CAS-206
Level 2

Rheumatic Fever

By
Medical Microbiology & Immunology Department
Faculty of Medicine
Merit University

Objectives:

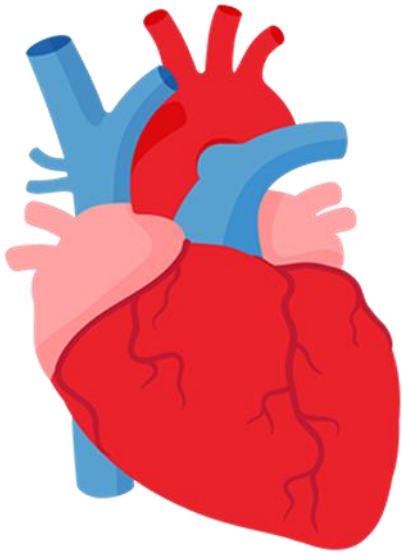
- Identify the leading cause of the disease **(post *Streptococcus pyogenes* infection)**

- Understand the **mechanism and pathophysiology** of the disease

- Recognize the role of **molecular mimicry and type II hypersensitivity**

- State the **diagnosis** of the disease

- Learn the most important **preventive measures**



Definition:

Delayed complication that usually occurs 2–4 weeks after throat infection caused by **group *A β-hemolytic streptococcal* (GAS)**

Epidemiology:

- **Peak incidence**: 5–15 years
- **Prevalence:**
  - ***Developing countries:*** the most common cause of cardiovascular disease in children and adolescents
  - ***Developed countries:*** rare

Etiology:

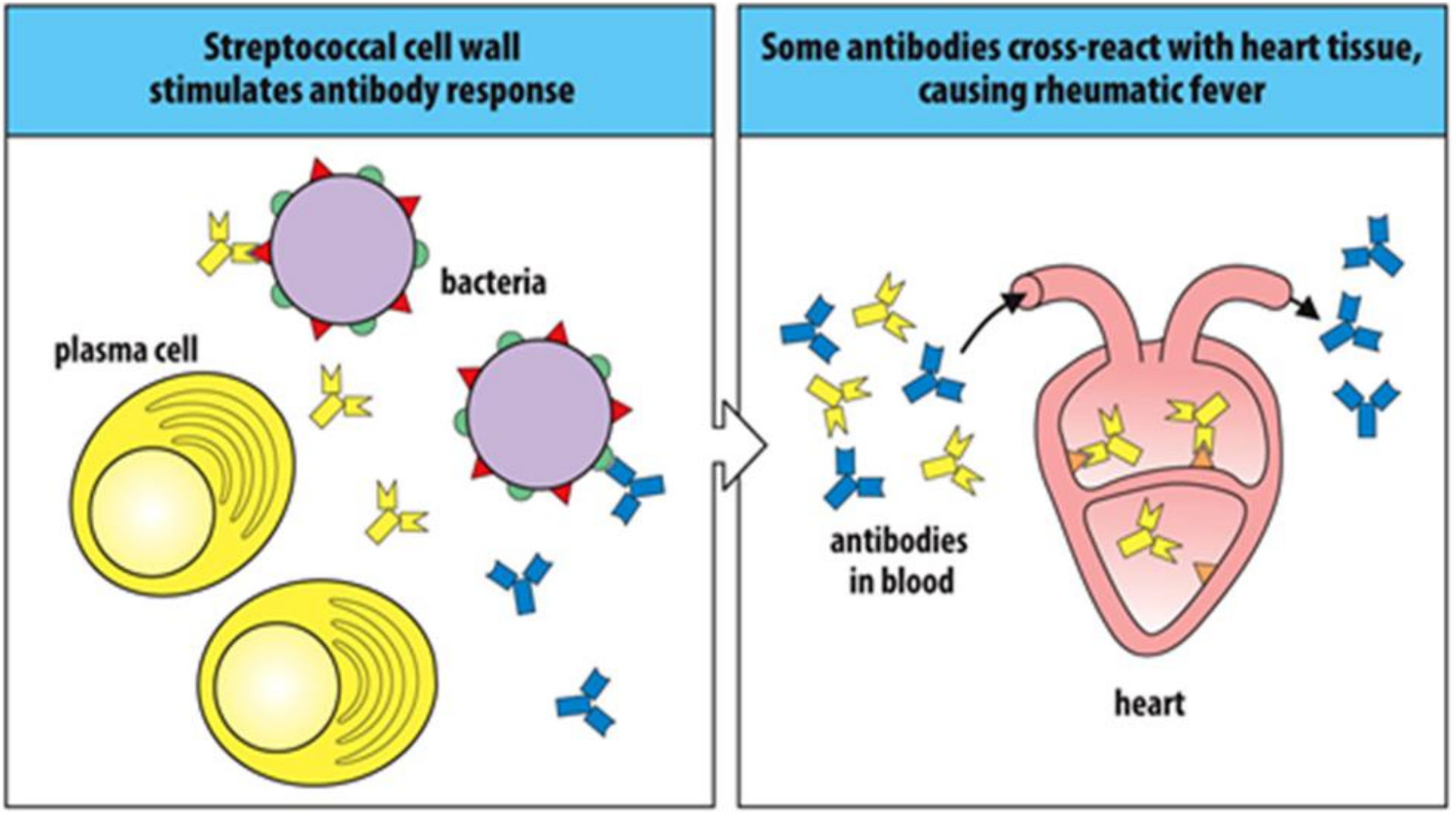
The most accepted mechanism is ***Molecular mimicry:***

➢*Streptococcus pyogenes* possess antigenic determinants **(M protein)** that are similar to **myosin** of the heart tissues.

➢In case of acute **strep throat** infection without antibiotic treatment → antibodies formed against **M protein of the pathogen** may cross-react with **myosin** of the heart tissues and cause rheumatic fever.

❑ Rheumatic fever is **not associated** with streptococcal **skin infections**

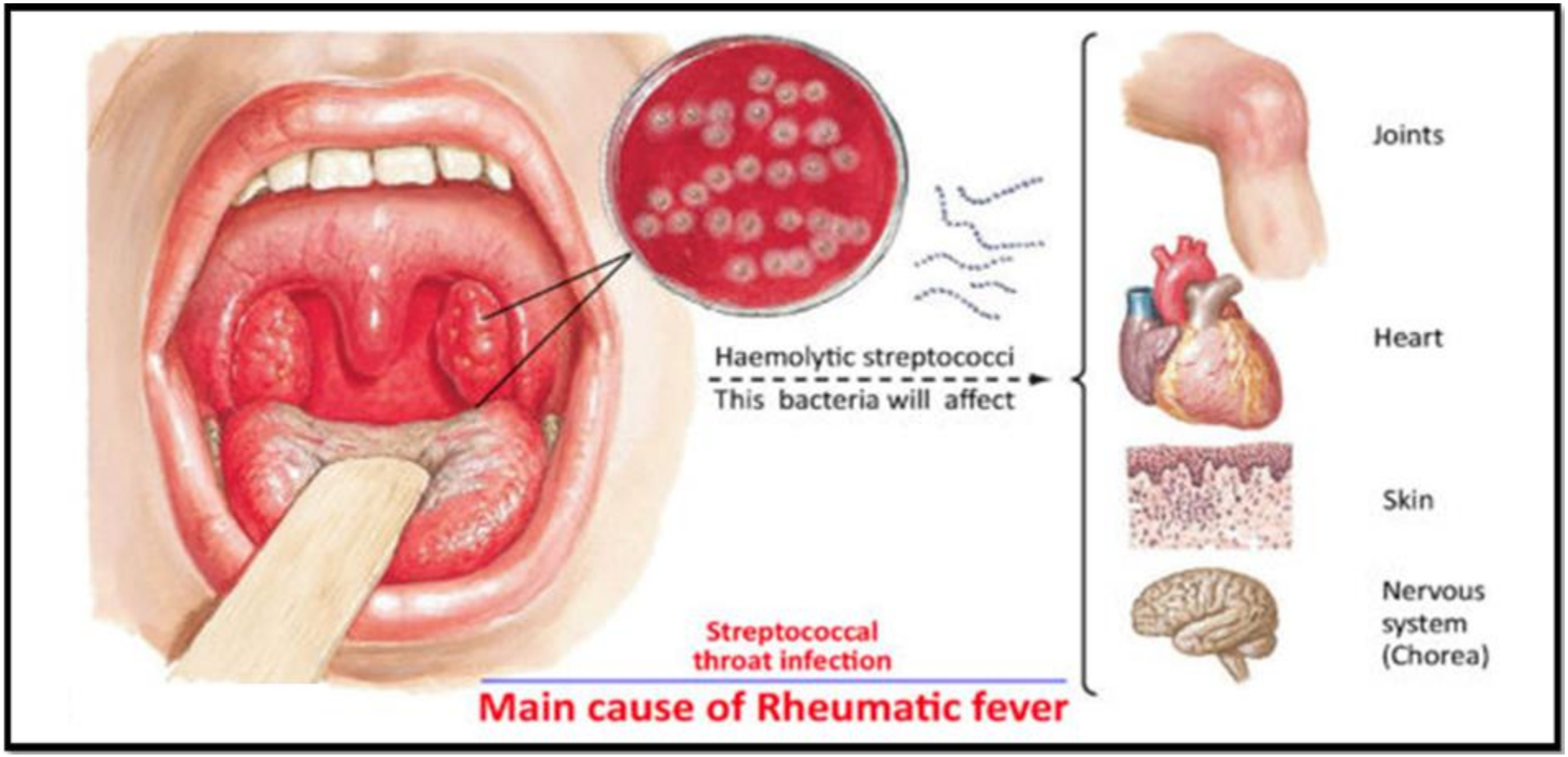
➢**Type II hypersensitivity reaction** → acute inflammatory sequel



Clinical features:

Constitutional symptoms (fever , malaise, fatigue) + (**J♥NES criteria)**:

- **Joints**: migratory poly-arthritis
- **Heart**: Pancarditis (endocarditis, myocarditis, and pericarditis).
- **Subcutaneous nodules**
- **Erythema marginatum:** Painless non-pruritic ring-like lesion on trunk
- **Sydenham chorea:** Involuntary irregular movements of the limbs, neck, head, and/or face.



- ***Chronic* valvular lesions** can occur as a complication of acute rheumatic fever

Diagnosis:

based on the **JONES criteria** + evidence of a preceding throat GAS infection as confirmed by laboratory test.

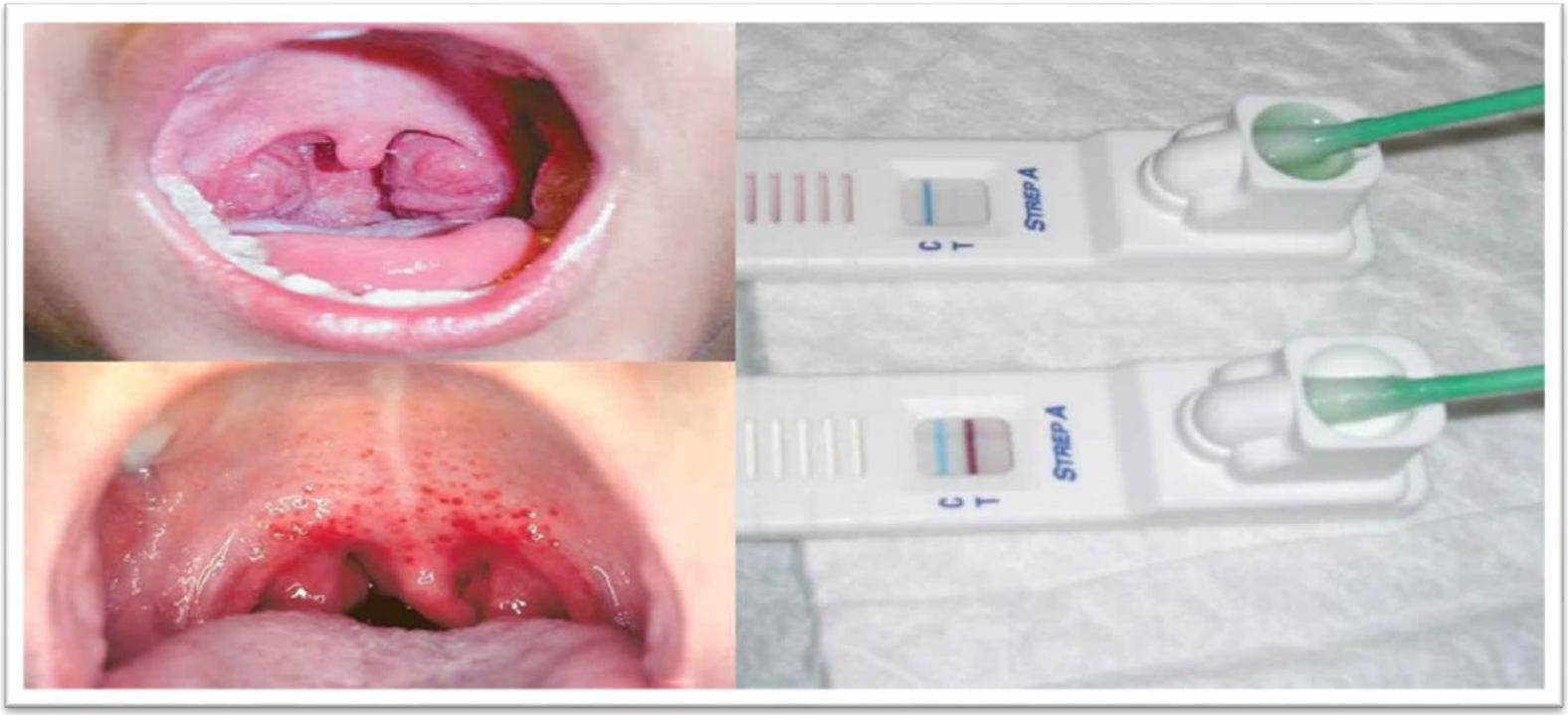
- ***Confirmation of GAS infection***
  - ↑ **Antistreptolysin O titer (ASOT)**
  - **Positive rapid streptococcal antigen** test from throat swab

Laboratory Tests

Specimens: Swabs from throat and blood for serology

N.B: Blood cultures are all **negative**

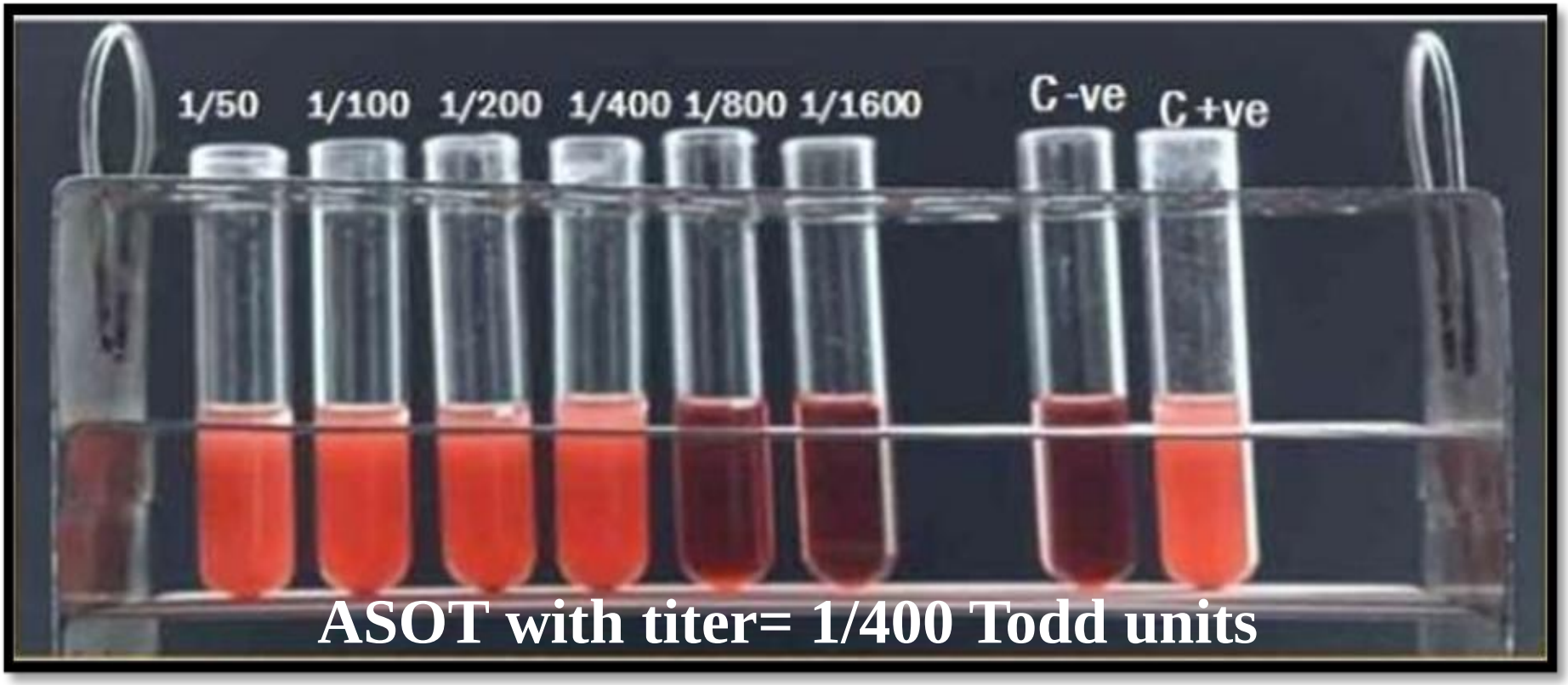
1. Rapid antigen detection test (RADT): in throat swabs. Negative result **doesn't confirm** the absence of GAS.



2. Streptococcal antibody tests:

a. Anti-streptolysin O test (ASO test):

- **Streptolysin O:** Protein toxin produced by GAS that causes lyses of RBCs (causes β-hemolysis when organism is cultured on blood agar)
- **ASO:** Host antibodies formed against the toxin.
- Antibody titers get raised within 1 week and reaches to the maximum level within 3-6 weeks post-infection.
- Anti-streptolysin O (ASO) antibody titers (≥ 200 Todd units) is **CONFIRMATORY for Rheumatic Fever**.



ASOT with titer= 1/400 Todd units

b. Antideoxyribonuclease B:

- Titers get raised within 1-2 week and it reaches to the maximum level within 6-8 weeks.

3- PCR based diagnosis assay:

- **more exact** than serology.
- helps in early **diagnosis** of rheumatic heart disease.

4- Acute phase reactants (ESR, CRP):

- Serum proteins synthesized by the liver.
- Elevated in cases of active RF as well as in other degenerative and inflammatory conditions.
- **A positive CRP, and a high ESR** are helpful in the diagnosis and follow up of cases of RF.

Complications:

- **Cardiac involvement** is the most important prognostic factor during an initial rheumatic fever episode.

- Early death in rheumatic fever is usually due to **myocarditis**.

- **Chronic valvular heart lesions** cause recurrent episodes of rheumatic heart disease.

Treatment:

- ***General measures:*** bed rest (especially important in patients with carditis)
- ***Antibiotics:*** to eradicate GAS
- ***Symptomatic treatment:*** of fever, arthritis and cardiac affection.
- ***Damage to the cardiac valves:*** interventional measures may be considered at least one year after the acute inflammatory phase.

- **Prevention:**

➢ Rheumatic fever is preventable if the patient is treated within the first 10 days following onset of acute pharyngitis.

➢ Prolonged **(**least 5 years) prophylactic antibiotic therapy (by beta lactams or macrolides) is indicated after an episode of rheumatic fever to reduce the risk of subsequent episodes if the patient is again infected with *S. pyogenes.*


TIME FOR QUESTIONS
12
1
2
3
4

MCQ:

1-which one of the following tests can diagnose prior infection with GAS in patients with acute rheumatic fever?

1. Blood culture.
2. Culture of a heart valve in a patient with carditis.
3. A high titer of antibody against the hyaluronic acid capsule.
4. A high titer of antibody against streptolysin O.

2-Which one of the following organisms causes tonsillopharyngitis, which may later be complicated by acute rheumatic fever?

1. *Staphylococcus aureus*
2. Group A β-hemolytic *streptococcus*
3. Group B *streptococcus*
4. *Enterococcus*

3-Which one of the following is not a clinical feature of acute rheumatic fever?

1. Migratory arthritis
2. Carditis
3. Sydenham's chorea
4. Painful skin rash

4-which one of the following describes acute rheumatic fever?

1. Direct tissue damage by the bacteria is responsible for the development of acute rheumatic fever
2. Genetic predisposition is not required for the development of acute rheumatic fever
3. It is usually diagnosed by positive blood culture
4. Immune mediated damage is the most widely accepted theory for the pathogenesis of acute rheumatic fever

5-Which of the following is the structure of GAS against which the antibody formed may cross react with the heart myosin and cause rheumatic fever?

1. Protein A
2. M protein
3. The capsule
4. Lipid A

Complete:

1. The most commonly accepted mechanism of rheumatic fever is …….

2. The main cause of rheumatic fever is type ……. Hypersensitivity reaction