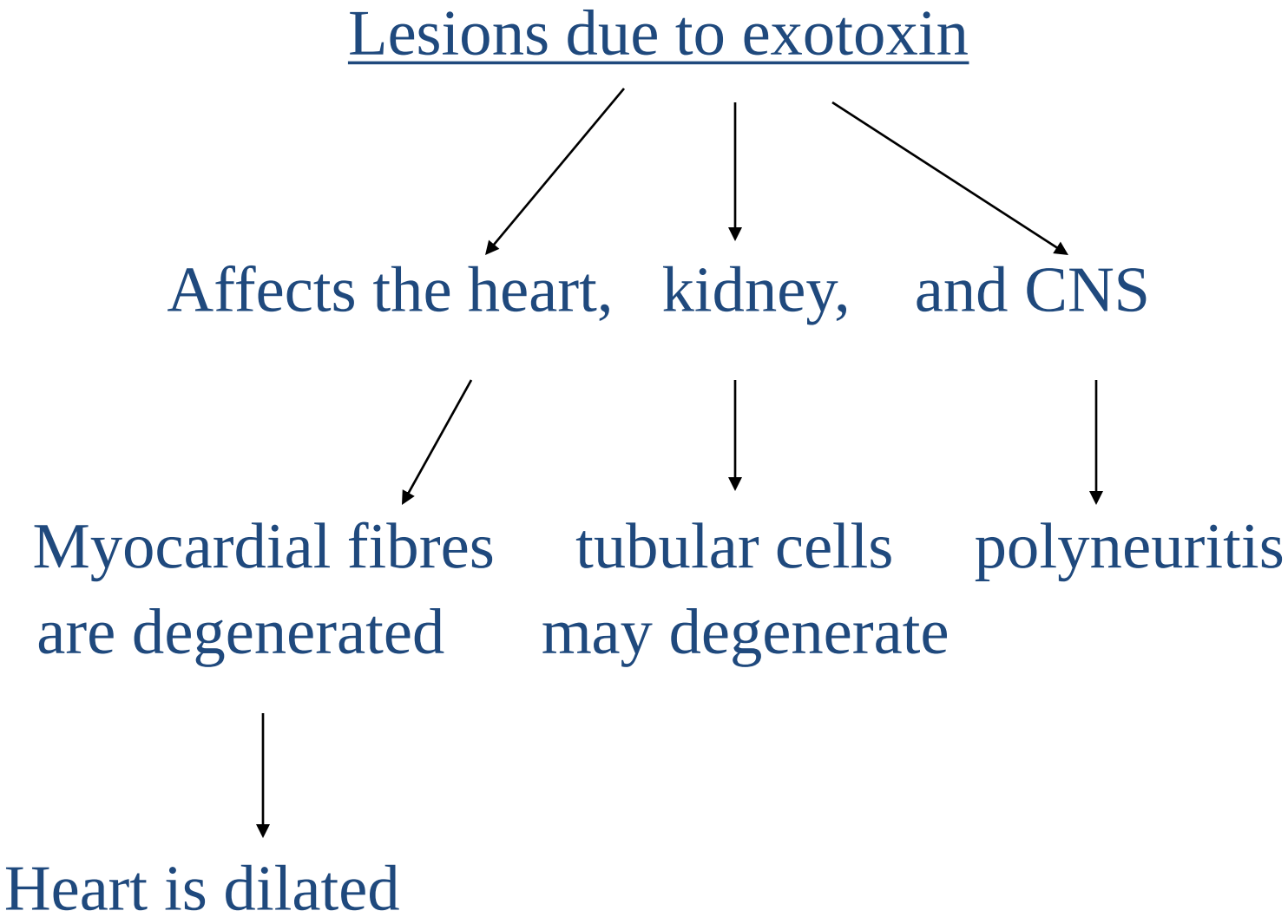
necrosis of epithelial cells and discharge of Serous fibrinous material

↓

Grayish, white pseudo membrane

↓

Which bleeds on being dislodged


Lesions due to exotoxin
Affects the heart,
kidney,
and CNS
Myocardial fibres are degenerated
tubular cells may degenerate
polyneuritis
Heart is dilated

Clinical Features

Types of clinical diphtheria

1) Respiratory

    -anterial nasal

    - Faucial

    - Laryngeal

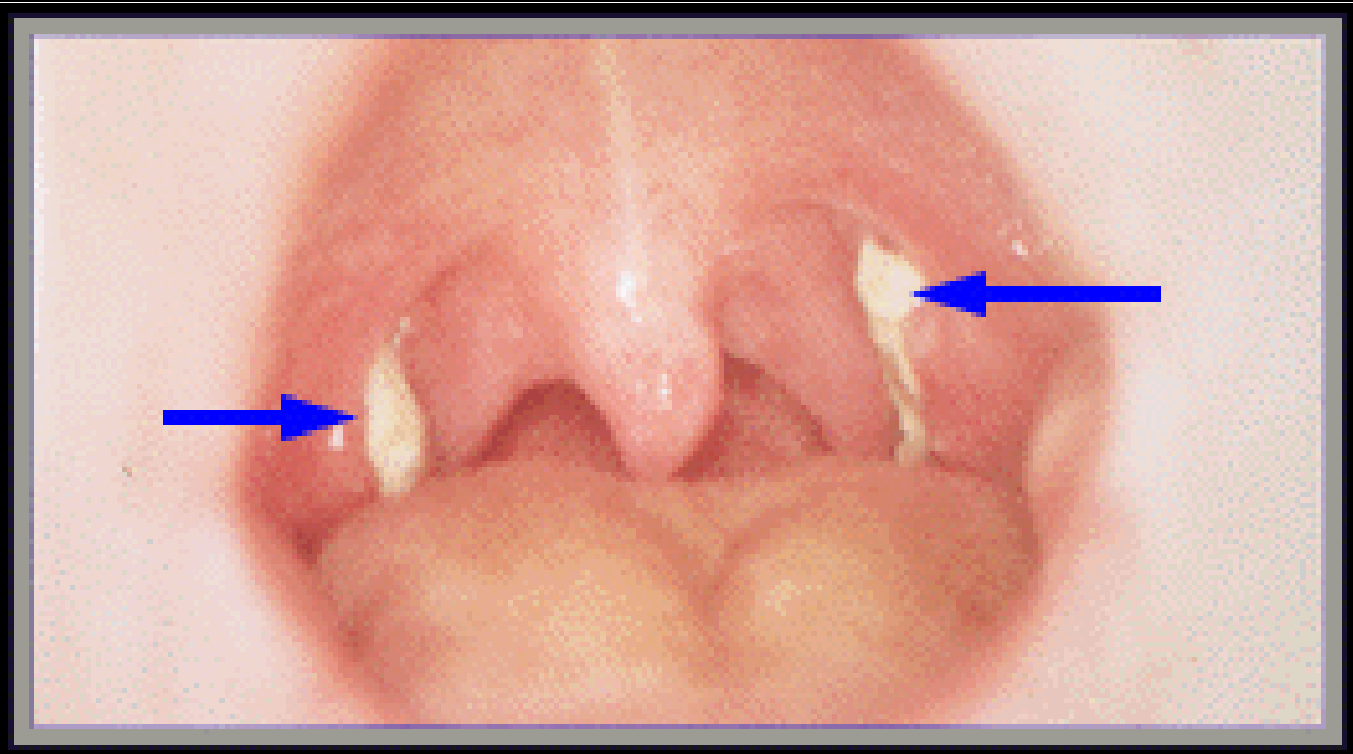
2) Non respiratory –

        Skin, conjuctiva, genitalia

- Symptoms develop after about 2-5 days starting with a mild temperature
- The damage is caused by a poison (toxin)

The most serious aspect is a grayish membrane in the throat which blocks the breathing

Pharyngeal Diphtheria



Pseudomembrane

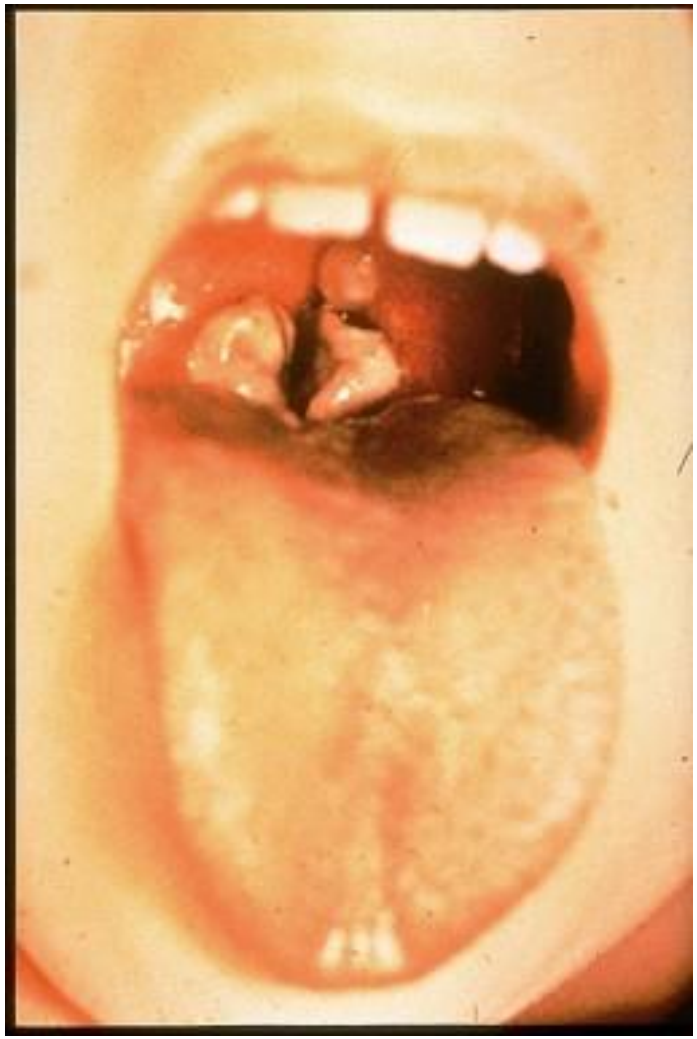
A thick, gray-green fibrin membrane, often forms over the site(s) of infection.

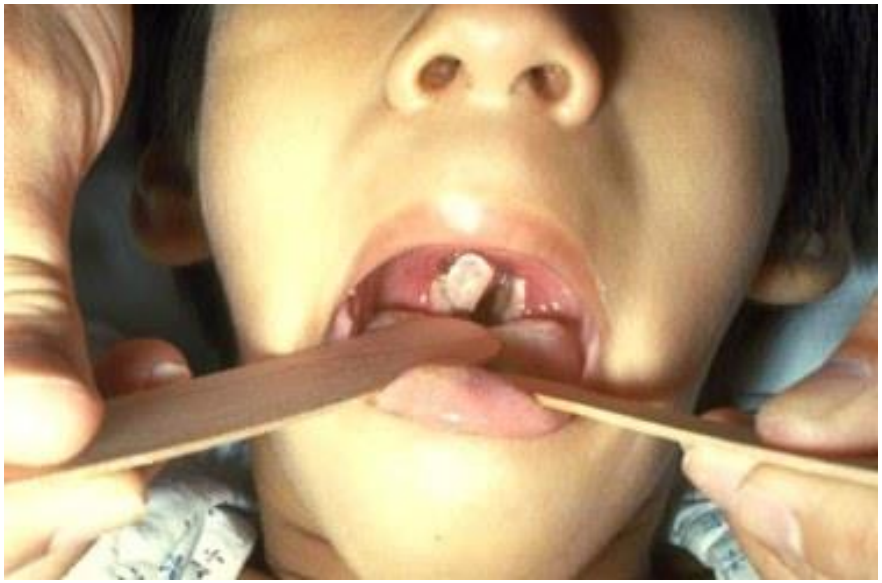
Pseudomembrane in diptheria

- The membrane may be localized as
- a patch of posterior pharynx or
- tonsil may cover the entire tonsil or
- less frequently, may spread to cover the soft or hard palates & posterior portion of pharynx.

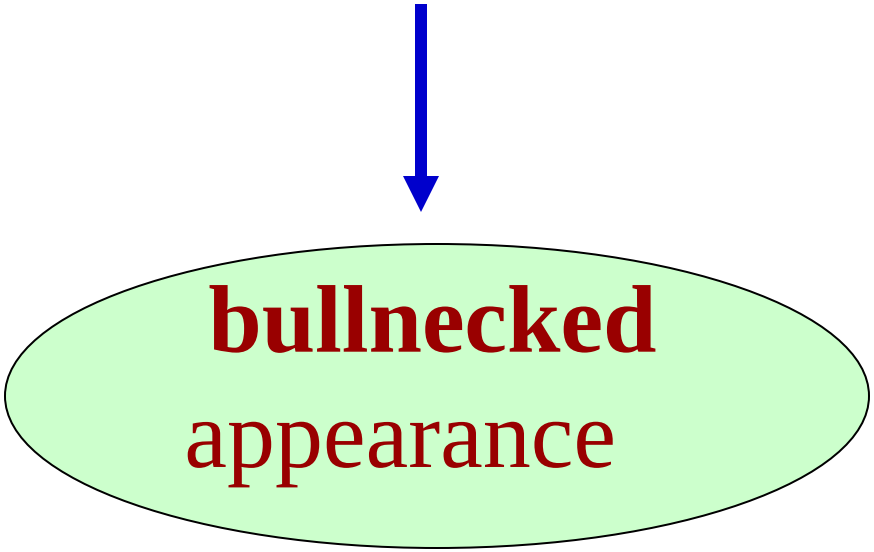
Pseudomembrane in diptheria

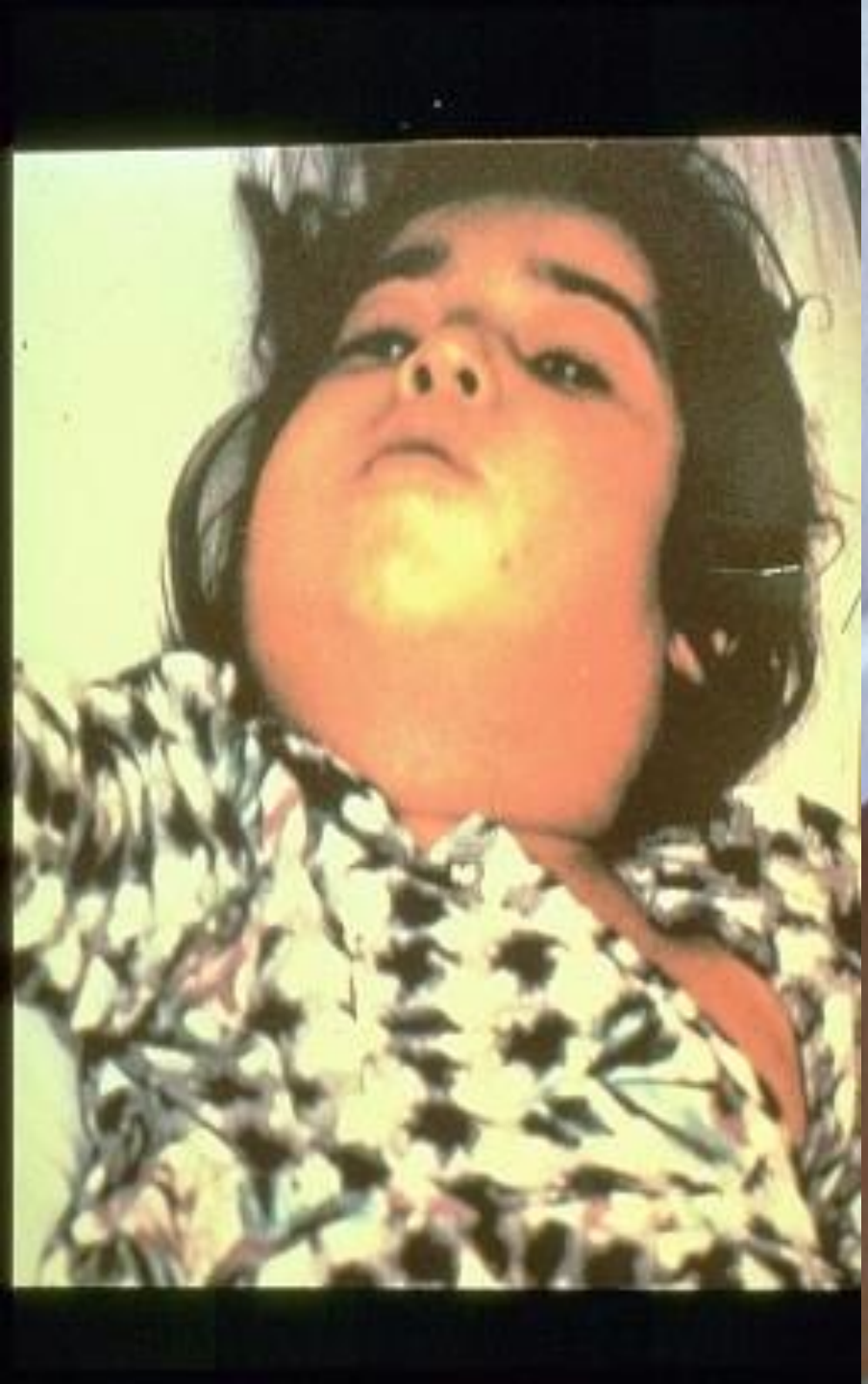
- **Composed of** fibrin, bacteria, and inflammatory cells.
- **It is a result of** the combined effects of
  - -bacterial growth,
  - -toxin production,
  - -necrosis of underlying tissue, and
  - -the host immune response.

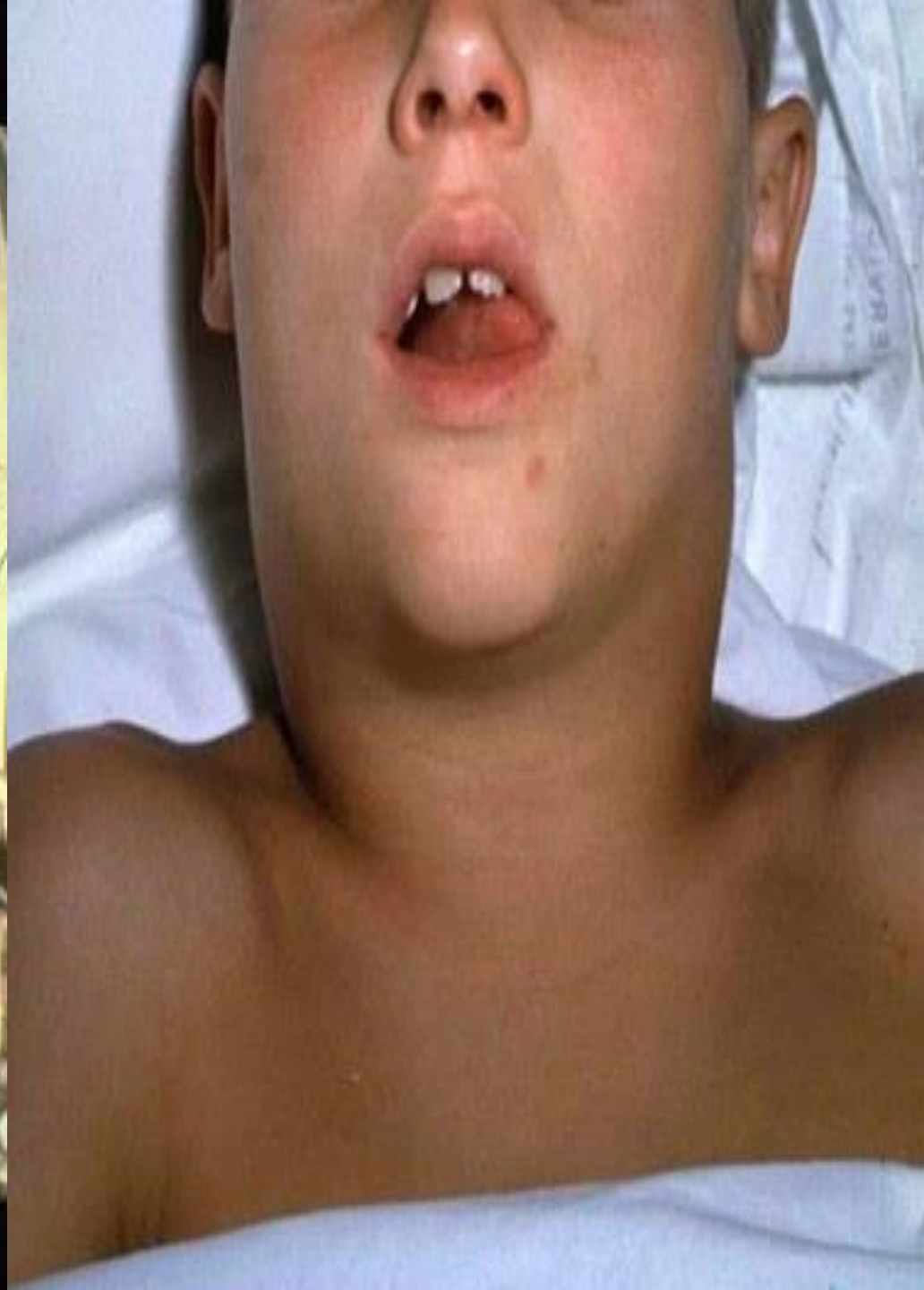


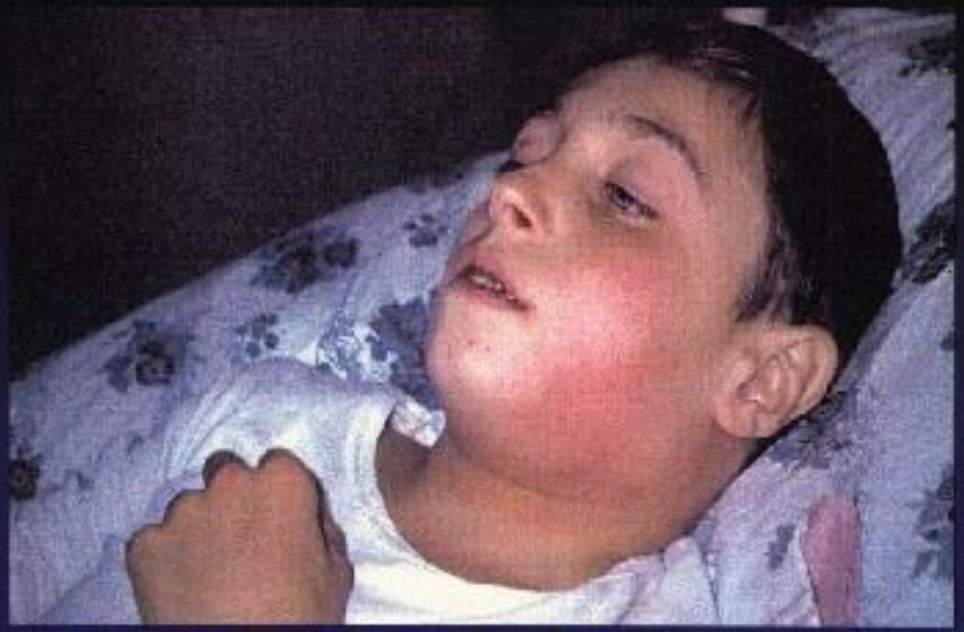


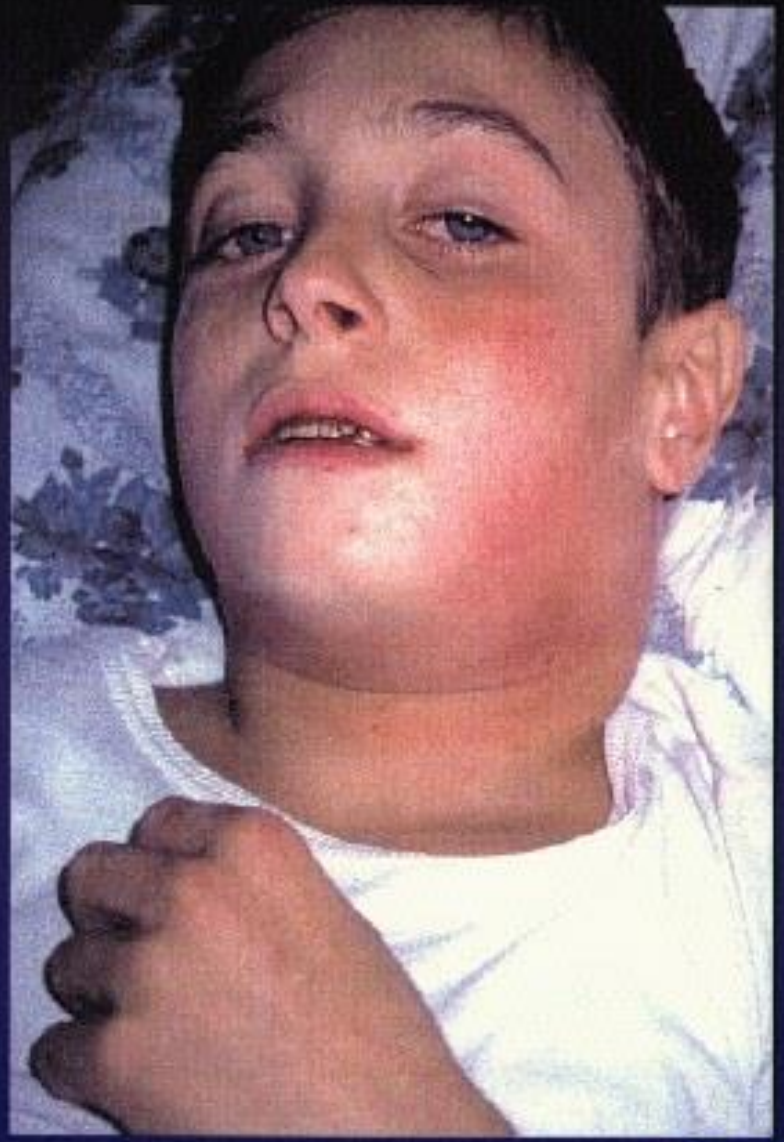
- In severe cases marked edema of submendibular area and anterior portion of the neck along with lymphadenopathy











10 y/o boy with severe diphtheria

- conjunctivitis
- pharyngeal membrane
- bull neck
- severe myocarditis
- all vaccines contraindicated

CDC

Pharyngotonsillar diptheria

- Sore throat
- Difficulty in swallowing
- Low grade fever
- Malaise
- Bull neck
- Loss of appetite
- Child looks sick and toxic
- Circulatory collapse due to myocarditis or adrenal insufficiency may occur

2). Laryngotracheal

Usually preceded by Pharyngotonsillar diph.

Hoarseness and croupy cough

3) Nasal

Mildest form, usually localized to septum or turbinates of one side of the nose

4). Non respi mucosal surface

Conjunctiva and genitals

5). Cutaneous diph.

Toxin is responsible for

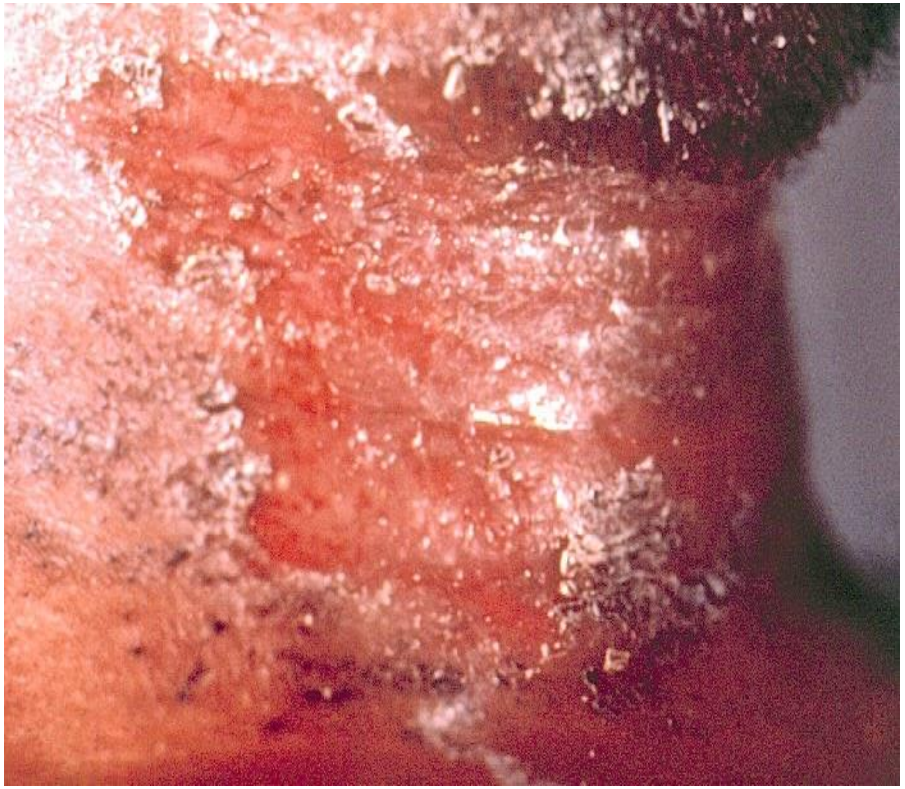
a) Formation of grayish yellowish membrane ("false membrane") commonly over the tonsils, pharynx, larynx with well defined edges & membrane cannot be wipped away

b) Marked congestion, oedema & local tissue distruction

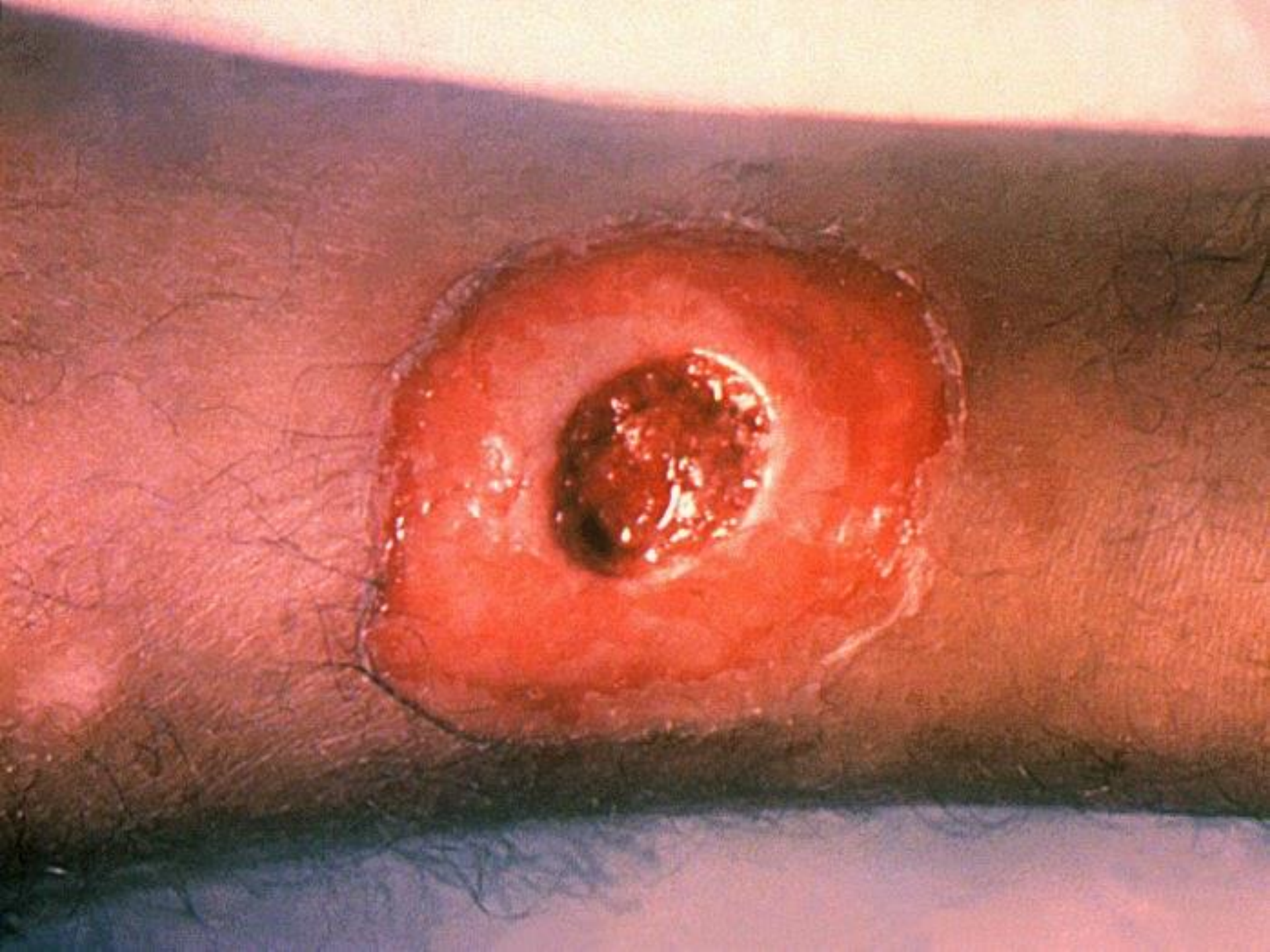
c) Enlargement of regional lymphnodes &

d) S/S of toxemia

Cutaneous diphtheria



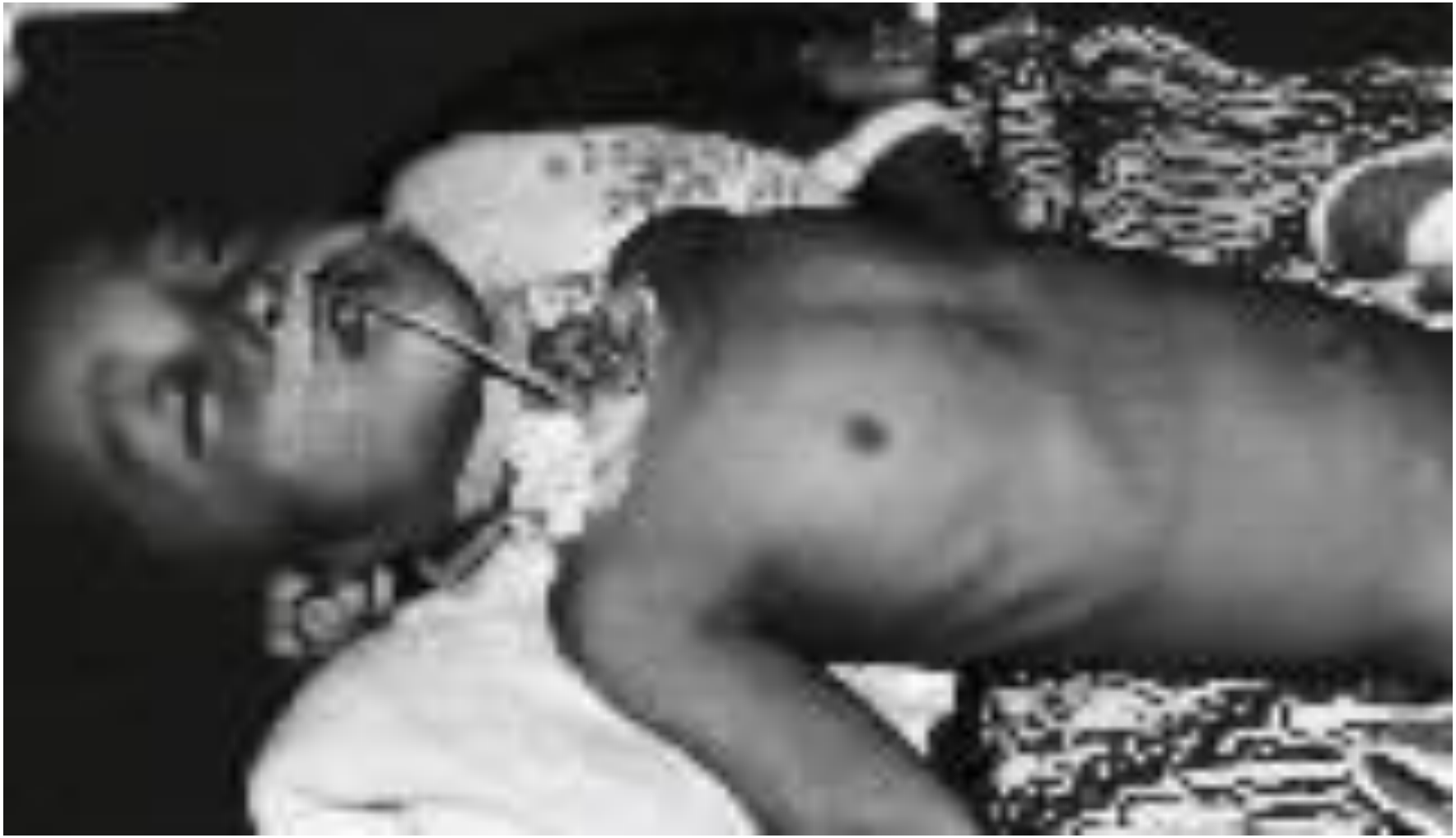
- Usually a secondary infection of a previous skin abrasion
- Usually covered by a gray-brown pseudomembrane.



Cutaneous diphtheria

- Pustular sores - are painful, swollen, and red, resembling impetigo.
- Symptoms usually appear two to four days after infection.

Indonesian child kept alive



Complications

- **Myocarditis**

  at the end of 1st week or beginning of 2nd week

  abdominal pain, vomiting, dysponea, tachycardia, extra systole, thready pulse.
- **Neurological**

  palatal paralysis, loss of accommodation and general polyneuritis.
- **Renal**

  oliguria and proteinuria
- **Sudden death**

  due to respiratory obstruction, myocarditis and respiratory paralysis

Complications

- Who survive - residual cardiac damage may be left.
- About 5% people with the disease die in spite of treatment

Diagnosis

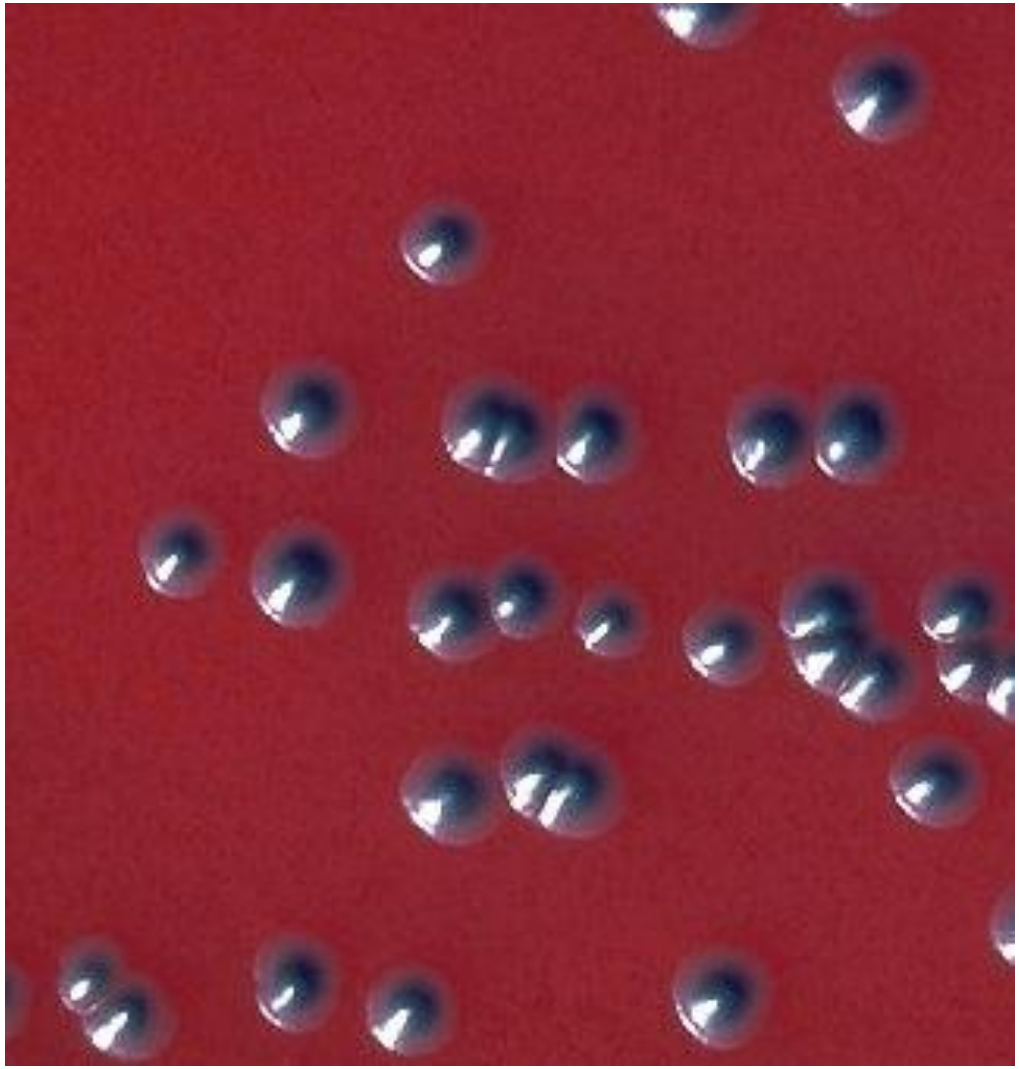
- Clinical diagnosis depends upon culture-proven toxigenic *C diphtheriae*–
- Toxigenicity is identified by a variety of
  - *in vitro* gel immunodiffusion, tissue culture or
  - *in vivo* (e.g., rabbit skin test) method.

Throat examination

- Mild erythema, localized exudate or a membrane.

Diagnosis
Throat or lesion cultures

- Sterile cotton-tipped applicators are used to swab the pharyngeal tonsils or their beds.
- Since diphtheritic lesions are often covered with a pseudomembrane, the surface of the lesion may have to be carefully exposed before swabbing with the applicator.

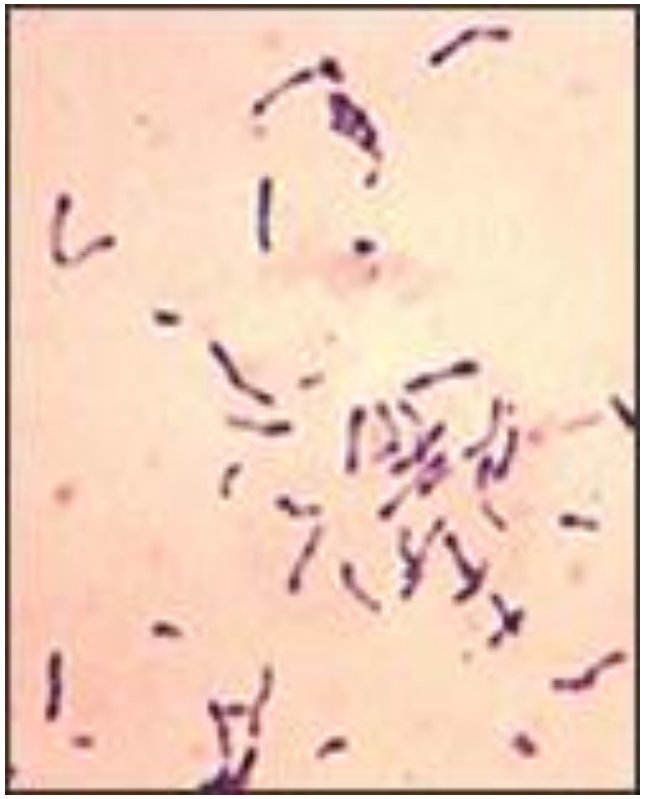


- *C.diphtheriae* colonies blood agar

- **McLeod's agar plate culture of Corynebacterium diphtheriae, gravis biotype.**

Microscpy

- **Corynebacterium diphtheriae taken from an 18 hour culture, and using Albert's stain.**



Schick Test

Schick Test

- **Schick Test**: The intradermal skin test introduced by Schick in 1913.
- Use
  1) Presence of anti-toxin→ Immunity Status
  2) Hypersensitivity to diptheria toxin & other dipth. protein

- Site- Forearm
- Route - Intradermal injection of 0.2ml
  =1/50 MLD (minimal lethal dose)
  of diphtheria toxin
- Control→ Opposite arm

  Heat inactivated toxin or

  0.1 ml diluted toxoid vaccine
  (dilution 1to 10)

Result		Interpretation	Action
Negative	No reaction on both arms	Immune (>0.03 unit antitoxin per ml)	
Positive	**Test arm**-Red flush-10-50 mm dia,appear within 1-2 days., reaches max.4-7 days. Fades slowly with brown patch & dessquamastion of skin **Control arm-** no change	Susceptible to dipheria	Vaccination
Pseudo positive	Both arm-Red flush less circumscribed,Fads by 4-7days-10-50 mm dia,appear within 1-2 days., reaches ma	Immune but Allergic	
Combined	**Test arm**- true positive **Control arm**-Pseudo positive	Susceptible & allergic	Vaccination - with caution

Prevention

Primary

Isolation :-

In hospitals for at least 14 days or two culture 24 hours apart become negative

Active immunization :-

Combined and single vaccine

Immunization does not prevent the carrier state

Contacts

Should be throat swabbed

- **Immunized- primary immunization**

  a) within 2 years- no action

  b) >2 years – booster dose of vaccine

- **Non- immunized-** Contacts should be examined daily for a week

  -Antibiotics-prophylactic penicillin or erythromycin

  -Antitoxin- 1000-2000 units of dip antitoxin

  -Vaccination

Secondary

Early detection & Treatment of cases

Carrier only by culture from nose and throat

Principles of treatment

1) Immediate administration of diphtheria antitoxin and antibiotics.

- Antibiotic treatment usually renders patients non-infectious within 24 hours.
- Unless immunized, children and adults may repeatedly be infected with the disease

Treatment

- Antitoxin-IM/IV after test dose of 0.2ml
- Antibiotics- for 5-7 days

  Penicillin- 2.5 lakh units qds

  Erythromycin- 250 mg qds

- Supportive

  bed rest

  easily digestible high calorie diet

  Antipyretic and sedatives may be given

- Treatment of complication

■ Treatment of carriers

- 10 day course of oral erythromycin

Epidemic control

- The most effective method is mass immunization of the entire population.
- Those individuals who are in close contact with a sick person should be identified and treated immediately with antibiotics.
- Early diagnosis and proper case management procedures (i.e. immediate treatment and hospitalization) should be followed in order to prevent complications and death.

Vaccination

Prevention

- It is vital to immunize early in life
- If a child is suffering from an acute illness (in which case the immunisation should be postponed until they are fully well);

Vaccination

- **Diphtheria toxin is used as combined vaccine in the**

  -DTP-DTaP,

  -HIB,

  -PCV (strep).

Prevention

- DTaP vaccine- 95% efficacy

The Vaccine

- Widely used for over 60 years
- Made from the toxin which has been made harmless. It is called a ‘toxoid’.
- diphtheria toxoid (formaldehyde-inactivated toxin) following immunization.
- Highly effective vaccine (over 90% protection)
- The vaccine may cause a fever and soreness at the site of injection
- Not available on its own but combined with tetanus and polio vaccines and others as appropriate.

- **WHO perspective.**

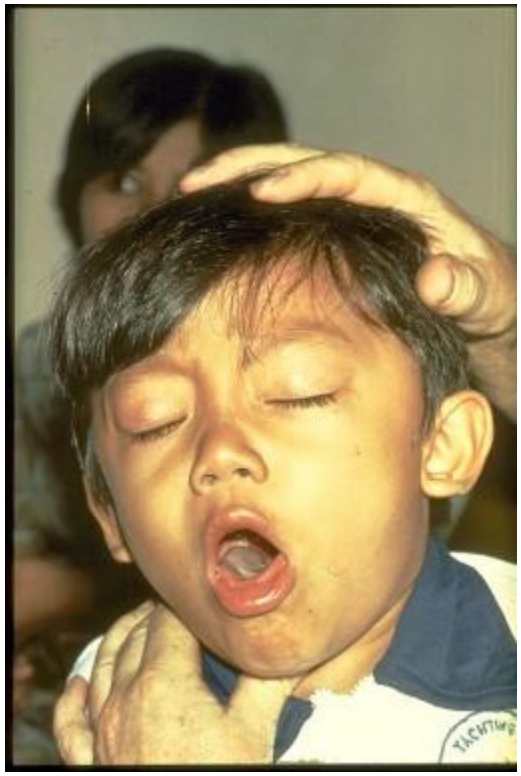
- at least 90% coverage with the 3 primary doses of diphtheria-tetanus-pertussis vaccine (DTP) as early as possible in the schedule.
- DTP is the core vaccine in childhood immunization services.
- Since 1990, the global coverage for this triple vaccine has only been around 80%.
- Additional doses of DTP should be given after completion of the primary doses.
- However, the need and timing for such additional booster doses should be addressed by individual national programs.

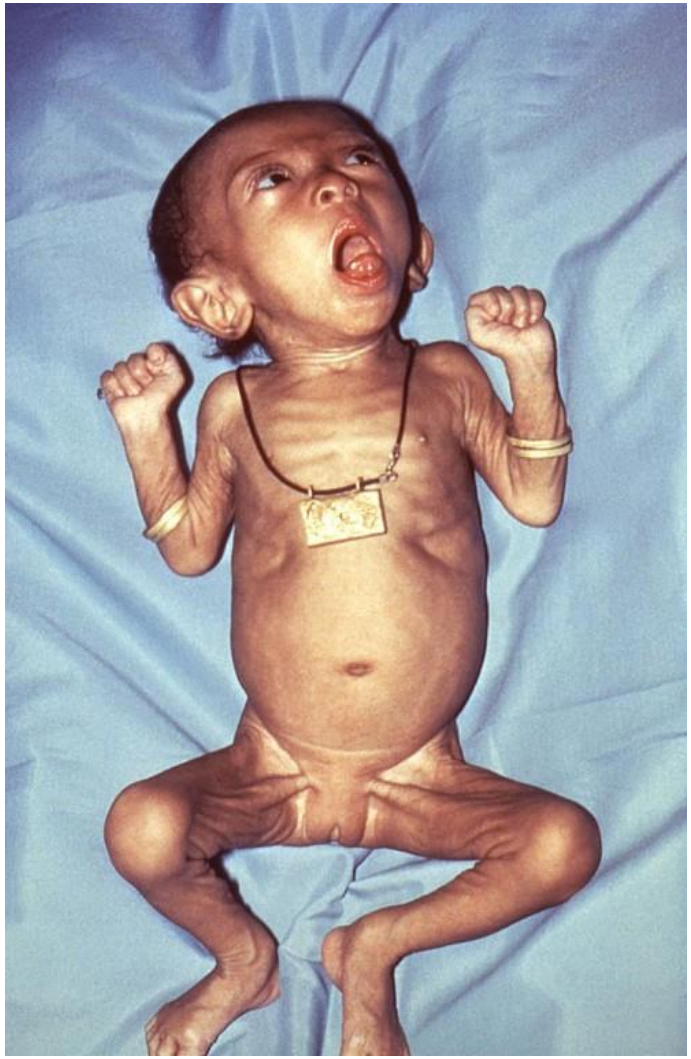
Thank you

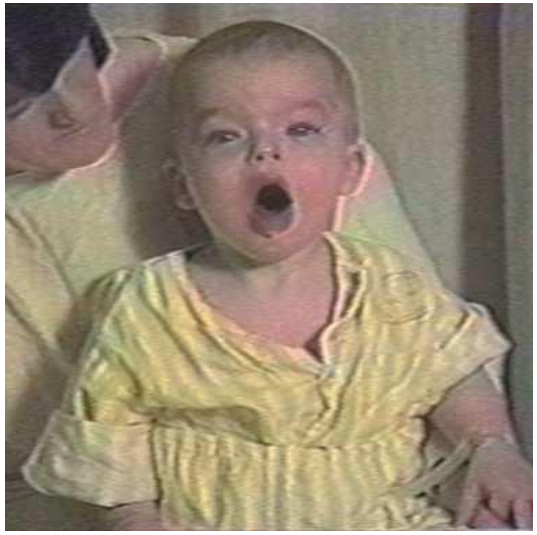
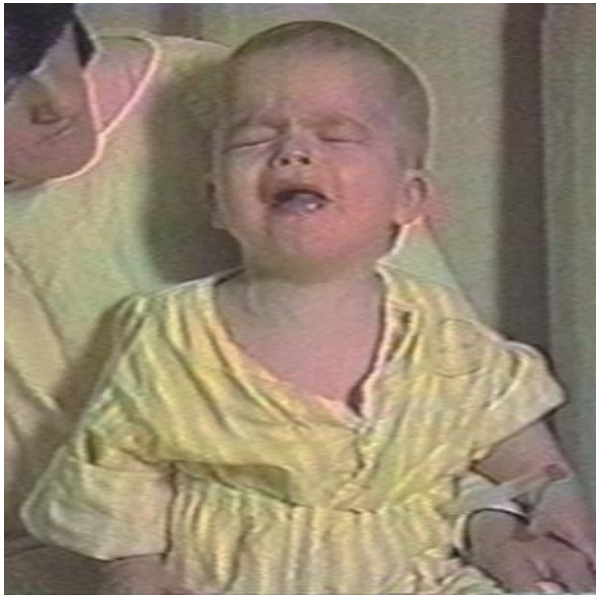
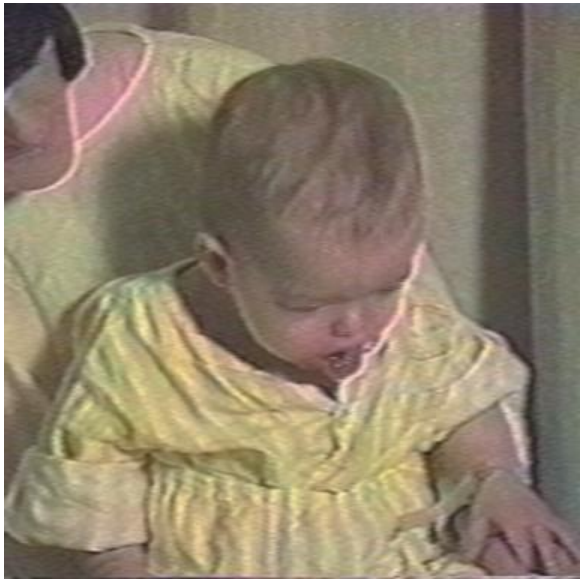

THANK
YOU

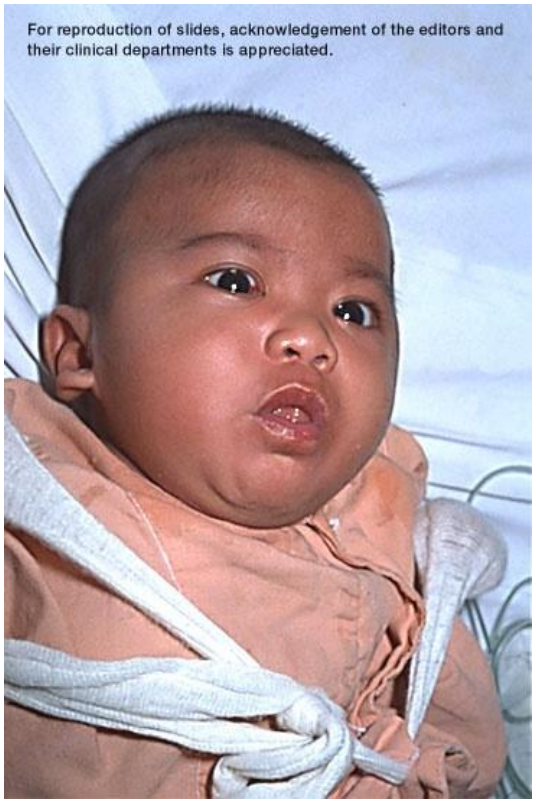
EPIDEMIOLOGY OF PERTUSSIS

Pertussis photos



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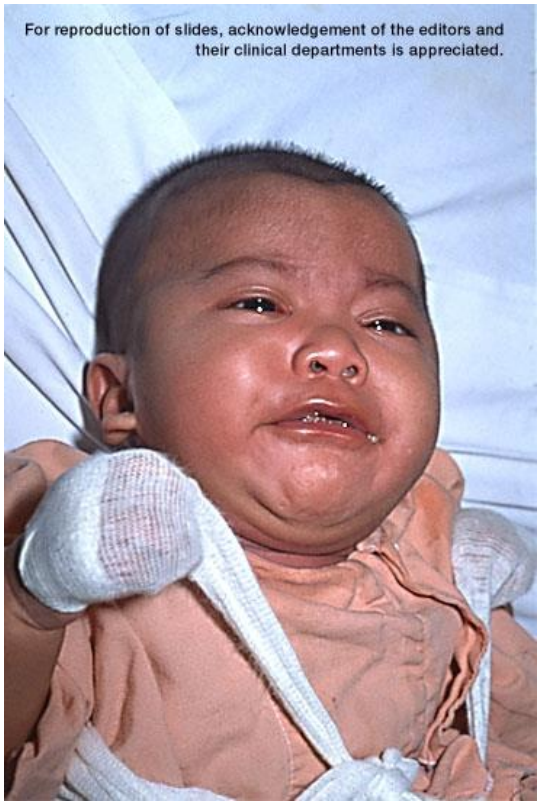
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