“Rheumatic fever” licks the joints but bits the heart

Dr. Sudhakar Sarker
MBBS,MD,FSCAI,MACC,MESC
Assistant Professor (Cardiology)
Green Life Medical College

Objective

- Definition of Rheumatic fever
- Pathophysiology
- Clinical features with diagnostic criteria
- Management of Acute Rheumatic Fever (ARF)
- Rheumatic prophylaxis
- Long term outcome of acute rheumatic fever
- Case scenario with management
- Take home message

References:

- Davidson’s Principles and Practice of Medicine (23rd edition)

- Manual of Cardiovascular Medicine (Griffin, 5th Edition)

Definition

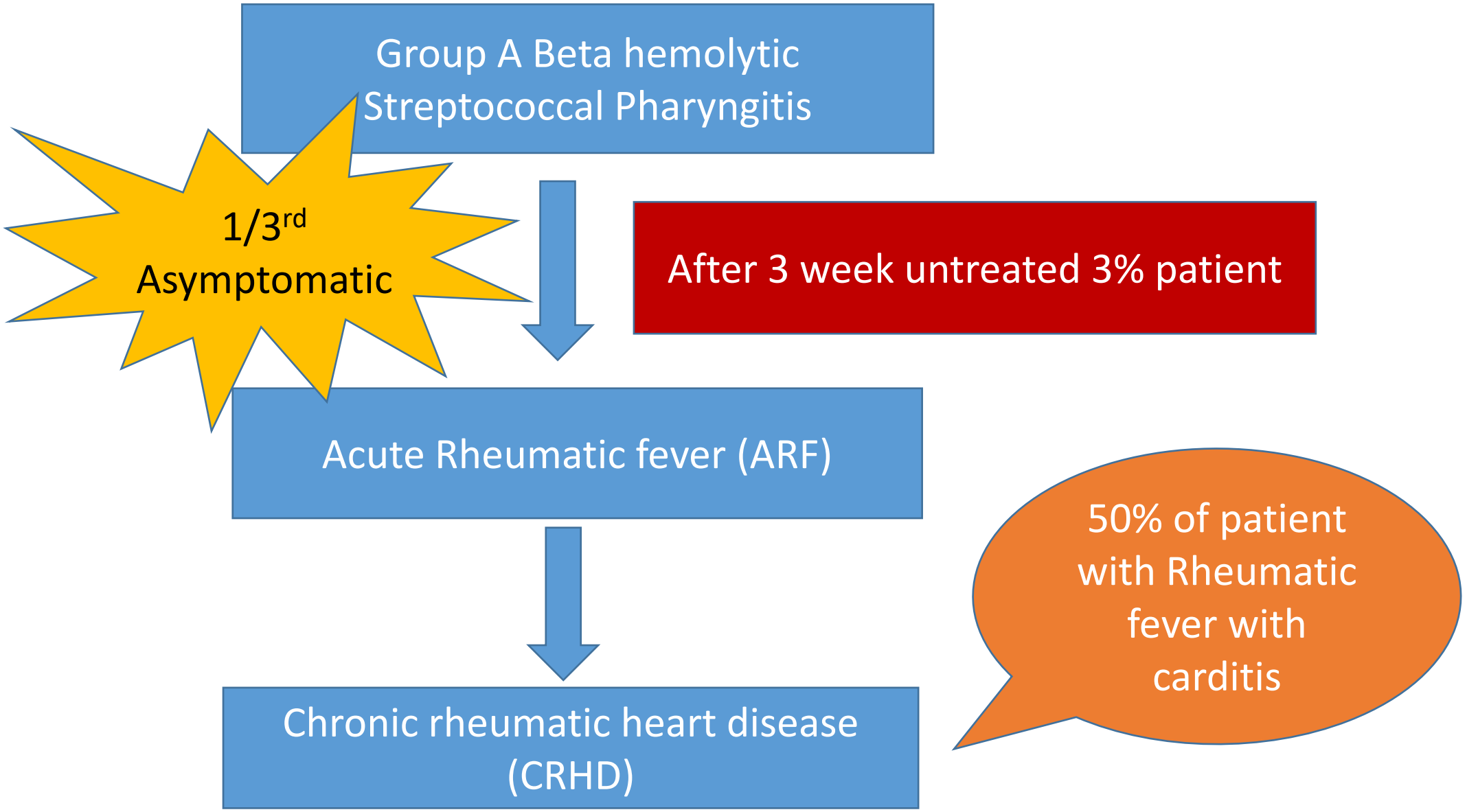
- Rheumatic fever is an immune mediated inflammatory disorder resulting from Group A Beta hemolytic streptococcal tonsillo-pharyngitis.

- It is a multisystem disorder involving heart, joints, brain and skin

Predisposing factors

- Overcrowding
- Poverty
- Poor nutrition
- Poor oral hygiene
- Poor access to health care
- Lack of primary and secondary prevention

- ✓Usually affects children and young adult
- ✓Between age 5 and 15 years
- ✓Rare in high income countries
- ✓Common in Indian subcontinent, Africa and south America
- ✓Incidence of RHD is 0.5 vs 13-150 cases per 10000 population between developed and underdeveloped country.


Group A Beta hemolytic Streptococcal Pharyngitis
1/3rd Asymptomatic
After 3 week untreated 3% patient
Acute Rheumatic fever (ARF)
Chronic rheumatic heart disease (CRHD)
50% of patient with Rheumatic fever with carditis

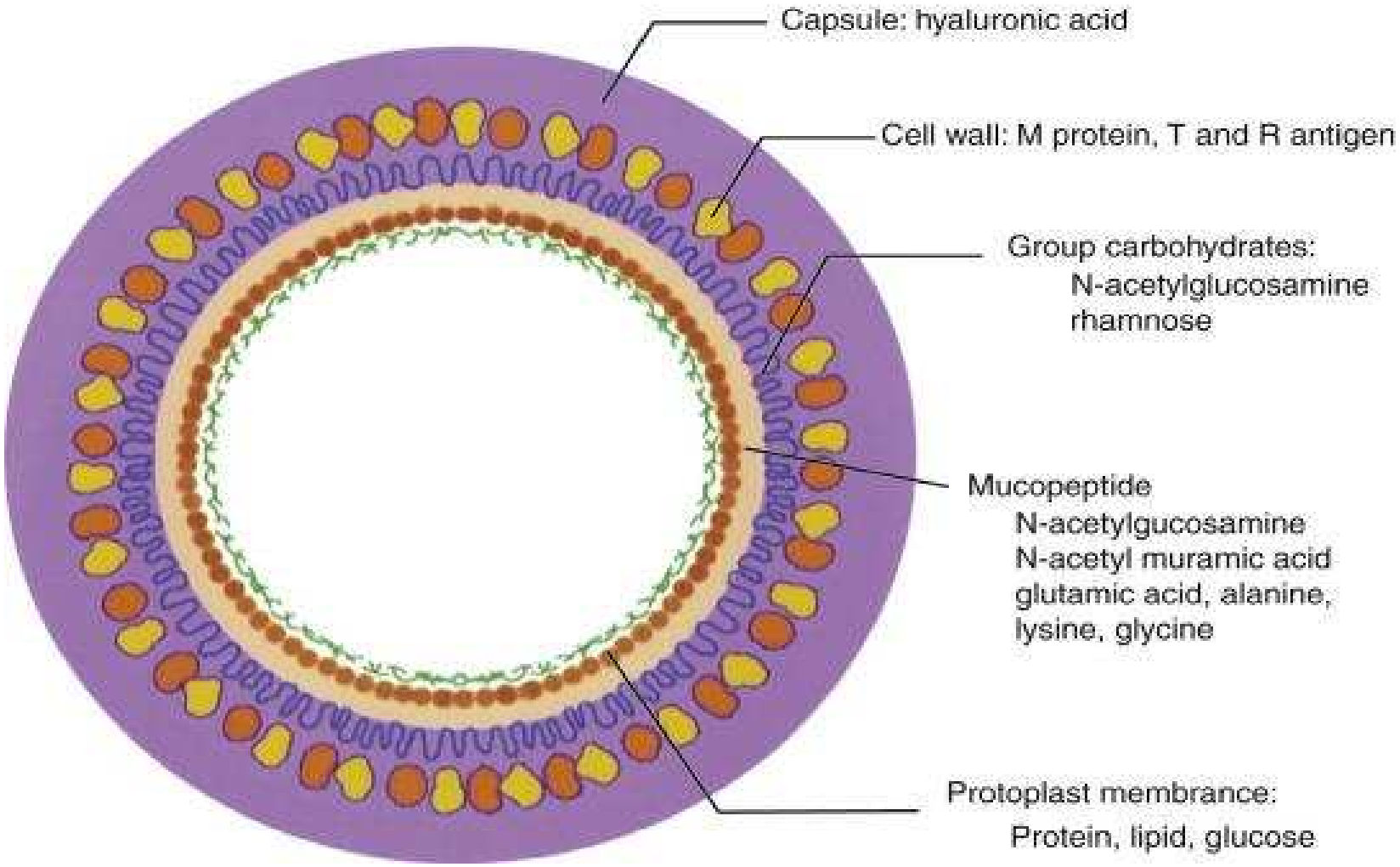
Pathogenesis: Phase 1:

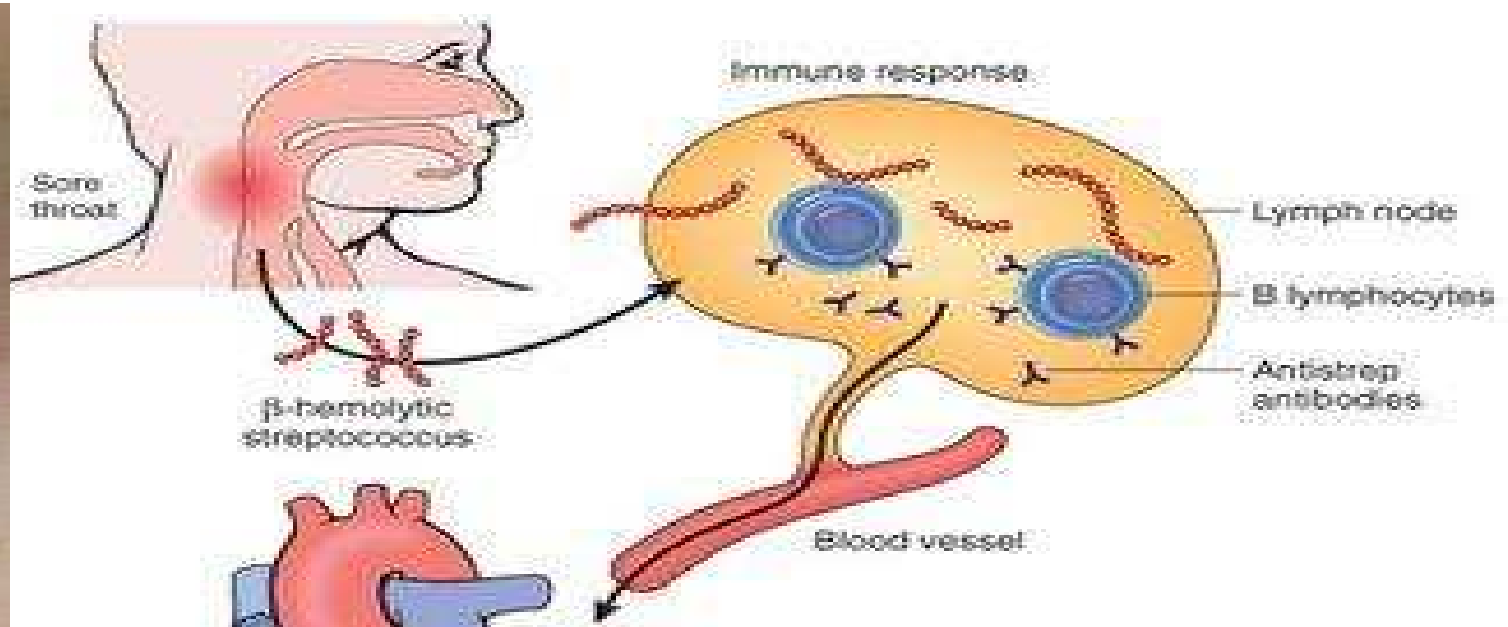
- β-hemolytic streptococcal (S.Pyogenes) **pharygitis** (Fever, sore throat)

- Formation of **antistreptococcal antibodies** which **cross reacts** with endogenous tissue antigens

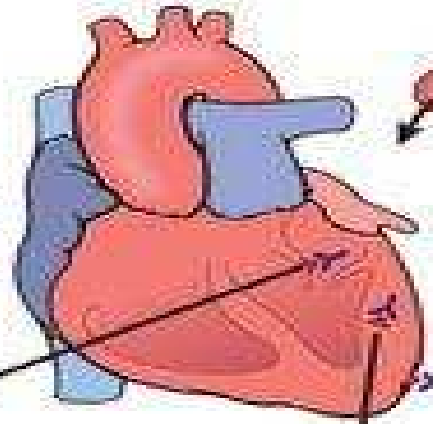
- In heart antibody against **Streptococcal M protein** cross reacts with Cardiac myosin and Sarcolemma

- In joints and other tissues antibody against **Streptococcal hyaluronic acid** cross reacts with connective tissue **proteoglycans**

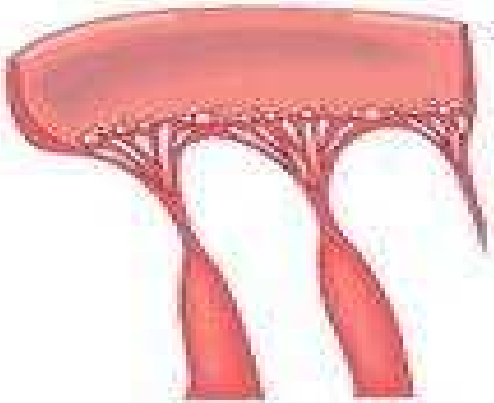

Capsule: hyaluronic acid
Cell wall: M protein, T and R antigen
Group carbohydrates:
N-acetylglucosamine
rhamnose
Mucopeptide
N-acetylgucosamine
N-acetyl muramic acid
glutamic acid, alanine,
lysine, glycine
Protoplast membrance:
Protein, lipid, glucose



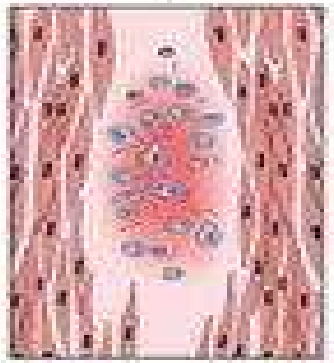
ACUTE RHEUMATIC HEART DISEASE



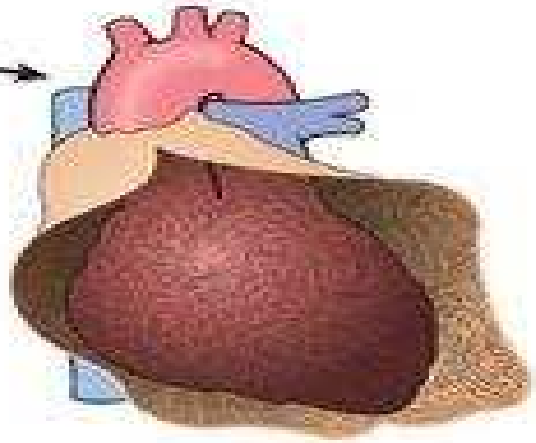
DEPOSITION OF CROSS-REACTIVE ANTIBODY



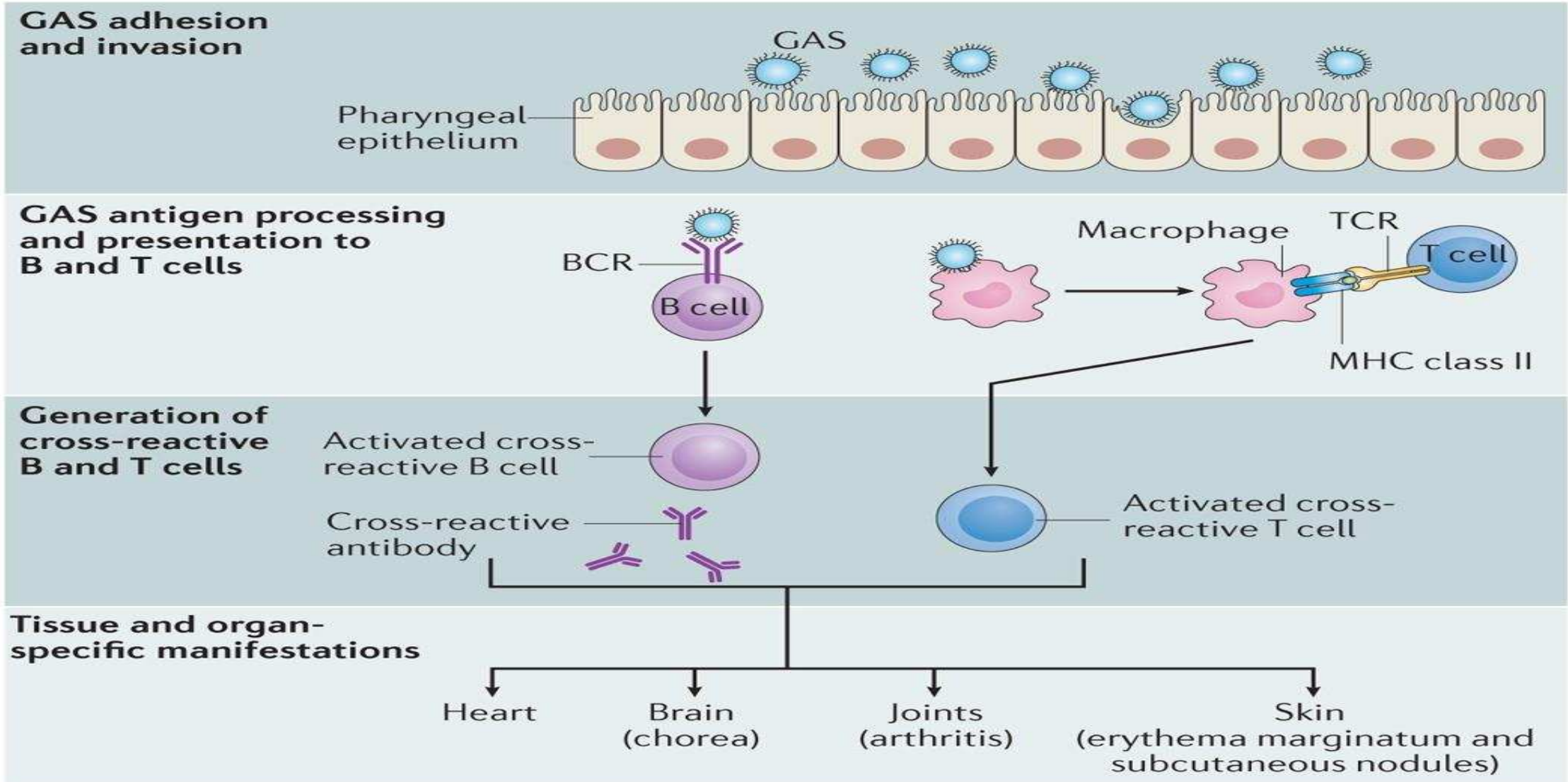
Vegetations



Myocardial Aschoff body



Fibrinous pericarditis


GAS adhesion and invasion
GAS
Pharyngeal epithelium
GAS antigen processing and presentation to B and T cells
BCR
B cell
Macrophage
TCR
T cell
MHC class II
Generation of cross-reactive B and T cells
Activated cross-reactive B cell
Cross-reactive antibody
Activated cross-reactive T cell
Tissue and organ-specific manifestations
Heart
Brain (chorea)
Joints (arthritis)
Skin (erythema marginatum and subcutaneous nodules)

Phase 2 (2-3 weeks Post-infection):

Heart: Carditis (50-70%)-most serious, most specific

- Pericarditis

  -Fever, chest pain, breathlessness

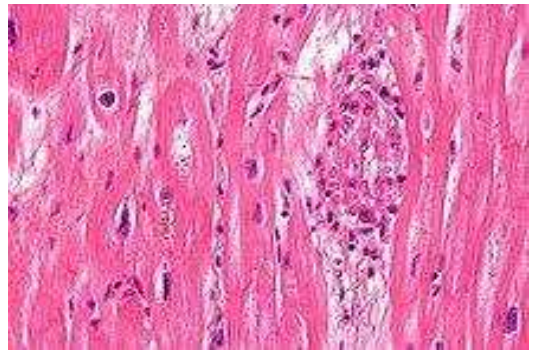
  -pericardial rub, pericardial effusion

- Myocarditis

  - Breathlessness due to heart failure, resting tachycardia.

- Endocarditis (Clinical/Subclinical-17%)

  - Breathlessness due to heart failure, Soft murmur of MR (Pansystolic), Carey Coombs murmur (mid diastolic),murmur of AR (Early diastolic)



- **Pancarditis:** Diffuse inflammation and Aschoff Bodies in any of the 3 layers of heart – pericardium, myocardium, endocardium (including valves)
- **Pericardium**: "Bread and Butter" Pericarditis (**Fibrinous or Serofibrinous)**
- **Myocardium:** Myocarditis (Scattered **Aschoff bodies** within interstitial connective tissue)
- **Endocardium:** Fibrinoid necrosis along the lines of closure of valves forming 1 to 2 mm vegetations (**verrucae**).

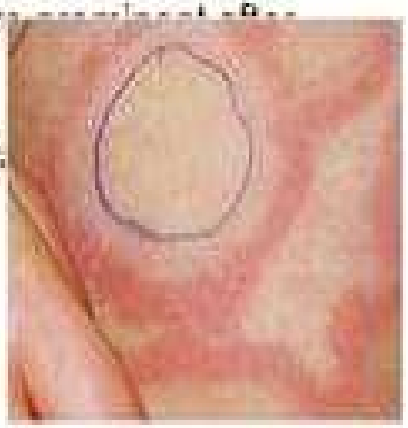
Rheumatic Verrucae

-Due to progressive inflammation causing necrotic collagen to project outwards from the valve, On which platelet thrombi deposit.
- Rheumatic verrucae occur on the atrial surface at sites of valve closure and on the chordae.
-The valves become edematous thickened and vascularised.

- Joints: Migratory arthritis
  - -Most common but less specific, affects 80% of patients
  - -Acute, painful, Asymmetrical and migratory large joint arthritis
  - -Benign and self limiting, usually cures within 4 weeks without any residual disability

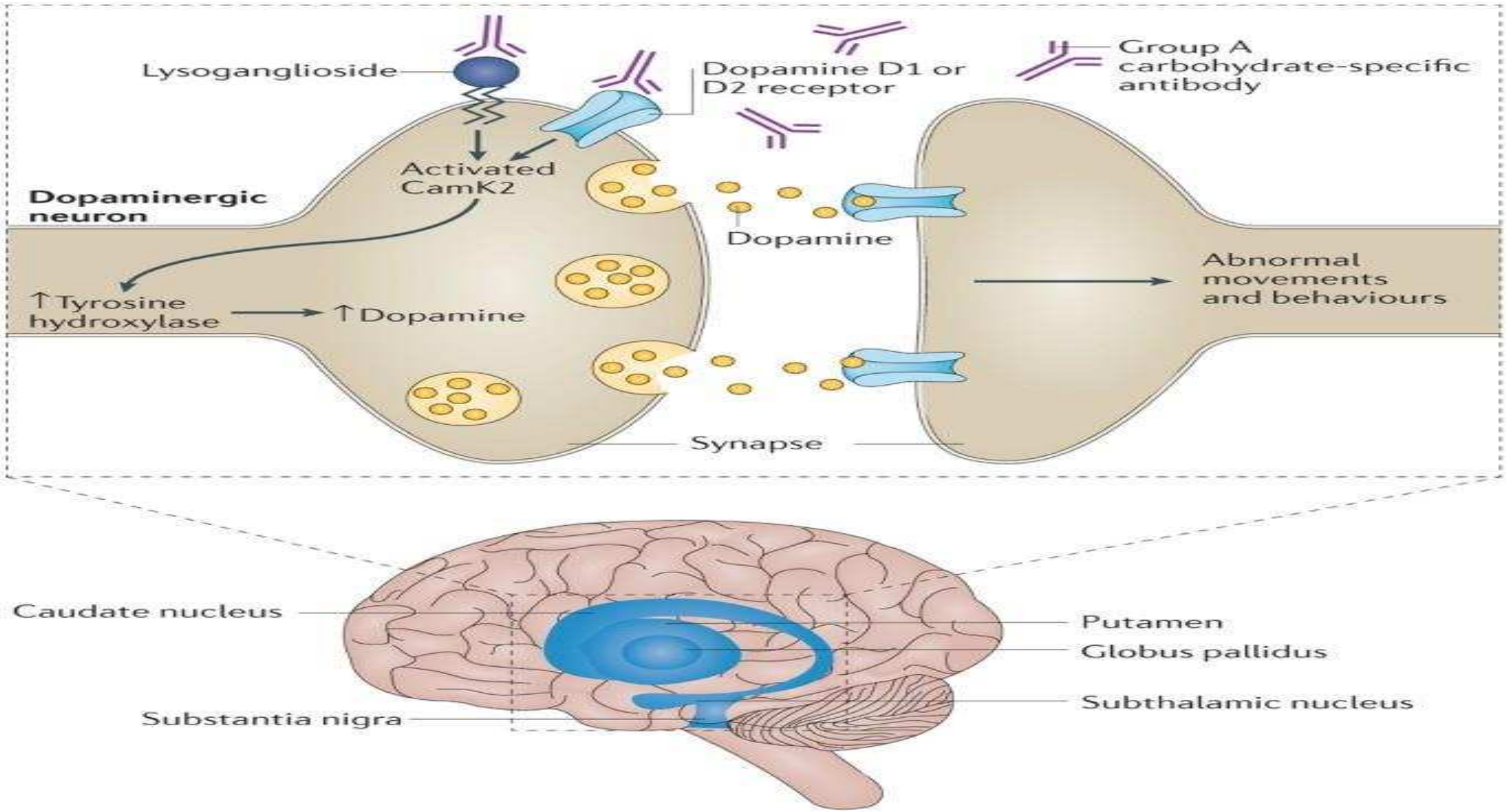
- Skin lesion
  - -Erythema marginatum (trunk, proximal extremities) <5 %
  - -Subcutaneous nodule (painless, extensor surface of bones) 20%

rheumatic fever
or trunk but not the
onpruritic.
an irregular,

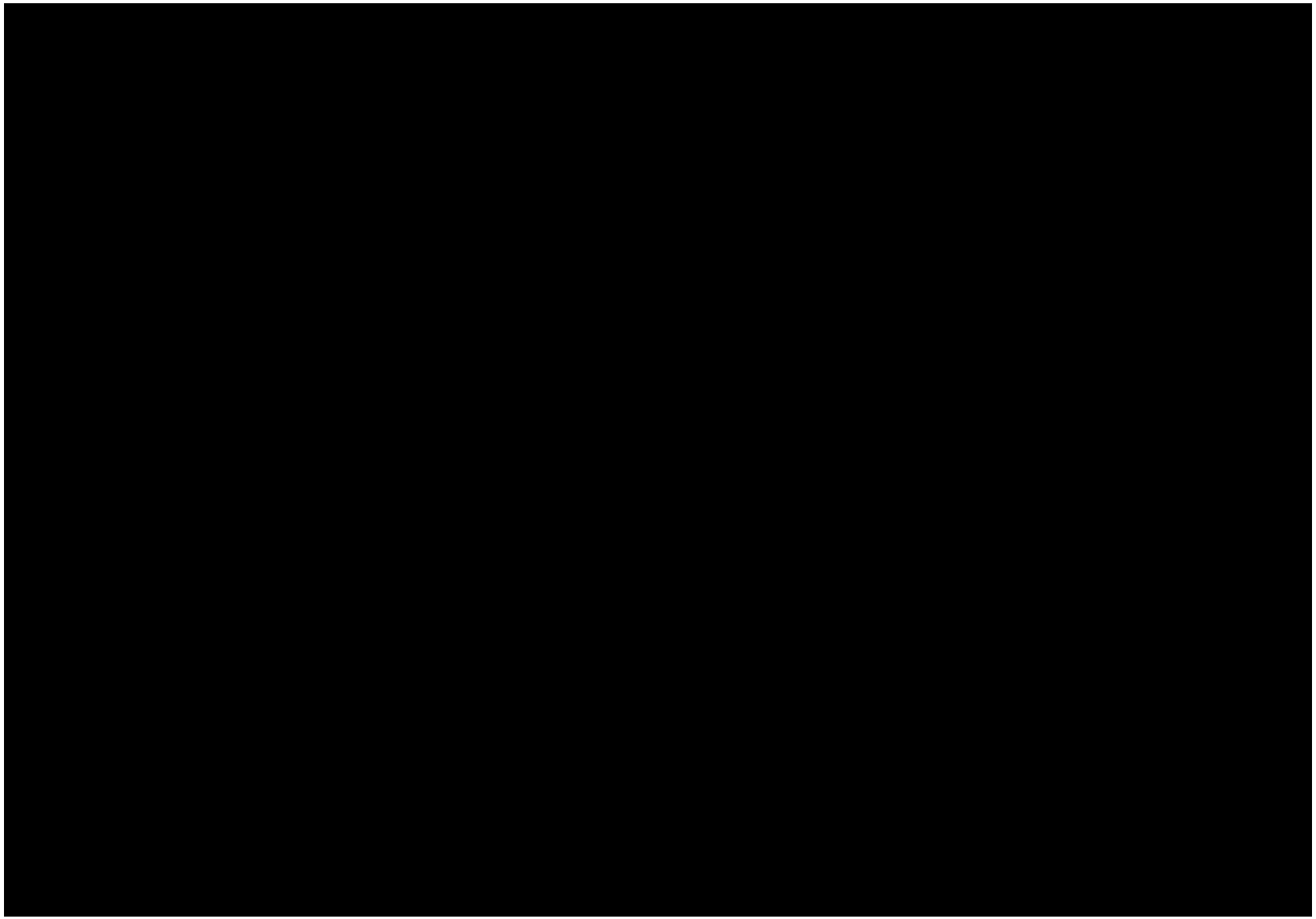


Source: Kevin J. Knoop, Lawrence B. Stack, Alan B. Storrow, R. Jason Thurman: The Atlas of Emergency Medicine, 3e

- Brain: Sydenham chorea (rare)
  - -Saint Vitus dance/ chorea minor
  - -Late neurological manifestation
  - -Affects after 3 months of pharyngitis
  - -Purposeless, involuntary movements of face, hands and feet
  - -Spontaneous recovery within few months
  - -Approximately 25% will develops CRHD



Nature Reviews | Disease Primers



Diagnosis of Rheumatic fever

Revised Jone's Criteria:

Major Criteria:

- Carditis
- Arthritis
  - -Polyarthritis only in low risk population
  - -Monoarthritis, Polyarthritis or Polyarthralgia in high risk population
- Sydenham Chorea
- Subcutaneous nodules
- Erythema Marginatum of Skin

Low risk population:
Incidence of ARF is ≤ 2 per 100000 school going children
or incidence of RHD ≤ 1 per 1000 all age population

Minor criteria:

- Fever
- Arthralgia
  - Polyarthralgia in low risk population
  - Monoarthralgia in high risk population
- Previous rheumatic fever
- Leukocytosis
- Raised ESR
- Raised CRP
- Prolonged PR interval on ECG (Exclude if Carditis is taken as major criteria)

Diagnosis of Rheumatic fever

≥ 2 major criteria

or

1 major criteria plus ≥ 2 minor criteria

Plus

Evidence of recent group A Streptococcal Pharyngitis

WHO criteria for diagnosis of rheumatic fever or Rheumatic heart disease

DIAGNOSTIC CATEGORIES	CRITERIA
Primary episode of RF	2 Mayor/1 Mayor+2 Minor manifestations + evidence of a preceding GAS infection
Recurrent attack of RF in a patient without established RHD	2 Mayor/1 Mayor+2 Minor manifestations + evidence of a preceding GAS infection
Recurrent attack of RF in a patient with established RHD	2 Minor plus evidence of a preceding GAS infection
Rheumatic chorea Insidious onset of rheumatic carditis	Other major manifestations or evidence of GAS infection not required
Chronic valve lesions of RHD	Do not require any other criteria to be diagnosed as having RHD

Investigations

- CBC (Leucocytosis, raised ESR)
- CRP
- ECG (AV block, ST-T changes,Resting tachycardia)
- Echo (Valvular dysfunction, Cardiomyopathy, Pericardial effusion)
- X ray chest (Cardiomegaly)
- Biopsy: Aschoff nodule
- To detect supportive evidence
  - ASO titre
  - Throat swab culture

Management of ARF

- **Bed rest** (Very important in carditis and arthritis)
  - Duration is guided by symptoms, ESR and CRP

- **Treatment of arthritis:** (Aspirin/NSAID/Steroid)

  1. Aspirin

  -Responds within 24 h

  -Starting dose is 60 mg/Kg/day in 6 divided dose

  -In adult 100 mg/Kg/day, maximum dose 8 gm/day

  -Should be continued until ESR fallen, then gradually tailed off.

2.Steroid

-Produce more rapid symptomatic relief than aspirin

-Prednisolone 1-2 mg/Kg/day (Maximum 60 mg/day) in divided dose

-Should be continued until ESR fallen, then gradually tailed off.

-Start Aspirin during tapering phase and continue for 3-4 week after discontinuation of steroid.

- **Treatment of cardiac failure**

  -Medications, Valve replacement, Permanent pacemaker (PPM)

Primary prevention

- Patient has pharyngitis but don’t develops rheumatic fever yet therapy started **as late as 9 days** after onset of pharyngitis is still effective to prevent acute rheumatic fever.

❖Benzathine benzylpenicillin IM 1.2 mu (weight ≥ 27 kg),
0.6 mu(≤ 27 kg) single dose

OR

❖Phenoxymethyl penicillin 250 mg 4 times daily for 10 days

OR

❖Azithromycin/Erythromycin/Cephalosporin/Amoxicillin

Secondary prevention

- To prevent recurrent attack of Rheumatic fever
- Should be started as soon as possible after diagnosis of Rheumatic fever or Rheumatic heart disease

❖Benzathine benzylpenicillin IM 1.2 mu (weight ≥ 27 kg)

0.6 mu(≤ 27 kg) once monthly

OR

❖Phenoxymethyl penicillin 250 mg 2 times daily

OR

❖Azithromycin/Erythromycin/Cephalosporin

Duration of secondary prophylaxis

Disease state	Duration of therapy
RF without Carditis	5 year or until the age 21 year whichever is longer
RF+ Carditis without valve involvement	10 year or until the age 25 year whichever is longer
RF+ Carditis+ mild valve disease	10 year or until the age 40 year whichever is longer
RF+ Extensive valve disease or Valve surgery	Life long

Fate of acute rheumatic fever

- Spontaneous recovery in most of the cases

- 50% of patient with acute rheumatic fever with carditis develops chronic rheumatic heart disease

- **Valvular involvement**
  - >90% mitral valve
  - 5% mitral and aortic
  - <3% Isolated aortic valve
  - Tricuspid and pulmonary valve very rare

Chronic Rheumatic Heart Disease:

- Organization of Acute Inflammation and Subsequent Fibrosis**:**
- Valve leaflet thickening
- Commisural fusion and calcification
- Thickening and fusion of chordae tendinae
- “**Fish mouth” or “Button hole” Stenoses:** Fibrous bridging across the valvular commisures and calcification

Longterm Consequences:

- Valvular stenosis and regurgitation
- Stenosis > Regurgitation
- Dilated left atrium
- Pulmonary hypertension
- RV failure (Leg edema, Ascites, hepatomegaly, raised JVP)

Case scenario

- Mr X, 25 year old, non diabetic, normotensive, non smoker presented with palpitation for 1 day and exertional breathlessness for last 2-3 years.

- Palpitation started spontaneously associated with aggravation of breathlessness at rest, not associated with chest pain, tea or coffee intake or syncopal attack. There was no history of haemoptysis or hoarseness of voice.

- He gave history of recurrent attack of sore throat with fever with irregular intake of antibiotic, no history of joint pain, skin changes and movement disorder. He lives in lower socioeconomic condition, no other family members were affected with such illness and denied any immunization history.

On general examination

-**Pulse:**110/min, irregularly irregular, low volume, pulse deficit 30/min, no radioradial or radiofemoral delay

-**BP :** 90/60 mmHg

-**JVP:** raised with absent a wave

-B/L pitting type pedal edema

-non anemic, non icteric, no lymphadenopathy, no bony tenderness

Examination of precordium

-Apex beat normal in position

-Tapping in nature

-Diastolic thrill on apical area

-Left parasternal heave present

-P2 was palpable

On auscultation :

-First heart sound was variable, P2 was loud

-There was mid diastolic murmur on apical area

-Low pitch localized, rough rumbling

-Best heard with the bell of stethoscope in left lateral position

-There was opening snap

-**No presystolic accentuation**

-Pansystolic murmur over left lower sternal edge, no radiation

-Lung base were clear

- Examination of other system were normal

Provisional diagnosis:

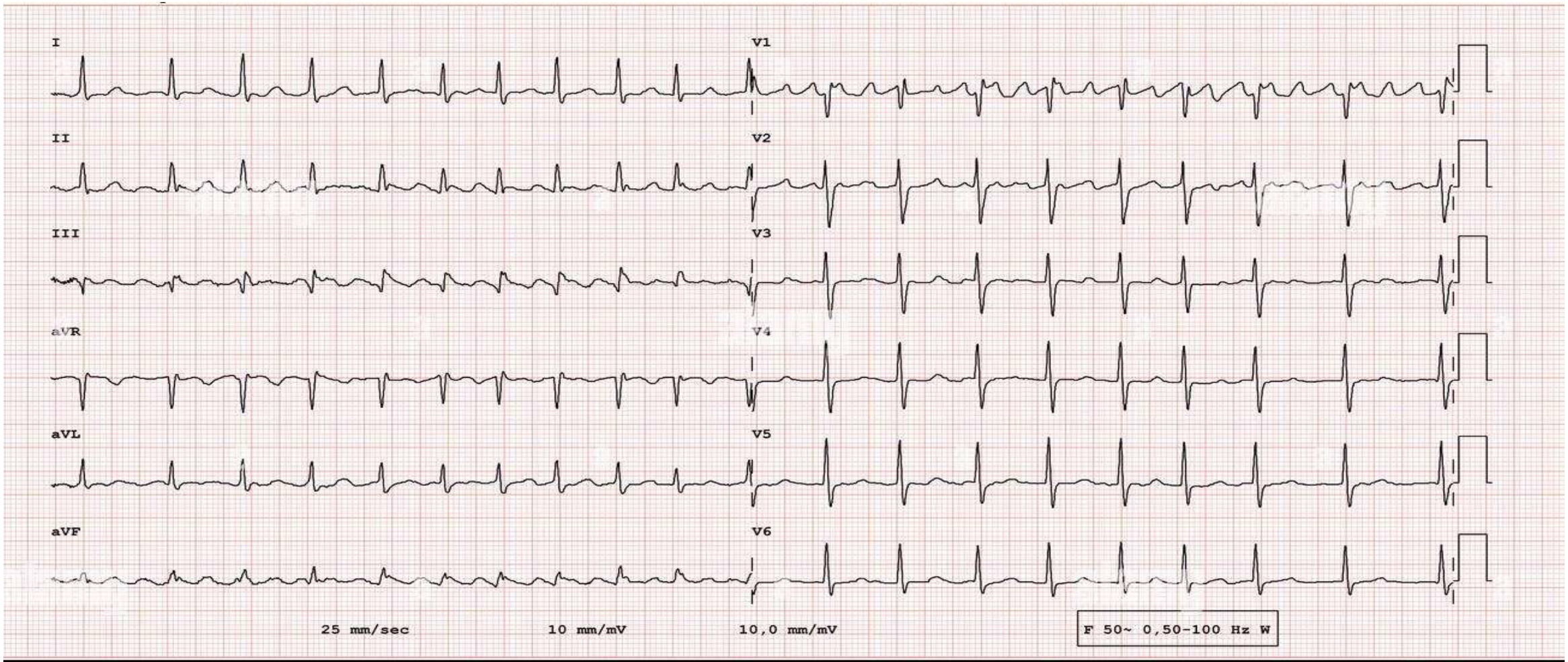
Mitral stenosis, Atrial fibrillation, TR with Pulmonary hypertension, RV failure

Differrential diagnosis:

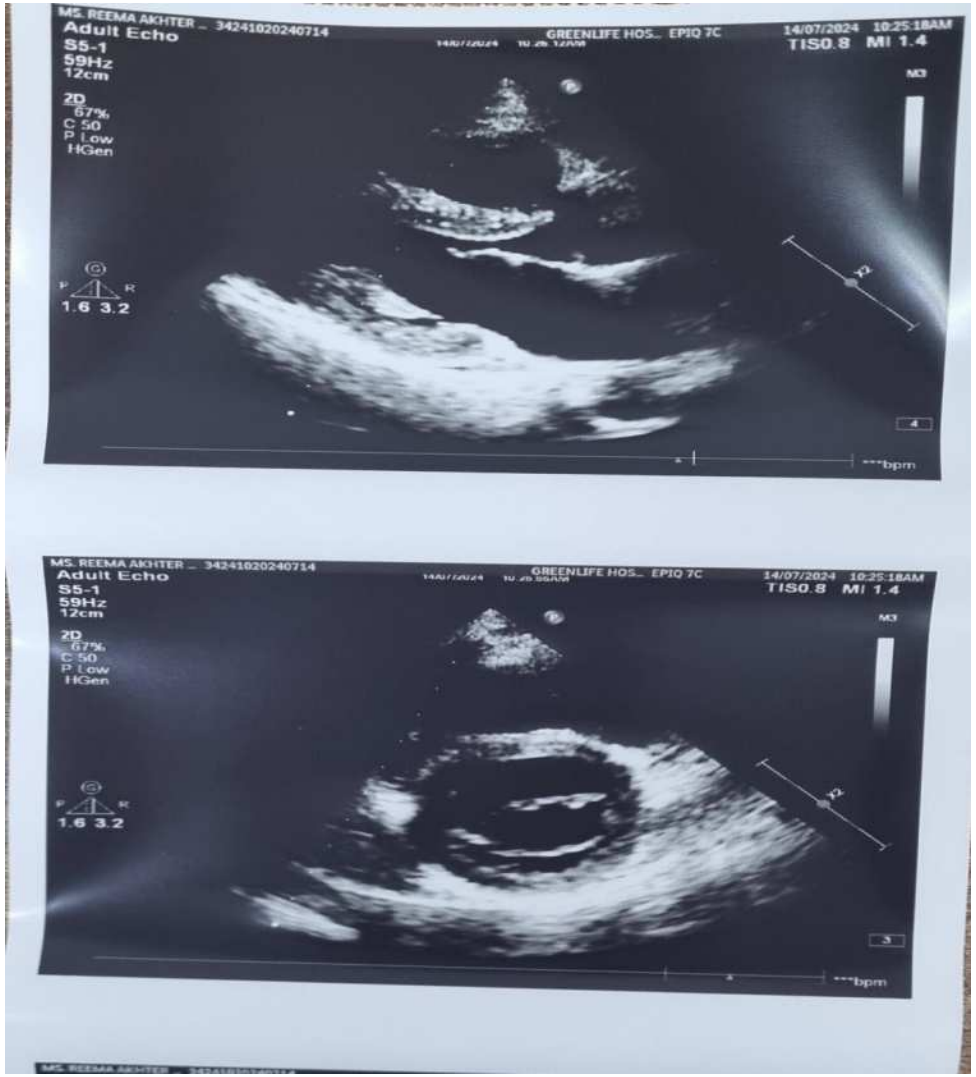
Left atrial myxoma

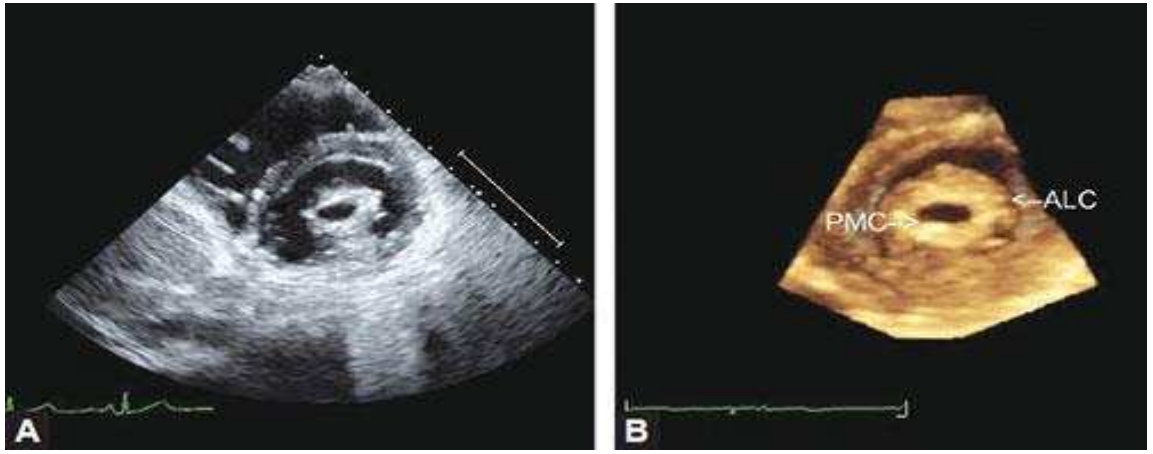
Investigation

- ECG



Normal vs Rheumatic mitral valve





- Straightening of left heart border
- Enlarged left atrium, RV type apex
- Double right heart border
- Upper lobe diversion
- Widening of tracheal carina

All other routine investigations were normal

Final diagnosis

Chronic Rheumatic heart disease
Severe mitral stenosis-Wilkin’s score 8/16
Severe TR with Severe pulmonary hypertension (PASP 80 mmHg)
Atrial fibrillation with fast ventricular rate
Right ventricular failure

Management

- **Management of Atrial fibrillation**

-**Rate control:** Beta blocker, Digoxin, Amiodarone, rate limiting CCB

-**Rhythm Control:** Amiodarone, DC shock, Pace and ablate therapy

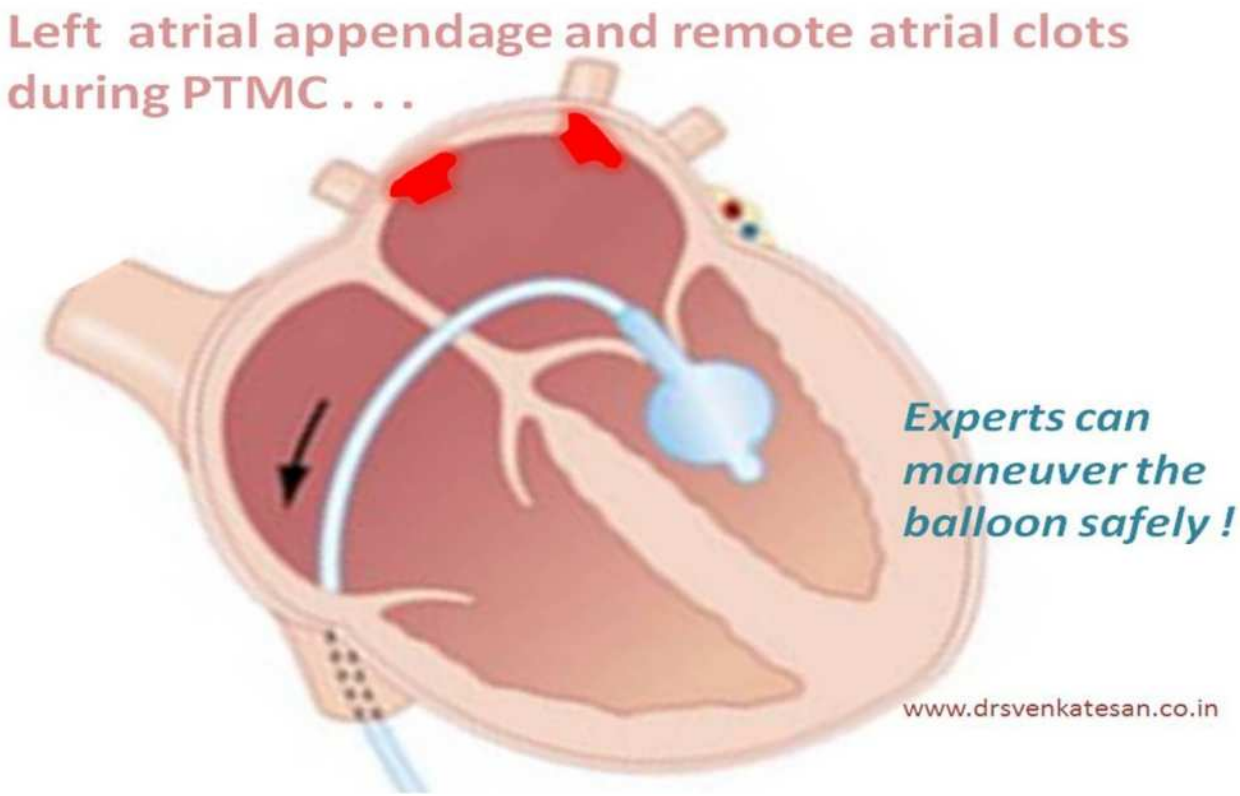
-**Prevention of thromboembolism:** Anticoagulant (Warfarin,heparin)

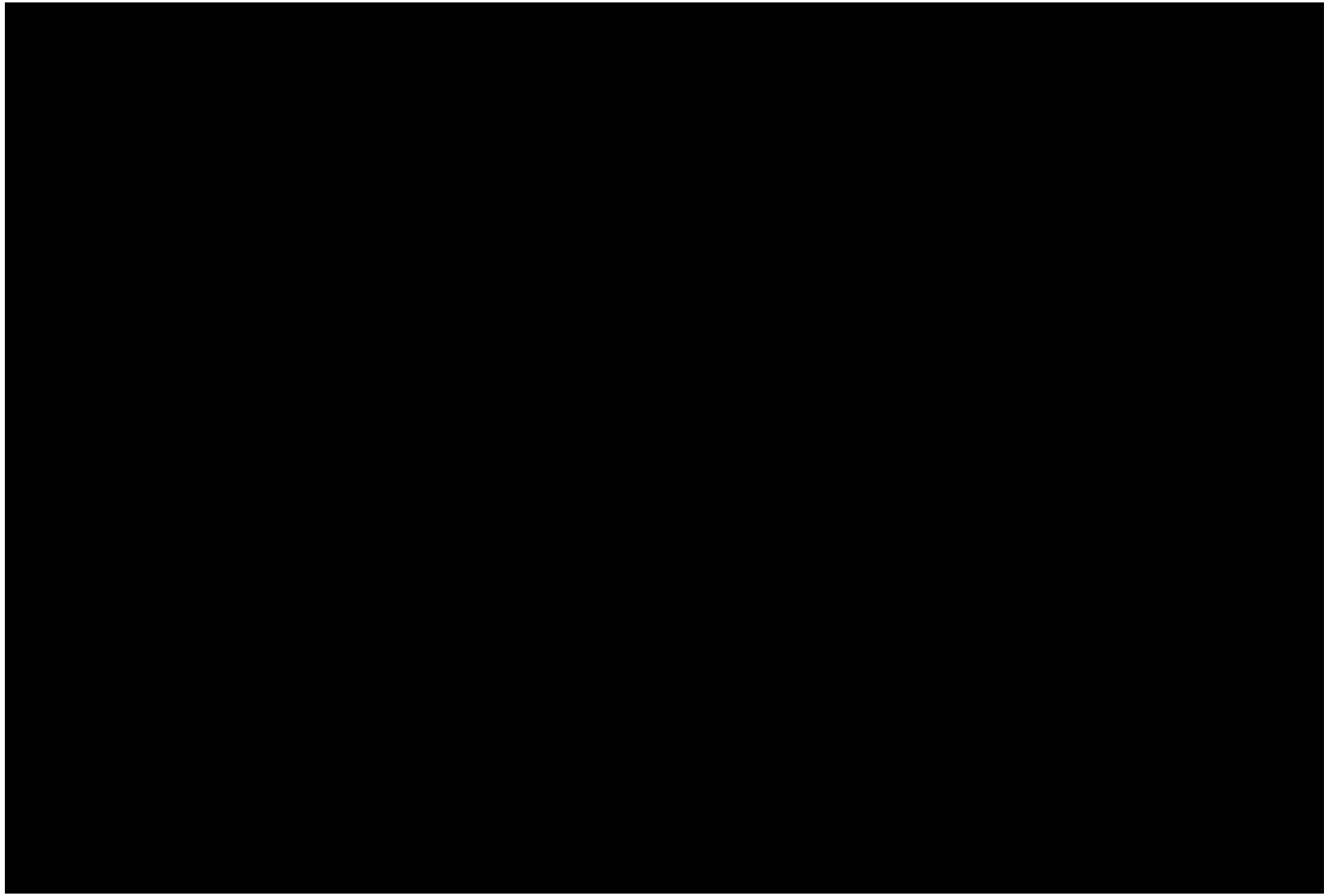
Treatment of underlying cause: Mitral stenosis

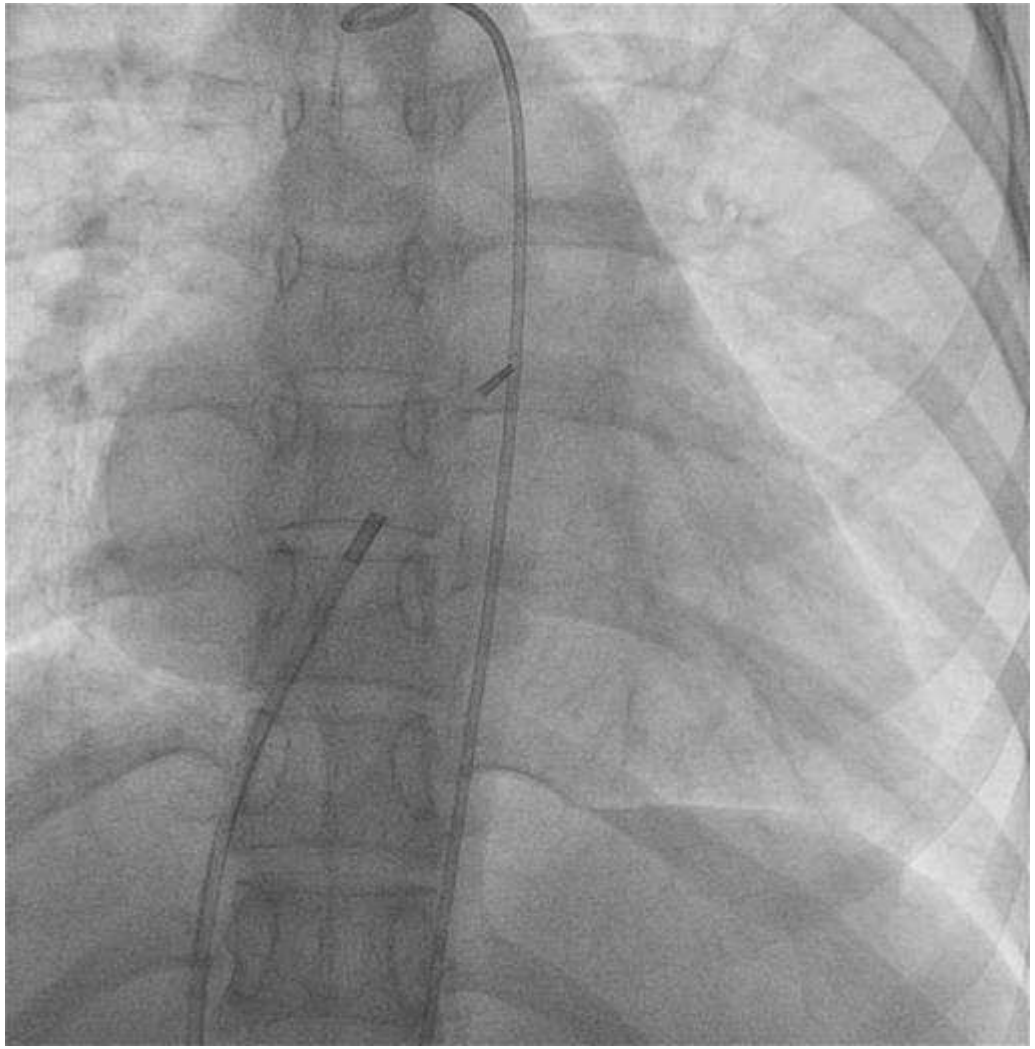
- Baloon valvuloplasty-PTMC (Percutaneous Transluminal Mitral Commissurotomy)
- Mitral valvotomy-Open/closed
- Mitral Valve replacement (MVR)

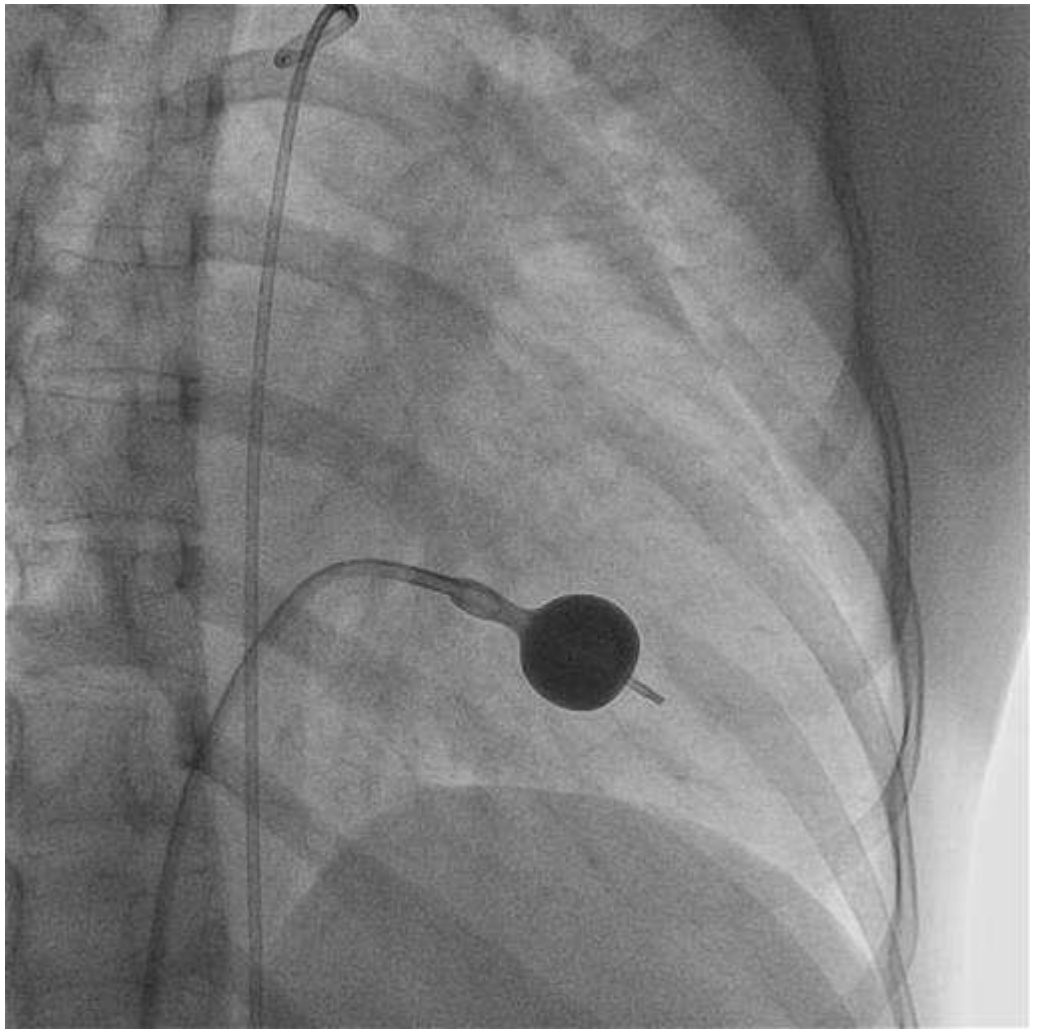
Without advance treatment
- 40% mortality at 10 year
- 80% mortality at 20 year

We have treated our patient by PTMC







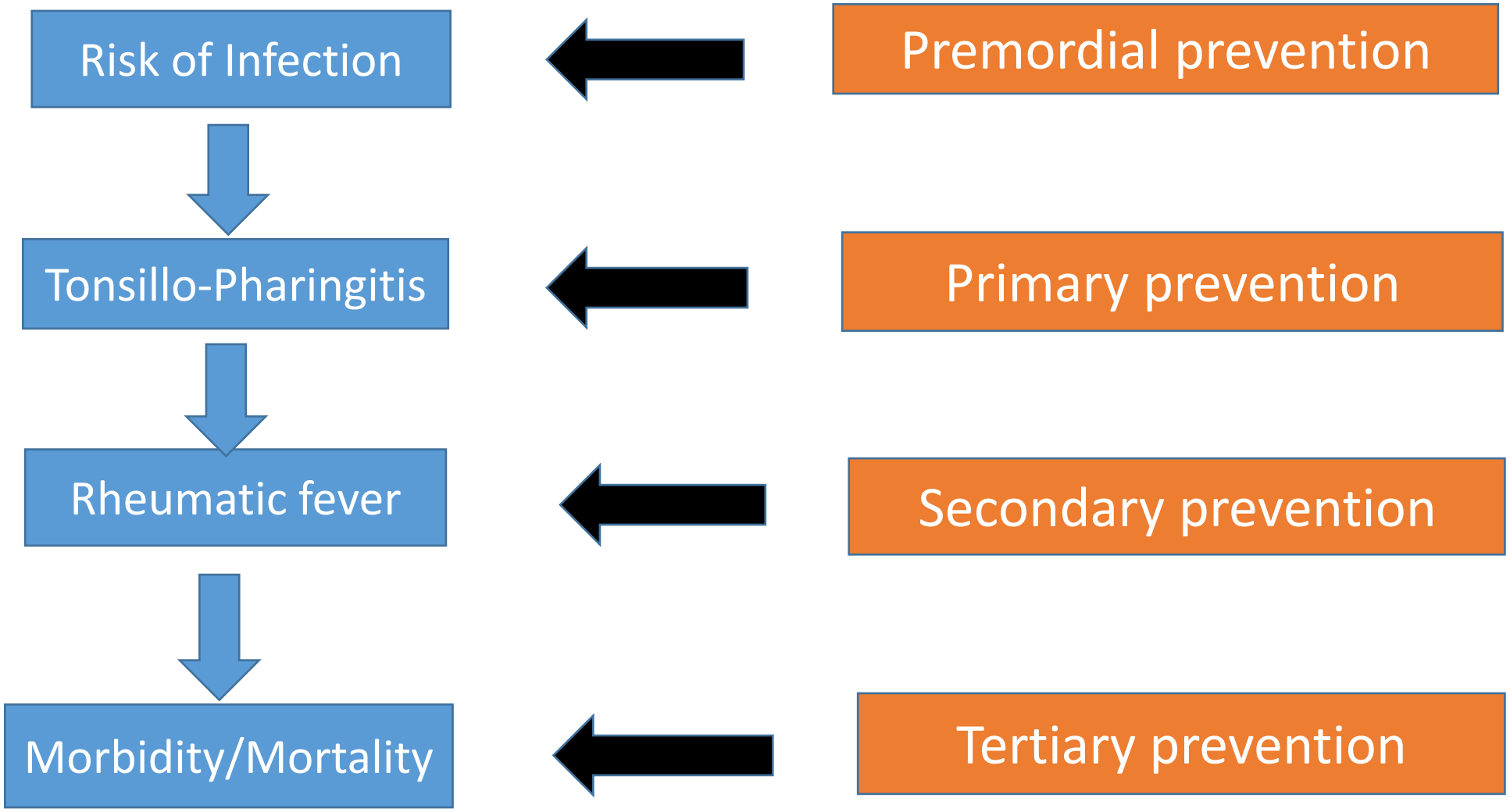


Life long medication

- Phenoxymethyl Penicillin 250 mg twice daily
- Beta blocker or rate limiting CCB
- May need digoxin
- Diuretic
- Warfarin

In future
PTMC /MVR

Model of prevention



Take home message

- Now a days acute rheumatic fever is very rare due to wide use of antibiotic
- However chronic rheumatic heart disease is still very common
- Arthritis with joint deformity think other causes of arthritis
- Raised ASO titre without other manifestation is not a indication for long term rheumatic prophylaxis
- In patients with tonsillo-pharyngitis prescribe proper antibiotic with adequate dose and duration to prevent acute rheumatic attack.


THANK
YOU!