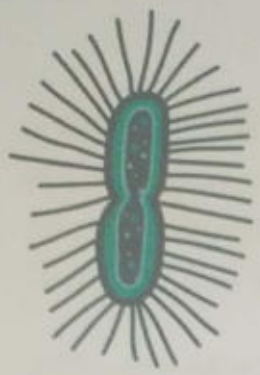

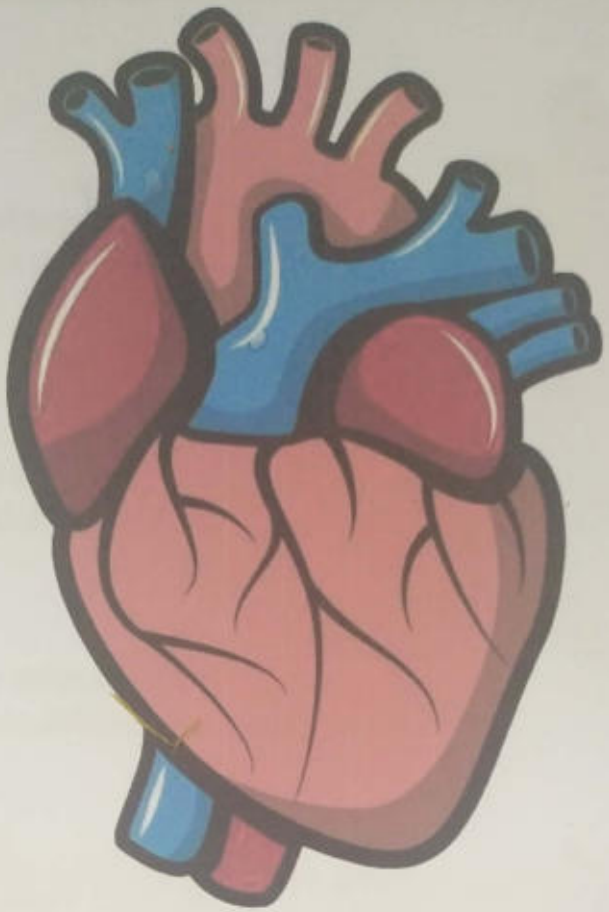

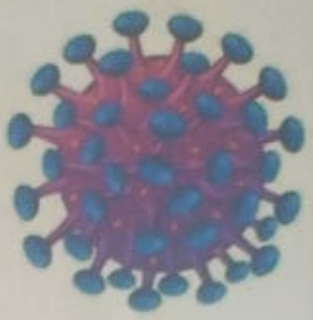

CVS

Micro Biology

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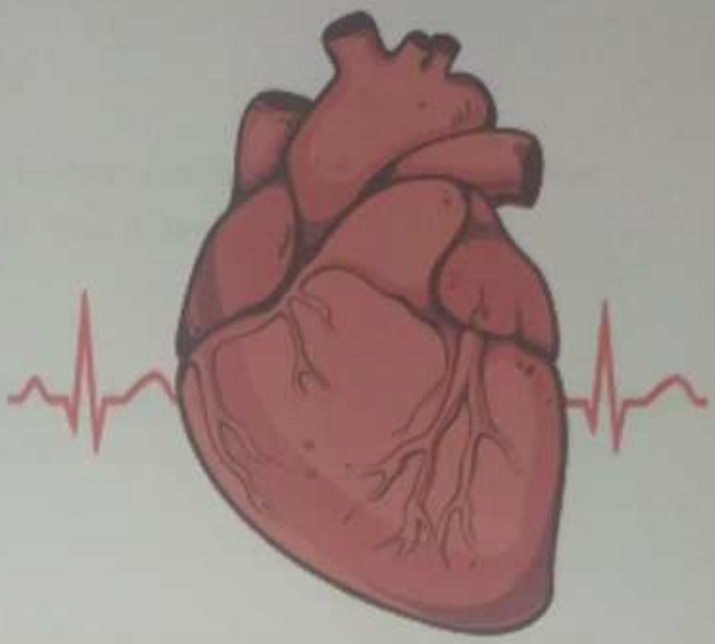
Endocarditis

Inflammation of the endocardium (the endothelial lining of the heart Chambers and valves).



Myocarditis

Inflammation of the myocardium (the muscular walls of the heart).

Pericarditis

Inflammation of the pericardium (the membranous sac around the heart).

Infective Endocarditis

Pathology

- **Endocarditis** is the inflammation of the endocardium (the endothelial lining of the heart chambers and valves.
- **Infective endocarditis occurs when** microbes attack healthy or diseased valve or the lining of the heart, leading to endothelial damage that allows circulating microorganisms to colonize on heart valves or other cardiac surfaces.
- **Colonization leads to** development of a **vegetation** and subsequent inflammatory and embolic complications.
- **Clinically manifested by** :
  1) constitutional symptoms (fever).
  2) new murmur .
  3) embolic Phenomena.

Result

Clinically

Threads

Classification of Endocarditis

Acute, or **subacute** according to the virulence of the causative organism and the progression of the disease.

Acute bacterial endocarditis (ABE): (High virulence organisms)

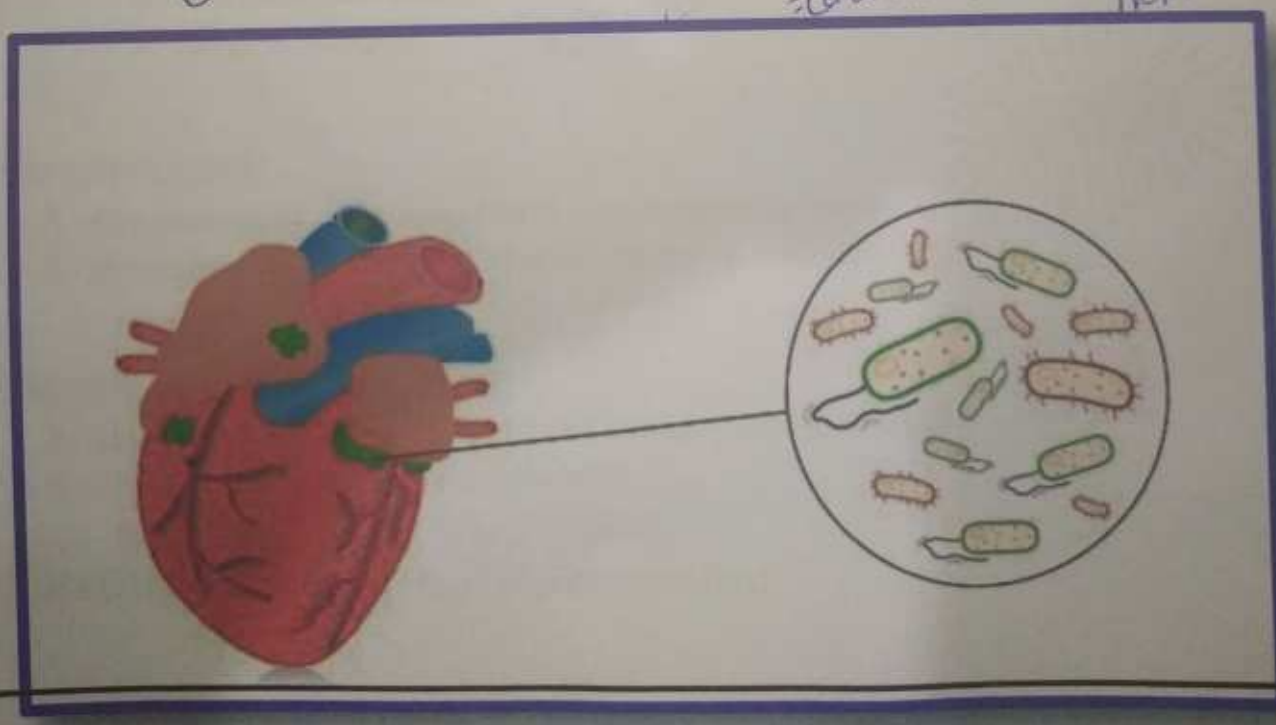
- *Staphylococcus aureus.*
- *Streptococcus pyogenes.*
- *Pneumococci.*
- *Gram -ve bacilli.*

(rapid onset, large vegetations on previously normal valves)

Subacute bacterial endocarditis (SBE): (Low virulence organisms)

- *Streptococcus viridans.*
- *Enterococcus.*
- *Haemophilus influenza*

(gradual onset, smaller vegetations on congenitally abnormal or rheumatically affected or prosthetic heart valves, mainly sequela of dental or pharyngeal procedures)

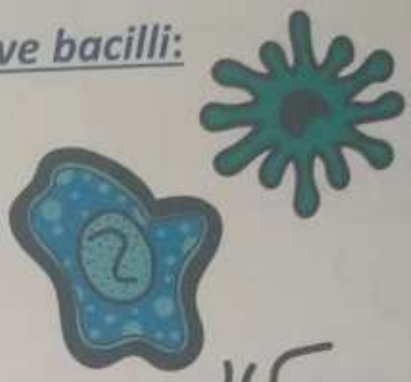


Microbial causes of endocarditis

Common causes:

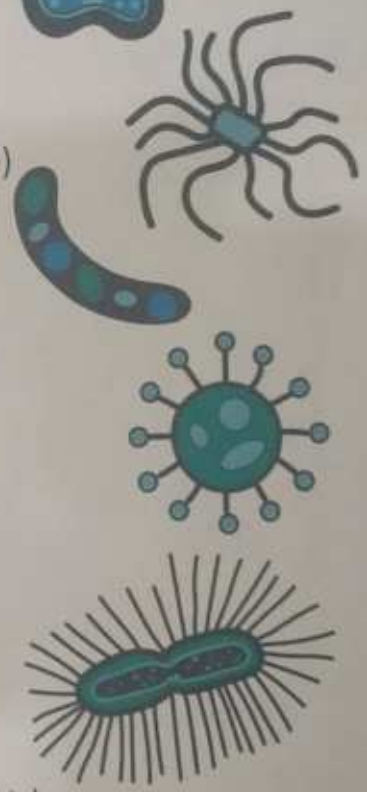
1. ***Staph aureus*, and *enterococci*:**
   in **IV drug users** and in **Prosthetic-valve** endocarditis.

2. ***Coagulase negative staph* and *gram negative bacilli*:**
   in **IV drug users**



Less common causes (HACEK organisms):

- Group of small gram-negative bacilli.
- Part of the normal oropharyngeal flora.
- **HACEK** (These organisms typically are culture negative)
  - ***Haemophilus aphrophilus.***
  - ***H parainfluenzae.***
  - ***H paraphrophilus.***
  - ***Aggregatibacter*** (formerly ***Actinobacillus***).
  - ***Actinomycetemcomitans.***
  - ***Cardiobacterium hominis.***
  - ***Eikenella corrodens.***
  - ***Kingella kingae.***



Streptococci:

- ***Streptococcus pyogenes*** (ABE) and rheumatic fever.
- ***Streptococcal viridans*** (Subacute bacterial endocarditis)

Staphylococci:

- ***Staphylococcus aureus*** (acute bacterial endocarditis)
- ***Coagulase-negative Staphylococci***

Enterococci (subacute bacterial endocarditis)

Myocarditis

Definition: Inflammation of the myocardium (the muscular walls of the heart).

Pathophysiology:

infection of the myocardium most frequently occurs following hematogenous spread of virus or other pathogen to the heart muscle.

Clinical manifestations:

patients with myocarditis present with sign and symptoms of heart failure.
Also, they have signs and symptoms of systemic infection (fever).

Causes:

Viral

- *Adenovirus*
- *coxsackie B*
- *parvovirus B19*
- *HIV*
- *HHV-6.*

Bacterial

- *Borrelia burgdorferi*
- *Mycoplasma pneumoniae*
- *Corynebacterium diphtheria.*

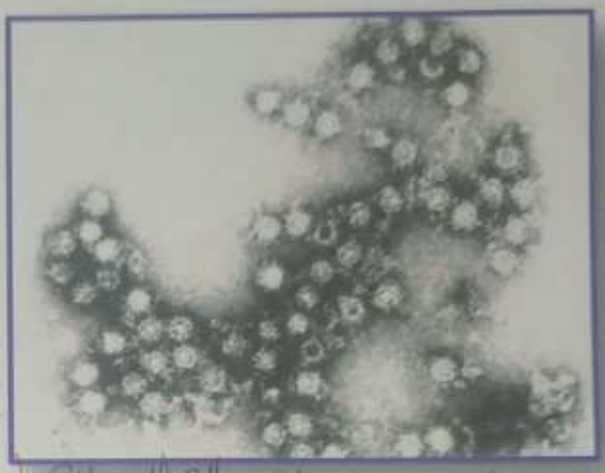
Coxsackie virus

Properties

- Positive, single-stranded RNA virus has an icosahedral capsid.
- It belongs to picornavirus family.

Transmitted by :

fecal-oral route and also through droplets.



Diseases

Group A:

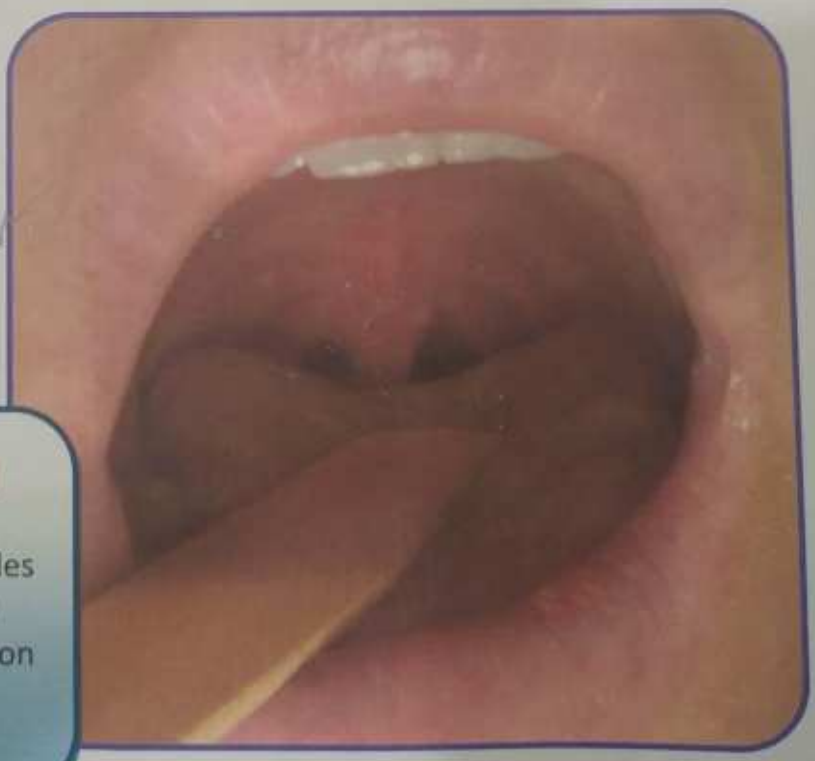
- **herpangina**
- hand-foot and- mouth disease.

Group B:

- cardiomyopathy (acute myocarditis and pericarditis),
- aseptic meningitis
- pleurodynia

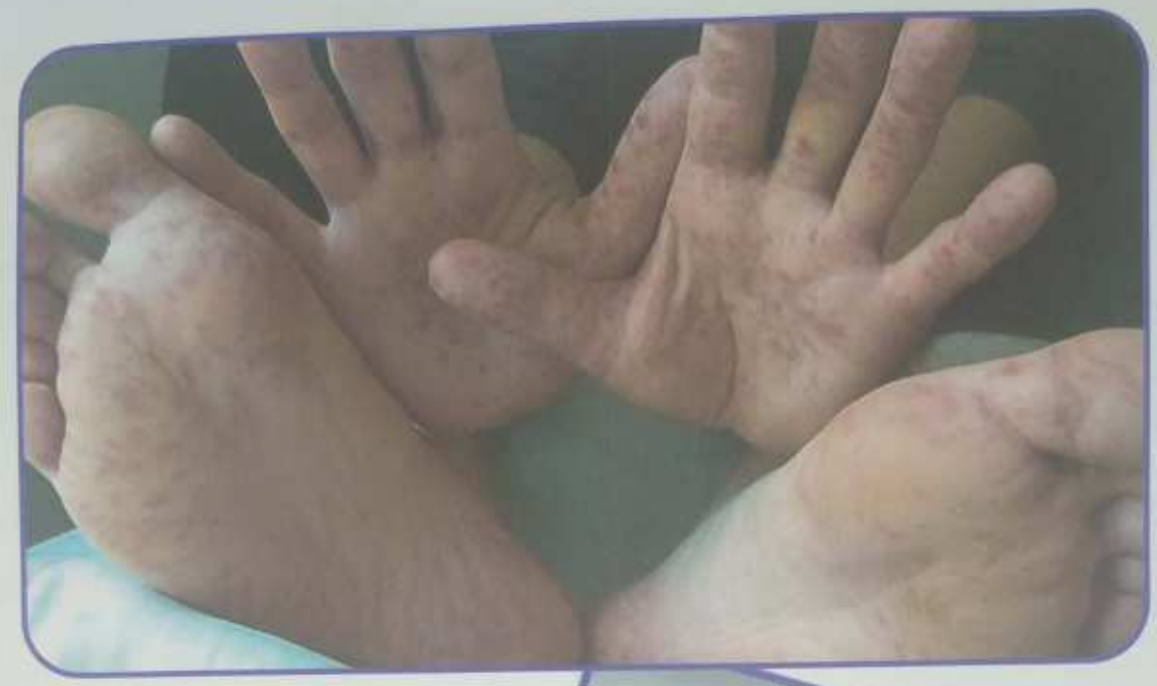
Diagnosis:

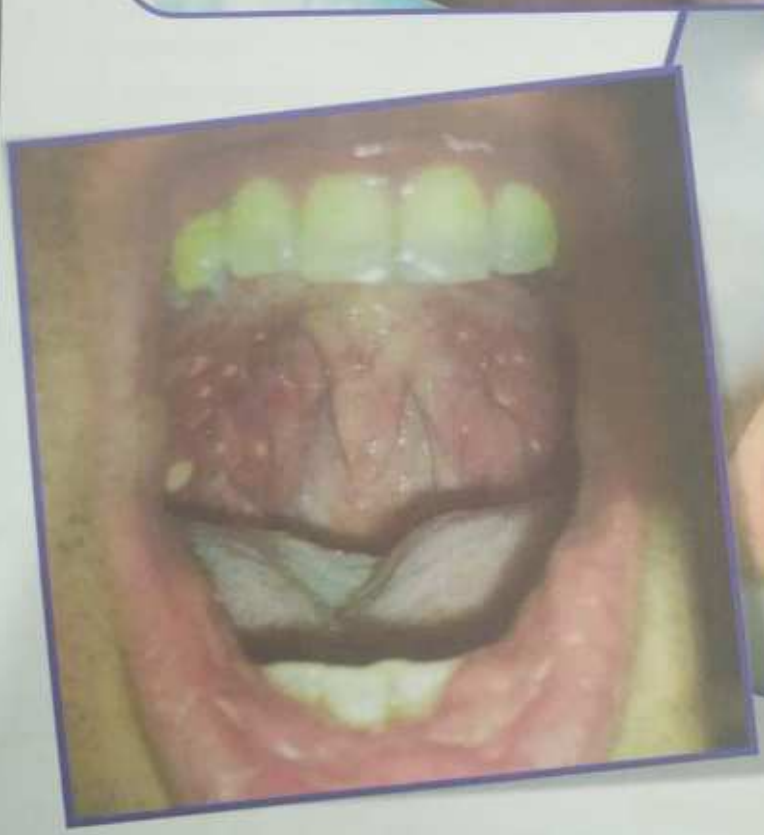
serological tests such as ELISA.

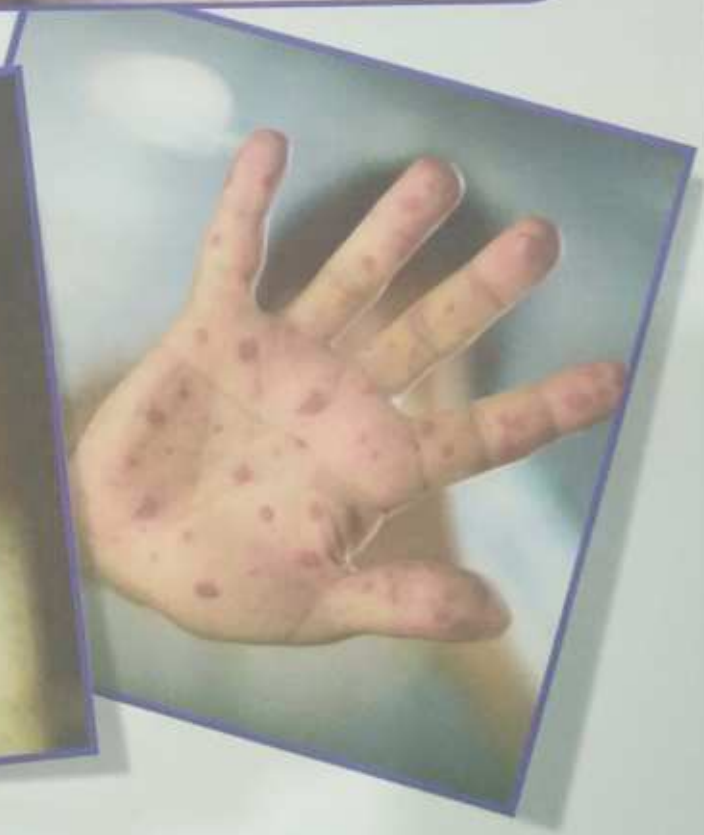


Herpangina

Multiple, small vesicles and erosions with erythematous halos on the soft palate.





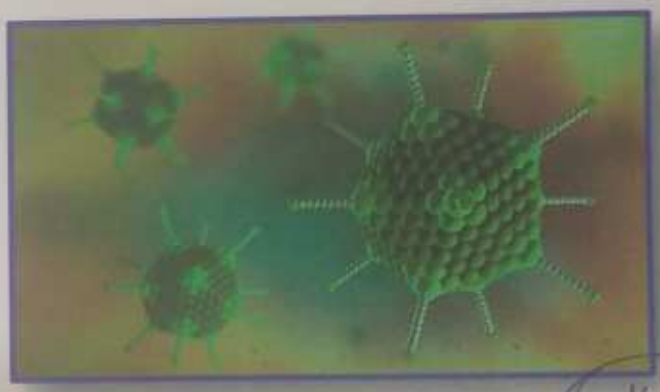


Hand, Foot and mouth disease

Adenoviruses

Properties

- dsDNA, naked, with icosahedral capsid.
- Has a unique fiber protruding from each of 12 vertices of its capsid, this fiber helps in the attachment of the virus to the host cell.
- Adenoviruses can infect several organs in the human body and causes latent infection in the adenoids, tonsils and lymphoid tissues.

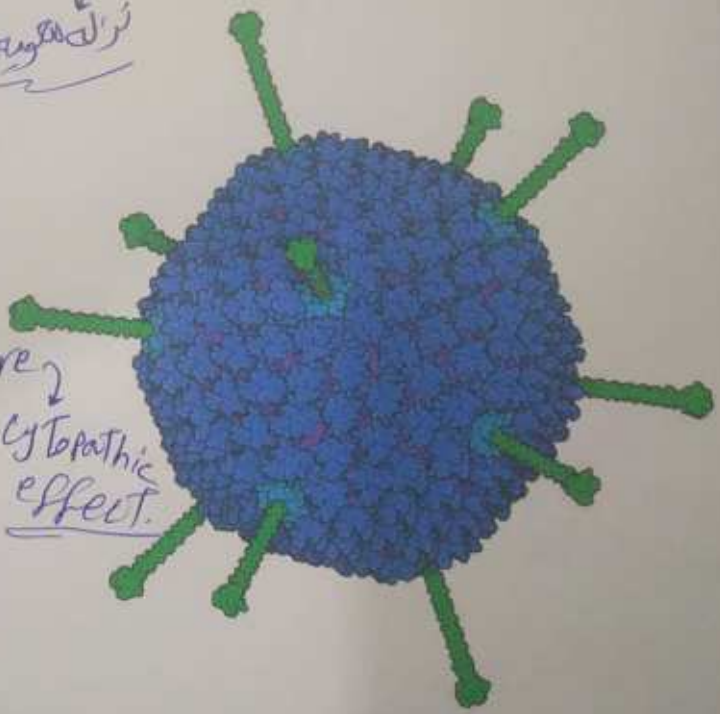


Transmission :

1. aerosolized droplets
2. contact
3. fecal-oral route.
4. Swimming Pool

Diseases: There are over 52 serotypes.

1. **Respiratory tract diseases:** acute febrile pharyngitis
2. **Eye diseases:** swimming-pool conjunctivitis
3. **Gastrointestinal diseases:** Gastroenteritis in infants
4. **Others:** *myocarditis*



Diagnosis:

1. Serology
2. virus isolation → Tissue Culture → Cytopathic effect.
3. PCR.

Top 5 Pediatrics

Parvoviruses B19

Properties:

- ssDNA, naked, linear virus with icosahedral capsid.
- it is also one of the **five** most common pediatric viral exanthems (diseases that cause a **rash**).

Transmitted by

1. respiratory route
2. transplacental
3. blood transfusion.

Diseases

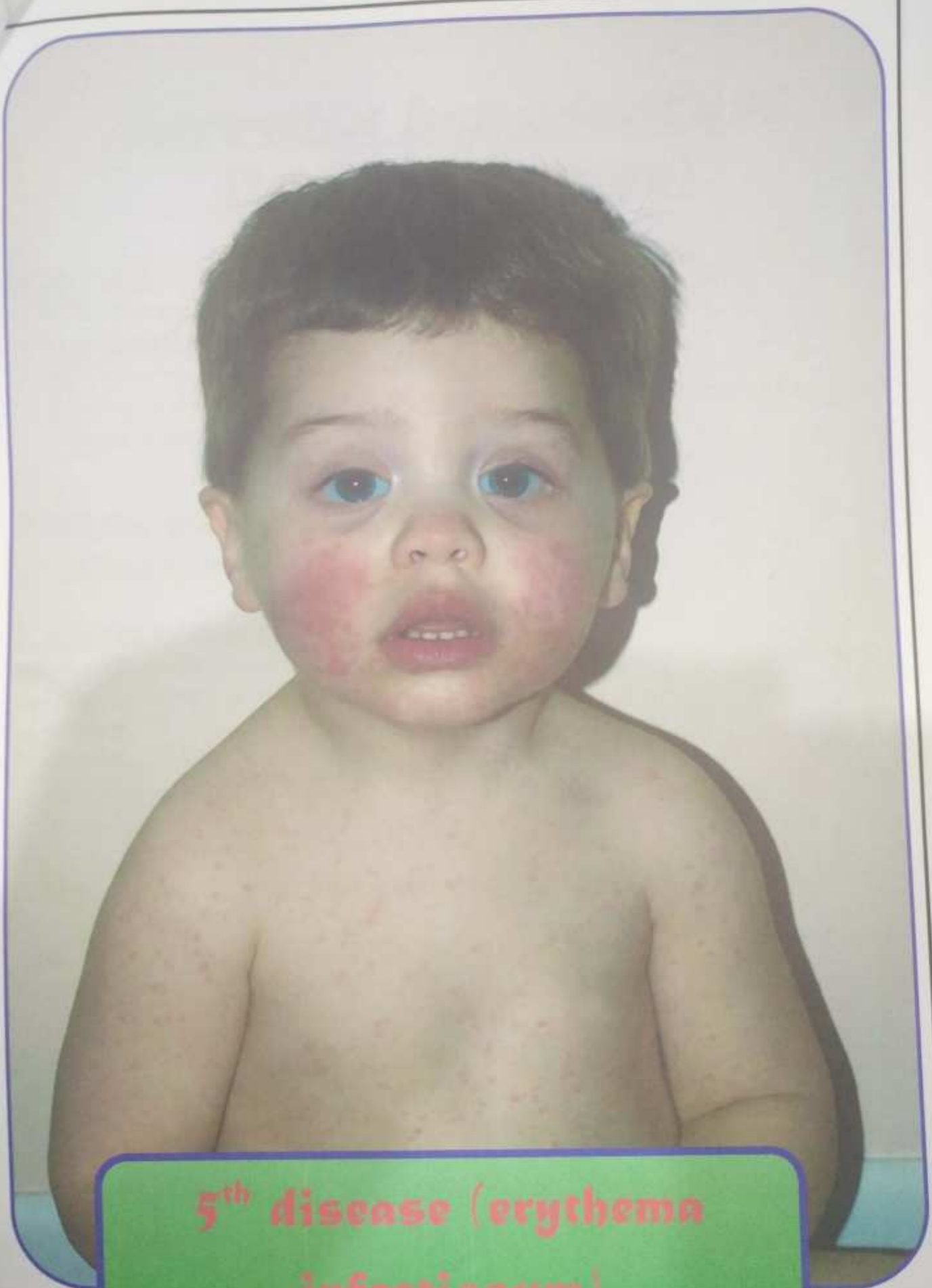
1. **Fifth disease of children** (**erythema infectiosum, slapped cheek syndrome**):
   bright red rash mainly in cheeks and flu-like symptoms.
2. **Immune complex deposition** results in a lacy red rash and arthralgias.
3. **Aplastic anemia** (especially in patients with sickle cell anemia).
4. **immunocompromised individuals** may develop a **severe chronic anemia.**
5. **Fetal infections**, including hydrops fetalis.

Diagnosis:

1. serology
2. detection of viral DNA by PCR.

Treatment:

1. Supportive care with blood transfusions as needed
2. immunocompromised patients may require IV immunoglobulins.



5th disease (erythema infectiosum)

Borrelia burgdorferi
(Lyme Disease)

Properties

- *Borrelia burgdorferi* is a tick-borne agent .
- **transmitted to man by** : tick bite.
- Reservoirs include rodents (mice) and deer.
- *B. burgdorferi* invades skin and spreads via blood to involve primarily the heart, joints, and CNS.

Disease: Lyme disease

there are **three** clinical stages of Lyme disease:

1. Primary (early): Erythema chronicum migrans (ECM)

annular skin lesion at site of bite with an erythematous leading edge and central clearing "bull's eye" associated with :

- fever
- chills
- muscle pain
- headache.

2. Secondary, disseminated phase (days to weeks after infection):

- Myocarditis
- atrioventricular (AV) block
- neurologic manifestations

3. Tertiary, late (months to years after infection):

Artheralgias and migrating arthritis due to immune complex deposition

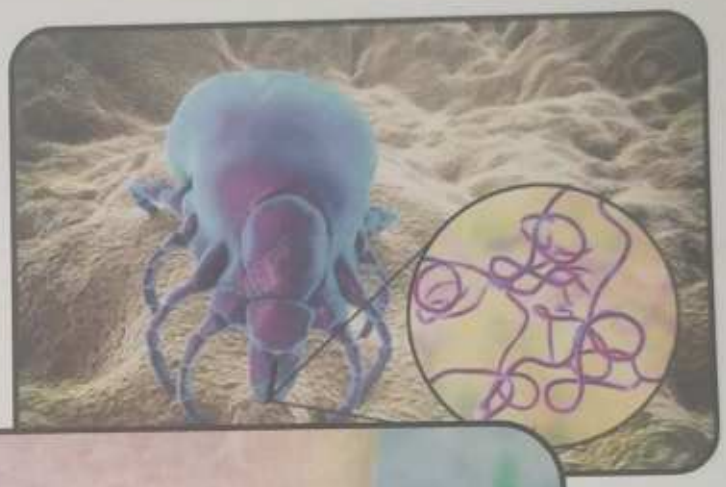
(erythema chronicum migrans) Rash in the pattern of a bull's-eye of the first stage of Lyme disease.

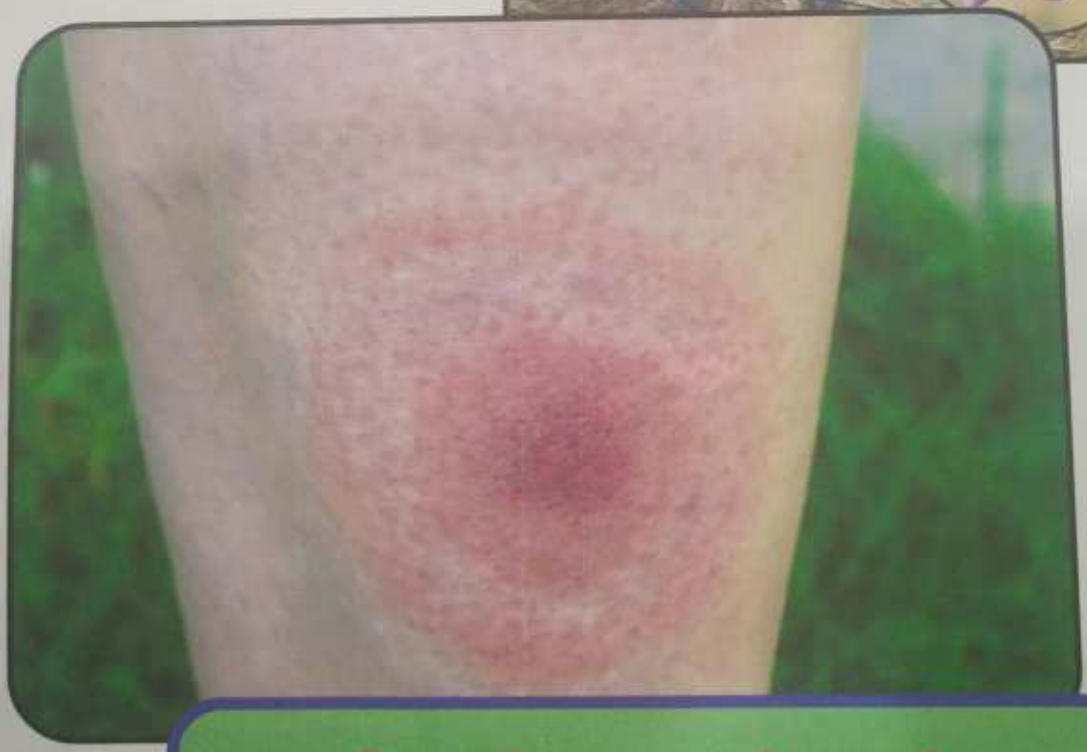
Diagnosis: based on clinical finding and history of tick bite.

1. ***Skin biopsy*** from skin lesion ECM, is cultured for *B. burgdorferi*
2. ***Skin biopsy***, motile spirochetes are visible under darkfield microscopy.
3. ***serology***: detection of anti *B. burgdorferi* antibodies in serum by ELISA
4. ***Other diagnostic tests*** include **PCR**.

Treatment

1. **Doxycycline (oral)** for primary-stage Lyme disease
2. **Ceftriaxone (IV)** for later-stage disease.





Erythema chronicum migrans (ECM)

Mycoplasma

General characteristics

- Mycoplasma are the smallest free-living bacteria in nature.
- **They do not possess cell walls** → therefore drugs that inhibit cell wall synthesis (penicillin, cephalosporins and vancomycin) are ineffective against mycoplasma.
- **Mycoplasma also have a plasma membrane reinforced with cholesterol** → a sterol usually found in eukaryotic cells.
- Mycoplasma can be grown (very slowly) on artificial media in the lab but have complex nutritional requirements.
- **They assume a fried-egg appearance** after a few weeks of culture.
- ***They spread by :***
  1. direct contact
  2. respiratory droplets.

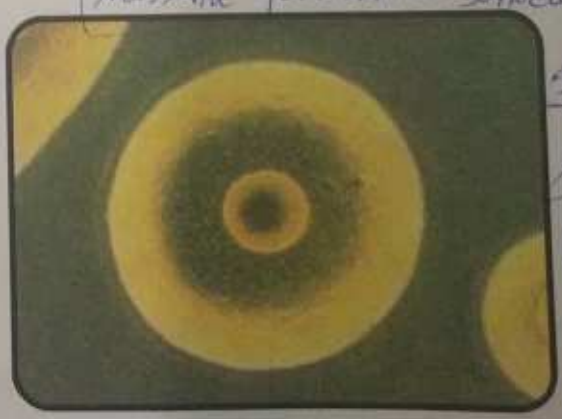
Important pathogens and Diseases

1. ***M. pneumoniae***: causes atypical pneumonia and also can cause myocarditis.
2. ***M. hominis***: causes postpartum fever.
3. ***U. uredlyticum and M. genitalium***: cause non-gonococcal urethritis.

Diagnosis

1. Direct detection of:

- Antigens by immunofluorescence.
- Viral nucleic acid using PCR or DNA probes.



2. Serology:

- **Detection of IgM or a rising titer of IgG by ELISA.**
- **Detection of cold agglutinin**: anti-*mycoplasma* antibodies **cross-react** with type O RBCs and agglutinate them but **only at low temperatures (4ºC).** Thus, the **cold agglutinin test** is a simple (but nonspecific) test that can be performed bedside.

Treatment

1. Tetracyclines.
2. Macrolides (erythromycin or azithromycin).

Corynebacterium diphtheria

- Diphtheria is a serious infection caused by Corynebacterium diphtheria, which produce a powerful exotoxin. Nowadays diphtheria is extremely rare after mass immunization.

- **It is transmitted by** : droplet infection, the organism multiplies locally releasing the exotoxin causing inflammation of the throat, local necrosis and formation of pseudo-membrane.

- The exotoxin diffuses to blood stream and can affect heart leading to myocarditis accompanied by arrythmias and circulatory failure and death may occur.

Acute pericarditis

Definition: Inflammation of the pericardium (the membranous sac around the heart).

Pathophysiology:

- Pathogen reach the pericardium by either hematogenous spread through the blood or direct spread from adjacent intrathoracic structures.
- Inflammation of the pericardium can result in the formation of pericardial effusion and cardiac tamponade.

Clinical manifestation:

- Chest pain is the most common manifestation of pericarditis.
- Pain often worsen with inspiration or coughing.
- Sitting up and leaning forward often improve the pain.

Causes:

1. **Idiopathic** (most common; presumed viral).
2. **Confirmed infection** (Coxsackievirus B).

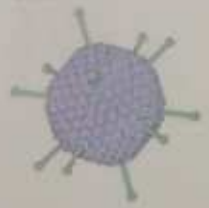
Tuberculosis pericarditis

It is an important complication of tuberculosis (TB) caused by *Mycobacterial tuberculosis* bacilli.

It arises most frequently by:

- Direct spread from involved mediastinal lymph nodes or adjacent pulmonary lesions Or from hematogenous spread.

Pericardial effusion is the most common complication.

	Coxsakie V	Adenoviruses	Parvovirus	Mycoplasma	Borrelia burgdorferi
Transmission	1. Feco oral 2. droplets	1. aerosolized droplets 2. contact 3. fecal-oral route.	1. respiratory route 2. transplacental 3. blood transfusion.	1. direct contact 2. respiratory droplets.	Tick bite. 
Diseases	**Group A:** • **herpangina** • hand-foot and- mouth disease. **Group B:** • cardiomyopathy (acute myocarditis and pericarditis), • aseptic meningitis • pleurodynia.	1. **Respiratory tract diseases:** *acute* febrile pharyngitis 2. **Eye diseases:** swimming-pool conjunctivitis 3. **Gastrointestinal diseases:** Gastroenteritis in infants 4. **Others:** *myocarditis*	1. **Fifth disease of children Immune complex :** bright red rash mainly in cheeks and flu-like symptoms. 2. **deposition** results in a lacy red rash and arthralgias. 3. **Aplastic anemia** (especially in patients with sickle cell anemia). 4. **immunocompromised individuals** may develop a **severe chronic anemia.** 5. **Fetal infections**, including hydrops fetalis.	1. ***M. pneumoniae***: causes atypical pneumonia and also can cause myocarditis. 2. ***M. hominis***: causes postpartum fever. 3. ***U. urealyticum and M. genitalium***: cause non-gonococcal urethritis. 	**Lyme disease** **1. Primary (early):** Erythema chronicum migrans (ECM) annular skin lesion at site of bite with an erythematous leading edge and central clearing "bull's eye" associated with fever, chills, muscle pain, headache. **2. Secondary,** disseminated phase (days to weeks after infection): Myocarditis, atrioventricular (AV) block, neurologic manifestations **3. Tertiary,** late (months to years after infection): Artheralgias and migrating arthritis due to immune complex deposition
Diagnosis	ELISA 	1. Serology 2. virus isolation 3. PCR. 	1. serology 2. detection of viral DNA by PCR. 	**1. Direct detection of:** ❖ Antigens ❖ Viral nucleic acid **2. Serology:** ❖ **Detection of antibodies by ELISA.** ❖ **Detection of cold agglutinin.**	1. ***Skin biopsy*** from skin lesion ECM, is cultured for *B. burgdorferi* 2. ***Skin biopsy,*** motile spirochetes are visible under darkfield microscopy. 3. ***serology***: detection of anti *B. burgdorferi* antibodies in serum by ELISA 4. ***Other diagnostic tests*** include **PCR.**
Treatment	Symptomatic	Symptomatic	1. Supportive care with blood transfusions as needed 2. immunocompromised patients may require IV immunoglobulins.	1. Tetracyclines. 2. Macrolides (erythromycin or azithromycin).	1. **Doxycycline (oral)** for primary-stage Lyme disease 2. **Ceftriaxone (IV)** for later-stage disease.

CVS Micro Biology

Part II

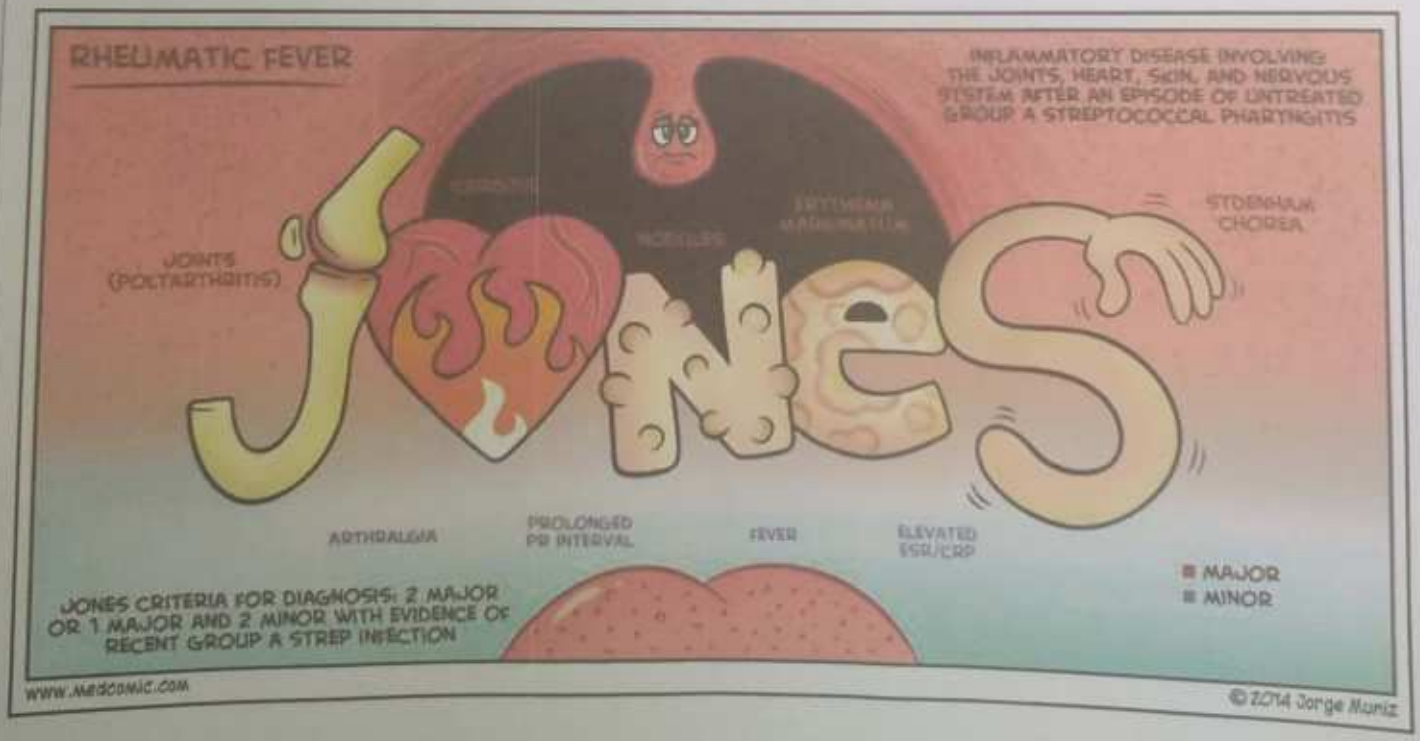
Rheumatic fever

Occurs as :

Complication of pharyngeal infection with ***group A β hemolytic streptococci,*** which affects heart and heart valves.

J ♥ NES (major criteria) :

1. Joint → migratory polyarthritis.
2. ♥ → carditis. PanCarditis
3. Nodules in skin → subcutaneous.
4. Erythema marginatum → rash with ring margin.
5. Sydenham chorea.



Pathogenesis:

Immune mediated (type II hypersensitivity) → antibodies to M protein cross-react with self-antigens (Molecular Mimicry).

Clinical Symptoms:

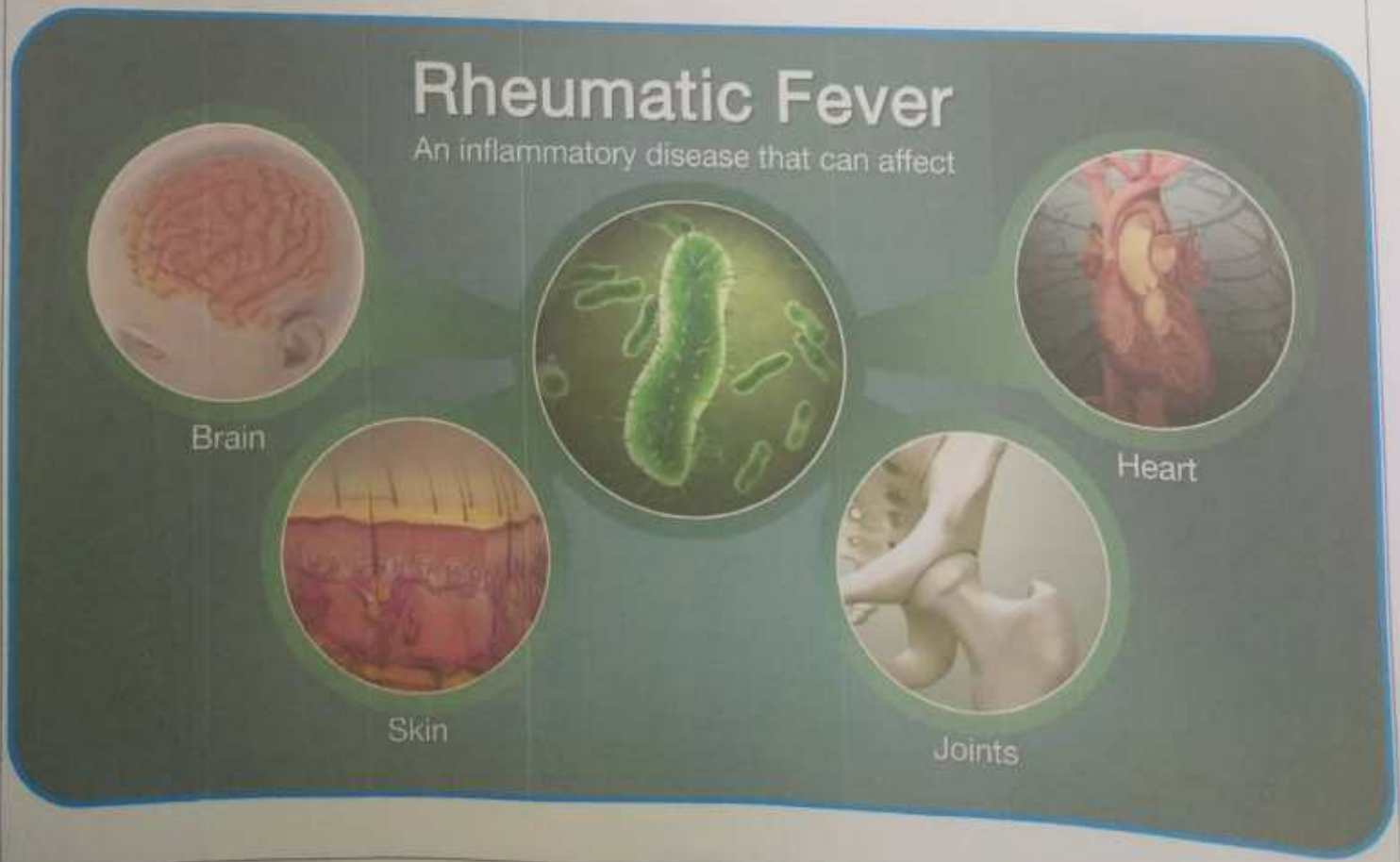
1. symptoms of valvular cardiac disease.
2. joint, cutaneous, and neurologic involvement is common.
3. J ♥ NES (major criteria).

Laboratory test to confirm diagnosis :

1. Elevated **Anti-streptolysin O titer** (**ASO**)
2. **C-reactive protein** (**CRP**) .
3. **Erythrocytes Sedimentation Rate** (**ESR**).

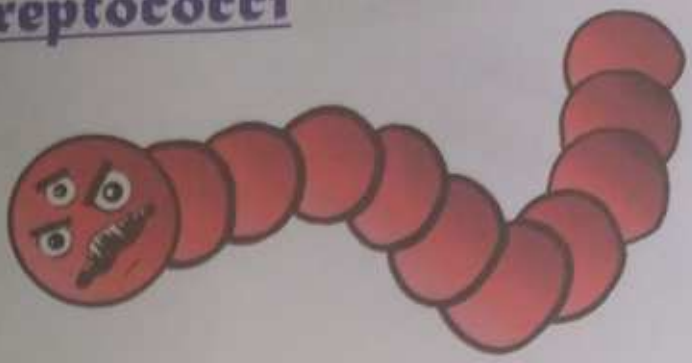
Prevention and treatment:

1. **early diagnosis and treatment** of streptococcal pharyngitis with antibiotics.
2. **Those affected by rheumatic fever** can have recurrences with subsequent streptococcal infections → prevented by prophylactic long acting penicillin administration.



Streptococci

- Gram +ve cocci .
- arranged in chains.
- Catalase negative.
- Grow best in blood agar.



Classification

According to Oxygen requirements

1-Aerobic streptococci :

According to growth on blood agar :

A-α haemolytic. [Partial] → Strept Viridans

B-β haemolytic. [Complete]

GAS ← 1- Group A → *strept. Pyogenes.*

2- Other groups.

C-λ haemolytic. [gamma]

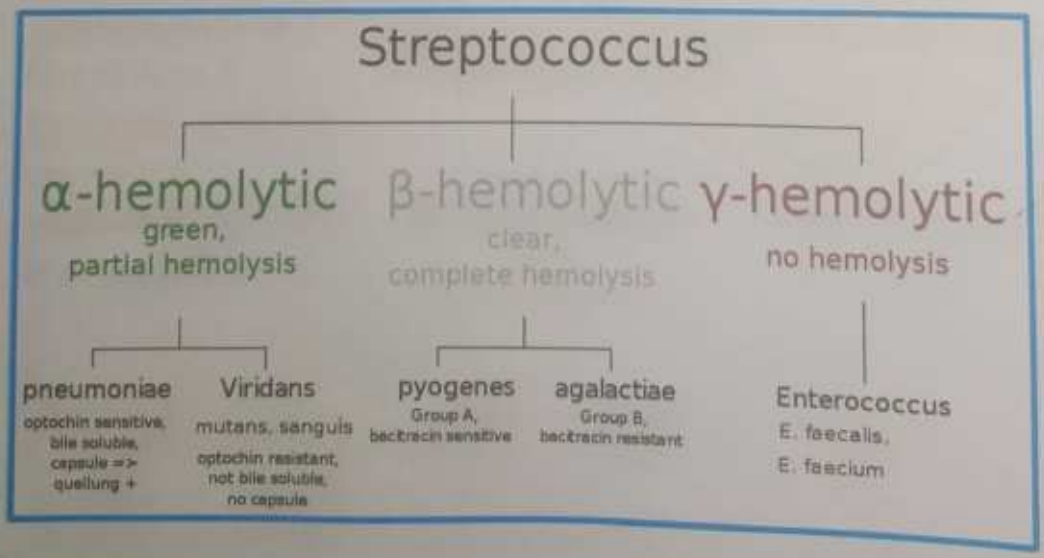
G-+ve

chain

XX Catalase

Blood agar

MCQ **2-Anaerobic streptococci :** *peptostreptococci*



Streptococcus pyogenes

Streptococcus Pyogenes

- **Pyogenic means** : a pus-producing organism.
- Gram-positive cocci .
- arranged in chains.
- β-hemolytic.
- Catalase-negative.
- Bacitracin-susceptible.
- Colonizes the upper respiratory mucosa (especially the oropharynx)

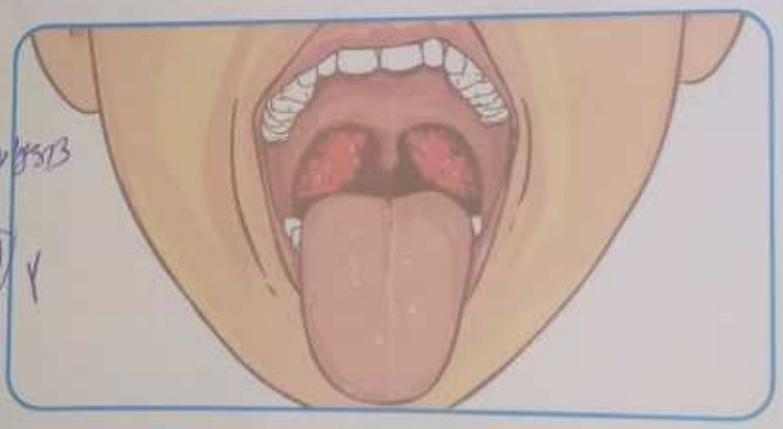
Pathogenesis of S. pyogenes (virulence factors)

1- M Protein

It is the most important virulence factor as it is antiphagocytic

2- Enzymes

1. **Streptokinase** (fibrinolysin)
2. **Streptodornase** (DNase)
3. **Hyaluronidase**



3- Toxins

1. **Streptolysin** (Hemolysin):
   Streptolysin O
   Streptolysin S
2. **Pyrogenic exotoxin**
   exotoxin A
   exotoxin B
   erythrogenic toxin.

Diseases caused by Streptococcus pyogenes

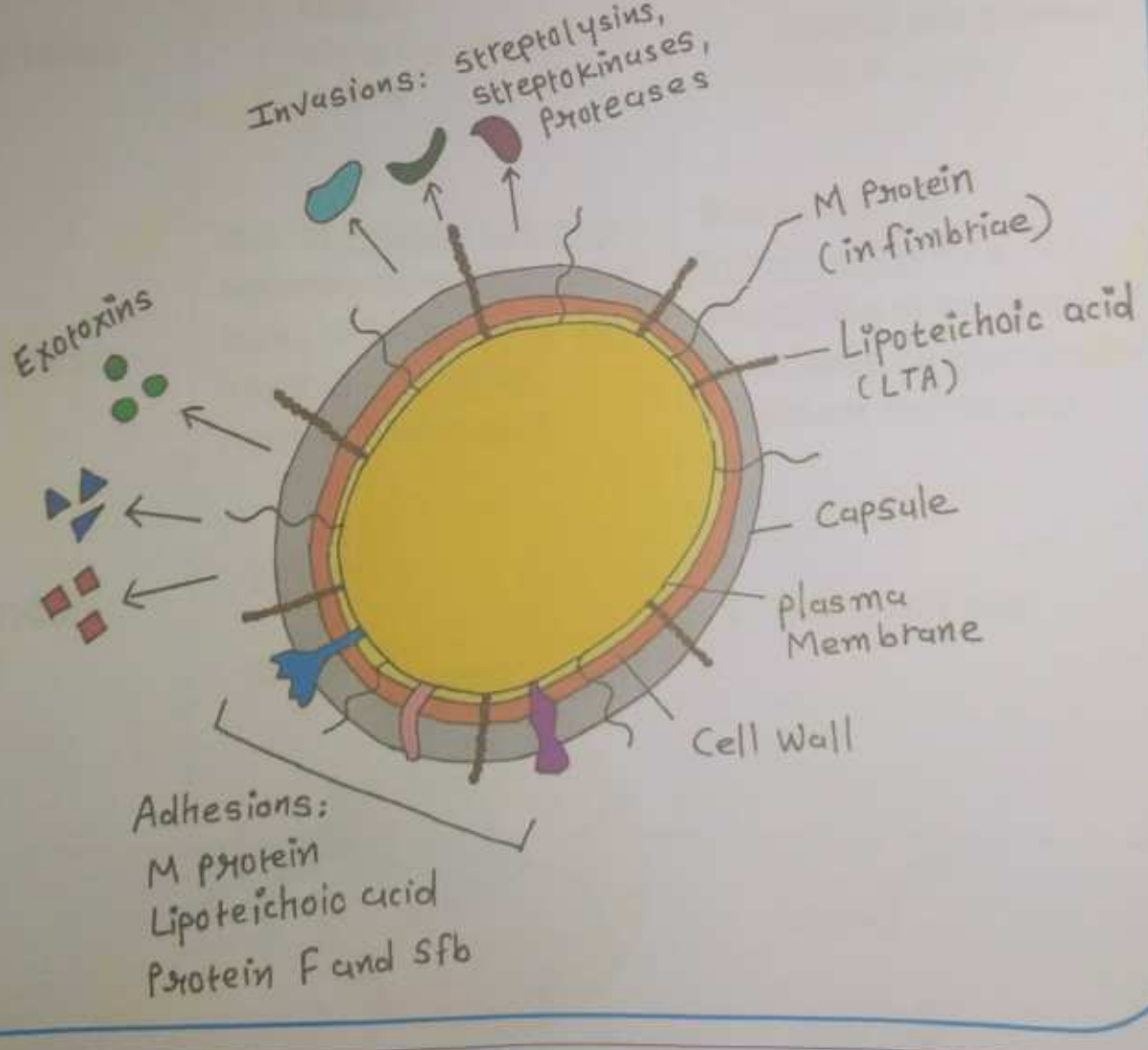
1. **Pyogenic local infections**
   1) Sore throat (follicular tonsillitis)
   2) Impetigo

2. **Invasive diseases**
   Acute bacterial endocarditis

3. **Toxigenic diseases**

4. **Post-streptococcal diseases**
   1- Rheumatic fever
   2- Acute glomerulonephritis

STREPTOCOCCUS ANTIGENIC STRUCTURE



Post-streptococcal diseases

- Occur weeks after acute infection with Strept. Pyogenes.
- **Rheumatic fever** usually occur after streptococcal infection of upper respiratory tract (tonsillitis).
- **Glomerulonephritis** usually occur after streptococcal infection of skin (impetigo)

	Acute Rheumatic fever	Acute glomerulonephritis
Occurrence	Following streptococcal **tonsillitis**	Following streptococcal **impetigo**
Symptoms	1- damage to heart muscles and valves. 2- Fever 3- Malaise 4- Migrating arthritis 5- carditis	1- Oedema 2- nitrogen retention 3- presence of blood, albumin and granular casts in urine
Mechanism	**Due to antigenic sharing between some M protein types of Streptococci and heart tissues (cross reacting antibodies)**	**Due to type III hypersensitivity = deposition of immune complexes on glomerular basement membrane**
Diagnosis	1- ASO 2- CRP 3- ESR	1- Anti DNASE test

Streptococcus viridans
(α-hemolytic streptococci)

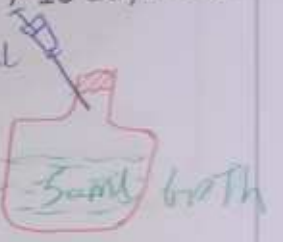
- Normal flora in oral cavity.
- a major cause of dental caries.

They may get accessibility to blood stream after tooth extraction or tonsillectomy → settle on abnormal heart valves → cause subacute bacterial endocarditis (SBE).

Diagnosis of SBE :

blood culture :

5-10 ml blood added to 50-100 ml broth–incubated at 37°C for 7-10 days with repeated subculture on blood agar.



Diagnosis of infections by Streptococci

2- **Specimen**.
3- **Direct smears** : stained by Gram.
4- **Antigen detection test**: by ELISA
5- **Culture** :
   on blood agar
   Blood culture in case of endocarditis
6- **Identification** of the colonies.

7- **For post-streptococcal diseases**:
   a) Anti-streptolysin O titer (ASO).
   b) C-reactive protein (CRP).
   c) Erythrocytes Sedimentation Rate (ESR).
   d) Anti-DNase antibodies.

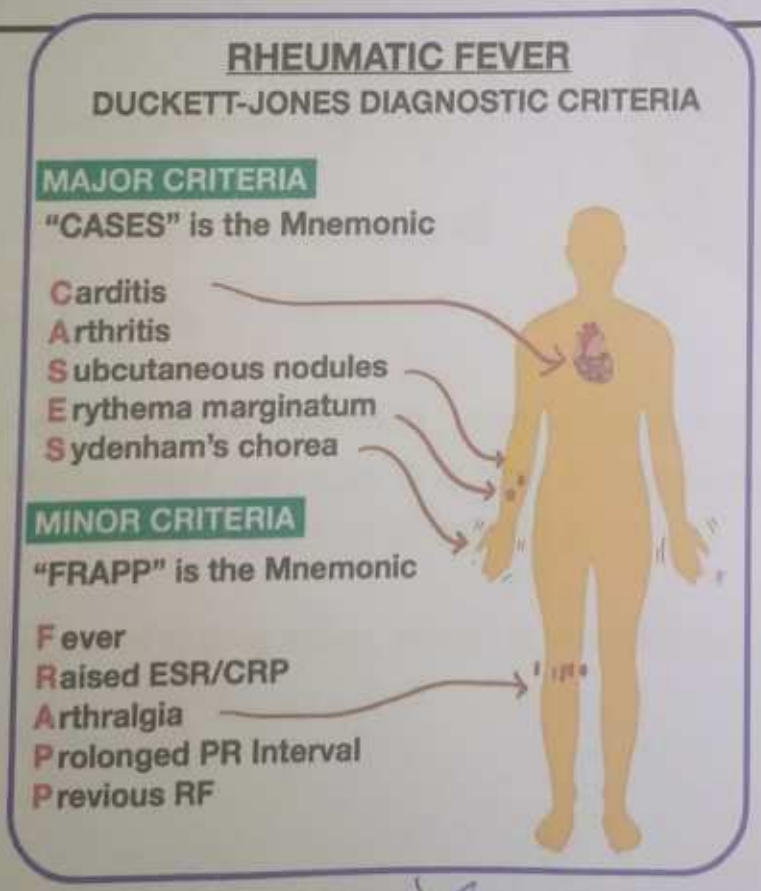
Treatment

1. **Penicillin** is the drug of choice.
2. **In cases of allergy** → erythromycin is the alternative.
3. **combination of vancomycin + aminoglycoside** (streptomycin or gentamycin) is essential for severe infections as endocarditis.

beta-hemolysis
Streptococcus pyogenes

alpha hemolysis
Escherichia coli

gamma hemolysis (no hemolysis)
Staphylococcus epidermidis



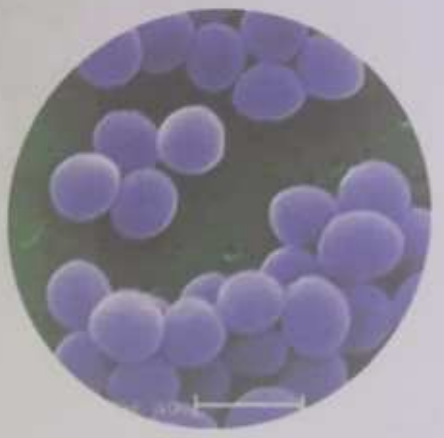
infective endocarditis

Common causes :

1. **Staphylococci:-**
   - Staphylococcus aureus (ABE).
   - Coagulase-negative Staphylococci.
2. **Streptococci:-**
   - Streptococcal pyogenes (ABE).
   - viridans streptococci (SBE).
   - Enterococci (SBE).

Staphylococcus aureus

☒ This is a classic case of acute bacterial endocarditis (ABE) .



☒ **symptoms** :
1) fever.
2) Malaise.
3) Chills.
4) new-onset cardiac murmur.

☒ **ABE also is seen most often in cases of** :
1) IV drug use.
2) indwelling catheters.

Staphylococcus aureus is the most common bacterial pathogen isolated in these cases, because it is part of the skin flora and enters the blood at needle sites.

☒ This patient's history of IV drug abuse, as well as auscultation of a murmur point to ABE.

Staphylococci

Morphology:

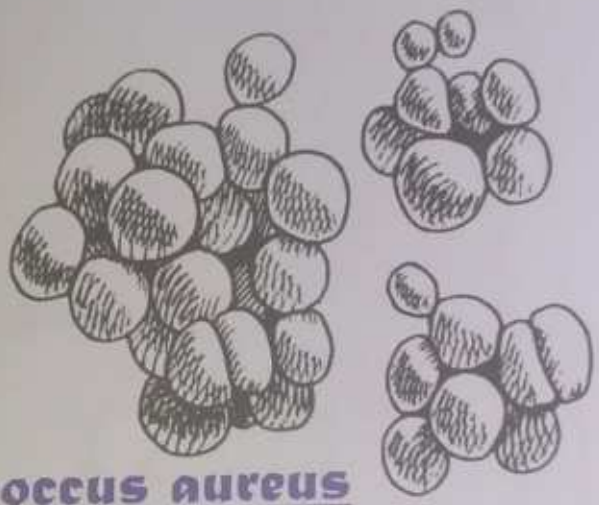
- ☒ Gram positive cocci
- ☒ arranged in grape like clusters

	Staphylococci	Streptococci
Microscopy	Clusters	Chains
Catalase	Present	Absent
penicillin	Rarely sensitive	Sensitive

Classifications :

1) **Coagulase positive**
   Staph aureus.

2) **Coagulase negative**
   Staph epidermidis.



Staphylococcus aureus

Morphology :

- **Because of its high degree of virulence** →
  S. aureus is a cause of both community-acquired and nosocomial infections.
- **Like other staphylococci** → it looks like purple clusters.

Culture :

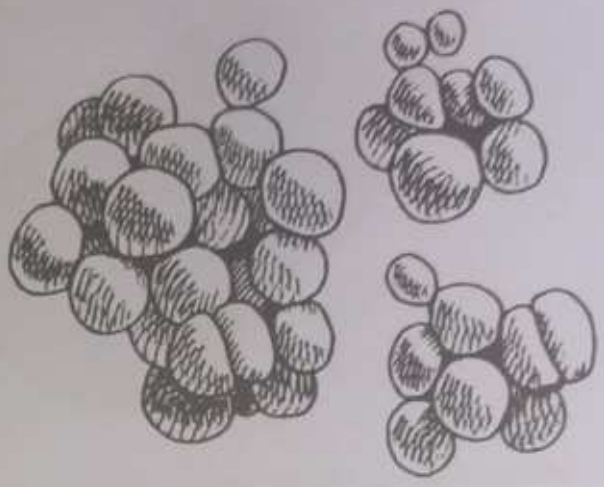
1. **Blood agar**: β-hemolytic (complete hemolysis) colonies
2. **Nutrient agar**: golden pigment colonies

Pathogenesis

Staph aureus have different virulence factors.

Protein A

preventing opsonization.

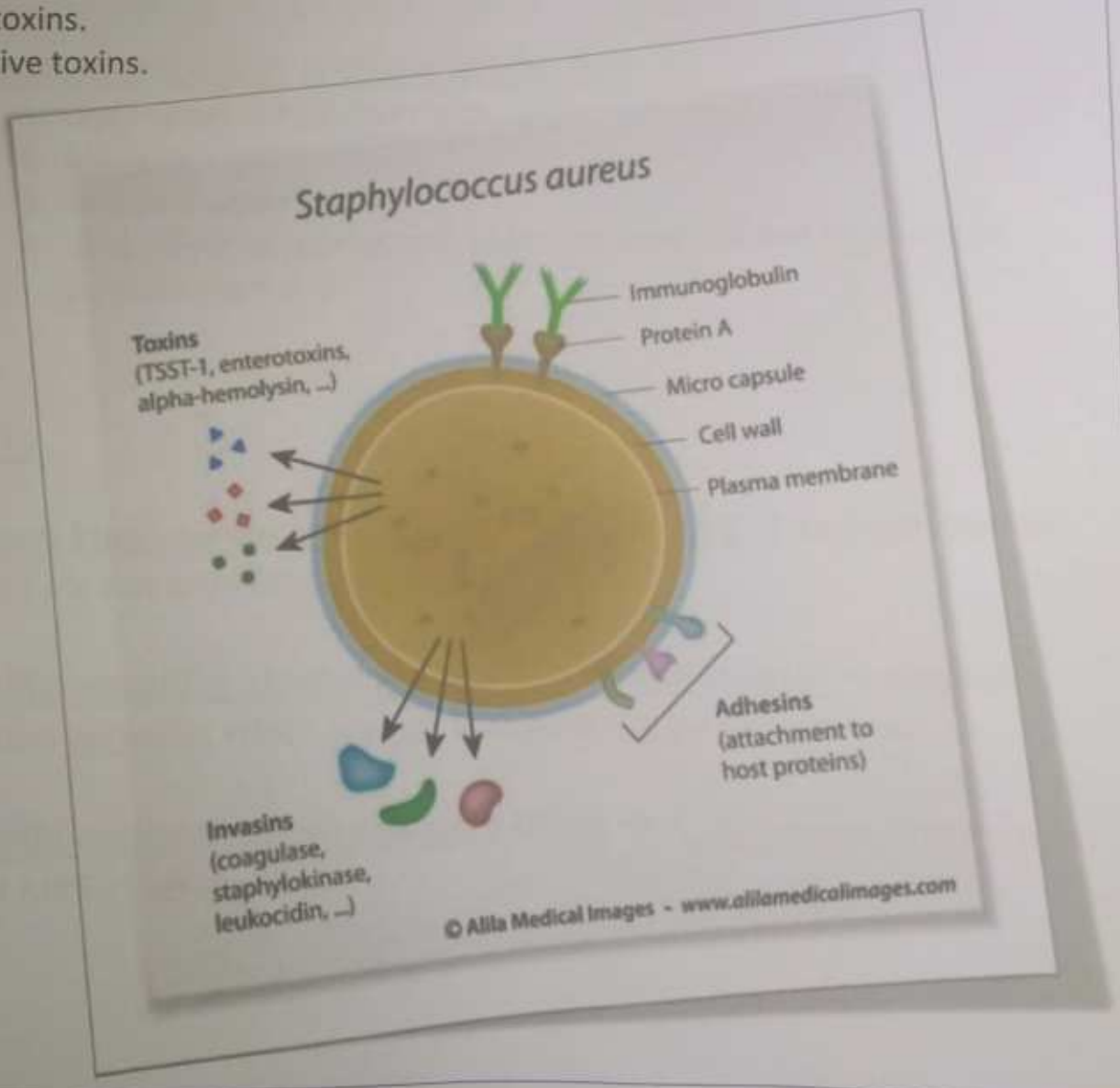


Enzymes :

1. Coagulase.
2. Catalase.
3. hyaluronidase .
4. staphylokinase.
5. Penicillinase (**β-lactamase**) .

Toxins :

1. Toxic shock syndrome toxin (**TSST-1**).
2. Enterotoxins.
3. Exfoliative toxins.



Diseases

1. Pyogenic diseases

1) **Focal suppuration** → abscess, boils.
2) **Invasive** → endocarditis (**ABE**).

2. Toxigenic diseases

1) Scalded skin syndrome (**SSS**).
2) Food poisoning.
3) Toxic shock syndrome.

3. Infective Endocarditis

- Infective endocarditis of undamaged (native) valves (**ABE**) is commonly caused by S. aureus.

- **acute endocarditis is characterized by :**
  1. rapid onset of high fever with rigors.
  2. Myalgias.
  3. cardiac murmur .
  4. large infective vegetations, which can break off and cause septic pulmonary emboli.

Treatment

- **Since most Staph aureus carry a penicillinase enzyme** → first-generation **penicillin** are not used for antibiotic therapy.

- **Methicillin-sensitive Staph aureus (MSSA) treated with** → second-generation **penicillin** which are not broken down by penicillinase.

- **Methicillin-resistant Staph aureus(MRSA)** → **Vancomycin** is the corner stone of MRSA therapy.

Coagulase-Negative Staphylococcus

staph epidermidis and Staph saprophyticus.

- **Both appear as :**
  1. gram-positive cocci in small clusters .
  2. catalase-positive.
  3. do not contain the coagulase enzyme.

- Staph epidermidis is sensitive to the antibiotic novobiocin, whereas Staph saprophyticus is resistant.

Staph. epidermidis

Pathogenesis

- **Staph. epidermidis** is a part of normal skin flora.
- **In healthy individuals,** this species is not a major cause of disease.
- Strains of Staph. epidermidis that produce a glycocalyx allows the organism to adhere to various surfaces (medical equipment), which can lead to opportunistic infections.

Clinical Symptoms

- **Infections of prosthetic implants** (prosthetic heart valves), vascular grafts as well as intravenous catheters.

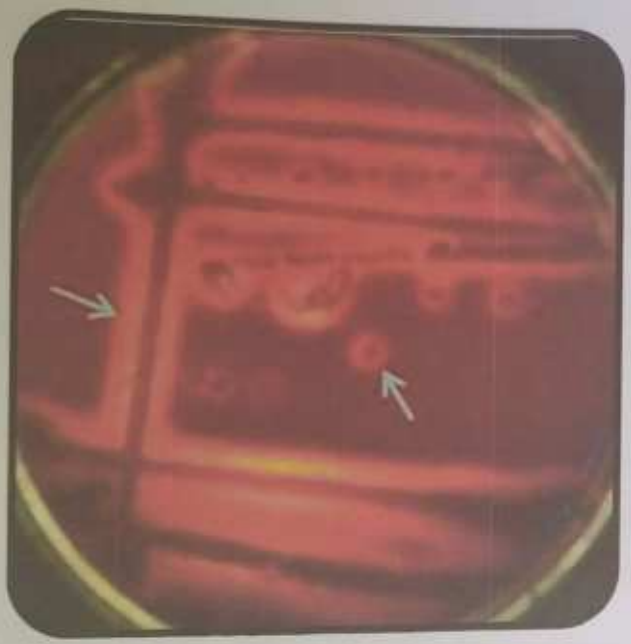
- These infections have a subacute course with slow development of symptoms.

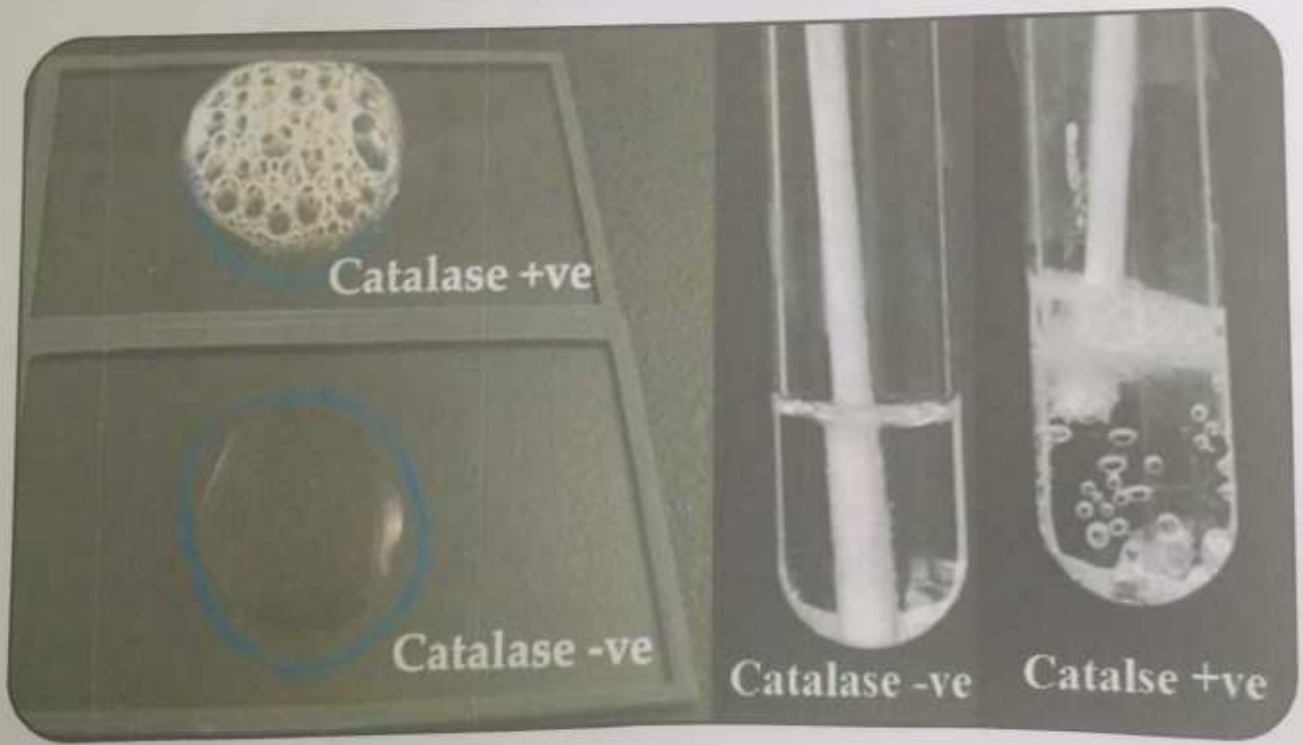
Treatment

Over 50% are methicillin-resistant and thus require vancomycin.

Diagnosis of infections by Staph aureus

1. **Specimen**: blood for blood culture in endocarditis
2. **Direct Gram stained smear**: gram positive cocci arranged in cluster
3. **Culture**: on nutrient and blood agar at 37 degree for 24 hours
4. **Gram stained film**: Gram positive cocci arranged in grape like clusters
5. **Biochemical reactions**: positive catalase and coagulase test
6. **Antibiotic susceptibility testing**: should be done routinely
7. **Serological identification**: by latex agglutination test.
8. **Molecular identification**: PCR or DNA probes.





Enterococci

Characteristics

- possess **group D Lancefield** antigen.
- distinguished from non enterococcal group D streptococci by their growth in 6.5% sodium chloride and 40% bile salts.
- mostly **γ-hemolytic**.
- **two species:**
  1. *Enterococcus faecalis*
  2. *Enterococcus faecium.*

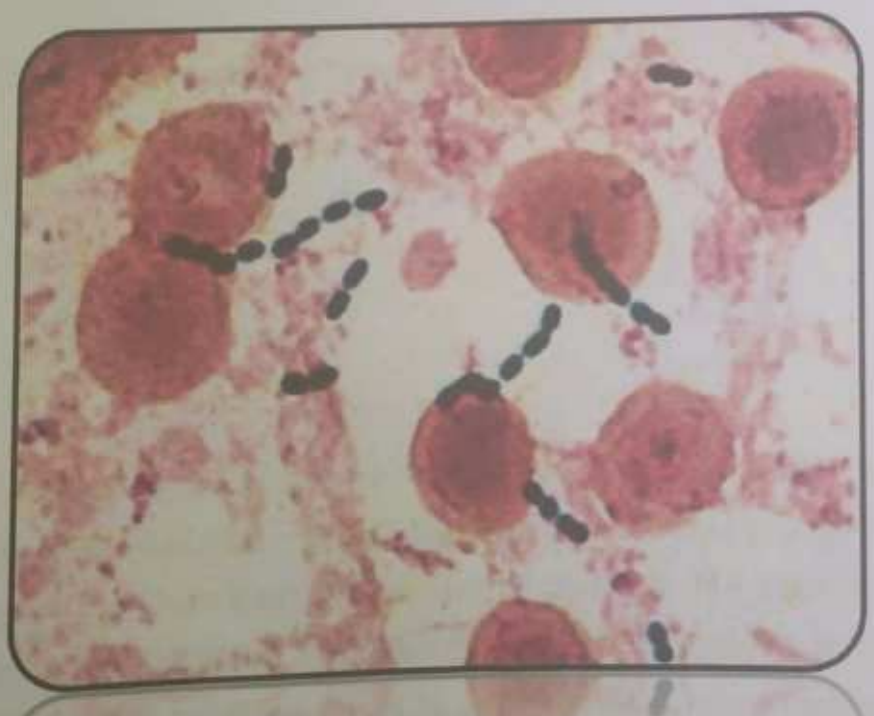
Pathogenesis (virulence factors)

- Enterococcal infections occur after genitourinary and gastrointestinal procedures.
- They possess virulence factors, like the **enterococcal surface protein (Esp).**

Diseases: Subacute bacterial endocarditis.

Treatment

- Vancomycin
- Vancomycin resistant enterococci (VRE): resistance to vancomycin is rising (up to 20% of E.faecium isolates) →
  1. Combination of two streptogramins [quinupristin/dalfopristin (synercid)].
  2. Linezolid, daptomycin and tigecycline.



Cases

Case (1)

A 12 years- old girl experience a group A streptococcus pharyngitis and within 3 weeks has chest pain and develops new murmurs of mitral regurgitation.

Which diseases he suffering from?

Case (2)

After extraction of a wisdom tooth, an 18 years-old male student is diagnosed with subacute bacterial endocarditis. He has a congenital heart disease that has been under control.

Which is the most likely organism causing the infection?

How to diagnose it?

Case (3)

A 24-year-old man presents to the emergency department with fever, chills, night sweats, malaise, and fatigue that started three days ago. In the past 24 hours, he has become short of breath. He admits to using intravenous drugs regularly. At presentation the patient is shaking and appears pale. Physical examination is remarkable for a temperature of

39.4°C, hypoxia, jugular venous distention, bilaterally decreased breath sounds at the bases of the lungs, and a systolic murmur heard best at the lower left sternal border.

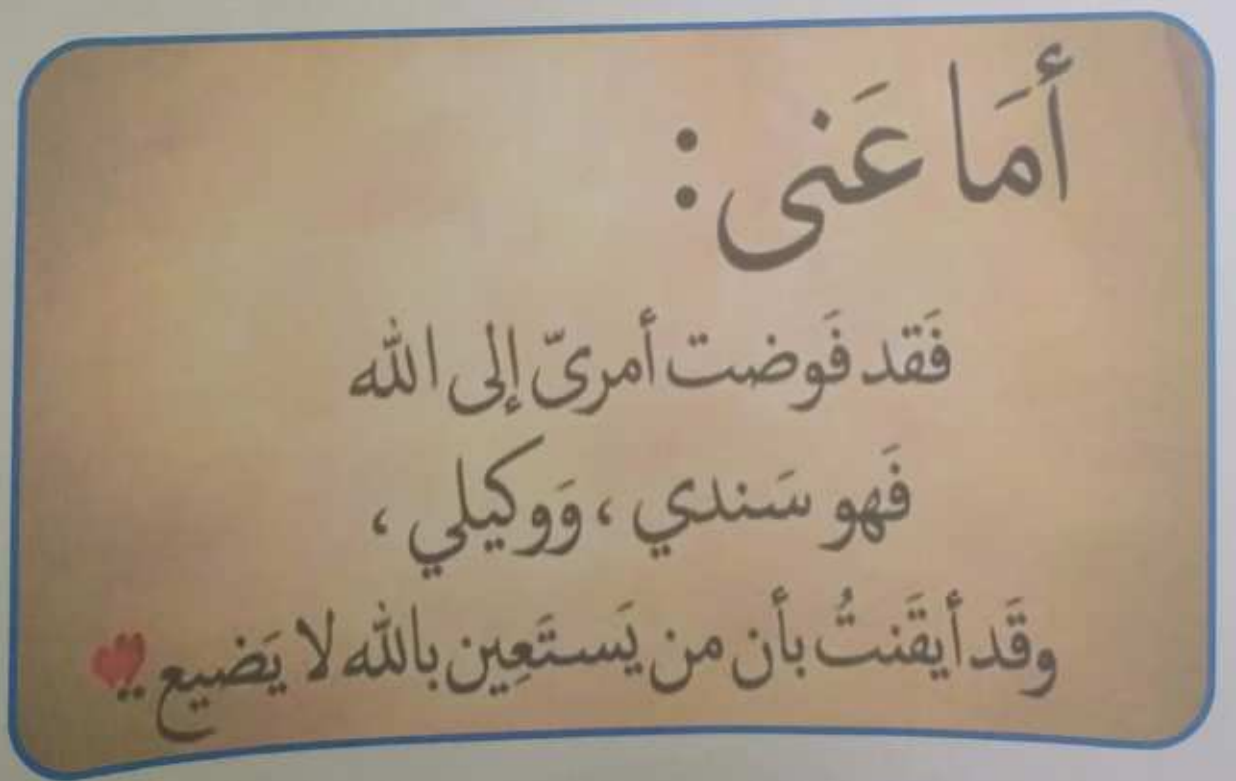
Which pathogen is most likely responsible for this patient's condition?

Case (4)

A70-year-old female patient was re admitted to a local hospital with fever and chills following cardiac surgery at a major teaching institution. Blood cultures were taken and a Gram-positive coccus grew from the blood cultures within 24 hours. Initial tests indicated that this isolate was resistant to penicillin.

The most likely identification is.....

Case	Answer
1	Rheumatic fever
2	Viridans streptococci
3	Staphylococcus aureus
4	SBE (Enterococci)

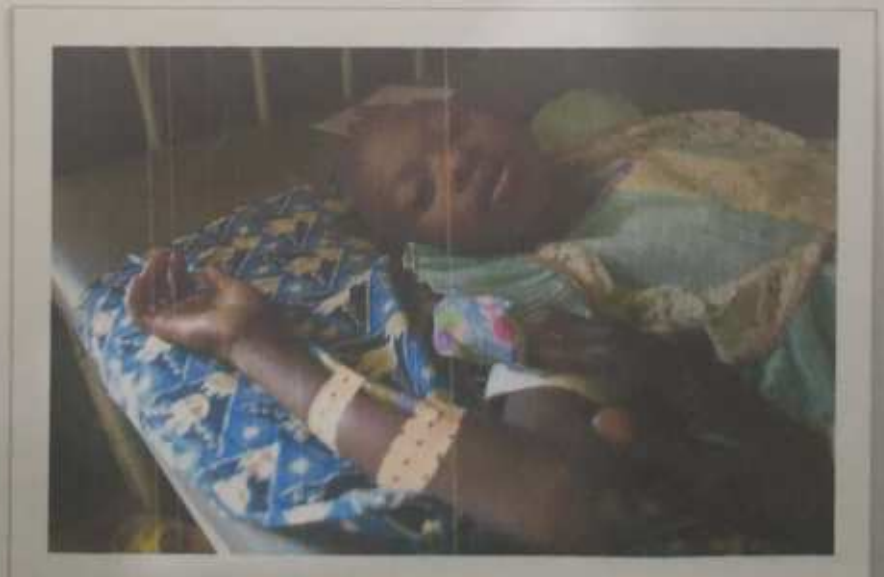


Viral Hemorrhagic fever

Viral hemorrhagic fevers

- **Viral hemorrhagic fevers (VHFs)** refer to a group of illnesses that are caused by several distinct families of viruses.
- It is a severe multisystem syndrome.
- **The overall vascular system** is damaged, **the body's ability to regulate itself** is impaired.

- These symptoms are often accompanied by hemorrhage.
- **The bleeding is itself** rarely life-threatening.
- **Some types** of hemorrhagic fever viruses can cause relatively mild illnesses.
- Many of these viruses cause severe, life-threatening disease.



Causes of viral hemorrhagic fevers:

VHFs are caused by viruses of four distinct families

1. Filoviruses :

- *Marburg virus.*
- *Ebola virus.*

2. Flaviviruses :

- *Dengue virus (Break bone fever).*
- *Yellow fever virus.*

3. Arenaviruses :

- *Lassa virus.*

4. Bunyaviruses :

- *Crimean-Congo hemorrhagic fever viruses (CCHF)*
- *Hantaviruses (Korean hemorrhagic fever)*
- *Rift Valley fever*

☒ **In Africa** → ***severe hemorrhagic fevers are caused by*** :

1) yellow fever virus.
2) dengue virus.
3) Roboviruses.
4) **in addition to a group of viruses** belonging to filoviruses.

Rodent borne

☒ **Roboviruses** : viruses that are transmitted directly from rodents to humans without an arthropod vector.

Humans are infected by exposure to infected rodents or their excreta →

1) Lassa virus
2) hantaviruses.

☒ **Severe hemorrhagic fevers** :

1) Lassa fever virus (**in Africa**) .
2) hantavirus infection (**in Asia**).

☒ **Arthropod-borne viruses** are called **arboviruses**, which are viruses transmitted by the bite of an arthropod vector.

Filoviruses

MCQ

Thread – like filamentous enveloped viruses that have non segmented negative sense ss-RNA.

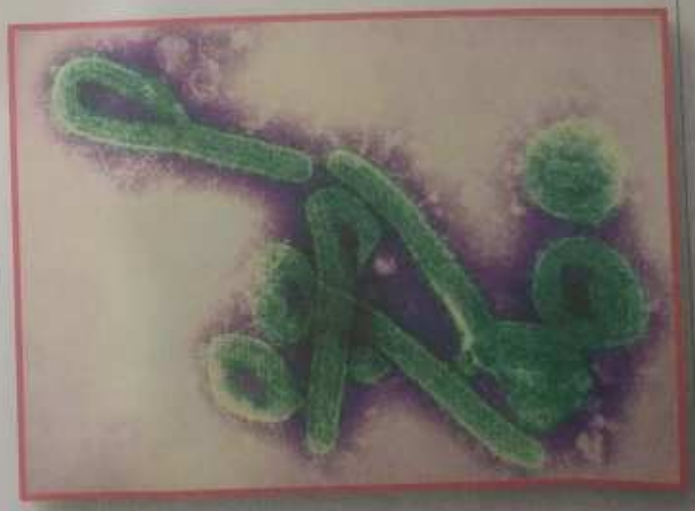
-ve ss-RNA

RNA Genome

The two known filoviruses are :

1) Marburg
2) Ebola viruses. MCQ

They are highly virulent viruses with infections usually ending in death.



Reservoirs :

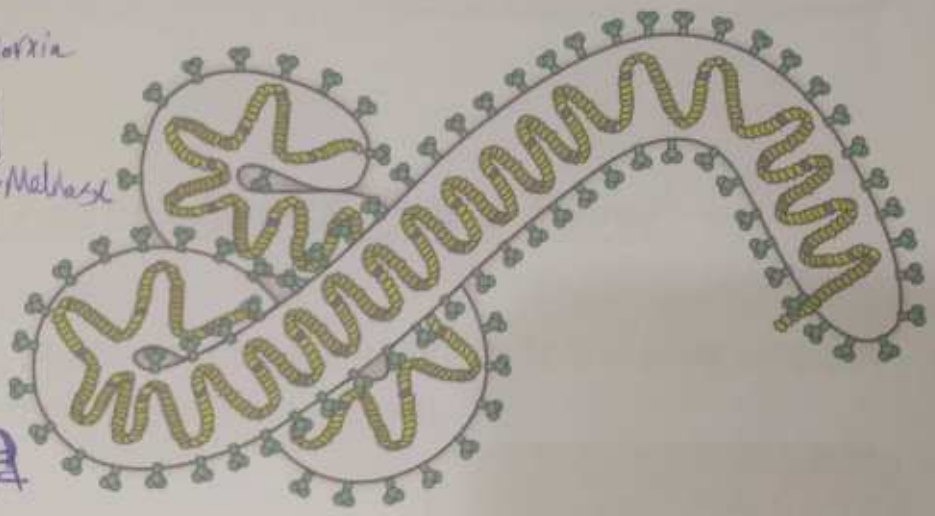
- ☒ have not been identified yet.
- ☒ **Perhaps monkeys or bats** are the reservoir and humans become infected accidentally.

Transmission :

- ☒ Human infections are **highly communicable** to human contacts.
- ☒ **This occurs by** direct contact with blood or body fluids.

Clinical picture :

- ☠ Fever.
- ☠ Headache.
- ☠ sore throat .
- ☠ muscle pain.



This is followed by →

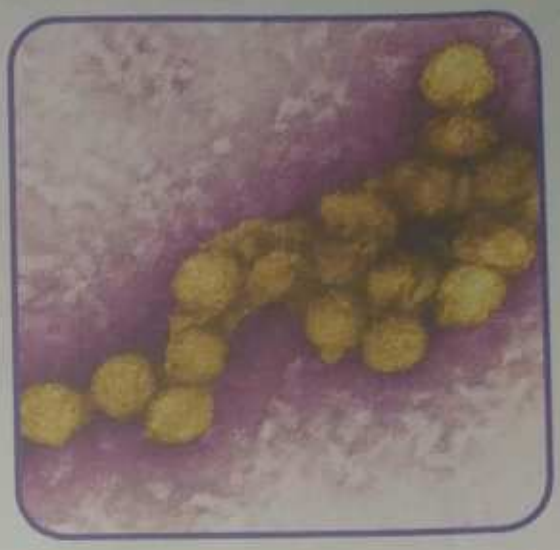
- ☠ abdominal pain.
- ☠ Vomiting.
- ☠ Diarrhea.
- ☠ skin rash.
- ☠ Internal and external bleeding follows leading to shock and death.
- ☠ **These viruses have the higher mortality rate** among all viral hemorrhagic fevers.

Treatment :

- ☒ symptomatic with no specific antiviral therapy.
- ☒ There is no vaccine till now.

Flaviviruses

Icosahedral, enveloped, (+) ss-RNA viruses.



The two known flaviviruses causing VHFs are :

1) Dengue virus
2) Yellow fever virus.

Dengue Fever (Break Bone Fever)

- ☒ **Four serotypes** are present.
- ☒ Infection by one serotype confers long life immunity to the same serotype but short-term immunity to the other serotypes.

Transmitted by :

- the mosquito *Aedes aegypti*.
- Humans are the reservoir of infection.

Clinical picture:

Classic dengue:

begins with flu-like symptoms consisting of :

- Fever.
- Chills.
- malaise.

pain

ain soon develops especially in the back, joints, muscles and eyeball.

- **Enlarged lymph nodes** and maculopapular rash may occur.
- **Recovery** occurs after few weeks.

Hemorrhagic dengue fever:

- **is a severe form of dengue** that is fatal.
- This occurs mainly in children and in those who are previously infected with a different serotype.
- **The initial picture** is the same as classic dengue.
- **Then** →
  1) shock
  2) hemorrhage, especially into GIT and skin.

Laboratory diagnosis:

1- **Serologic diagnosis** by **ELISA** to detect viral specific IgM. OR PCR for RNA
2- **Detection of viral Ags** or viral RNA in clinical specimens.
3- **Viral isolation**. → Tissue Culture
4- **Some hematological tests** may help in diagnosis as **WBCs** count which is lowered and the hematocrit value. → CBC → ↓ No. of RBCs & Hb

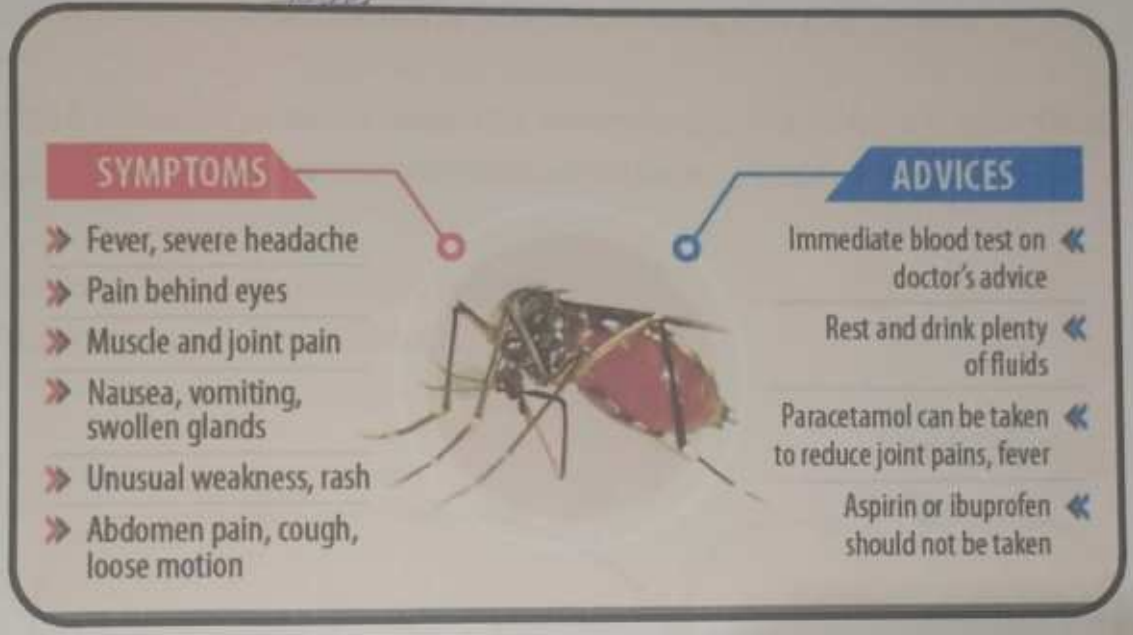
Treatment:

1- **Supportive and symptomatic treatment.**

Paracetamol is given as an analgesic.

Nonsteroidal analgesics are avoided as they affect the bleeding tendency of the patient.

2- **Hydration of the patient is very important.**



Yellow Fever

Yellow fever is an acute, febrile, mosquito-borne illness that occurs only in Africa and South America.

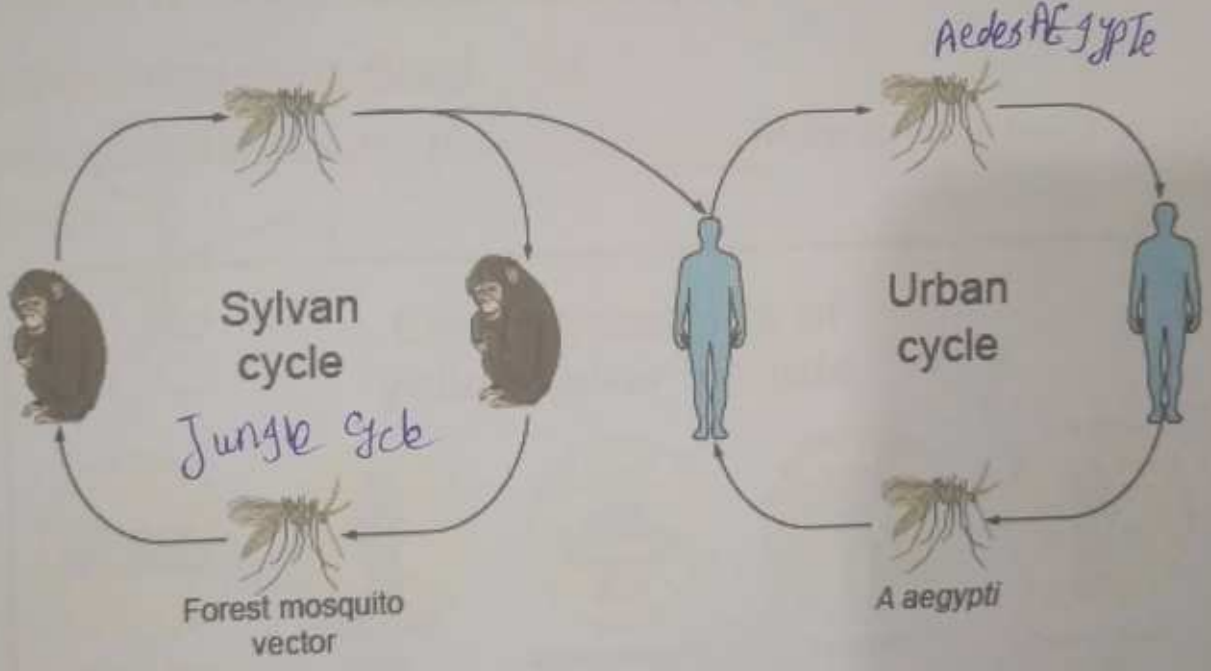
Severe cases are life threatening characterized by **liver** and **renal dysfunction** and **hemorrhage** with high mortality.

Two epidemiologic cycles for viral transmission are recognized:

(1) Urban yellow fever.

(2) Jungle yellow fever.

- In the jungle cycle **which occurs in tropical forests** → monkeys serve as the main reservoir.
- **The virus is transmitted** from monkey to another by **mosquito *Aedes africanus*** in Africa and ***haemogogus*** in south America.
- Humans become accidentally infected if they visit the forests.
- When infected persons return to urban areas, the virus is transmitted from human to human by the domestic mosquito ***Aedes aegypti***.
- This is called urban yellow fever.
- This may occur in epidemics.



Clinical picture:

The liver is usually the most affected organ leading to the development of deep jaundice, hence the name "yellow fever".

The clinical condition may pass in 3 stages:

liver → Jaundice

1st stage:

- a mild one.
- **The patient develops :**
  1- Headache.
  2- Fever.
  3- malaise .
  4- myalgia.
  5- Vomiting and jaundice may occur.

2nd stage (remission stage):

in which symptoms disappear and most patients recover.

3rd stage (intoxication stage):

about 15% of cases suffer from multi-organ dysfunction with liver and renal failure,

rophylaxis:

1- **Mosquito control** in endemic areas as in equatorial countries of Africa and South America and on airplanes going to or coming from these areas.

2- **Live attenuated vaccine** :
   - **prepared from** an attenuated 17D strain (17D vaccine).
   - It is **prepared in eggs** and thus those having egg allergy should consult doctors before taking it.

Arenavirus: Lassa virus

- Helical, circular and enveloped with RNA-encoded, segmented genomes.

The natural reservoir is :

- **small rodent** which inhabits rural homes and fields.

transmitted by :

- **contaminated food or water** with animal urine.

It causes a sever hemorrhagic fever characterized by multiple organ involvement.

- Lassa virus is associated with **high death rates in pregnant** women in 3rd trimester and fetuses (**~95%** fetal mortality rate).

Complications: Most common complication is deafness in **~1/3** of cases.

World Health Organization

LASSA FEVER

What is Lassa fever?

Lassa fever is a viral illness that typically occurs in West Africa.

How is Lassa fever spread?

The Lassa virus is transmitted to humans mainly through handling rats, food or household items contaminated by rats' urine and faeces.

The virus can spread between people through direct contact with the body fluids of a person infected with Lassa fever, as well as contaminated bedding and clothing.

You cannot get Lassa fever through hugging, shaking hands or sitting near someone.

What are the symptoms of Lassa fever?

Symptoms of Lassa fever typically occur 2-21 days after coming into contact with the virus. Many people who are infected do not show symptoms.

- Fever
- Headache
- Sore throat
- Chest and muscle pain
- Nausea, vomiting and diarrhoea
- Facial swelling
- In severe cases, bleeding from the mouth, nose, vagina or gastro-intestinal tract

Bunyaviruses

Helical, enveloped, (-) ss-RNA viruses.

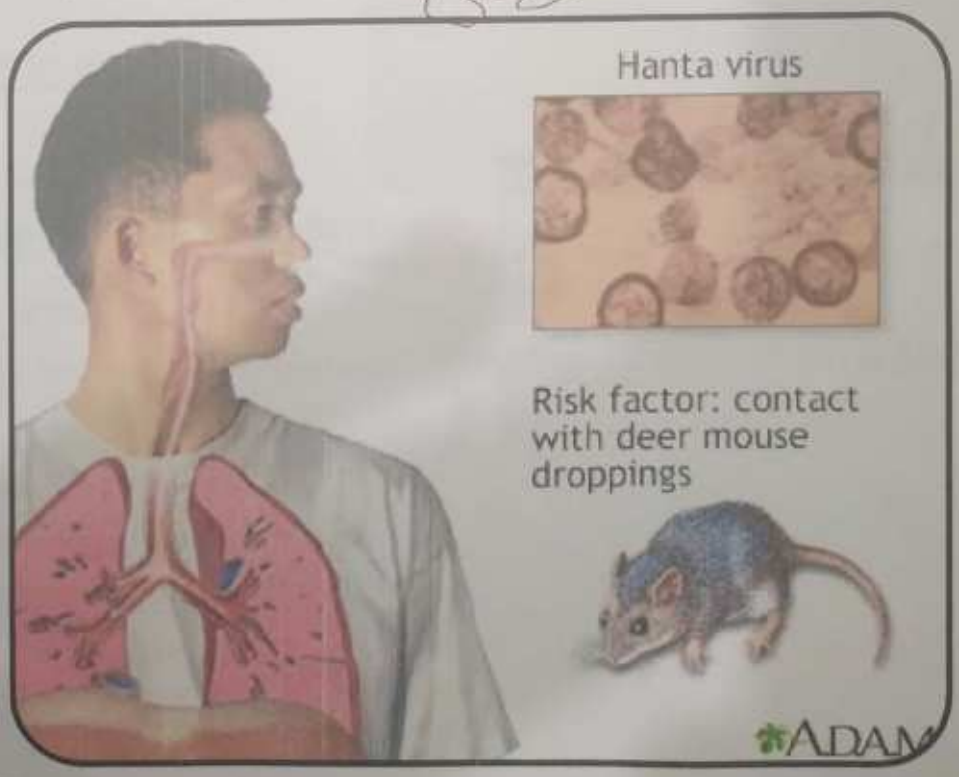
Crimean-Congo hemorrhagic fever viruses (CCHF):

It is carried by the ***Hyalomma spp. tick***.

Hantaviruses:

It is also known as Korean hemorrhagic fever.

- ☒ They are heterogenous group of viruses called roboviruses (**rodent-borne viruses**).
- ☒ It is **transmitted by** inhaled rodent urine/feces.
- ☒ There is no person to person transmission.
- ☒ **It causes :**
  1) hemorrhagic fever .
  2) renal disease .
  3) cardiopulmonary syndrome



Rift Valley Fever

The disease affects primarily domestic livestock →

1- sheep
2- cattle.

Transmission:

It can be transmitted to humans either by:

1- **Direct or indirect contact** with blood, fluids or organs of infected animals → placenta of aborted animal.
Those in contact with animals as veterinarians and those working in slaughterhouses are at high risk of infection.

2- Bite of ***Aedes aegypti mosquito***.

Clinical picture:

The incubation period : 2 to 6 days.

- ☒ Flu-like symptoms.
- ☒ Recovery is usually complete but sometimes the condition is **complicated by**:
  1- Ocular complication
  2- Meningoencephalitis.
  3- Hemorrhagic fever.

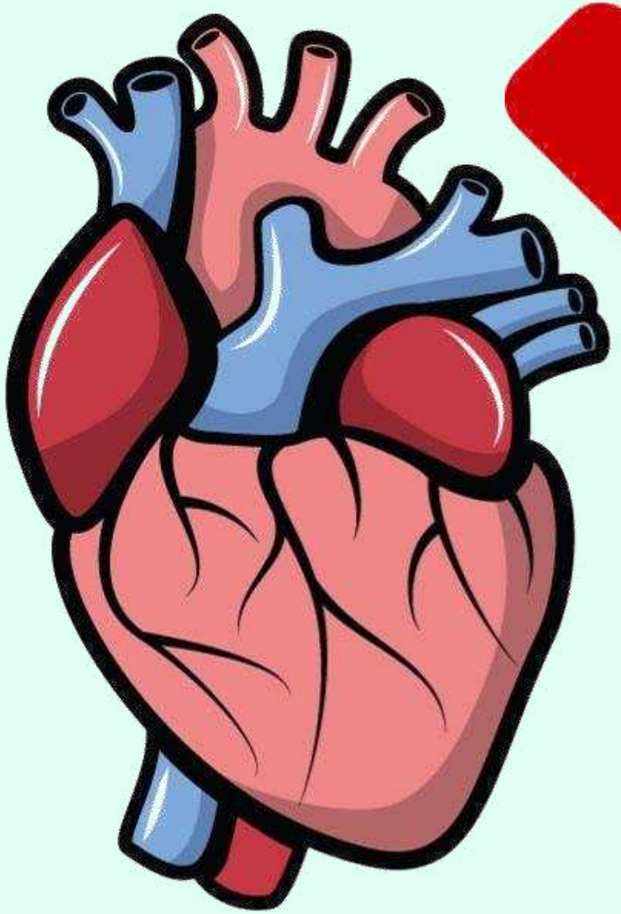
Prophylaxis:

- **A live attenuated vaccine** is used for animal (not human) immunization.
- **Protective clothing** is indicated for persons that have contact with animals to reduce the risk of exposure in addition to vector control.

There is only one bacterial cause for hemorrhagic fever:

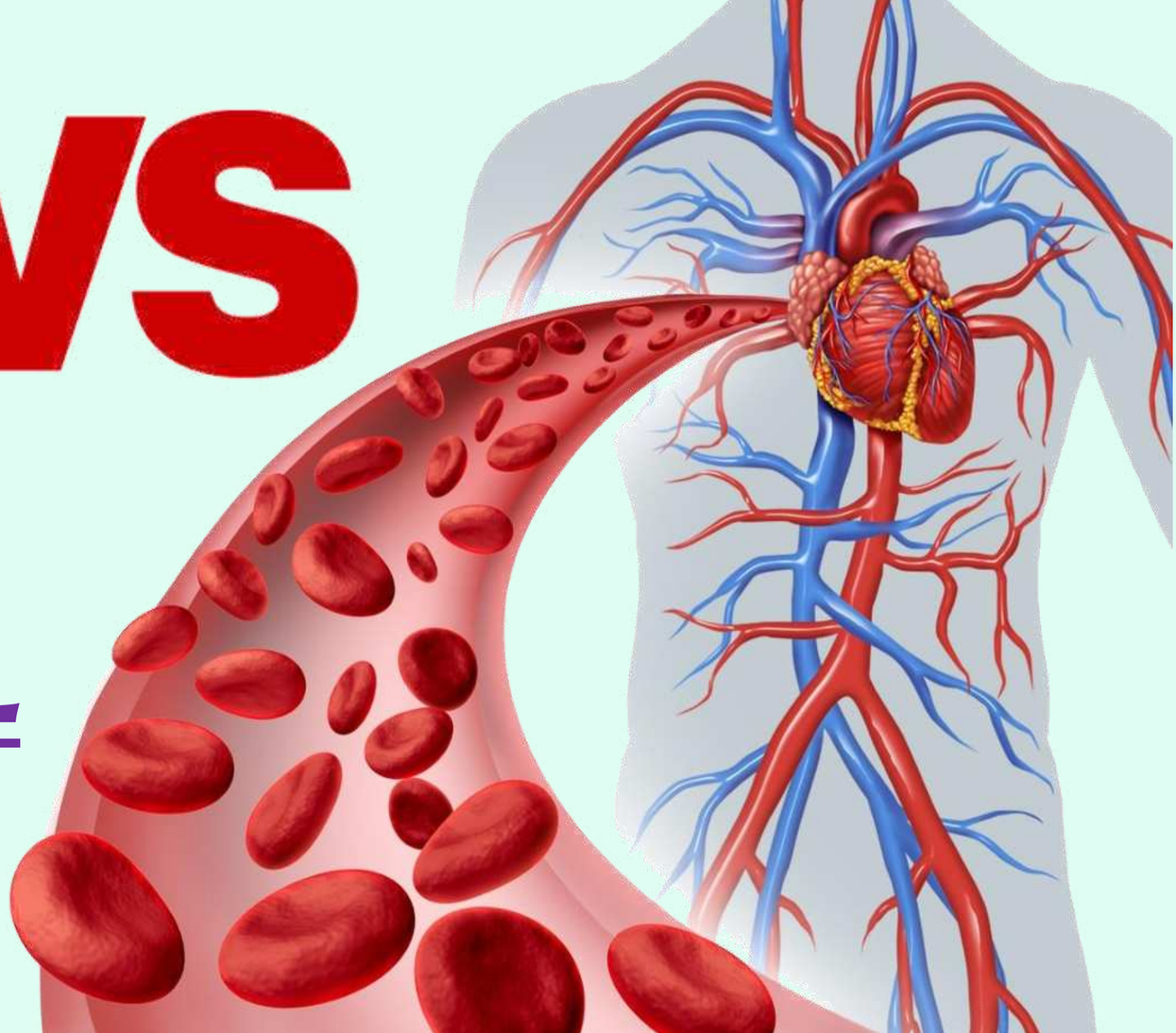
Leptospira icterohaemorrhagiae

causing Leptospirosis (Weil's disease).



CVS

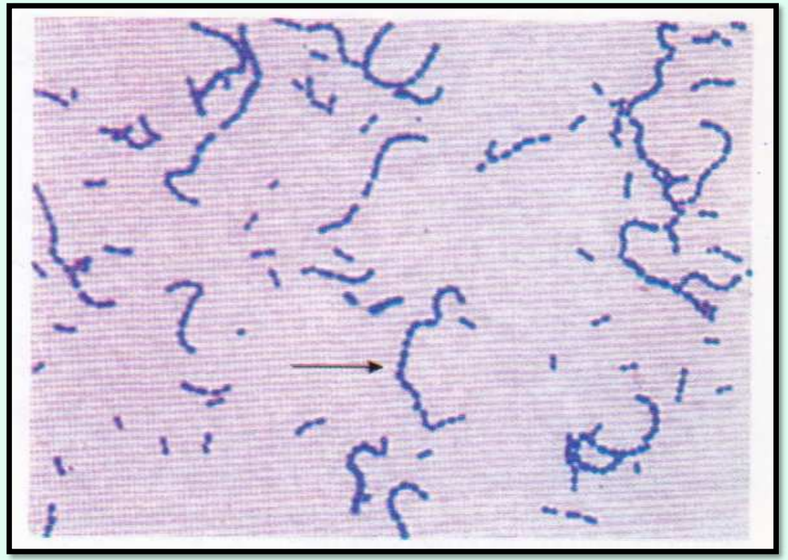
CLINICAL

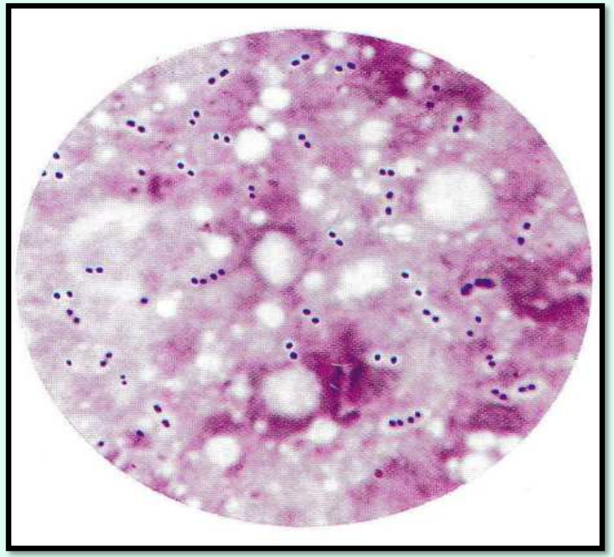


STREPTOCOCCI

MORPHOLOGY

Gram positive cocci arranged in pairs or chains. They are non-motile, non-spore forming, some strains are capsulated





Classification

Beta hemolytic:

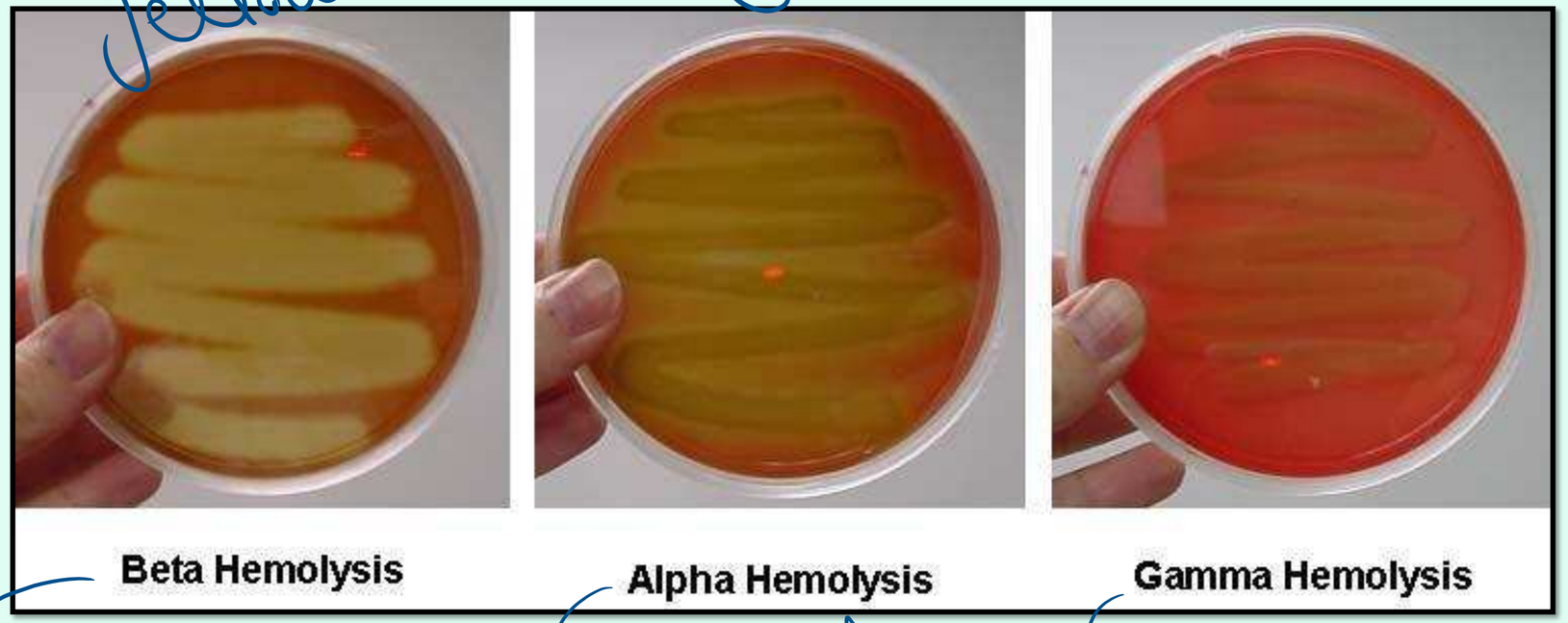
- ✓ *S. Pyogenes*
- ✓ *S. Agalactiae.*

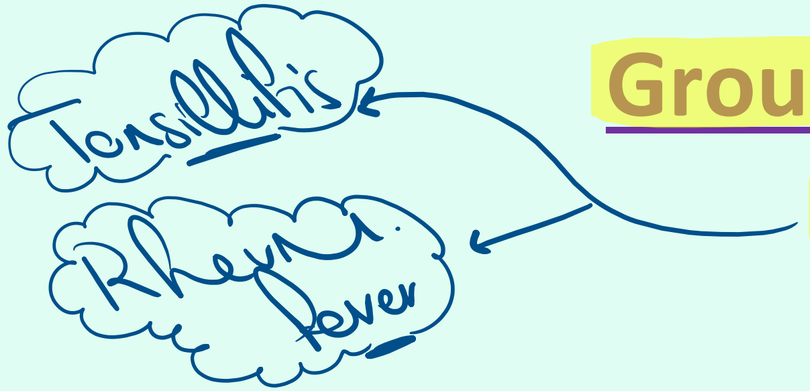
Alpha hemolytic:

- *viridans streptococci*
- *S. Pneumoniae.*

Gamma hemolytic:

S. bovis





Group A, β-hemolytic *Streptococci*

Streptococcus pyogenes

GAS

1-Specimen

according to site of infection

swabs, pus, or blood.

Blood for Blood cultures as in bacterial endocarditis

مزرعة دم

Blood culture

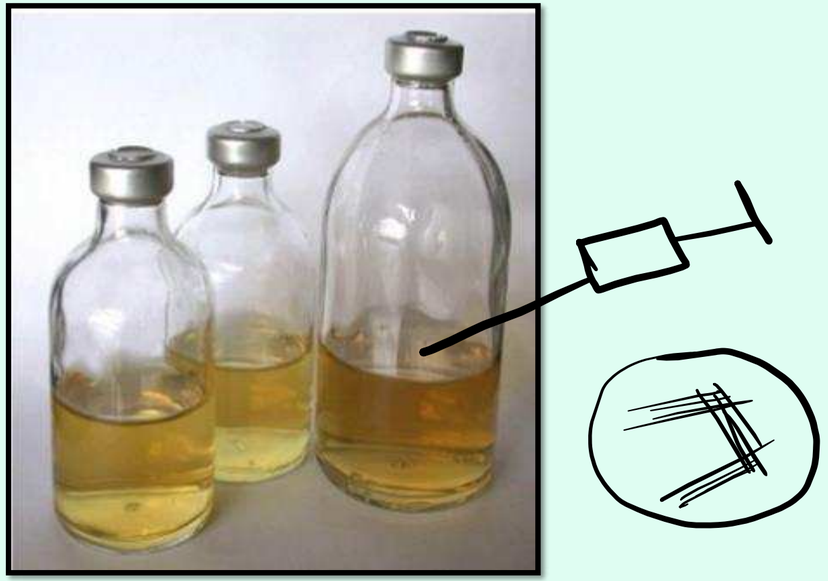
5 mL blood + 50 mL broth

Appropriate volume should always be withdrawn.

Obtain blood sample **prior to antibiotics use.**

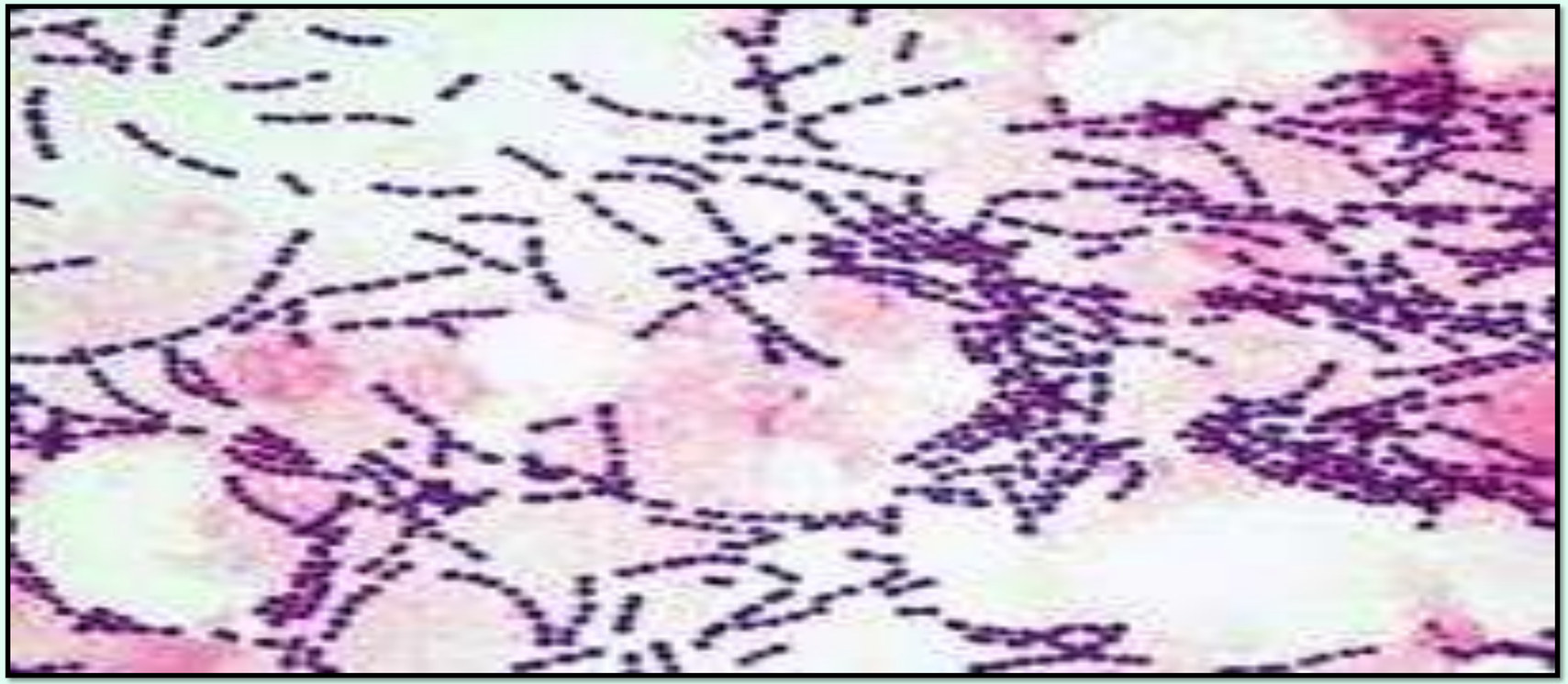
Blood is withdrawn using **sterile syringe** after **proper disinfection** of the puncture area to avoid contamination by skin commensals.

The blood sample is placed in blood culture bottle



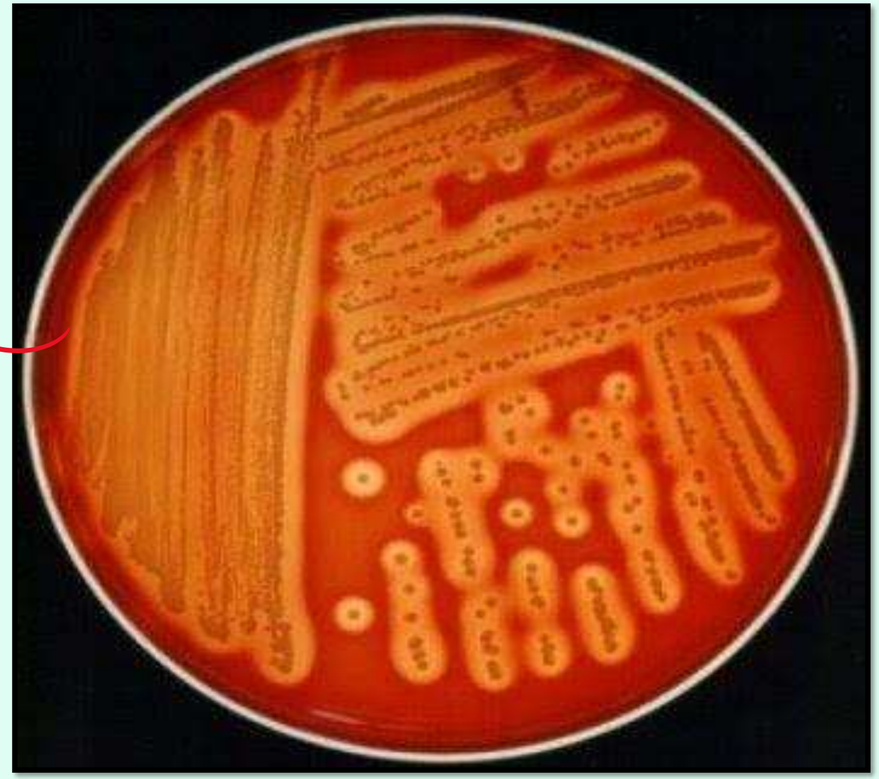
2. Gram-stained smears:

Gram positive cocci **arranged in chains** within pus cells



3- Culture

On blood agar → incubated at 37°C. Growth and hemolysis are enhanced by incubation at 5-10% CO_2.



GAS

Strept. Pyogenes

Blood Agar

β

4- Colonies are identified by:

1- **Morphology:**

Complete hemolysis (**ß-hemolysis**)

2- **Gram-stained film**

3- **Bacitracin sensitivity test**

A zone of inhibition around the bacitracin disc is indicative of group A *Streptococci*

4- **Commercially available latex agglutination kits**: for serotyping when needed.

5- **Antigen detection test**: by ELISA or agglutination tests.

Diagnosis of post-streptococcal diseases

Diagnosis of Rheumatic Fever

1-Antistreptolysin O (ASO) → ↑↑ 1200

2- C-reactive protein (CRP) ↑↑

3- Erythrocyte sedimentation rate (ESR) ↑↑

Diagnosis of Acute Glomerulonephritis

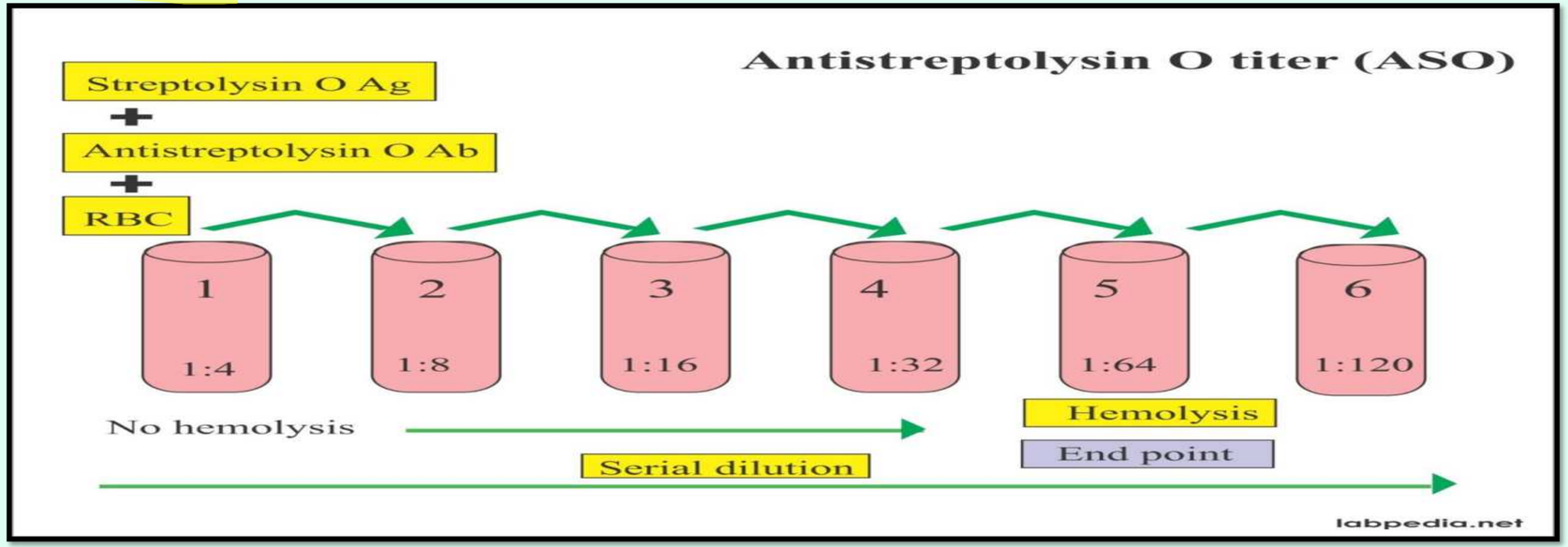
Anti-DNase B

+ Jones

Diagnosis of Rheumatic Fever:

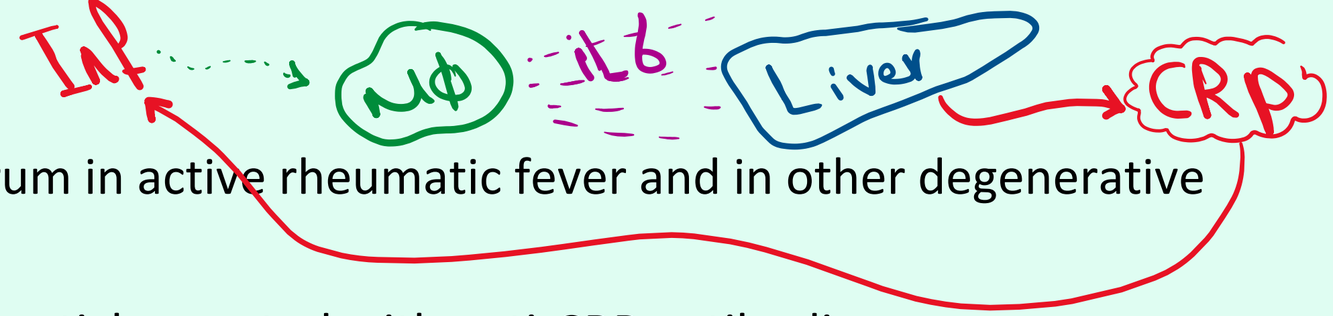
1- Antistreptolysin O (ASO):

- ✓ ASO antibodies are detected in the patient`s serum.
- ✓ **High ASO titers 1/200 or more** is significant and indicates **recent** streptococcal infection.




1/80

2- C-reactive protein (CRP):

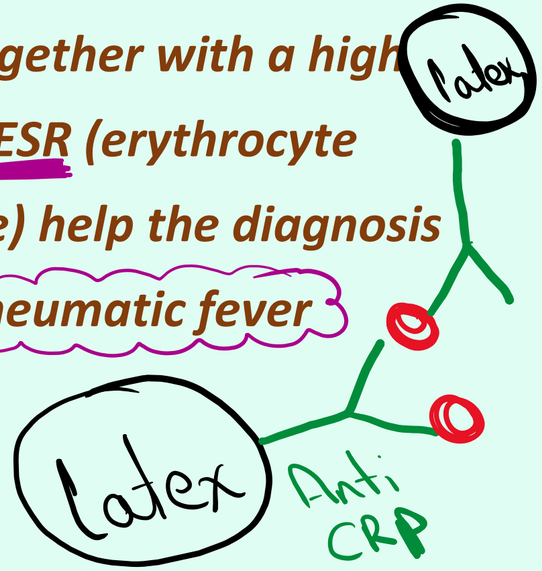


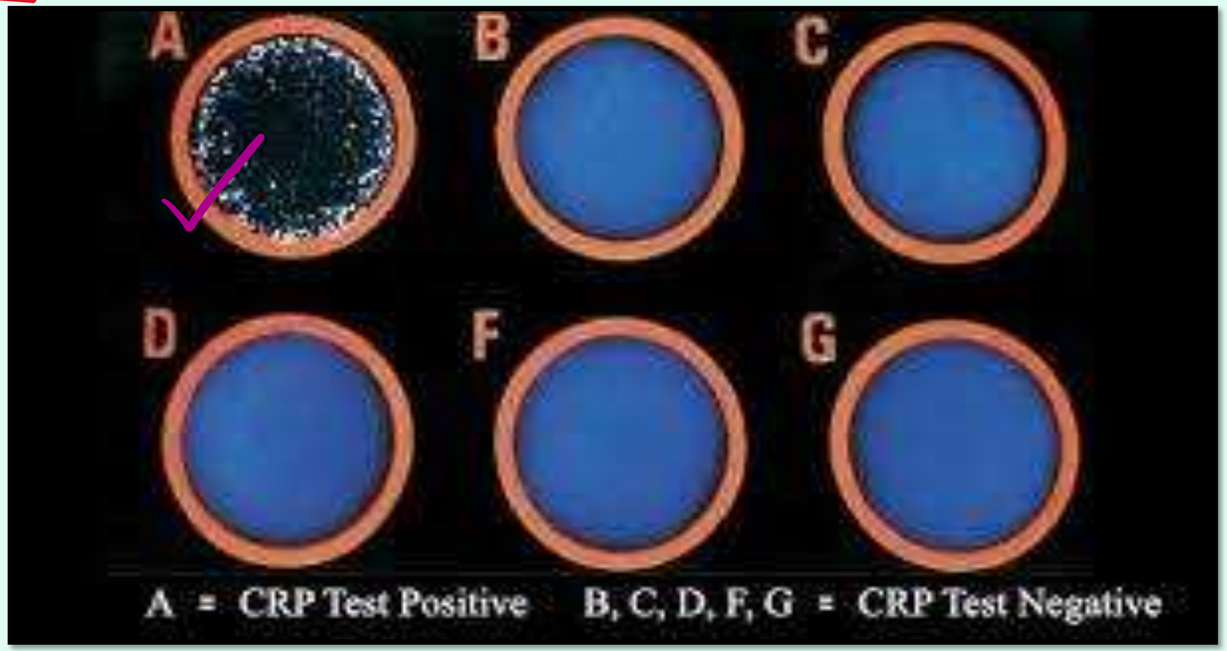
Abnormal acute phase protein, appears in serum in active rheumatic fever and in other degenerative and inflammatory conditions.

Tested by agglutination reaction using latex particles coated with anti-CRP antibodies.

≥ 1200

Presence of CRP together with a high ASO and elevated ESR (erythrocyte sedimentation rate) help the diagnosis and follow up of rheumatic fever

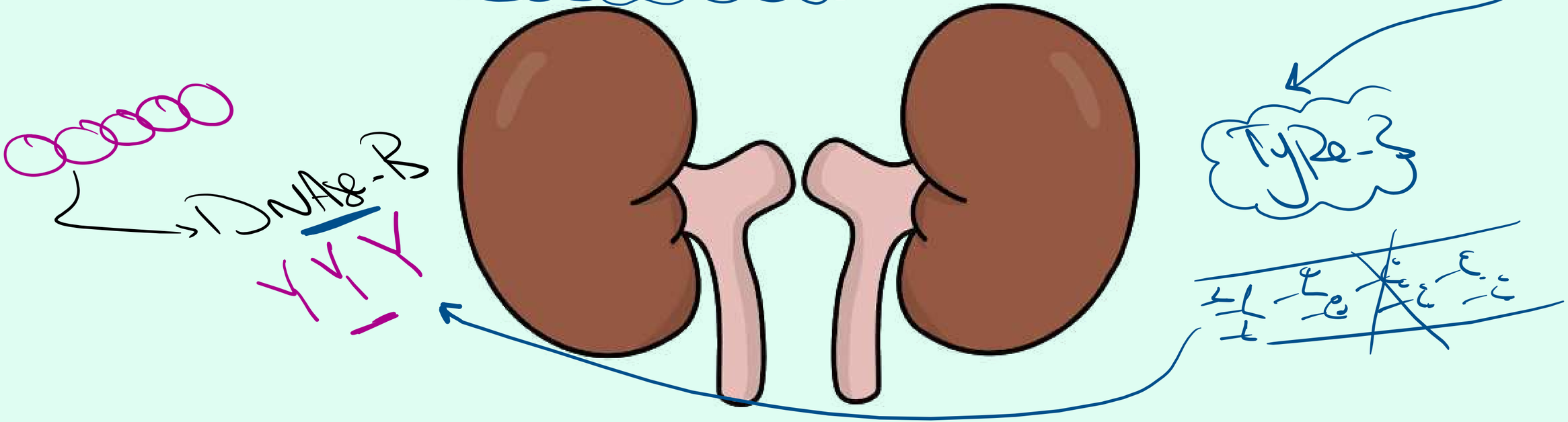




Diagnosis of Acute Glomerulonephritis

Anti-DNase B:

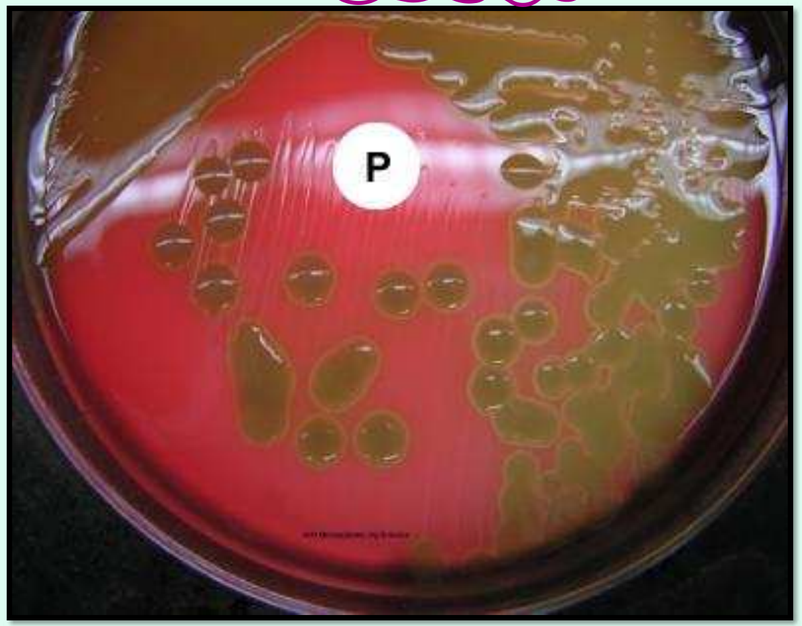
These antibodies are high in group A streptococcal skin infections and is an indicator of recent infections when suspecting **acute glomerulonephritis.**

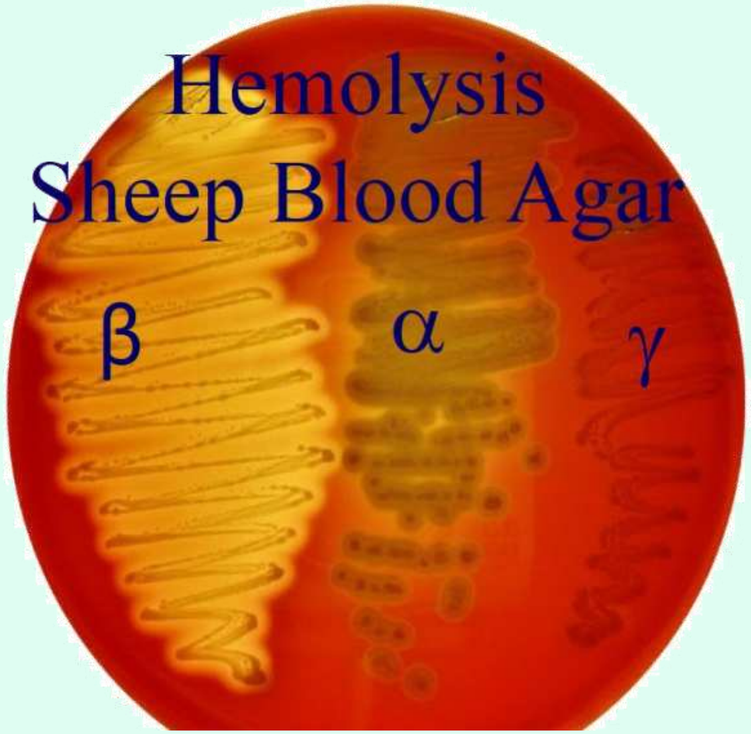


α-hemolytic *Streptococci*

α-hemolytic *Streptococci*: produce greenish discoloration of blood

- ***Viridans streptococci*** → Teeth
- ***Streptococcal Pneumoniae (pneumococci)***





Viridans *Streptococci*

- Viridans *Streptococci* is a large group of commensal streptococcal bacteria that are either **α-hemolytic**, or non-hemolytic, with no Lancefield antigens.

- **Diseases**
  - ✓ It is the most common causes of **subacute bacterial endocarditis.**
  - ✓ Present in large numbers in mouth, and can cause **dental caries**.

Laboratory diagnosis of subacute bacterial endocarditis is done by blood culture.