Epidemiology Of Diphtheria

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- Diphtheria is an acute infectious disease caused by the bacterium *Corynebacterium diphtheriae*.

- The bacterium produces a exotoxin that is carried in the bloodstream

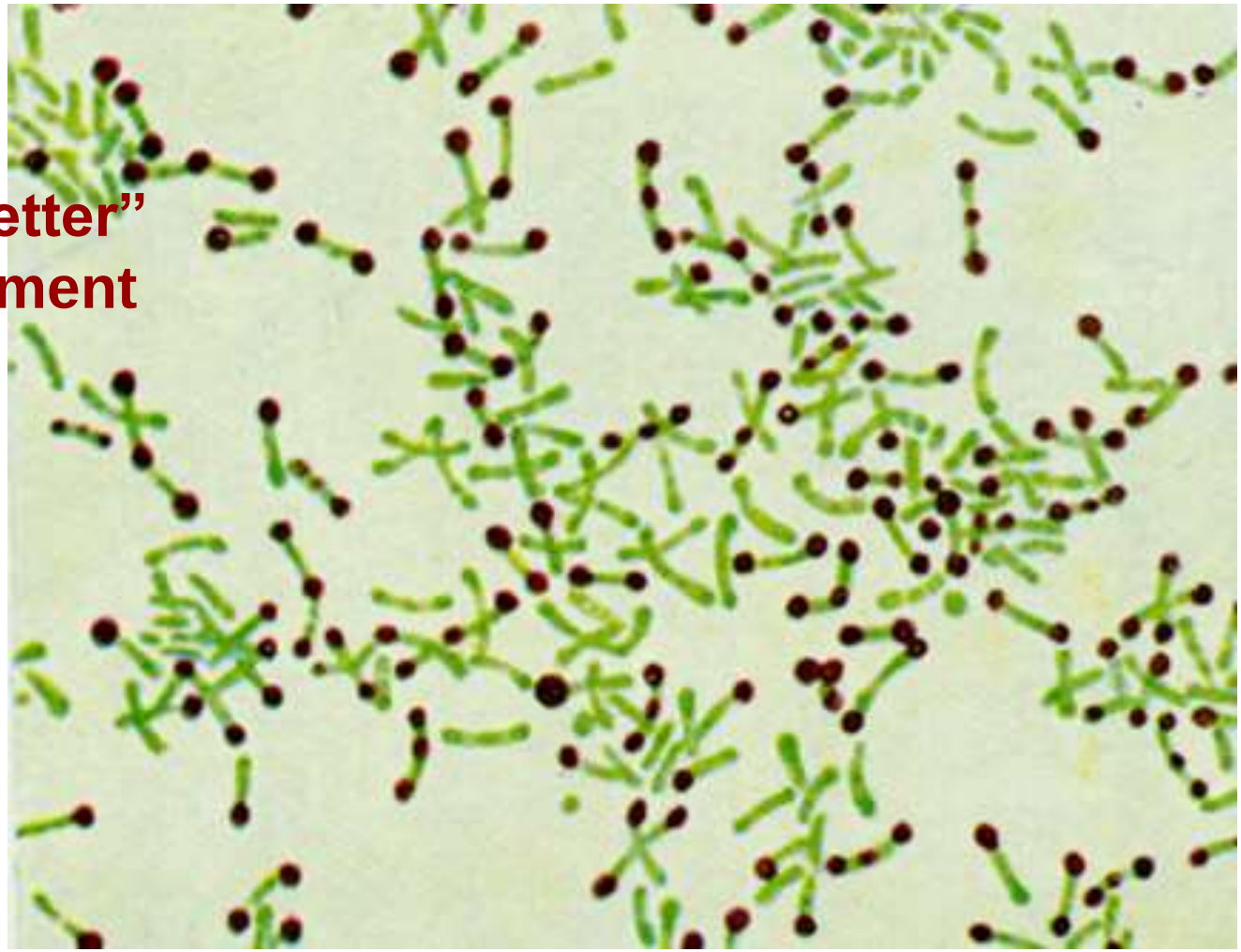
Diphtheria

- Diphtheria is a very contagious and potentially life-threatening bacterial infection that mainly affects the tonsils, throat, nose, pharynx, larynx and occasionally the skin.

- In more serious cases, it can attack the nerves and heart.

Agent

"Chinese-letter" arrangement



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

Agent

- Killed by chemical and heat
- May survive for short periods in dust and fomites

Toxigenic strain

- Bacteriophase in toxigenic strains is responsible for toxin production & produces a powerful exotoxin.
- A toxin that is absorbed into the tissues and bloodstream of the body, causing swelling and subsequent damage

Agent

- **Bio type-** mitis, intermedius and gravis.
- 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 the disease in untreated
  - Carriers– > 6 months
  - Antibiotics can reduce contagious **period < 2 days.**

Non communicable

2 negative cultures 24 hrs. apart

Host

Age

- 1to 5 years (80 % cases < 15 years age group)
- It is now affecting older children (5-19 years) and adults (Shift in age affected from preschool to school age)
- Females = males

Host

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

Immunity

- **Natural Infection** - long-lasting immunity

  Second attack is always mild/ subclinical
- **Vaccine immunity (acquired)** People may become infected with an atypical strain.
- **Maternal antibodies** Protection for first few weeks or months of life

Herd immunity-

70% to prevent epidemic spread

Environmental Factor

Environment

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

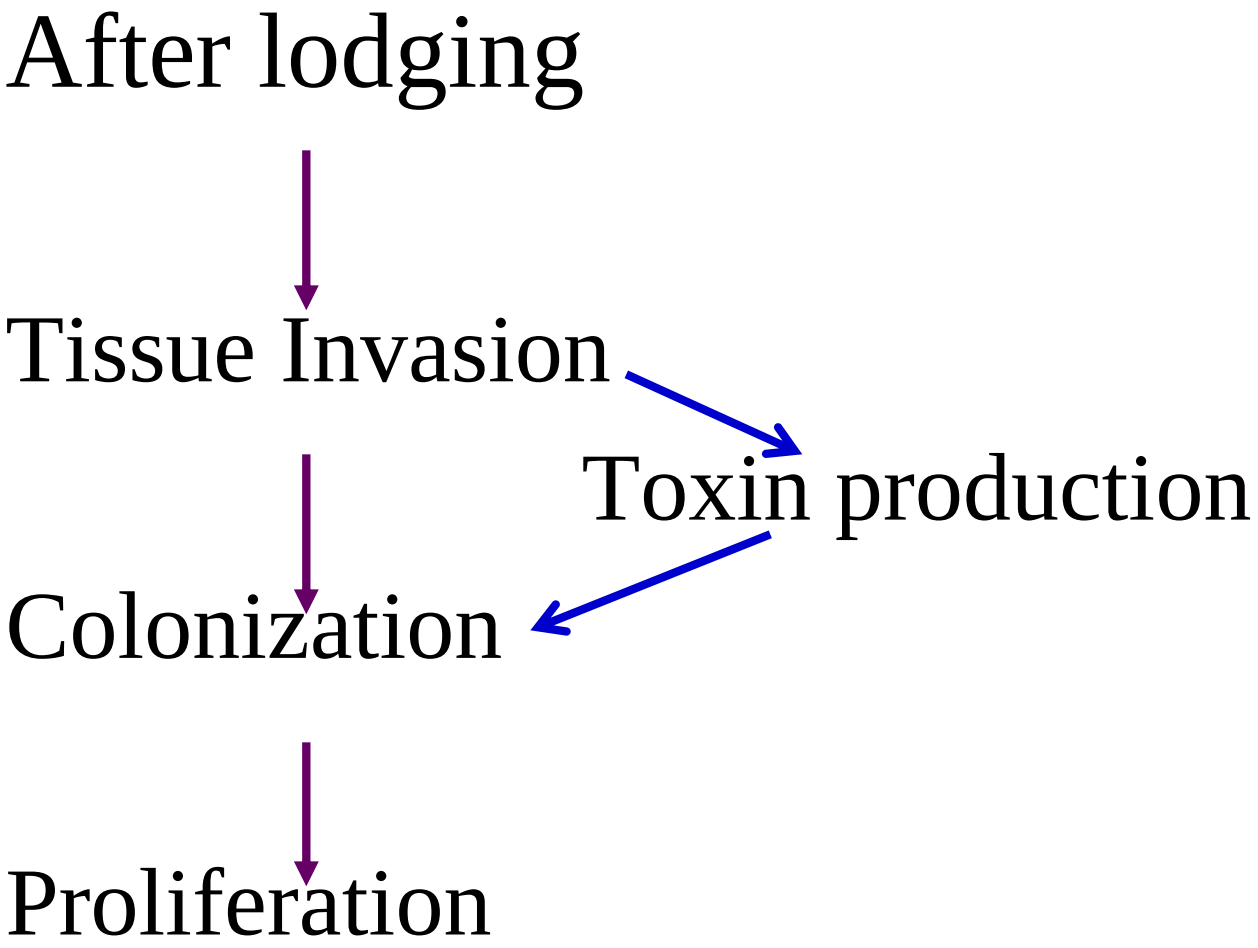
Spread

- Person to person by respiratory **droplets** from the throat through coughing and sneezing.
- **Air borne-** By close face to face contact with an infected person.
- Close contact- Infected cutaneous lesion
- **Fomite**
- Contaminated raw milk.

Portal of entry

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

Pathogenesis


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

↓

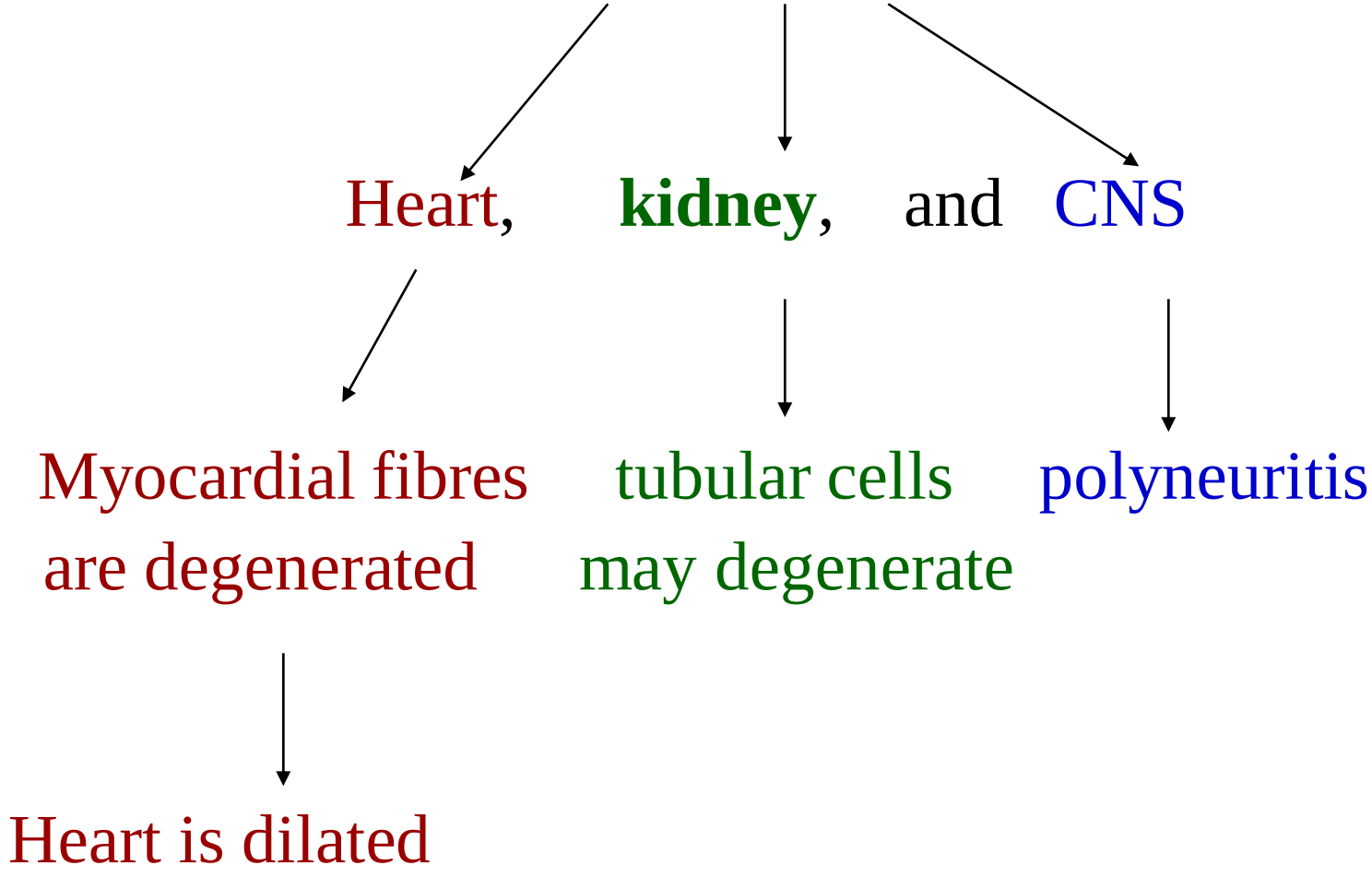
Which bleeds on being dislodged

- **Mitis , Intermedius & gravis -**based upon two primary determinants:

- (1) the ability of a given strain of *C diphtheriae* to colonize in the epithelial surface and
- (2) its ability to produce diphtheria toxin.

- The toxin is absorbed into the tissues and bloodstream of the body, causing swelling and subsequent damage.

Systemic effects of exotoxin



Clinical Features

Types of clinical diphtheria

1) Respiratory
   - -Anterial nasal
   - - Pharyngeal
   - - Laryngeal

2) Non respiratory
   - -Cuteneous
   - -conjunctiva,
   - -genitalia

- In Respiratory -Pharyngotonsillar

- In non- Respiratory -- Cutaneous is commonest.

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

Pharyngeal Diphtheria

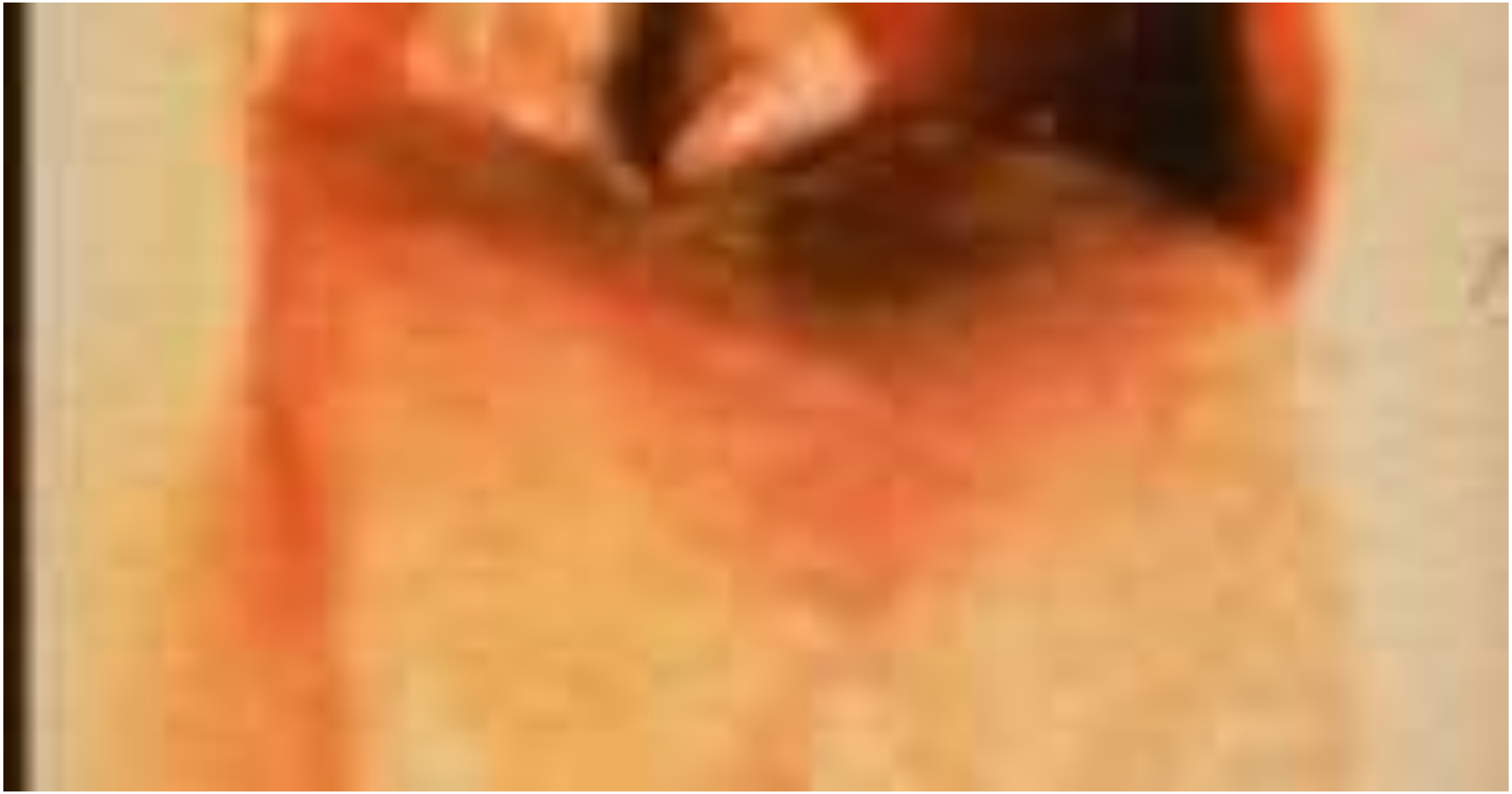
An adherent, dense, grey pseudomembrane covering the tonsils is classically seen in diphtheria

Pseudomembrane in diptheria

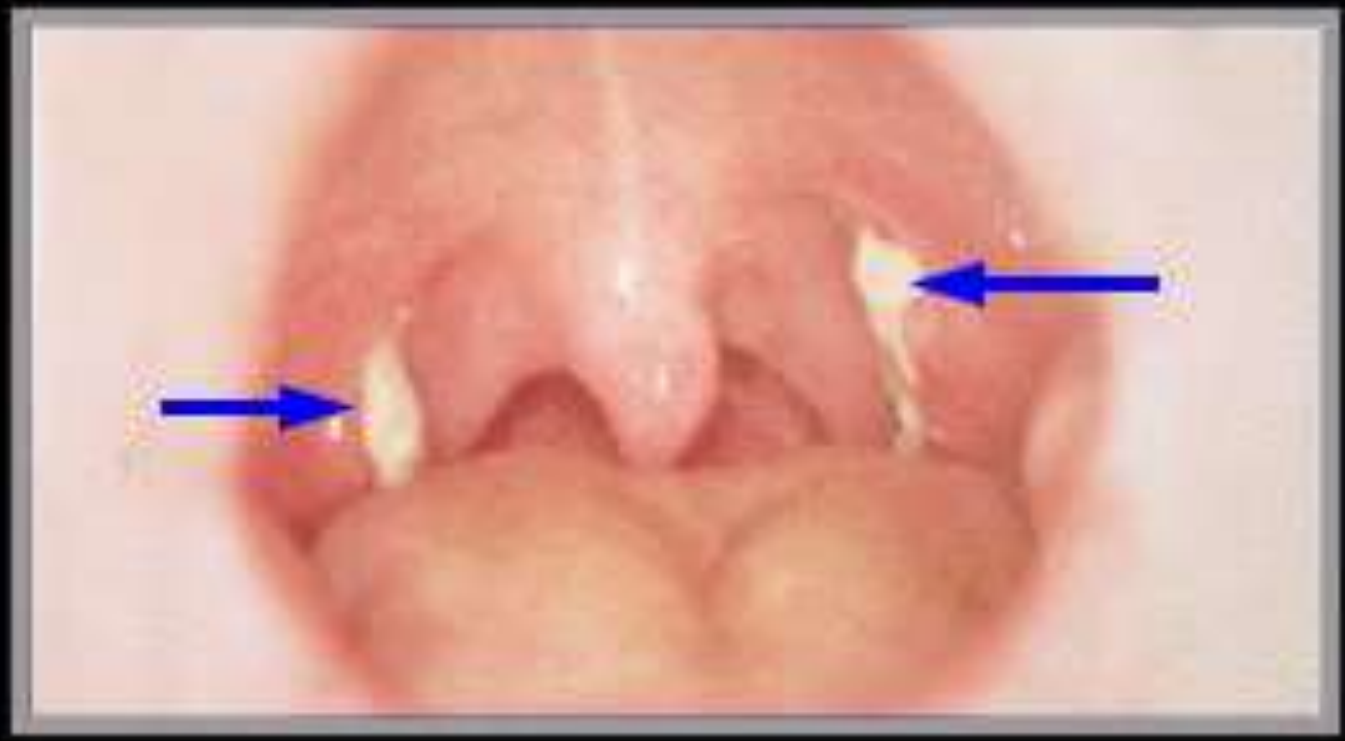
- The membrane may be localized as
- a patch of posterior pharynx or
- tonsil may cover the entire tonsil or
- less frequently, may spread to cover the soft or hard palates & posterior portion of pharynx.

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.

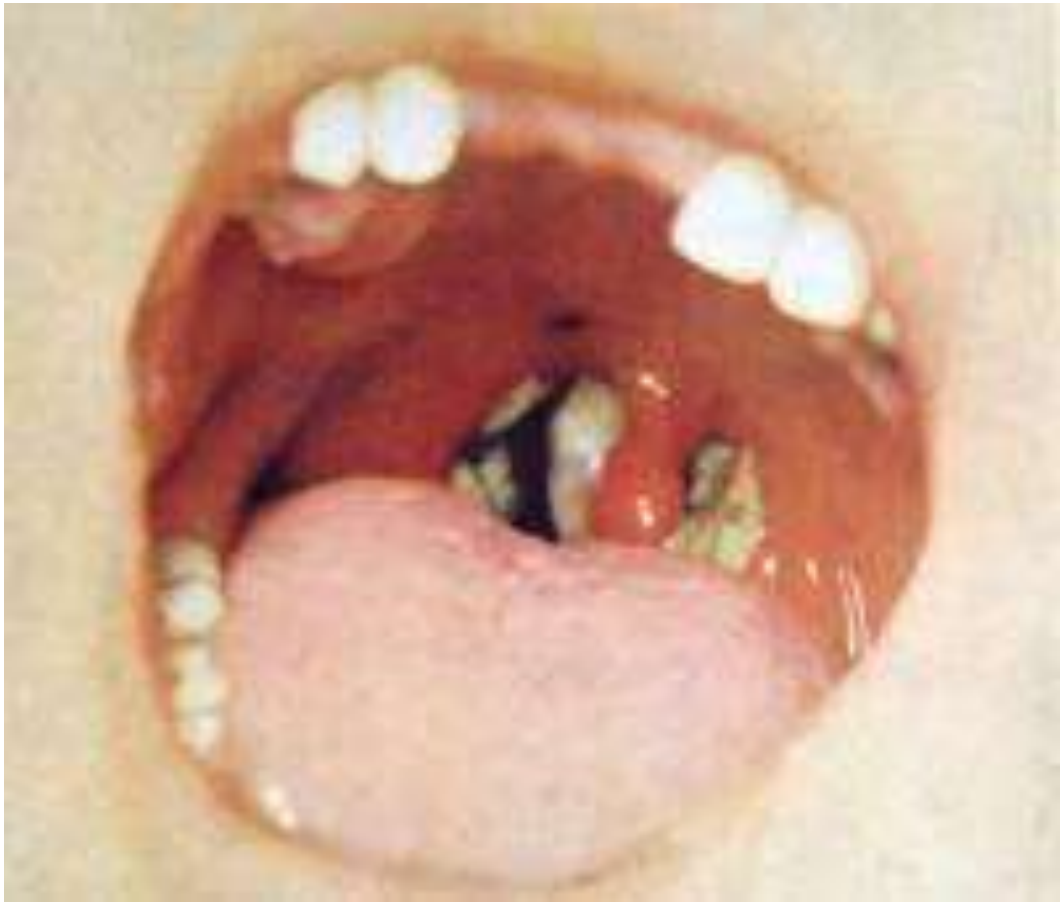


•Minimal area of mucosal erythema surrounds the membrane.



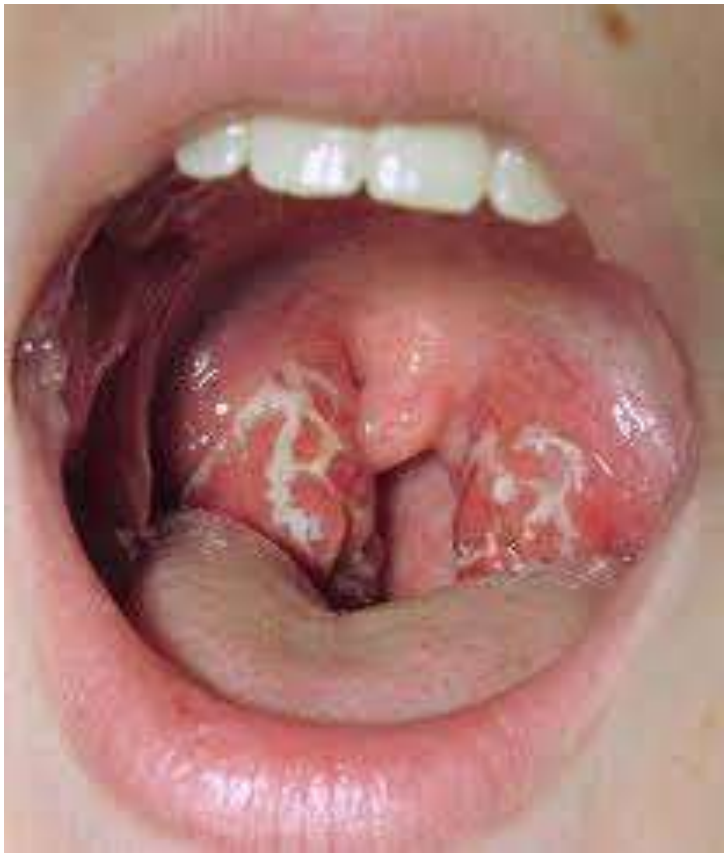
Pseudomembrane

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

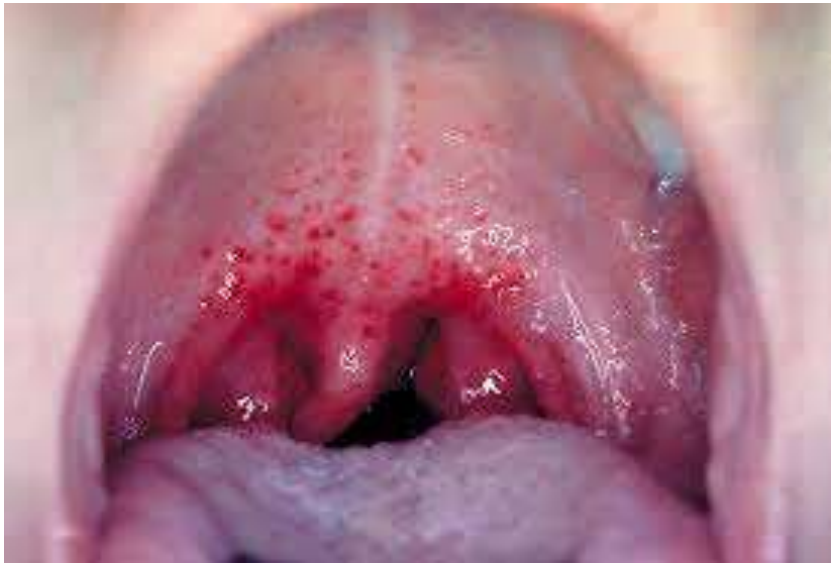


- Early stage – it is whitish & may wipe off easily.
- Later- thick, blue white to gray black & adherent.

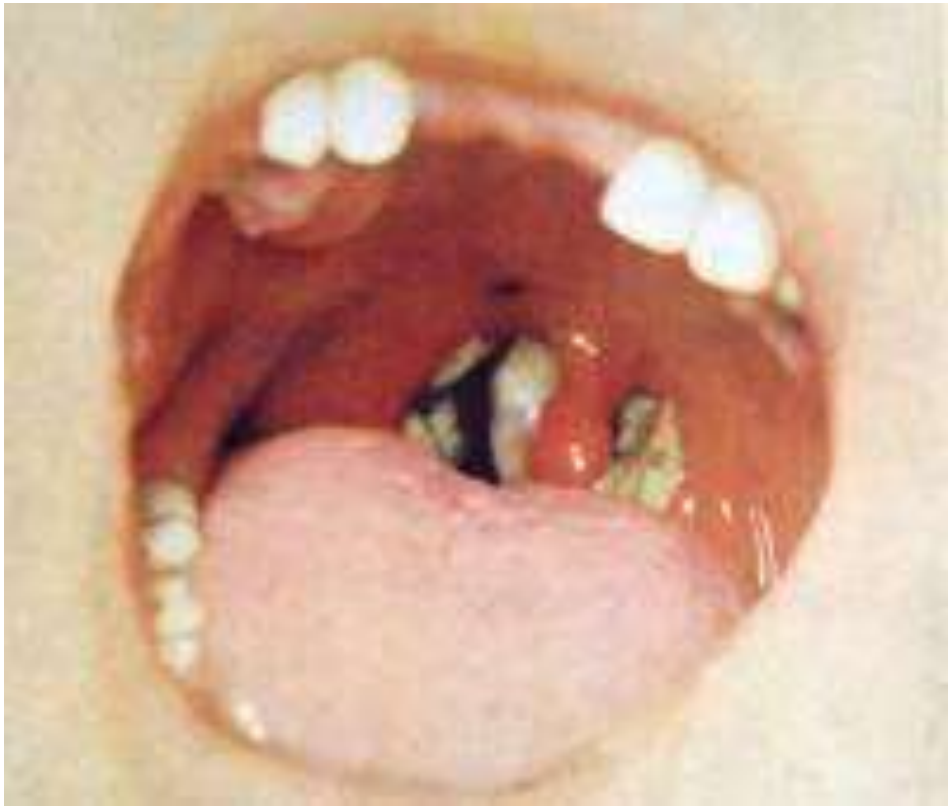
Diphtheria



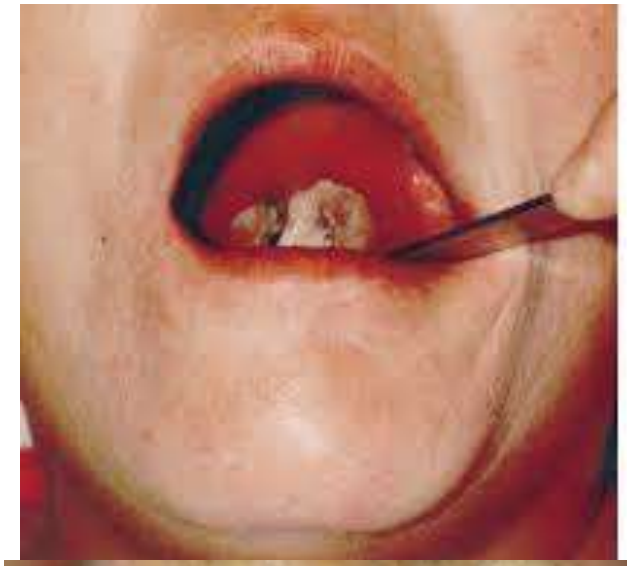
Enlarge Tonsils



The attempt to remove membrane may result in bleeding.

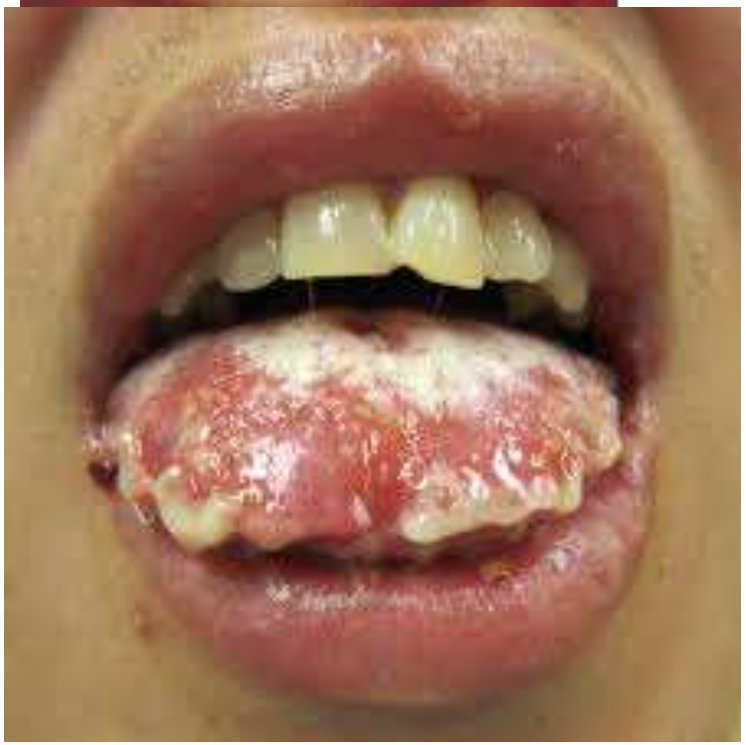


- Air way obstruction
- Difficulty in swallowing



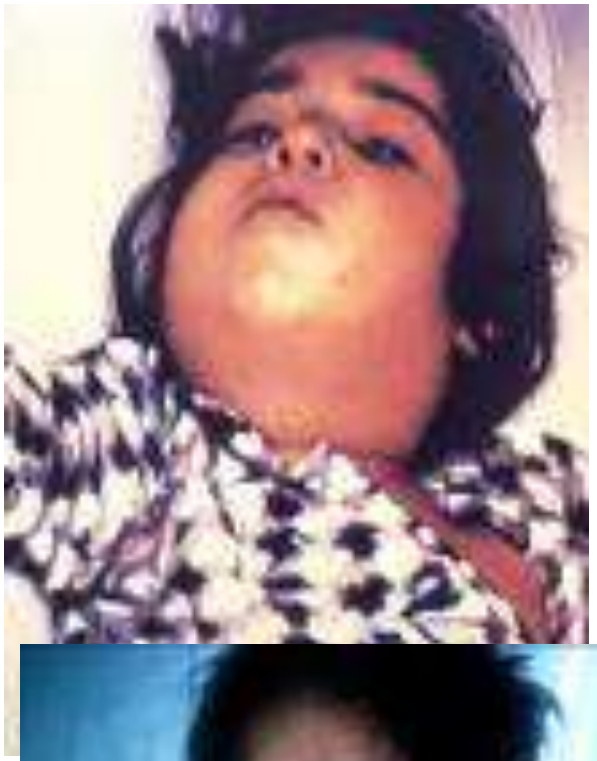
Pseudo Membrane

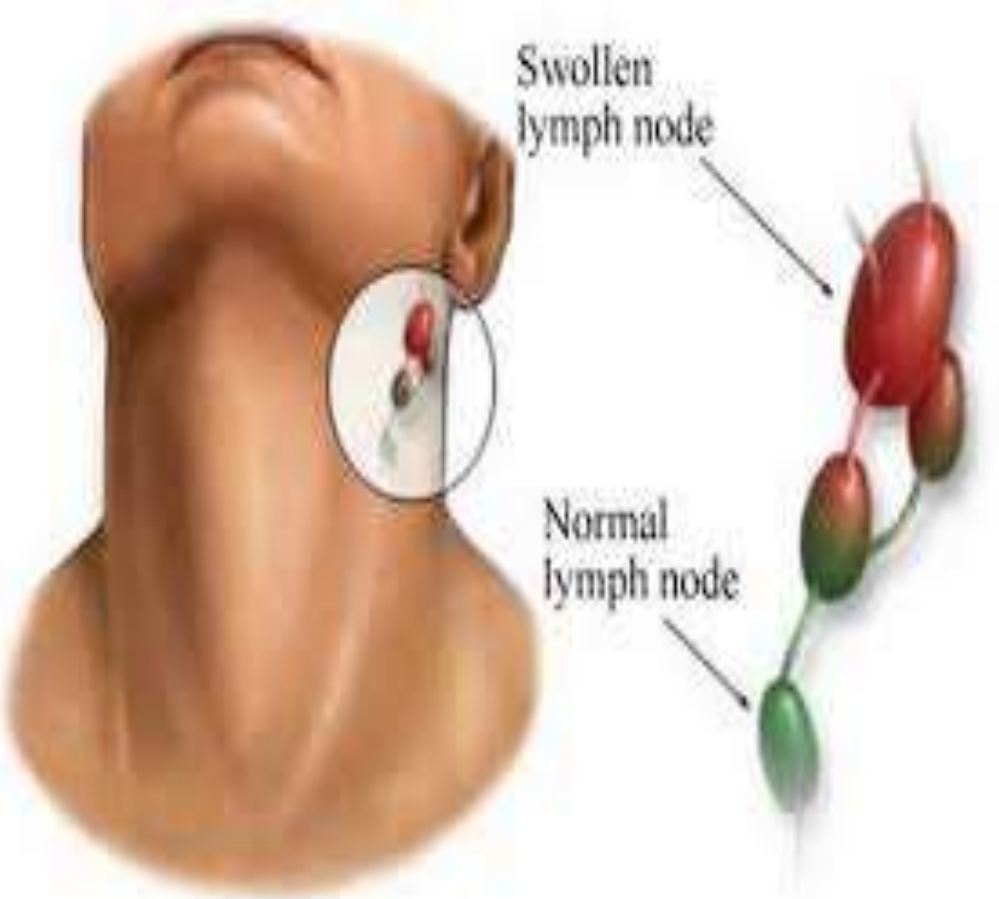
May spread to cover the soft or hard palates & posterior portion of pharynx.



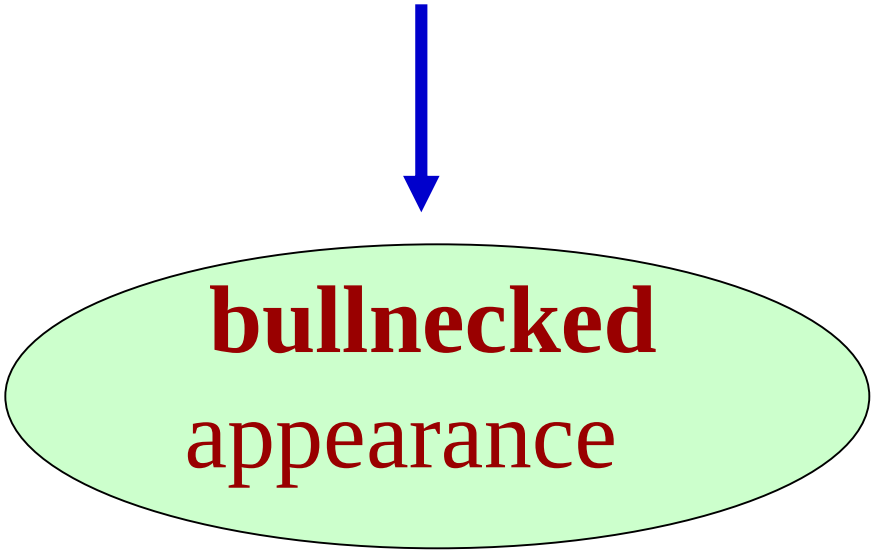
- Symptoms of pharyngeal diphtheria vary from mild pharyngitis to hypoxia due to airway obstruction by the pseudomembrane especially **in the throat** which blocks the breathing

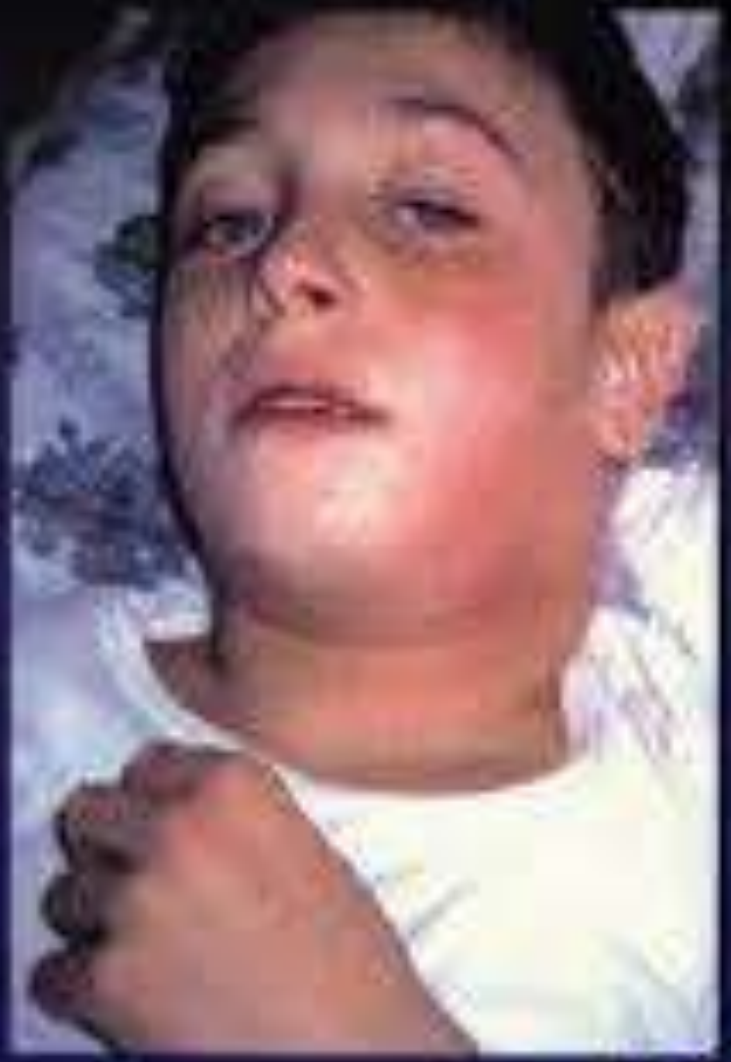
Bull neck Diptheria





- 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

Toxin is responsible for

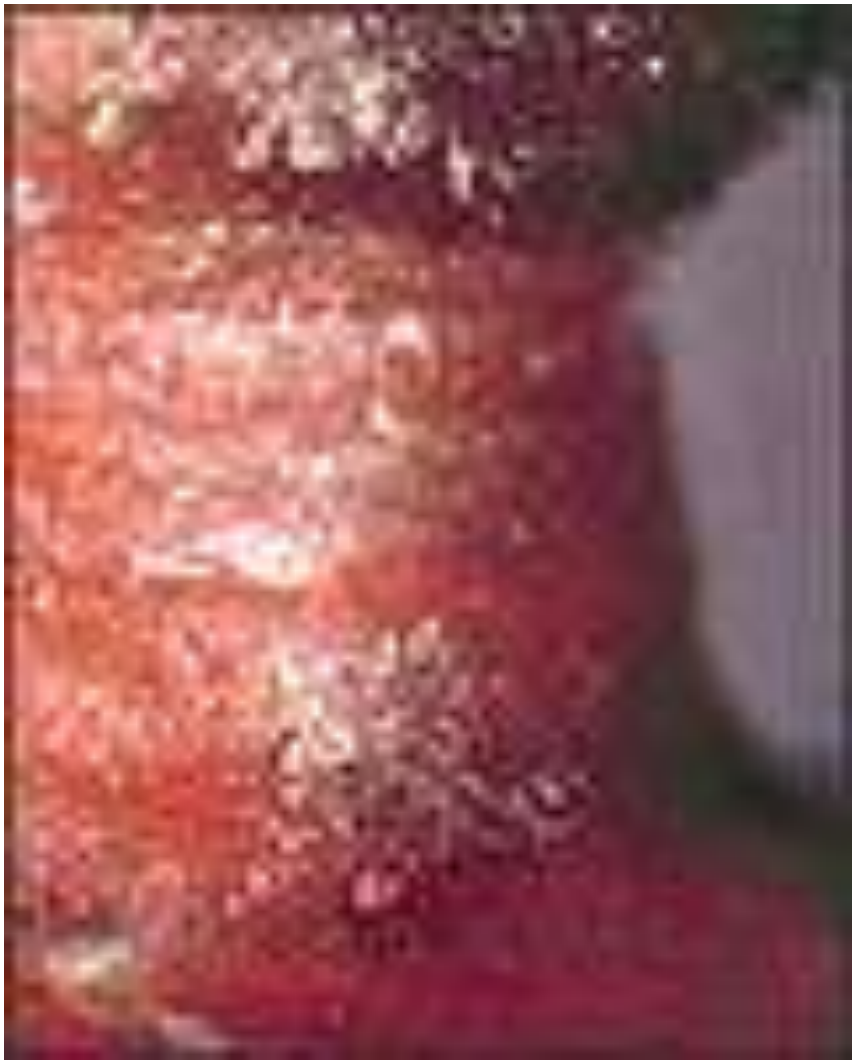
a) Formation of grayish yellowish membrane ("false membrane") commonly over the tonsils, pharynx, larynx with well defined edges & membrane cannot be wipped away

b) Marked congestion, oedema & local tissue distruction

c) Enlargement of regional lymphnodes &

d) S/S of toxemia

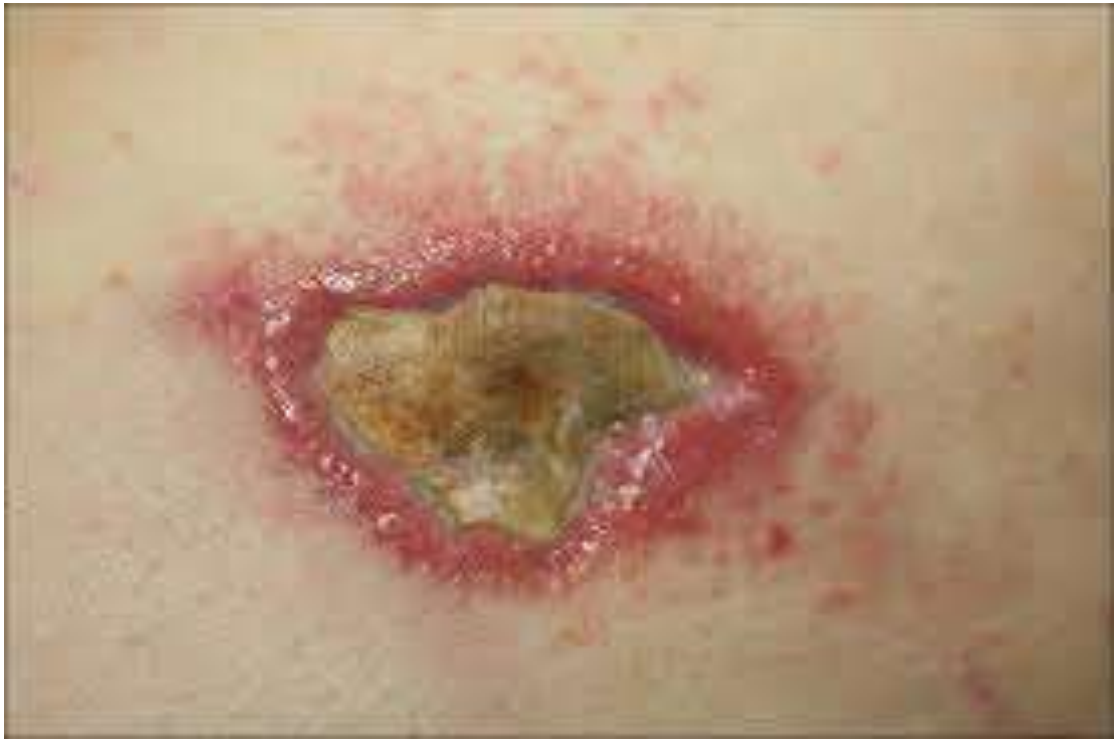
Cuteneous diphtheria



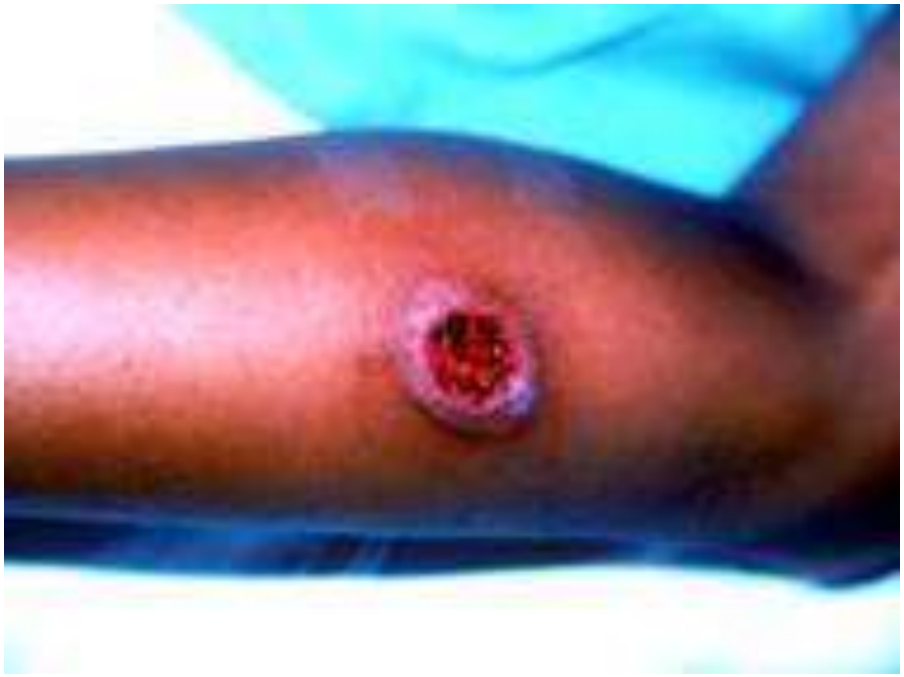
- Usually a secondary infection of a previous skin abrasion
- covered by a gray-brown pseudomembrane.

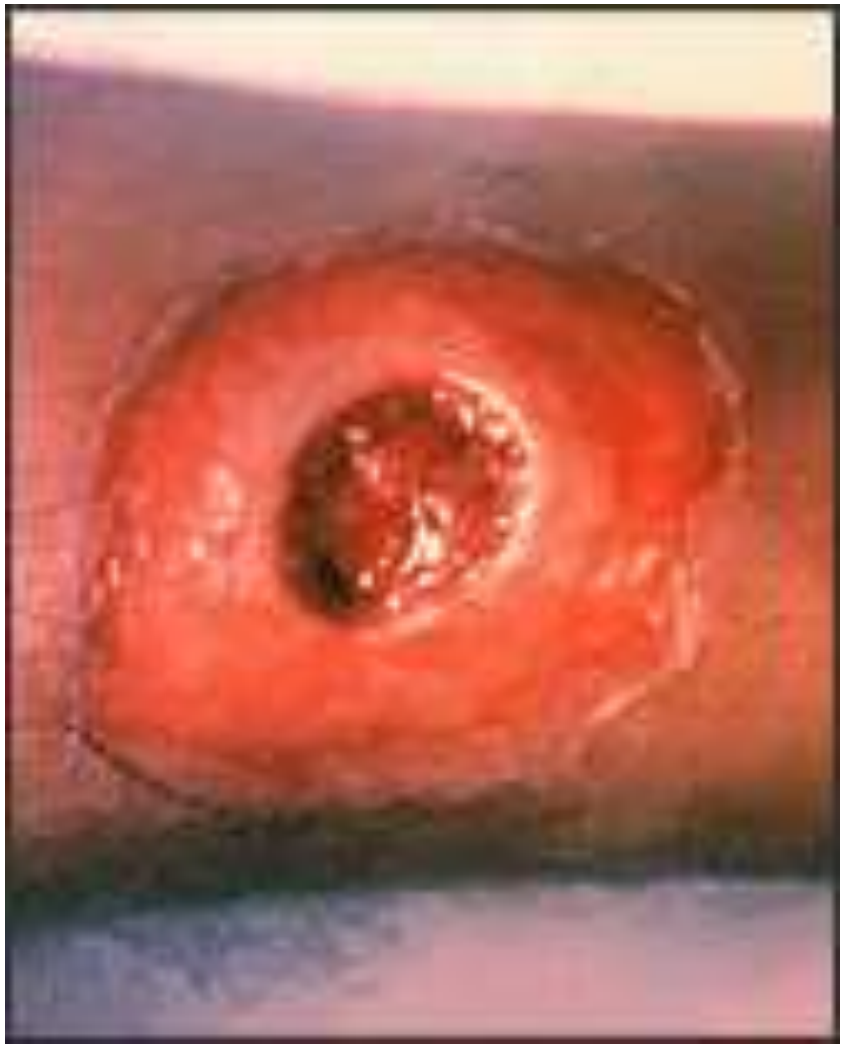
Cuteneous diphtheria

ulcer ,erythema & pseudo memb.



Cuteneous diphtheria

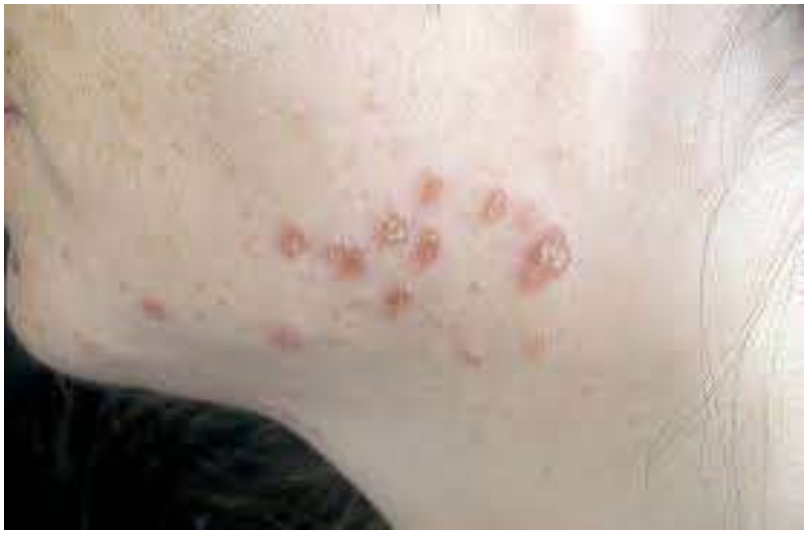


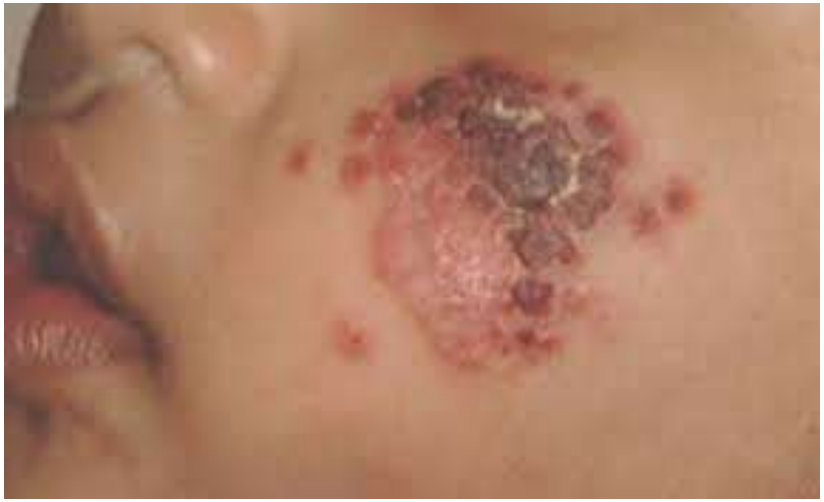


ulcer ,erythema &
pseudo memb.

Cuteneous diphtheria

Pustular sores - are painful, swollen, and red, resembling impetigo.





Symptoms usually appear two to four days after infection.

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.- Ulcer/ lesion like impetigo

Complication

- **Myocarditis**

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

  abdo pain,vomiting, dysponea, tachycardia, extrasystole, thready pulse.

- **Neurological**

  palatal paralysis, loss of accomodation and general polyneuritis.

- **Renal**

  oliguria and proteinuria

- **Sudden death**

  due to respi obstruction, myocarditis and respi paralysis

Complications

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

Diagnosis

Throat examination

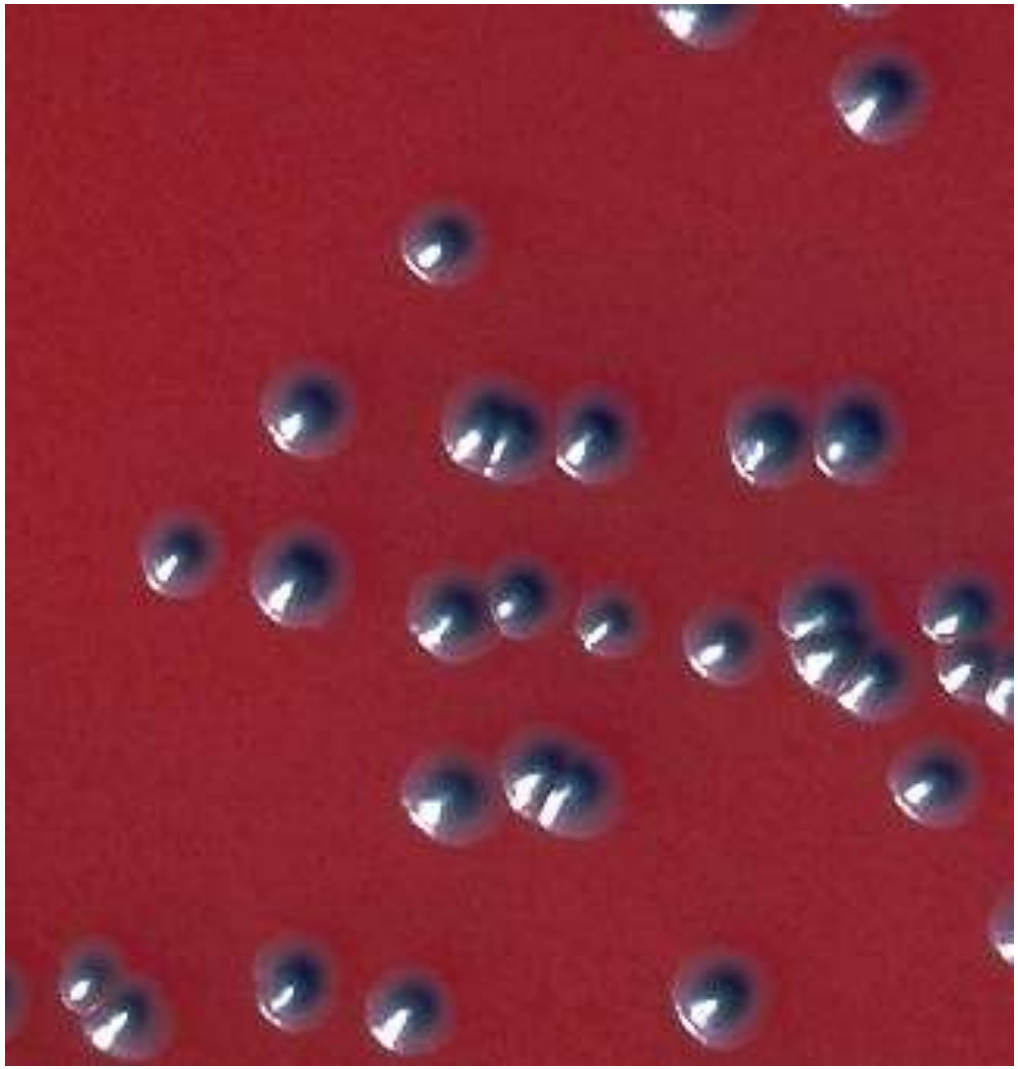
- Mild erythema, localized exudate or a membrane.

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.

Lab. diagnosis

- Culture-
- Toxigenicity is identified by a variety of
  - *in vitro* gel immunodiffusion, tissue culture or
  - *in vivo* (e.g., rabbit skin test) method.

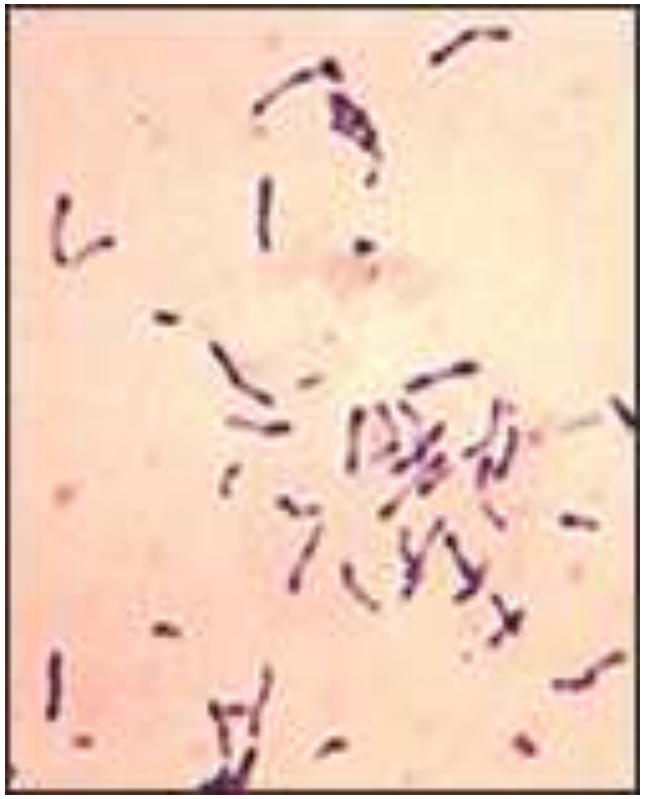


- *C.diphtheriae* colonies blood agar

- **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

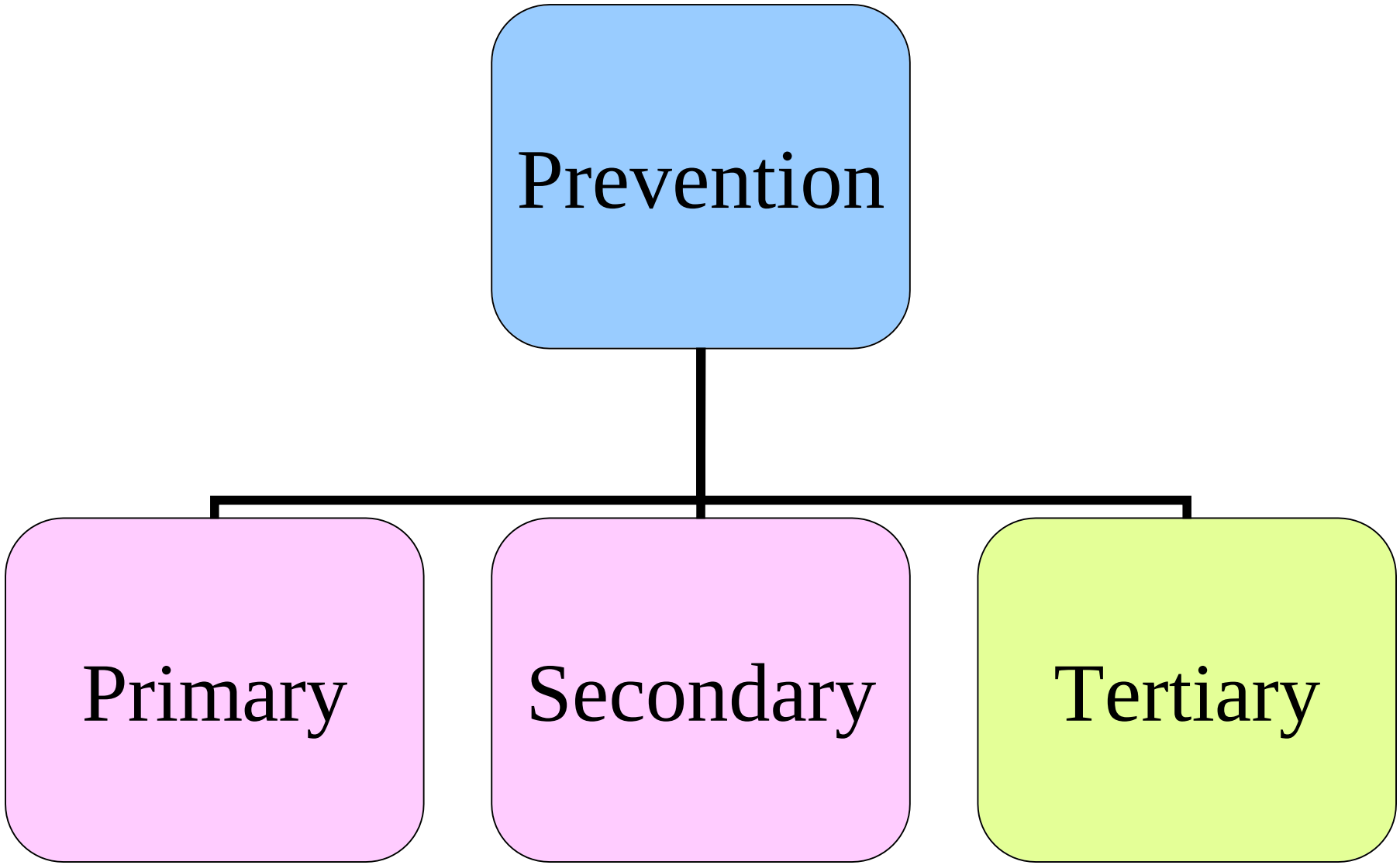
  Heat inactivated toxin or

  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 diptheria	Vaccination
Pseudo positive	**Both arm-** Red flush less circumscribed, Fads by 4-7days-10-50 mm dia,appear within 1-2 days.	Immune but Allergic	----------
Combined	**Test arm**- true positive **Control arm**-Pseudo positive	Susceptible & allergic	Vccination-with caution

- "By the use of a simple test, it is possible to find out those children who are at risk for the disease and those who are not."

Prevention


Prevention
Primary
Secondary
Tertiary

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

Care Of Exposed

- All contacts/ exposed should be throat swabbed
- **Immunized**
- **Unimmunized**

Contacts

- **Immunized- primary immunization**

  a) within 2 years- no action

  b) >2 years – booster dose of vaccine

Contacts

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

  -Antibiotics-prophylactic penicillin /erythromycin

  -Antitoxin- 1000-2000 units of dip antitoxin

  -Vaccination

Secondary

- Early detection & Treatment of cases
- Carrier only by culture from nose and throat

Secondary
Principles of treatment

1) Neutralization of free circulating toxin-
   Immediate administration of diphtheria antitoxin
   antitoxin is of little use after toxin has already been fixed to the tissues.

2) Prevent colonization- killing bacteria by antibiotic/s

3) Provide long term immunity- active immunization

Secondary

Antitoxin

Immediate administration of diphtheria antitoxin

- -IM/IV after test dose
- Doses : 10000 to 80000 units or more, after a test dose of 0.2 ml subcutaneously

Secondary

Antibiotics

Antibiotic turns patients non-infectious within 24 - 48 hours.

- Antibiotics- for 5-7 days

  Penicillin- 2.5 lakh units qds

  Erythromycin-250 mg qds

Treatment

- Treatment of carriers
  - 10 day course of oral erythromycin

Treatment

- Supportive

  bed rest

  easily digestible high calorie diet

  Antipyretic and sedatives may be given

- Treatment of complication

Active immunization

- 4 weeks after the completion of treatment

- Unless immunized, children and adults may repeatedly be infected with the disease

Epidemic control

- Mass immunization
- Close contact with a sick person - be identified and treated immediately with antibiotics.
- Early diagnosis and proper case management procedures (i.e. immediate treatment and hospitalization)

Prevention of Diphtheria

- **Primary prevention-** Immunization
- **Care of exposed-**

A-take throat swab

B-Examine contact daily for a week

C-Active immunization

a) within 2 years- no action

b) >2 years – booster dose of vaccine

- **Non- immunized-**

-Antibiotics-prophylactic penicillin /erythromycin

-Antitoxin- 1000-2000 units of dip antitoxin

-Vaccination

Secondary prevention

A. Anti toxin
B. Antibiotic- 5-7 days

   Erythromycine for 7 days to prevent carrier

A. Supportive
B. Immunization after 4 weeks of completing treatment

Vaccination

Vaccination

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

  -DTP-DTaP,

  -HIB,

  -Hep. B

Prevention

- DTaP vaccine- 95% efficacy

Immunisation

- Primary-Three vaccinations

  6-8, 10-12 and 14-16 weeks old,

- Booster- 1st -at 18-24 months

  2nd - 5-6 years- DPT

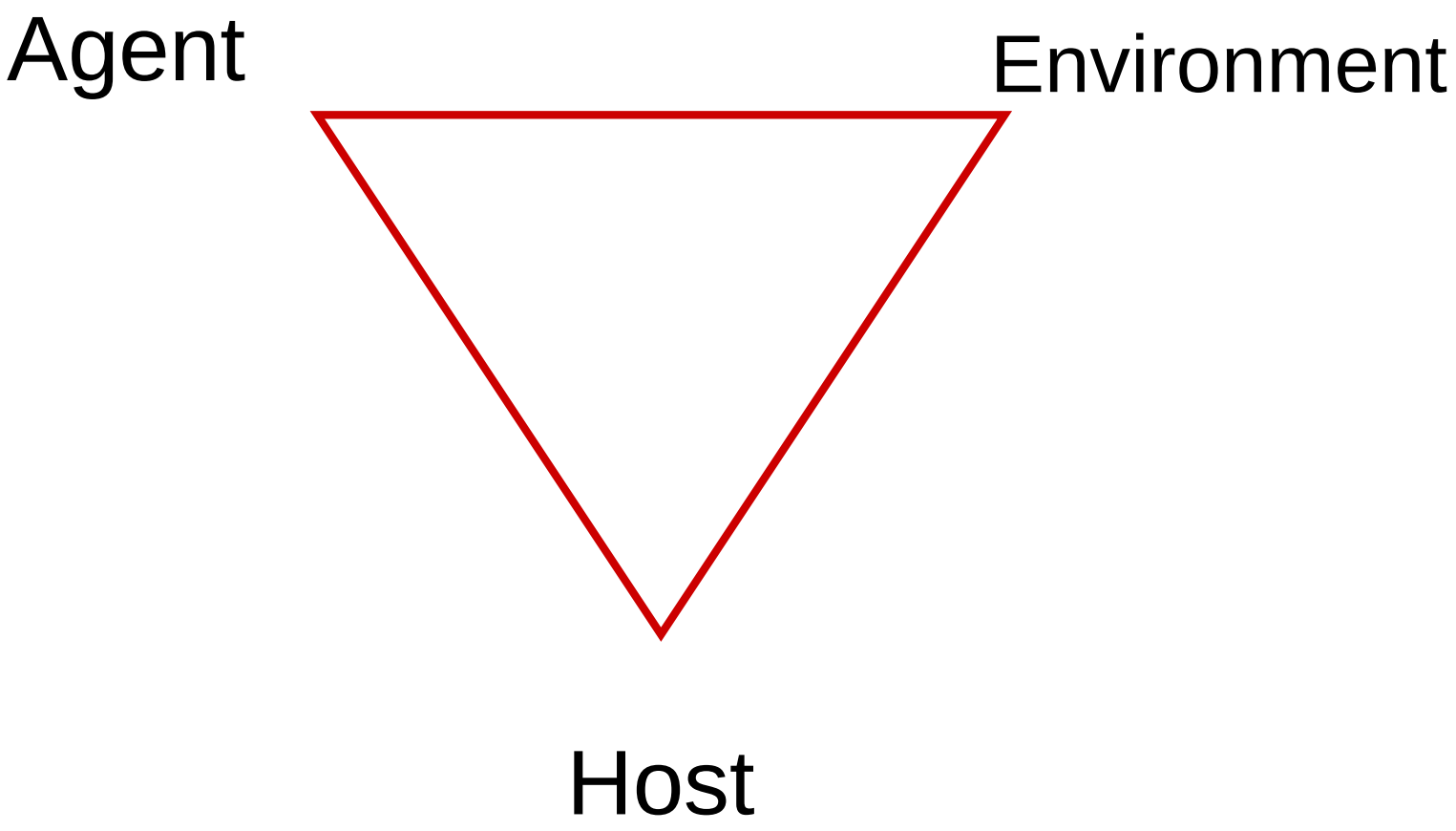
Thank you

Epidemiology of Pertussis (Whooping Cough)

ઊટાટીયું

- Pertussis or whooping cough, is a serious acute respiratory infection caused by ***Bordetella pertussis*.**

- It is characterized by a paroxysmal, spasmodic cough that usually ends in a prolonged, high-pitched crowing inspiration or whoop .


Agent
Environment
Host

Agent

Bordetella pertussis

Gram-negative aerobic cocobacillus

- Human infection- 2 subtypes

  B. pertussis – Antigenically highly complexed

  B. parapertussis- <5% of cases

  causes a mild diesease

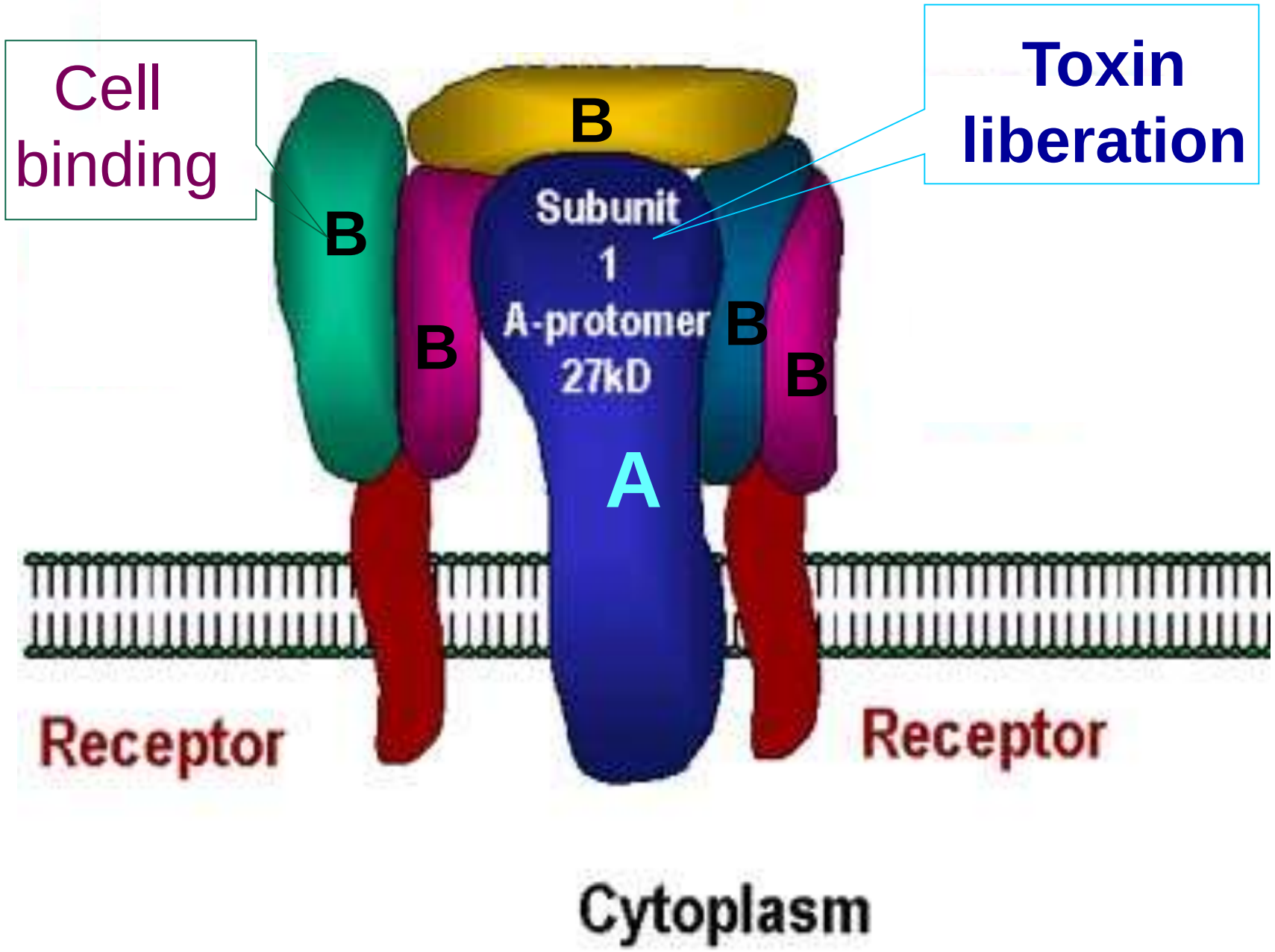

bacteria
cilia
nonciliated cells

Agent

- Toxin production- Endotoxin & exotoxin

1-It has been found in alveolar macrophages

2- Primarily it attaches itself to the ciliated epithelium of the respiratory tract.


Cell binding
Toxin liberation
B
B
B
B
B
Subunit 1 A-protomer 27kD
A
Receptor
Receptor
Cytoplasm

- These toxins paralyze the cilia and cause inflammation.
- Paralysis of cilia inhibits proper clearing pulmonary secretions.

- Source of infection- mankind is the only source
    - Case
    - No sub clinical or No carrier
- Infective material

    -Bronchial secretions,

    -Nasopharyngeal secretions

    - Droplets

    -Freshly contaminated fomites

- SAR- 90% in unimmunized close contacts

- Incubation period - 7 to 14 days, with a maximum of 21 days

- Infective Period-
  - From a week after the exposure to 3 weeks after the onset of paroxysmal stage.
  - Most infective during catarrhal stage.

Host

Age

- Any age.
- Milder in adult
- Infants- 20% cases , CFR– 4-15%
- Children from ages 1 to 4 years -60% of cases
- After the introduction of widespread immunization, age-specific attack rates shifted upward. – older children, adolescents

Host

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

Immunity

- Natural Infection & vaccine - long-lasting immunity to the typical clinical manifestations.
- People may become infected with an atypical strain.

- No protection from maternal antibodies

Environmental Factor

Clinical Features

Three stages.

1. ***The catarrhal stage- 1-2 weeks***
2. ***The paroxysmal stage- 2-4 weeks***
3. ***The convalescent stage-2-4 weeks***

1--*The catarrhal stage*
1-2 weeks

- Highly communicable.
- SAR more than 90% in non-immune households.
- Characterized by the attachment of **B. pertussis to the epithelium of the** respiratory tract.
- Clinical symptoms are very similar to that of a cold.

1--*The catarrhal stage*

- Cold-like symptoms
  - Mild fever - or no fever at all in early stages
  - Mild dry cough ---Night cough
  - Running nose
  - Sneezing
  - Sore throat
  - Tears
  - Tiredness
  - Loss of appetite

1--***The catarrhal stage***

- Cough- mild but hacking nocturnal cough that gradually becomes diurnal as well.
- by 7 to 10 days after the onset of illness, becomes explosive and episodic, heralding the onset of the paroxysmal stage.

2--The paroxysmal stage
2 to 4 weeks

- Once B. pertussis begins to produce toxin it enters the *paroxysmal* stage.
- Characterized by the infamous whooping cough.

2--The paroxysmal stage

- This is a number of rapid coughs, invoked because the body is **encountering difficulty in removing thick mucous from the tracheobronchial tree--- Paralysis of cilia**

2--The paroxysmal stage

- Each paroxysm is characterized by five or more rapid short coughs followed by a deep hurried inspiration.
- It is this hurried inspiration through a narrowed airway that produces the characteristic **high-pitched whoop sound.**

- Whooping cough was first recognized after an epidemic in Paris in 1578. It was then known as the **‘dog bark’,** the ‘chin’ cough or ‘kin’ cough, meaning convulsive cough. .

2--The paroxysmal stage

Infants

- Choking spells and cyanosis.
- The child is often exhausted following a paroxysm.
- May appear happy and relatively normal between episodes.

2--The paroxysmal stage Infants

- A variety of stimuli, including feeding, sucking, or crying, can trigger an attack.

- Very young infants tend to have apniatic spells rather than paroxysms of cough.

2--The paroxysmal stage (Infants)

Breathing difficulties

- Non-breathing periods (apnea)
- Cyanosis
- Convulsions
- Choking

Breathing difficulties are serious & very dangerous

2--The paroxysmal stage (Infants)

Feeding difficulties

- The act of feeding can also trigger a coughing fit, making it hard to feed an infant.

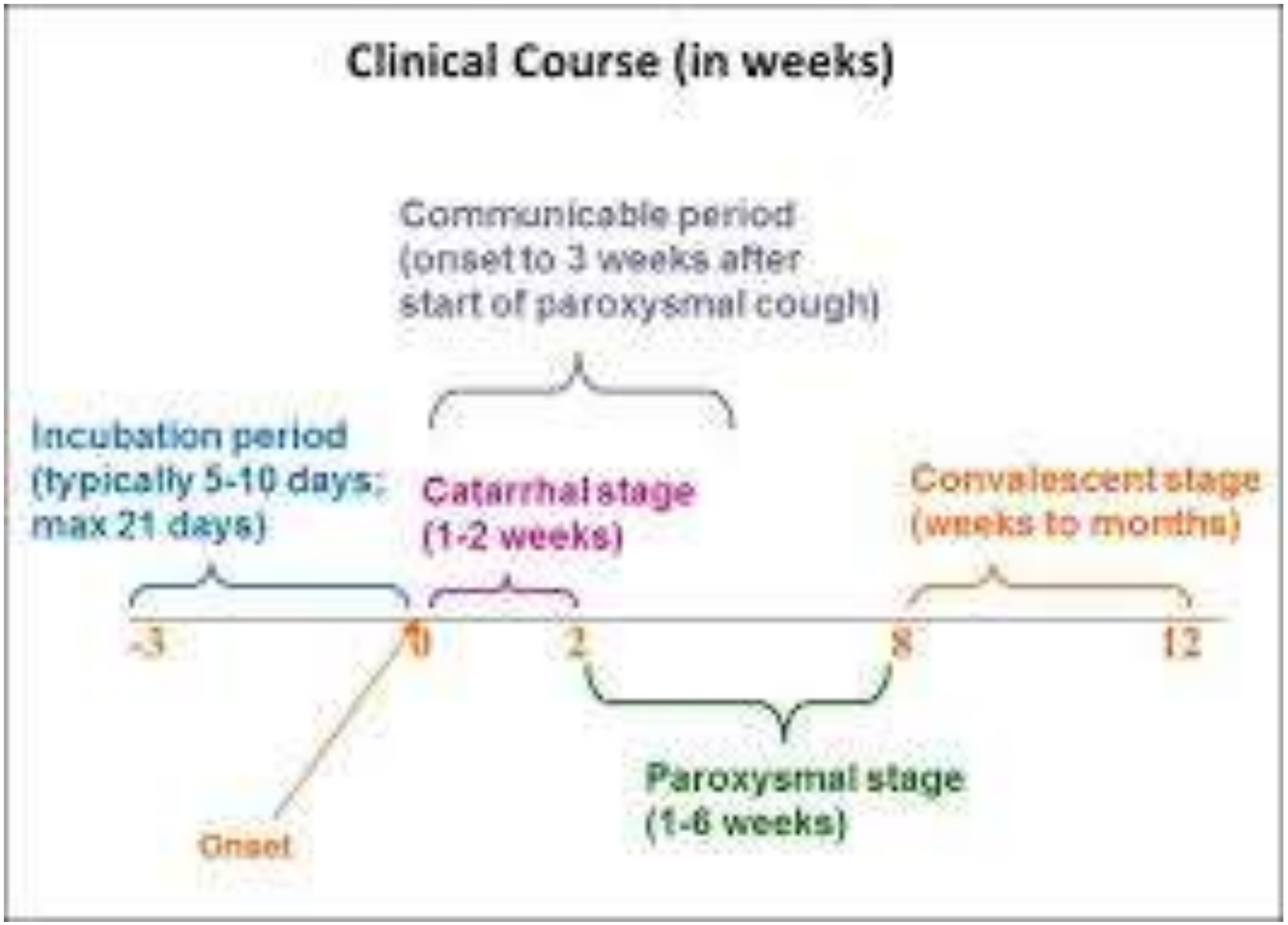
- Vomiting
- Retching
- Nosebleeds
- Diarrhea
- Fever

2--The paroxysmal stage

- Patients can become cyanotic and even exhausted or vomit after coughing fits.
- Patients typically suffer from about 15 coughing attacks a day.
- The first few days the coughing - increase. It can remain at this high level for 2-3 weeks, and then slowly decreases.

3--The convalescent stage
2-4 weeks

- The gradual recovery of the patient .
- Coughing fits become less severe and can disappear in two to three weeks.
- Despite a decrease in the clinical symptoms, any respiratory infections months following the disease can trigger the recurrence of the paroxysm coughing fits.


Clinical Course (in weeks)
Communicable period
(onset to 3 weeks after
start of paroxysmal cough)
Incubation period
(typically 5-10 days;
max 21 days)
Catarrhal stage
(1-2 weeks)
Convalescent stage
(weeks to months)
-3
0
2
8
12
Onset
Paroxysmal stage
(1-6 weeks)

Complication

- Due to cough
- Systemic effect of toxin

Figure 2: Subconjunctival haemorrhage: a potential complication of the pertussis cough.

Complications
Due to coughing

- Subconjunctival hemorrhages
- Epistaxis secondary to the paroxysmal coughing.
- Suppurative otitis media is a frequent complication in infants

Complications

Systemic effect of toxin

More Case Fatality Rate

- Respiratory,
- CNS and Heamorrhage
- GIT
- Nutritional

Complications

Respiratory

- **Respiratory**-Most common.

  Asphyxia in infants.

  Secondary bacterial pneumonia -in elderly people,

  Atelectasis, bronchiectasis, interstitial and subcutaneous emphysema, and pneumothorax.

Complications

- **CNS** – 2%- 7%

  Acute encephalitis ,

  Stupor-Coma

  Spastic paralysis,

  Mental retardation, or

Pathologic findings reveal cerebral hemorrhage and edema.

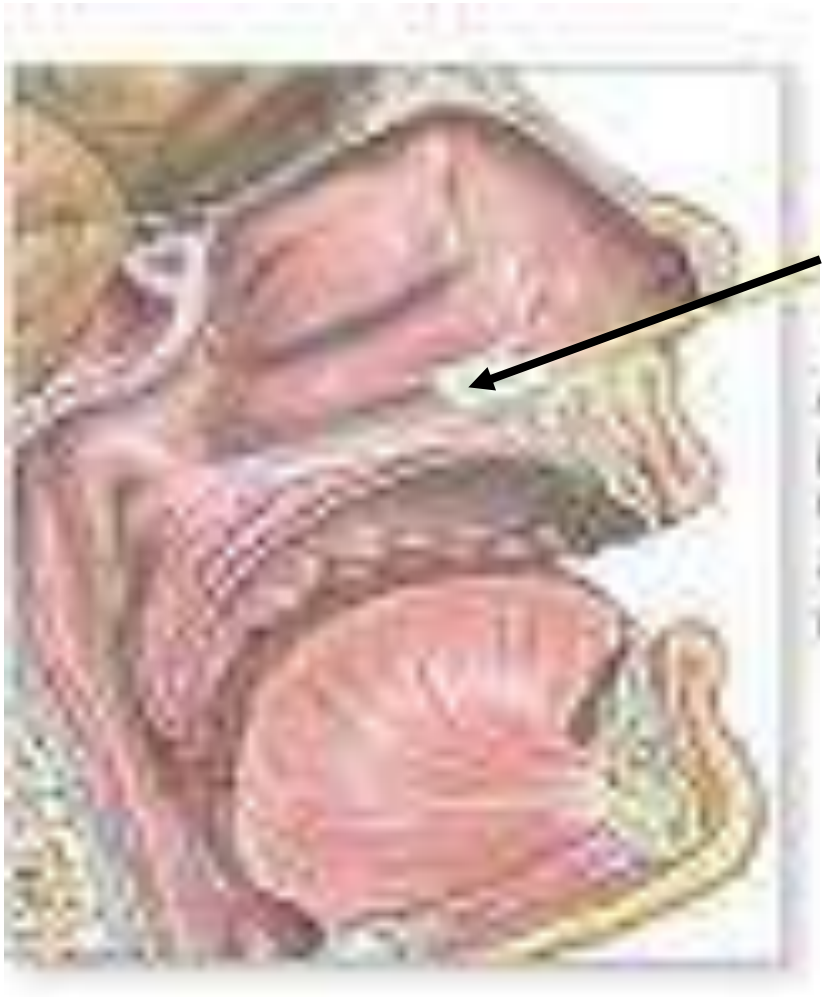
- GIT- Rectal prolapsed & hernias
- Severe malnutrition

Disease In Immunized

- As the effects of the vaccine wear off in adolescence and adulthood, those partially protected may become infected.
- Milder, - a persistent cough- may linger for more than seven days, is often indistinguishable from other respiratory infections.
- 7% of cough illnesses in older people are caused by B. pertussis.

Diagnosis

Diagnosis

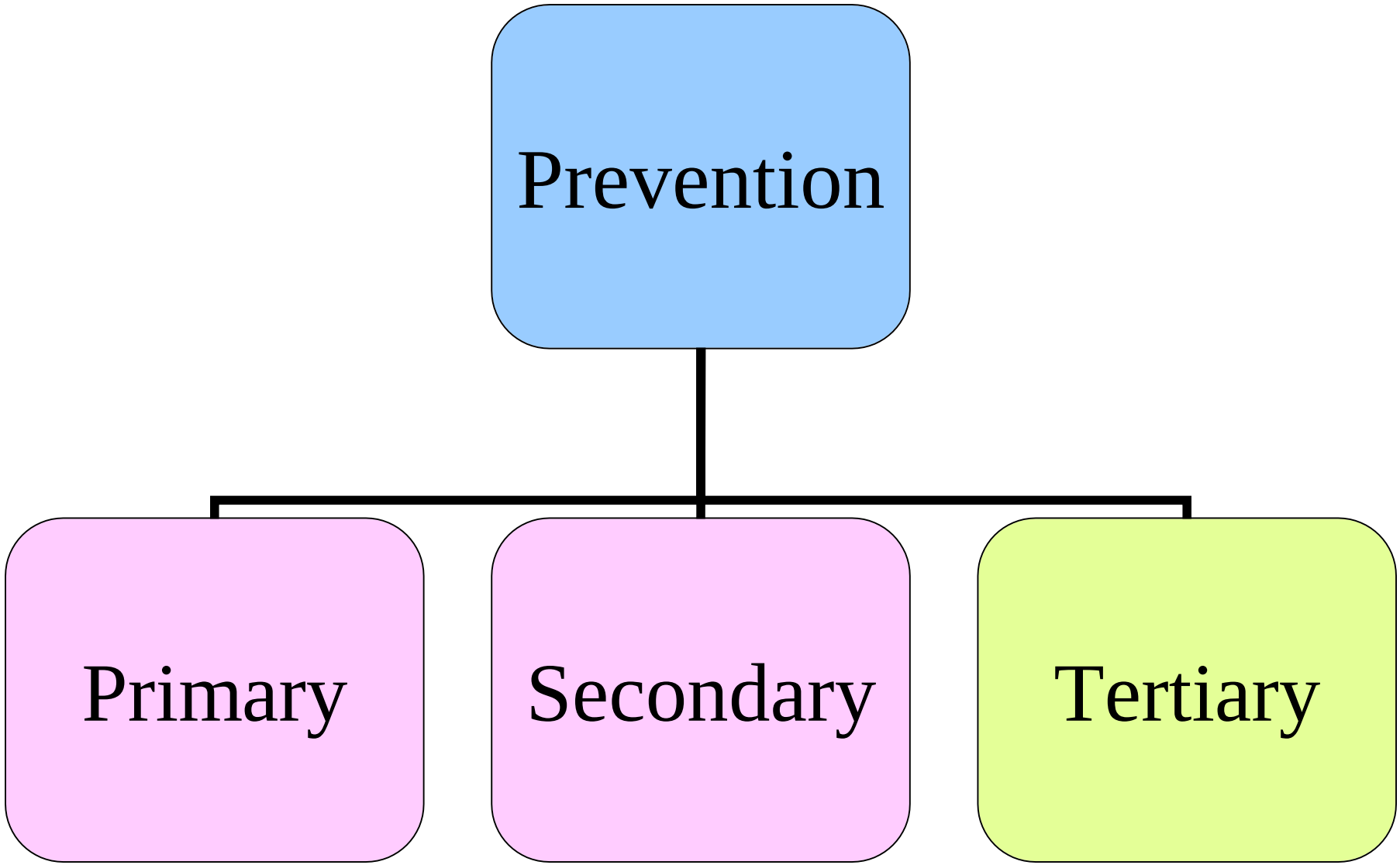


- *Culture ---Nasophsryngeal swab*
- A positive culture is diagnostic.
- **False-negative** cultures are common, particularly in persons receiving antibiotics .
- Most effective– catarrhal stage

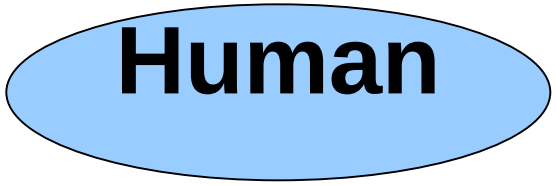
Diagnosis

- Immunofluorescence microscopy
- Serologic tests- ELISA, FHA
- PCR
- Lymphocytosis - lymphocyte count over 20,000 is associated with pertussis, but there may be no lymphocytosis in infants, children, or mild cases.

Laboratory Investigations


Prevention
Primary
Secondary
Tertiary

A- Reservoir/Source



- Isolation
- Vaccination
- Notification

Isolation

- 3 weeks in untreated
- 5 days after the initiation of antibiotic

Vaccination

- DPT– 0.5 ml deep IM,

  Efficacy 75%

3 dose at 4-6 wks interval, starting 2-3 months old

- Vaccine should contain both

Booster

- Pertussis vaccine– Antigens 1,2,3

0.5 ml IM

Schedule same as DPT

Preventive Measures

A- Reservoir/Source

B-**Increase Host resistance**

C- Interruption Of transmission

Chemoprophylaxix

- **Quarantine-** 2 weeks

- **Chemoprophylaxis**
  - Erythromysin or Co-trimoxazole for 2 weeks irrespective of immunization status

Preventive Measures

A- Reservoir/Source

B- Increase Host resistance

C- Interruption Of transmission

Secondary Prevention

A- Reservoir/Source

Early diagnosis & Rx

- Active case detection
- Passive surveillance
- Symptomatic
- Chemotherapy
- Immunoglobulin

Secondary prevention

- Early diagnosis

  -Positive culture is diagnostic

Epidemic– case definition-

cough more than 14 days

Secondary prevention

- Antibiotics
- Symptomatic
- Passive Immunization– Igs– poor efficacy

Treatment

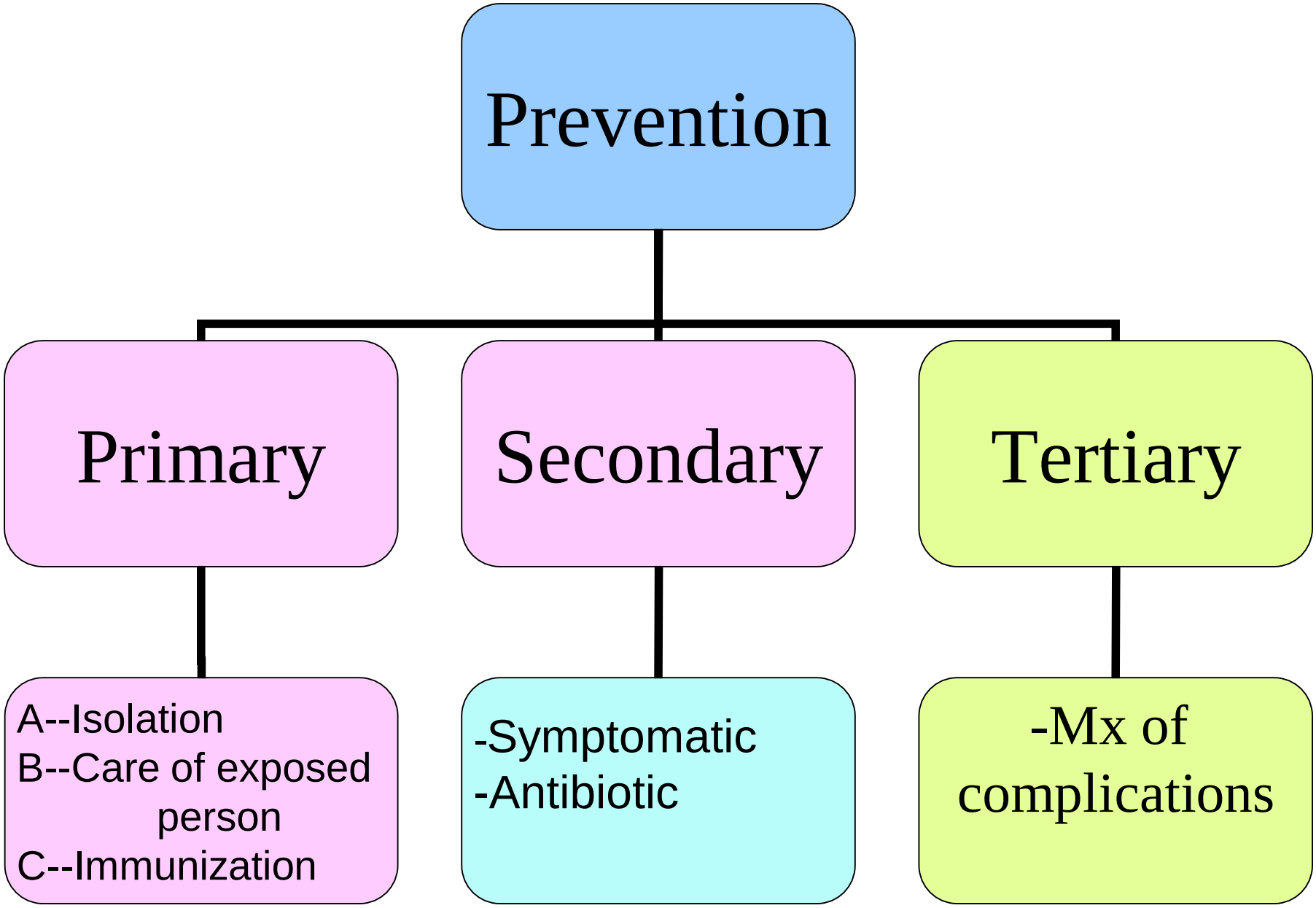
- Erythromycin - orally in doses of 40-50 mg/kg qds for 14 days
- **It kills the bacteria, but the toxins are still effective.**
- If the disease is diagnosed and treatment begins during the catarrhal stage, the symptoms can be lessened.
- Treatment after the cattarhal stage is ineffective in decreasing morbidity of the patient

- Antibiotics are used to decrease communicability- prevent or minimized transmission in households where there are unvaccinated children.

- In infants and potentially severe cases, the patient should be hospitalized for supportive care.

Symptomatic

- Bronchodilators- may relieve paroxysm
- Sedation to reduce anxiety


Prevention
Primary
Secondary
Tertiary
A--Isolation
B--Care of exposed person
C--Immunization
-Symptomatic
-Antibiotic
-Mx of complications

Thank You

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 diptheria	Vaccination
Pseudo positive	**Both arm-** Red flush less circumscribed, Fads by 4-7days-10-50 mm dia,appear within 1-2 days.	Immune but Allergic	
Combined	**Test arm**- true positive **Control arm**-Pseudo positive	Susceptible & allergic	Vccination-with caution