Myocarditis (especially viral) in children and adolescents

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MYOCARDITIS

- Is it an infective disorder?

The World Health Organization has defined myocarditis as an inflammatory myocardial disease diagnosed by a combination of histologic, immunologic, and immunohistochemical criteria

MYOCARDITIS- Dilated CMP

Myocarditis is collection of diseases of infectious, toxic, and autoimmune etiologies characterized by inflammation of the heart.

Subsequent myocardial destruction and fibrosis can lead to dilated cardiomyopathy.

CAUSES

- Amongst the infectious causes, viral acute myocarditis is by far the most common.
  - Especially the coxsackie-adenovirus-parvovirus
  - Other viruses implicated in myocarditis include influenza virus, echovirus, herpes simplex virus, varicella-zoster virus, hepatitis, Epstein-Barr virus, and cytomegalovirus.
  - Human immunodeficiency virus (HIV)

CAUSES

- Nonviral infectious causes are numerous and varied.
- Bacteria: chlamydia (*C. pneumonia*/psittacosis) haemophilus influence, brucella, clostridium, neisseria meningitis, mycobacterium (tuberculosis), salmonella, staphylococcus, streptococcus A, S. pneumonia
- Spirocheta: *Borrelia*, leptospira, *Treponema pallidum*
- Reckettsia: *Coxiella burnetii*, *R. rickettsii*/*prowazekii*
- Protozoa: *Entamoeba histolytica*, leishmania, *Plasmodium falciparum*,*Trypanosoma*
- Helmintic: ascaris, *Echinococcus granulosus*, Schistosoma, *Trichinella spiralis*,*Wuchereria bancrofti*

CAUSES

- Toxic myocarditis has a number of etiologies including both medical agents and environmental agents.

  - Numerous medications eg, lithium, doxorubicin, cocaine hydrochlorothiazide, methyldopa.

CAUSES

- Environmental toxins include lead, arsenic, and carbon monoxide.
- Scorpion, and spider stings
- Radiation therapy

CAUSES

- Immunologic etiologies of myocarditis encompass a number of clinical syndromes and include the following:
  - Connective tissue disorders such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and dermatomyositis.

Infective especially viral myocarditis

PATHOPHYSIOLOGY

Several mechanisms of myocardial damage

(1) Direct injury of myocytes by the infectious agent

(2)Myocyte injury caused by a toxin such as that from *Corynebacterium diphtheriae*

(3)Myocyte injury as a result of infection-induced immune reaction or autoimmunity

PATHOPHYSIOLOGY

A Host Response

The clinical course observed in patients with myocarditis is related to balance of infectious agents and host immune interactions during the different phases of disease. The initial *acute phase* is marked by viral infection and subsequent dissemination.

The virus causes direct damage to the myocytes and also leads to host immune activation by binding to cell receptors

PATHOPHYSIOLOGY

In the final *chronic phase*, there is resolution of the host immune inflammatory response with viral clearance and resolution of clinical symptoms.

In some patients, there is a persistent inflammatory response with ongoing tissue damage, remodeling, and scar formation, with or without viral persistence, leading to dilated cardiomyopathy and heart failure.

Pathophysiology

Triphasic disease process

- Acute Phase: Characterized by direct infiltration of cardiotropic virus into myocytes.
- Subacute Phase: Host attempts to clear the virus. Natural Killer cells, Macrophages, and Lymphoctes infiltrate infected heart tissue. There is subsequent pro-inflammatory cytokine release, antibody secretion.
- Chronic Myocarditis: Dilated heart with evidence of fibrosis

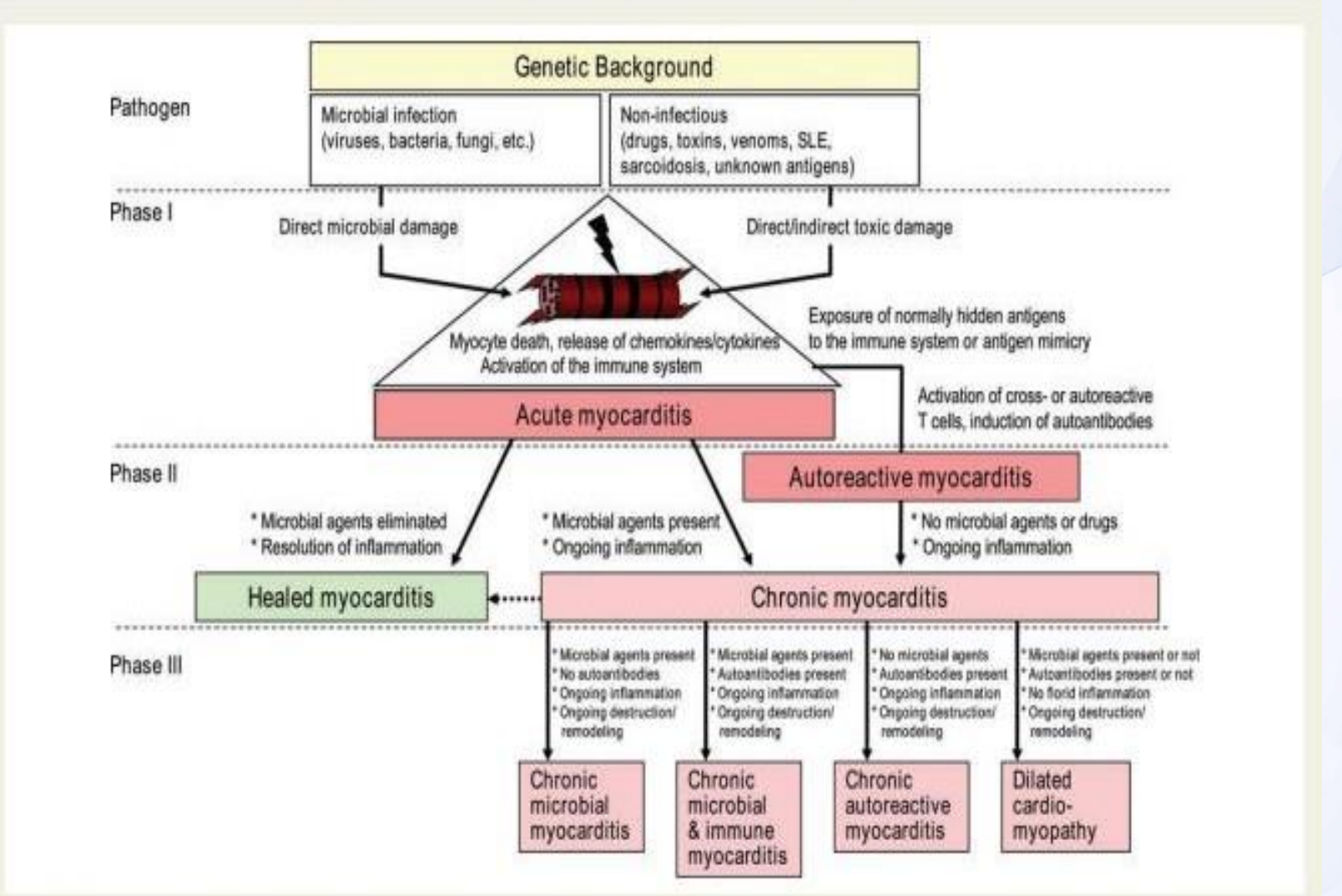
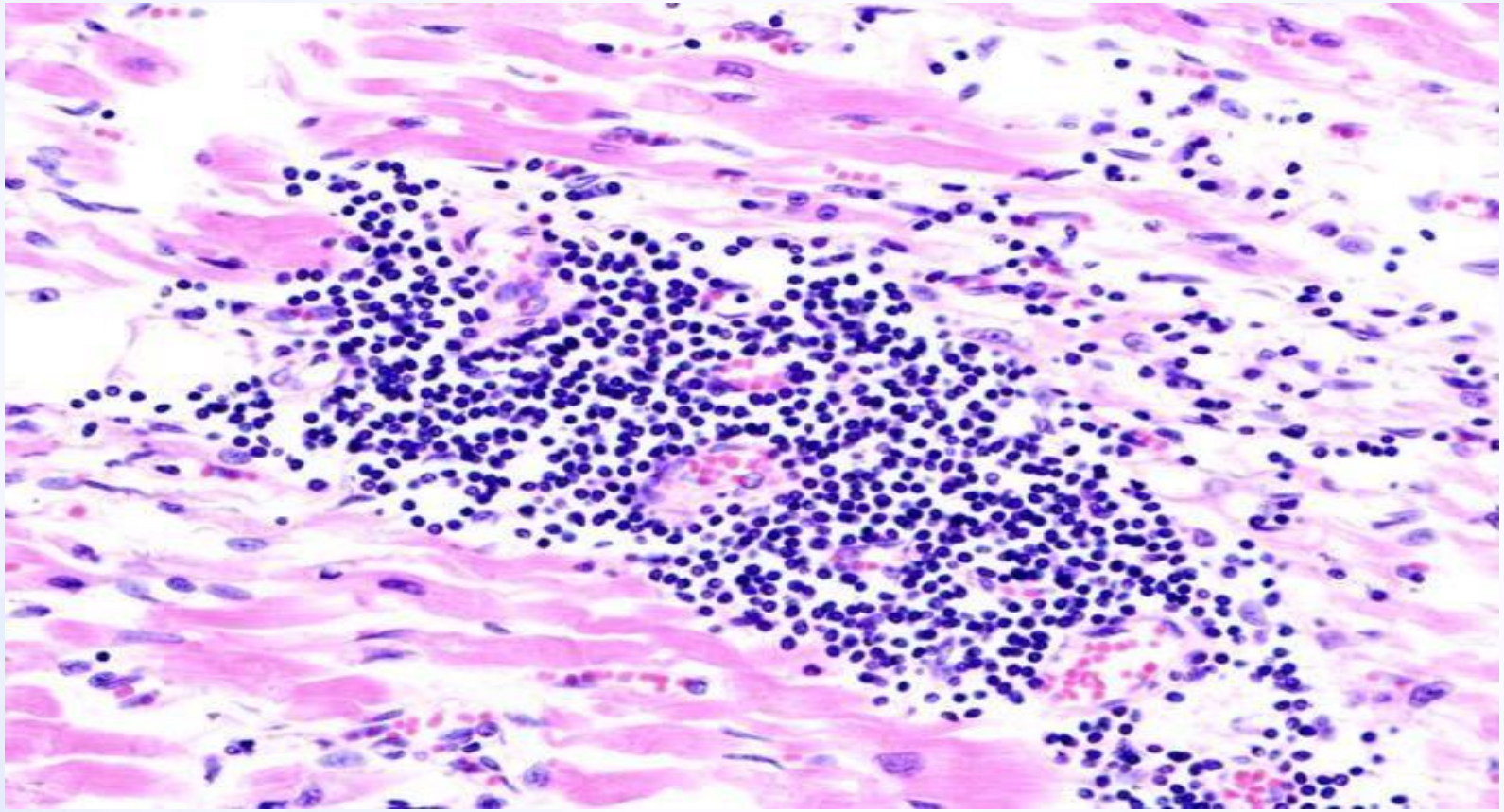


Figure 2 The picture shows the pathogenetic mechanisms involved in myocarditis and progression to dilated cardiomyopathy.



Histopathological image of viral myocarditis at autopsy in a patient with acute onset of congestive heart failure.

Clinical phenotypes

- **1- Dilated Cardiomyopathy**

The classic presentation of myocarditis includes a dilated LV with systolic dysfunction in the setting of acute-onset

heart failure after a viral prodrome

- **2- Fulminant Myocarditis**
- Described as a more severe form of myocarditis, fulminant myocarditis presents similarly with a history of recent viral illness followed usually within 2 to 4 weeks with sudden-onset heart failure.

- The magnitude of ventricular dysfunction and heart failure is more severe than typical myocarditis in most patients. Patients may present with **cardiogenic shock**, multiorgan failure, and/or life-threatening arrhythmias

Clinical phenotypes

- **3- Acute Coronary Syndrome**
- Acute coronary syndrome (ACS), particularly in adolescent and young adult males. Patients usually present with chest pain and dyspnea with ECG changes and elevated cardiac enzymes that are suggestive of a myocardial ischemia

- **4- Sudden Death**
- Myocarditis has long been recognized as a cause of sudden death in children and adults

بنظر شما کدام گزینه زیر از نشانه های نارسایی قلبی است؟

الف- اسپلنومگالی

ب- هپاتومگالی

پ- هپاتواسپلنومگالی

Details of symptoms and signs

- Patients(59%) frequently present days to weeks after an acute febrile illness, particularly a flu-like syndrome

- Myocarditis is most commonly **asymptomatic at first**, with no evidence of left ventricular dysfunction

  -Cardiac symptoms may result from systolic or diastolic left ventricular dysfunction or from tachyarrhythmias or bradyarrhythmias (dyspnea, fatigue, decreased exercise tolerance, palpitations)

Clinical Presentation

In most pediatric patients, myocarditis classically presents with symptoms of acute heart failure, usually days to weeks, and a history of recent viral prodrome consisting typically of respiratory or gastrointestinal symptoms with fever.

Respiratory symptoms are the predominant complaint in up to 80% of patients

Clinical Findings

- Physical Examination

-Tachycardia, hypotension, fever and tachycardia may be disproportionate to the degree of fever
-(Bradycardia is seen rarely)

- -Murmurs of mitral or tricuspid regurgitation are common

- **-Right heart failure:** Distended neck veins, and peripheral edema, **hepatomegaly (no splenomegaly)**

- **Left heart failure:** rales, wheezes, gallops

Symptoms and signs

- Diffuse inflammation (**and capillary leak syndrome**) may develop leading to pericardial effusion.

Laboratory Evaluation

Troponin T and I levels may be elevated as a marker of cardiac damage.

LABORATORY STUDIES

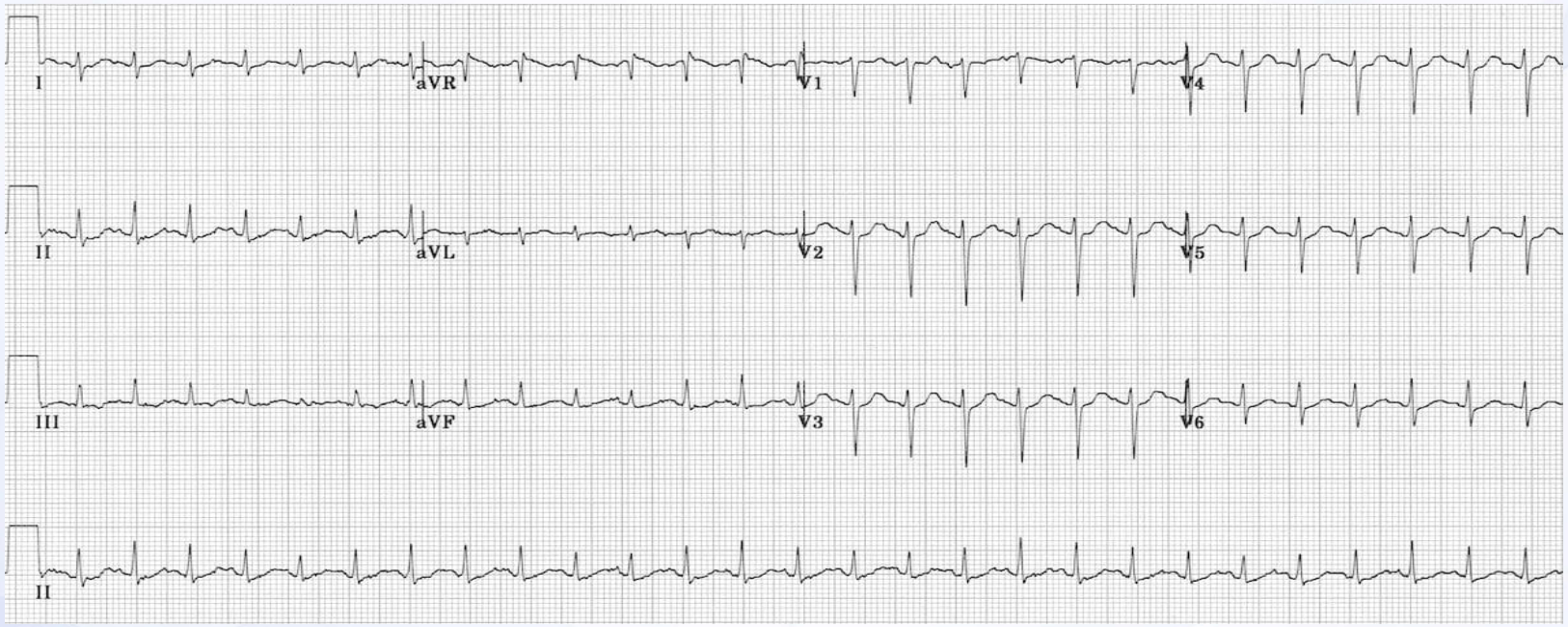
- ESR is elevated in 60% of patients with acute myocarditis as an inflammatory factor.
- Leukocytosis is present in 25% of cases.

Electrocardiography

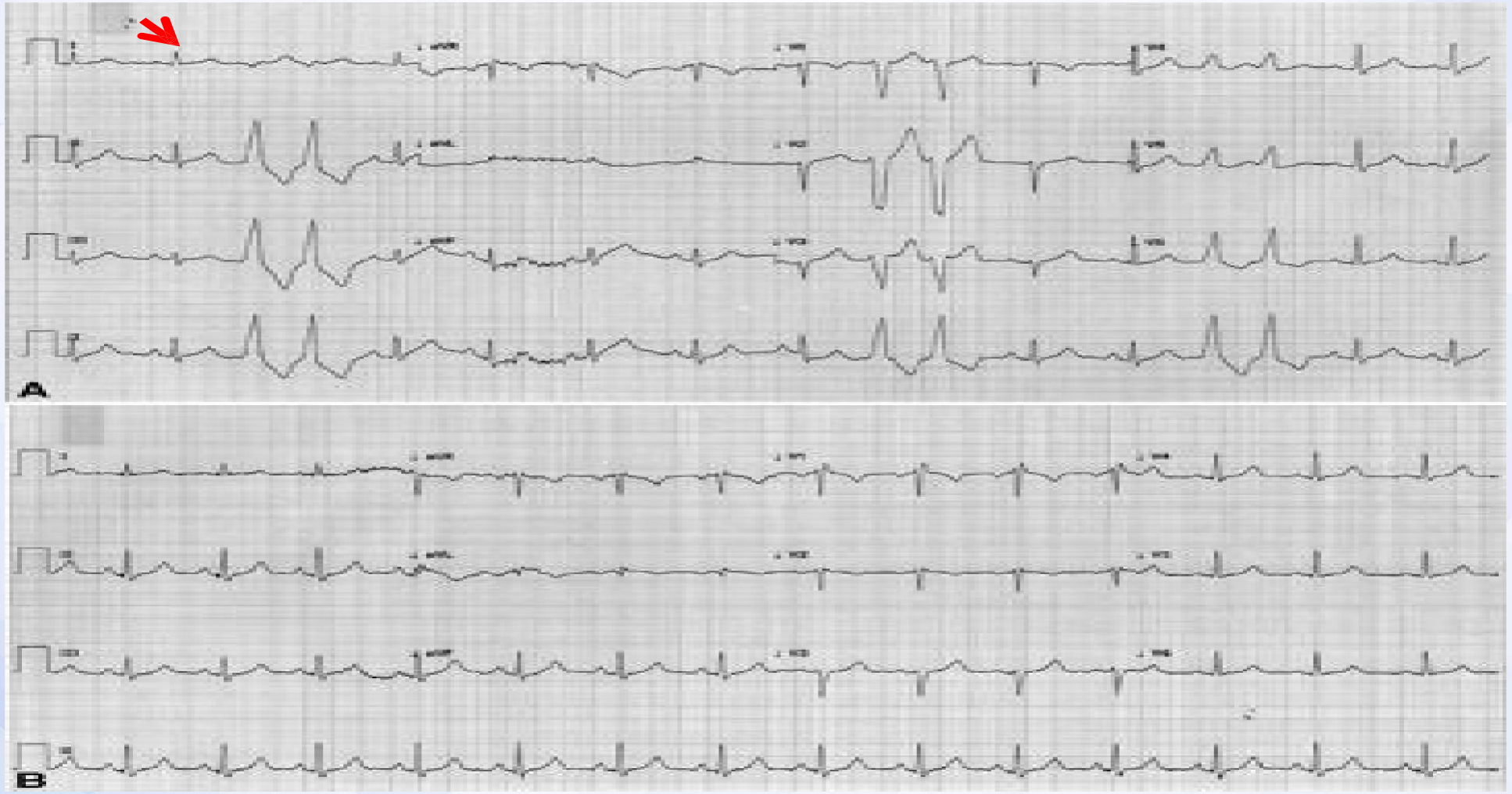
-The most common abnormality is sinus tachycardia.

- may show ventricular arrhythmias or heart block, or it may mimic the findings in acute myocardial infarction or pericarditis with ST segment elevation, ST segment depression, PR segment depression, and pathological Q-waves

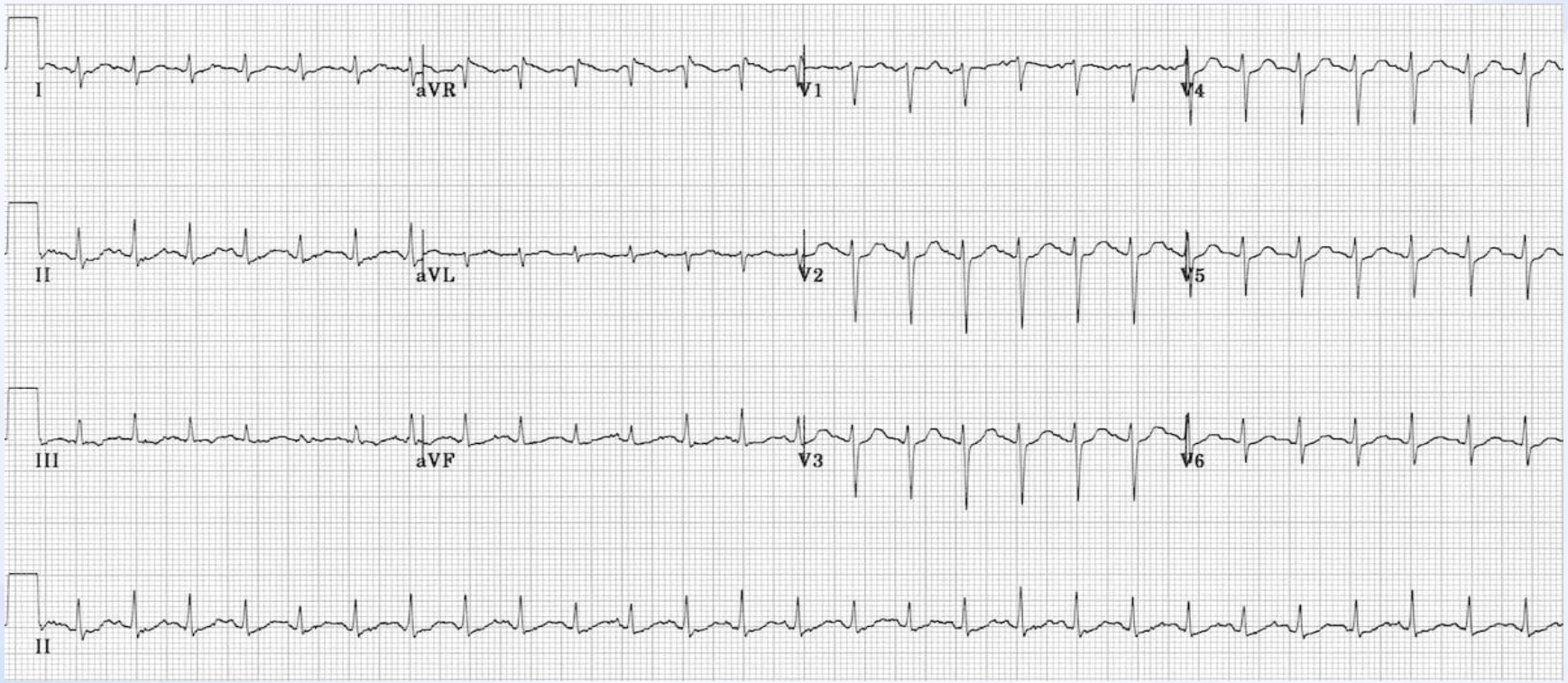
Tachycardia



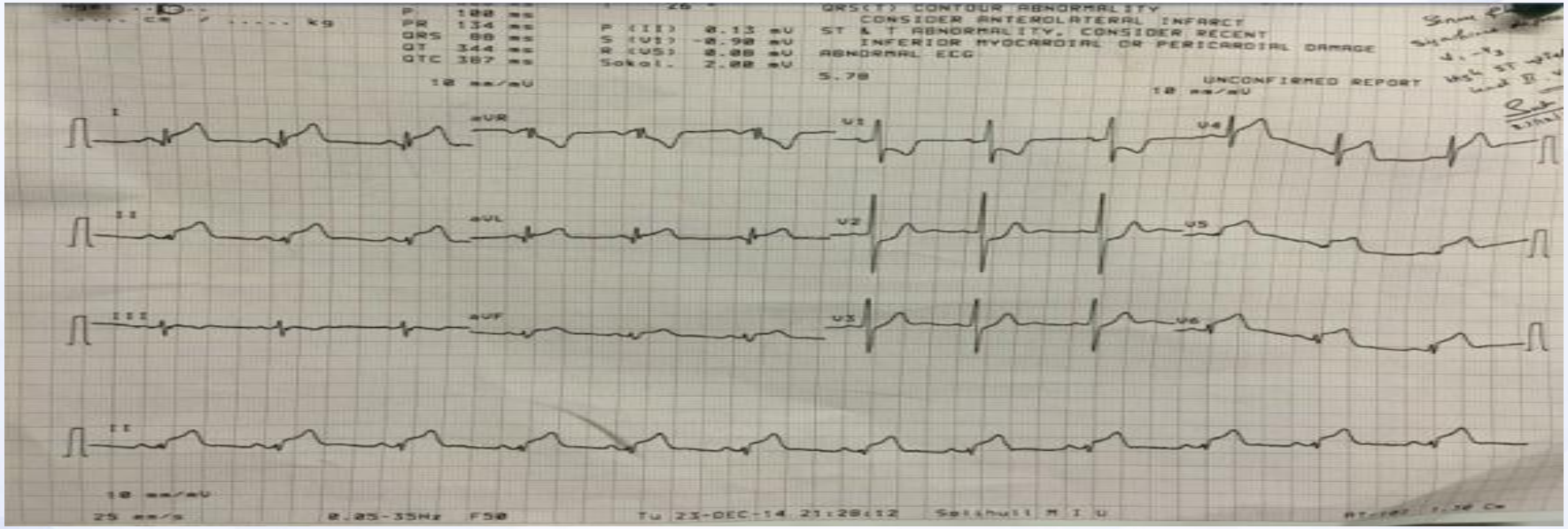
Bigeminy



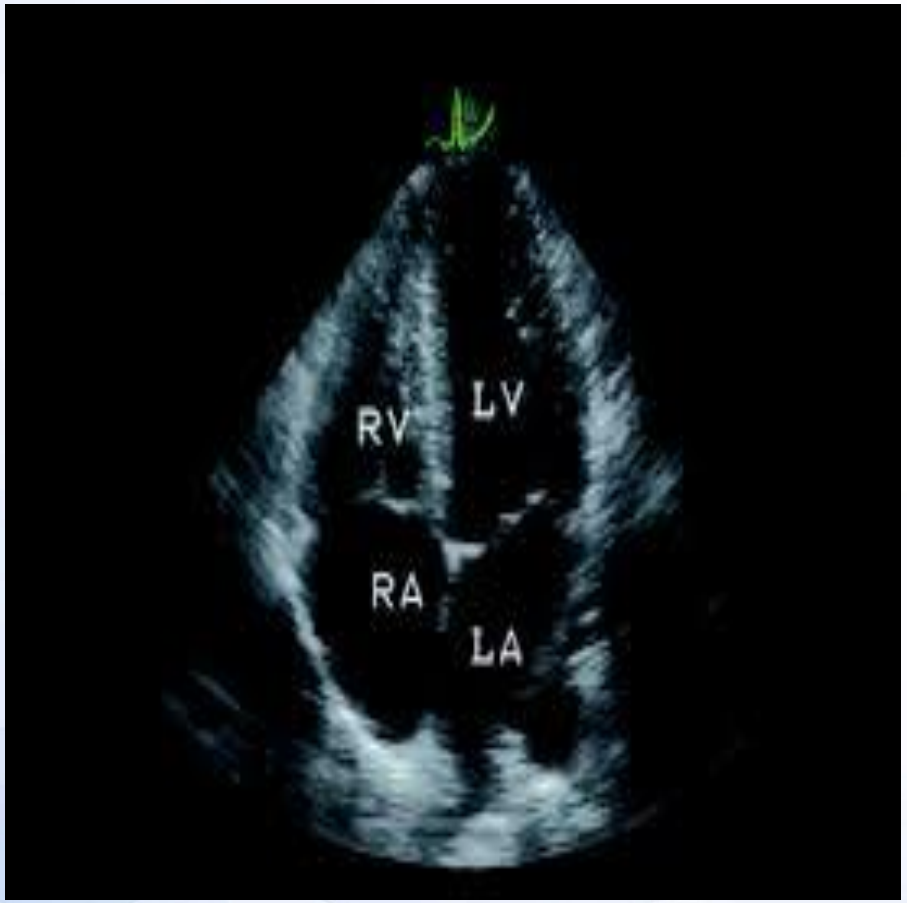
Low voltage

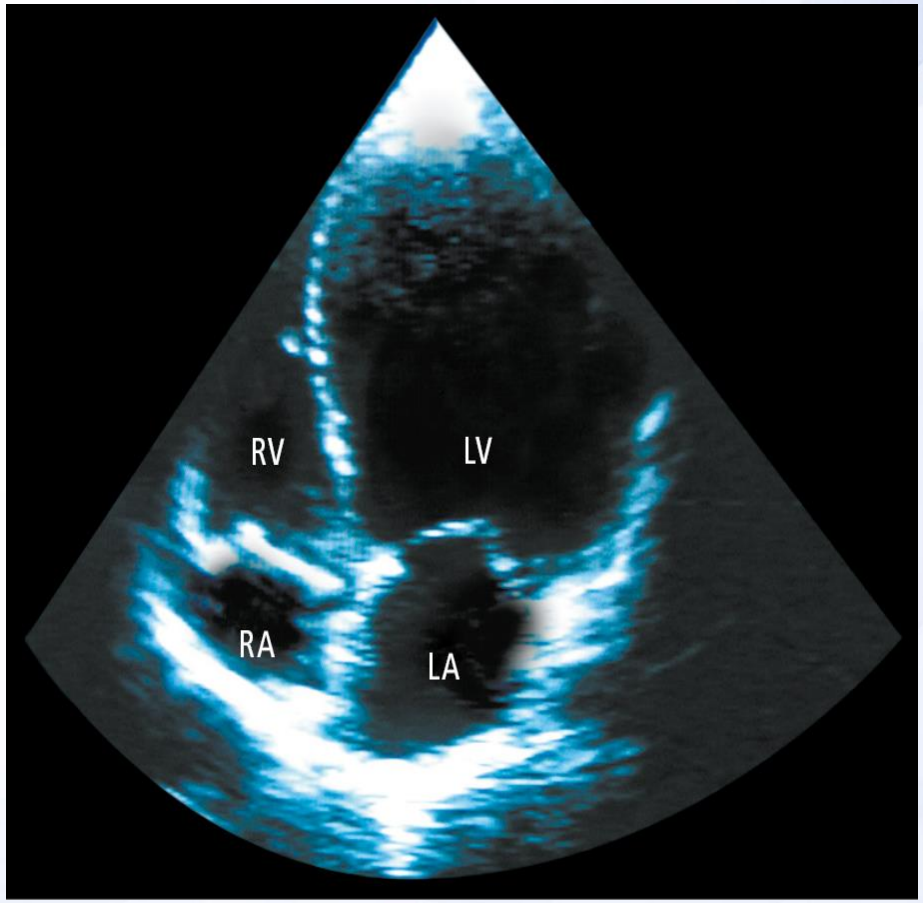


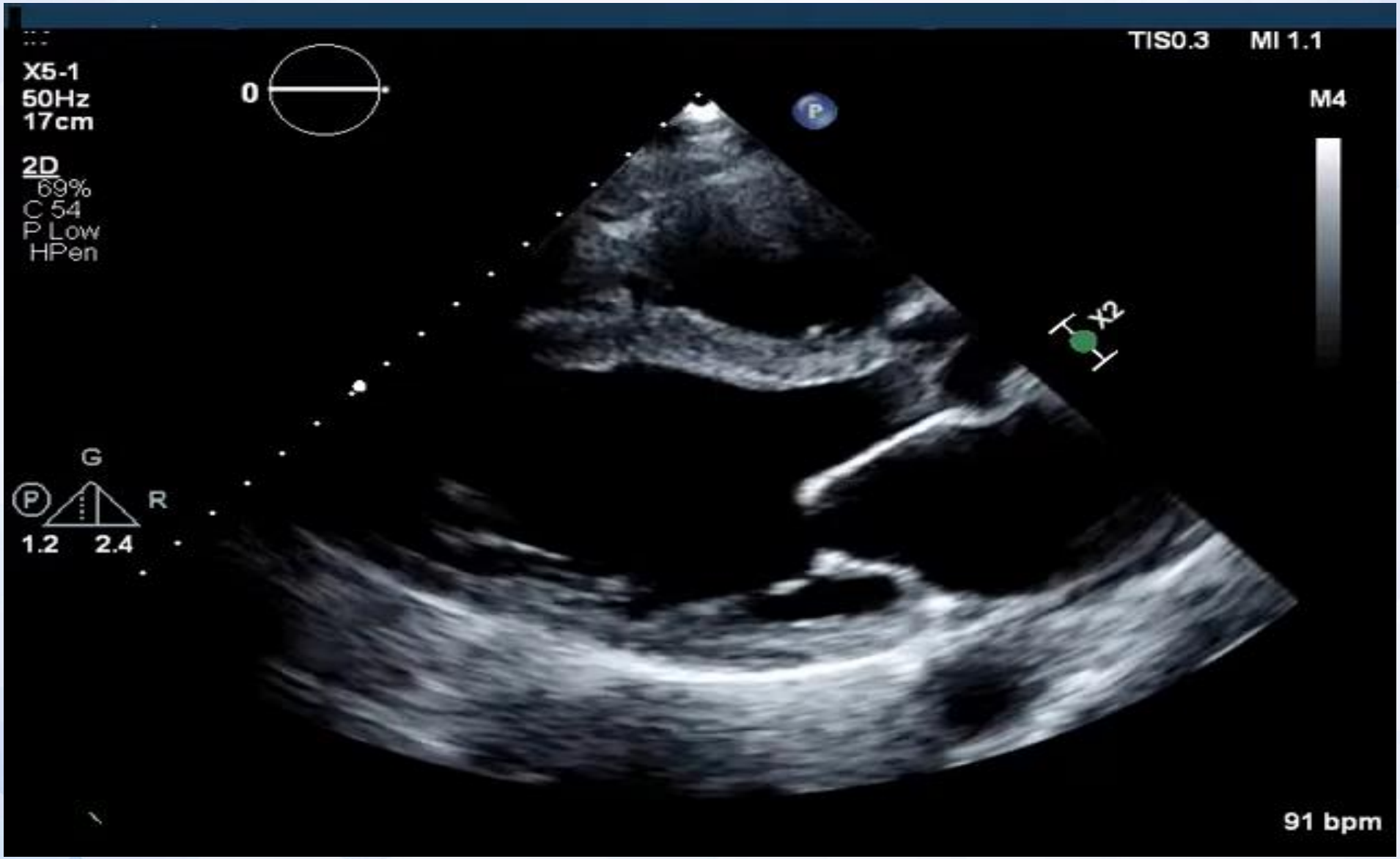
Non-specific



Echocardiography



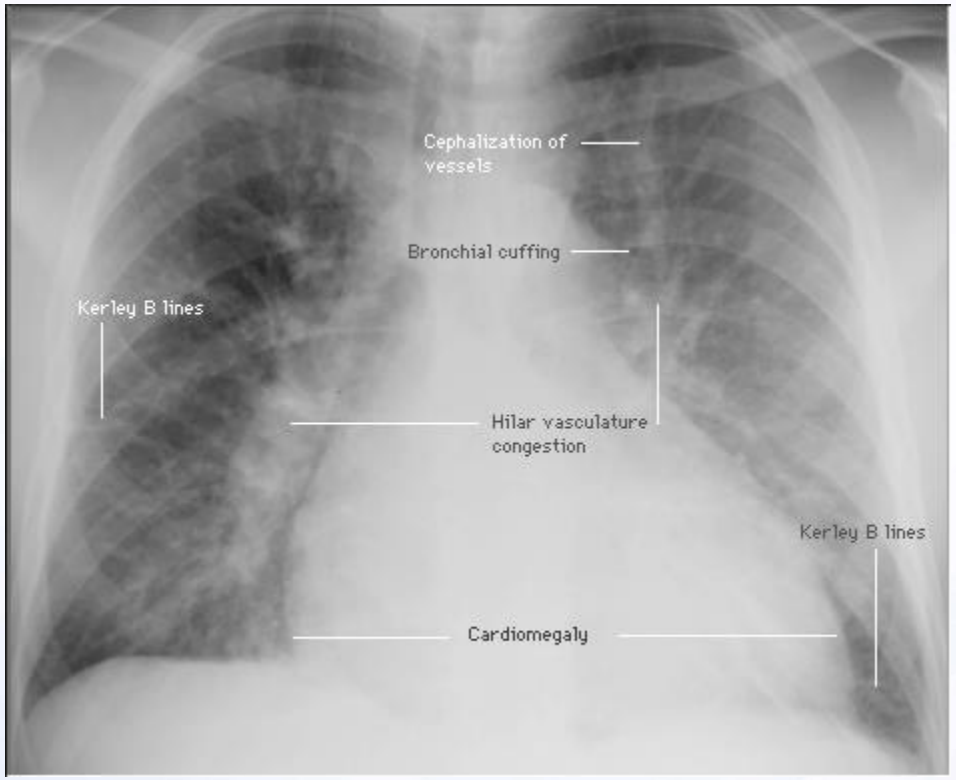


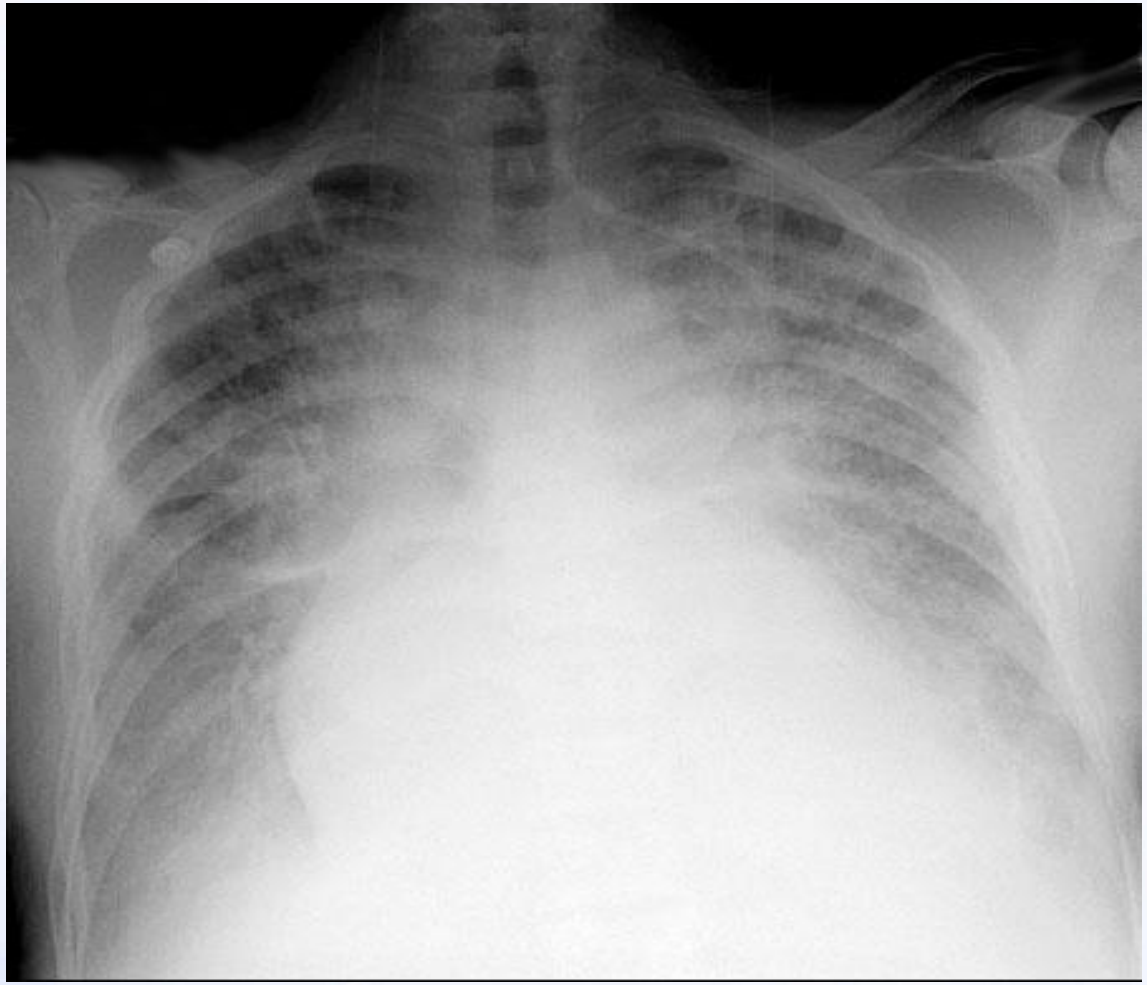

X5-1
50Hz
17cm
2D
69%
C 54
P Low
HPen
TIS0.3
MI 1.1
M4
G
R
1.2
2.4
91 bpm

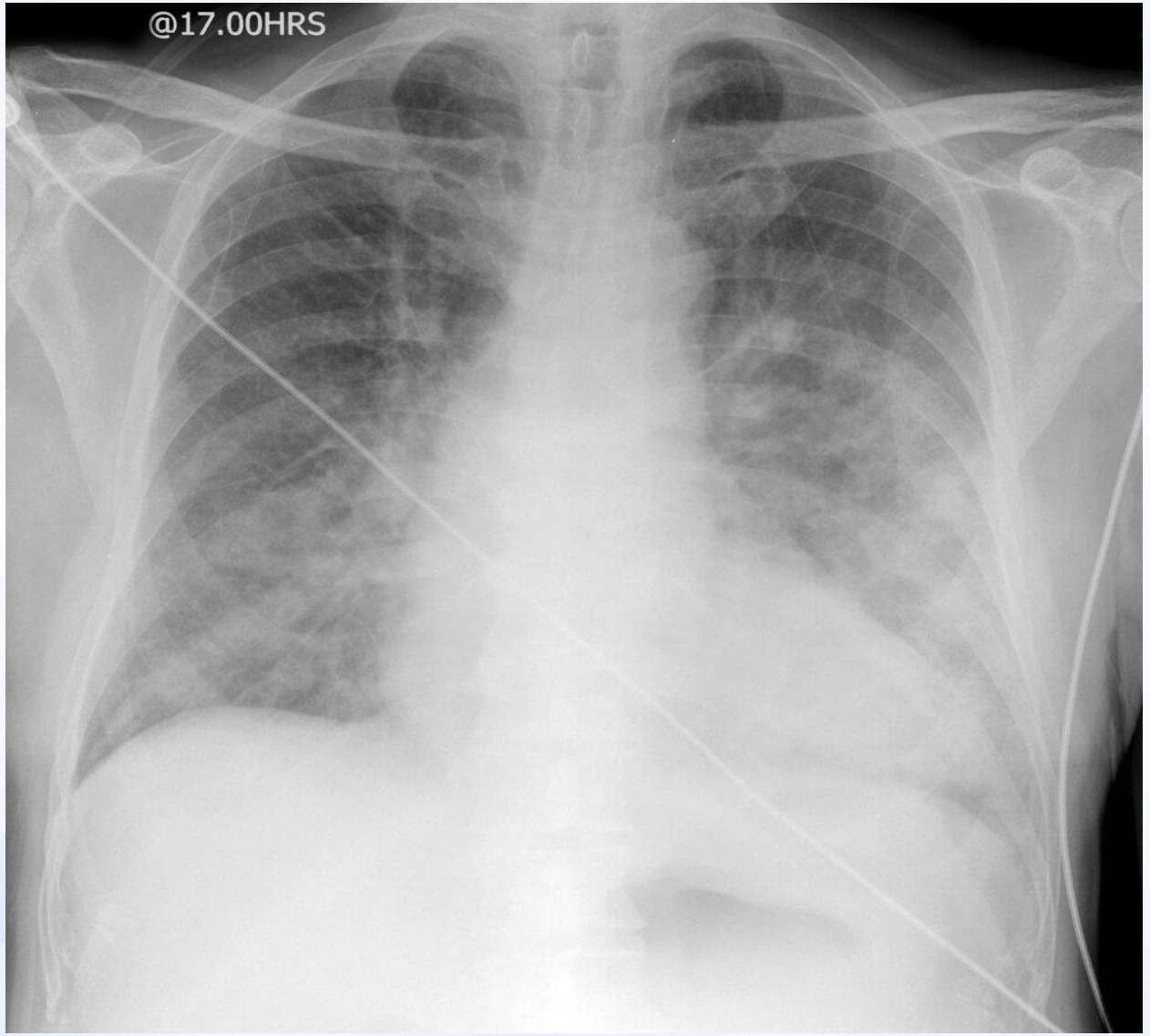
Radiographic Evaluation

CXR is commonly performed due to the high frequency of respiratory symptoms at presentation. Most
CXR are abnormal in patients with myocarditis (>90%), with cardiomegaly being the most common finding

Chest radiography






@17.00HRS

MRI

Table 5 Diagnostic cardiac magnetic resonance criteria for myocarditis

In the setting of clinically suspected myocarditis (*Tables 3–4*), CMR findings are consistent with myocardial inflammation, if at least two of the following criteria are present:

(1) Regional or global myocardial signal intensity increase in T2-weighted oedema images[a]
(2) Increased global myocardial early gadolinium enhancement ratio between myocardium and skeletal muscle in gadolinium-enhanced T1-weighted images[b]
(3) There is at least one focal lesion with non-ischaemic regional distribution in inversion recovery-prepared gadolinium-enhanced T1-weighted images (late gadolinium enhancement)[c]

A CMR study is consistent with myocyte injury and/or scar caused by myocardial inflammation if Criterion 3 is present

A repeat CMR study between 1 and 2 weeks after the initial CMR study is recommended if

- None of the criteria are present, but the onset of symptoms has been very recent and there is strong clinical evidence for myocardial inflammation
- One of the criteria is present

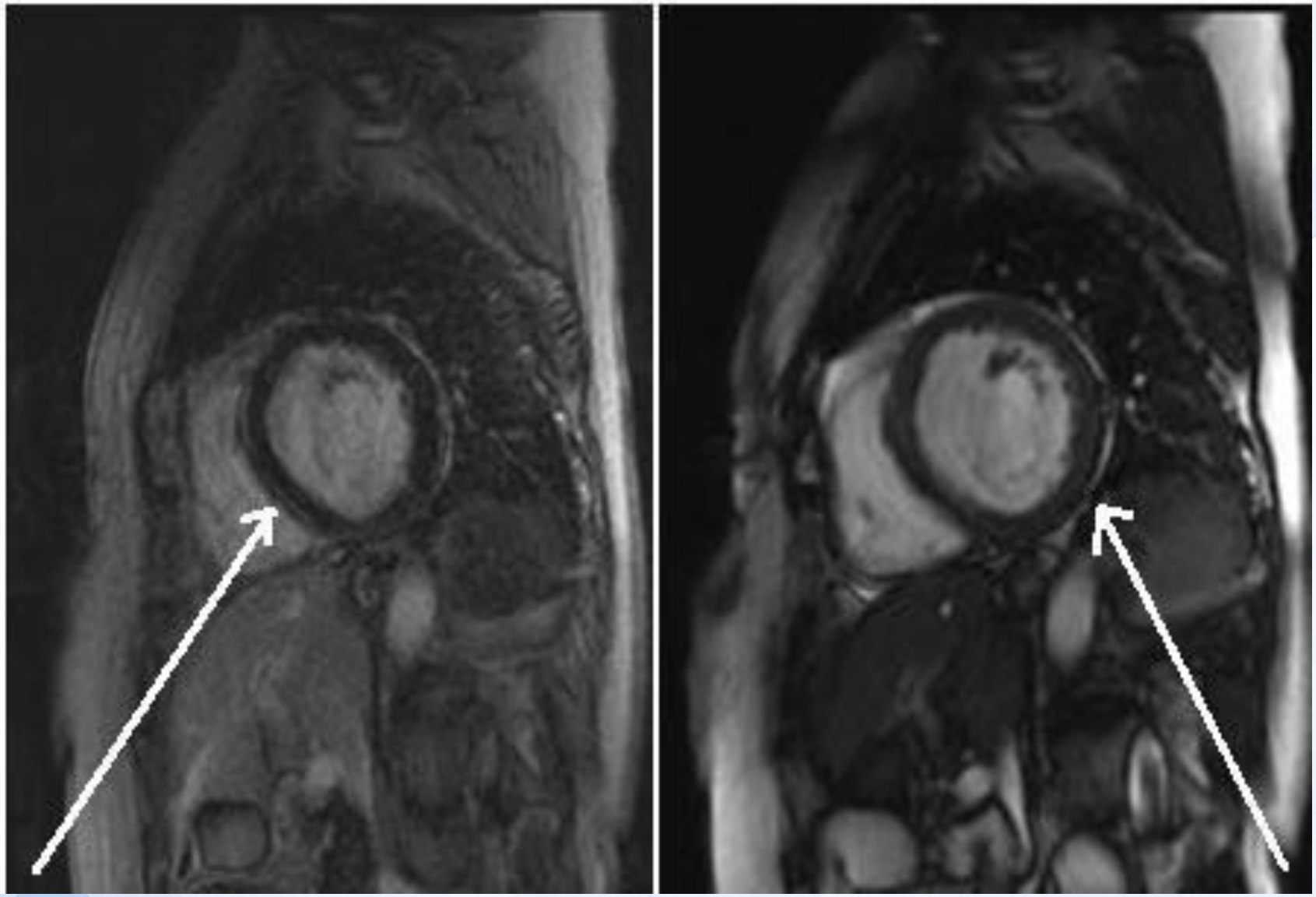
The presence of LV dysfunction or pericardial effusion provides additional, supportive evidence for myocarditis

Table reprinted with permission from (20).

[a]Global signal intensity (SI) increase has to be quantified by an SI ratio of myocardium over skeletal muscle of ≥ 2.0. If the edema is more subendocardial or transmural in combination with a colocalized ischaemic (including the subendocardial layer) pattern of late gadolinium enhancement, acute myocardial infarction is more likely and should be reported.

[b]A global SI enhancement ratio of myocardium over skeletal muscle of ≥ 4.0 or an absolute myocardial enhancement of ≥ 45% is consistent with myocarditis.

[c]Images should be obtained at least 5 min after gadolinium injection; foci typically exclude the subendocardial layer, are often multifocal, and involve the subepicardium. If the late gadolinium enhancement pattern clearly indicates myocardial infarction and is colocalized with a transmural regional edema, acute myocardial infarction is more likely and should be reported.



Endomyocardial biopsy

- gold standard for the diagnosis of myocarditis

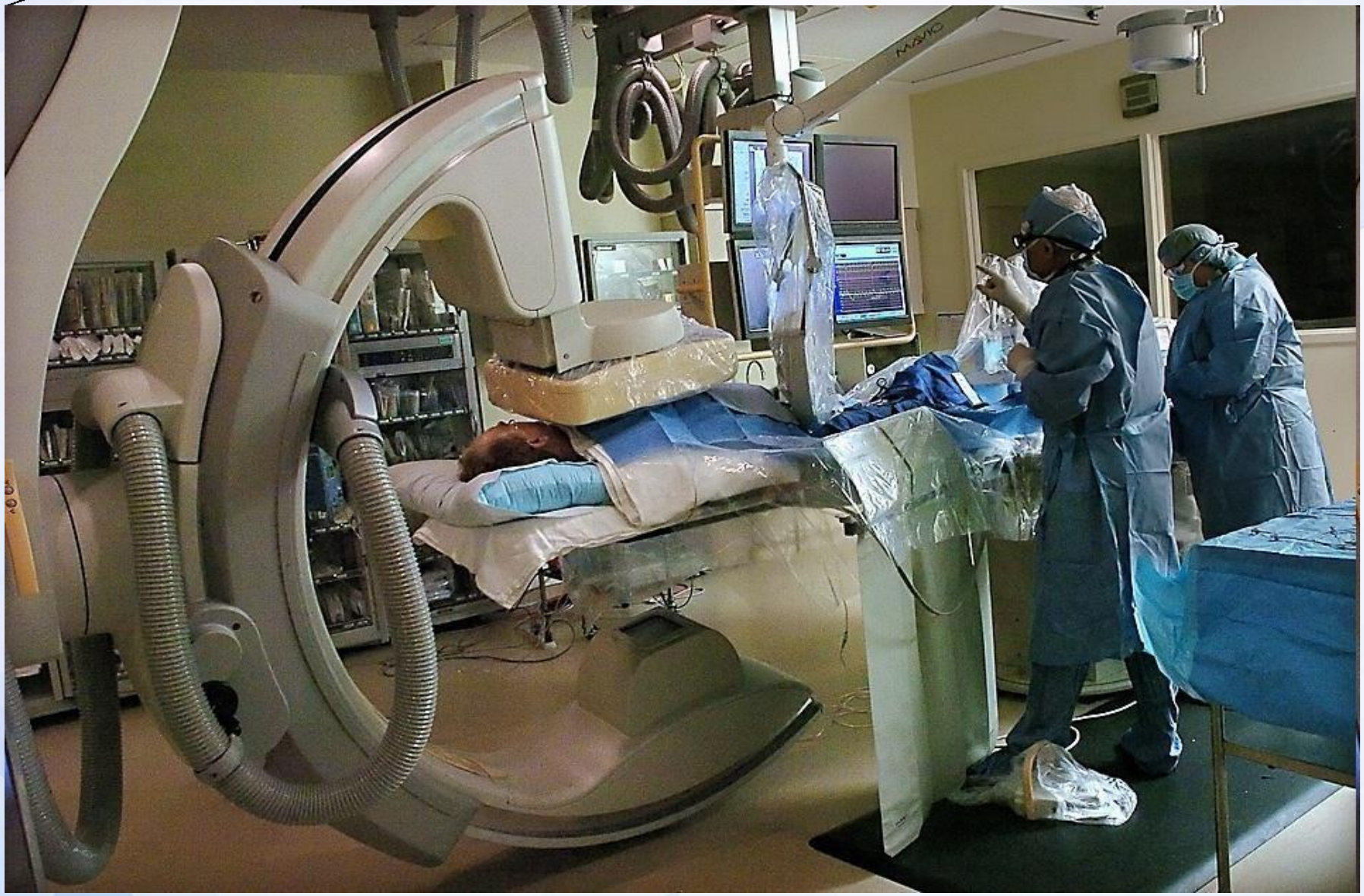
-Dallas criteria (an inflammatory infiltrate of the myocardium +injury to the adjacent myocytes)

-borderline myocarditis is made when the infiltrate is not accompanied by myocyte injury

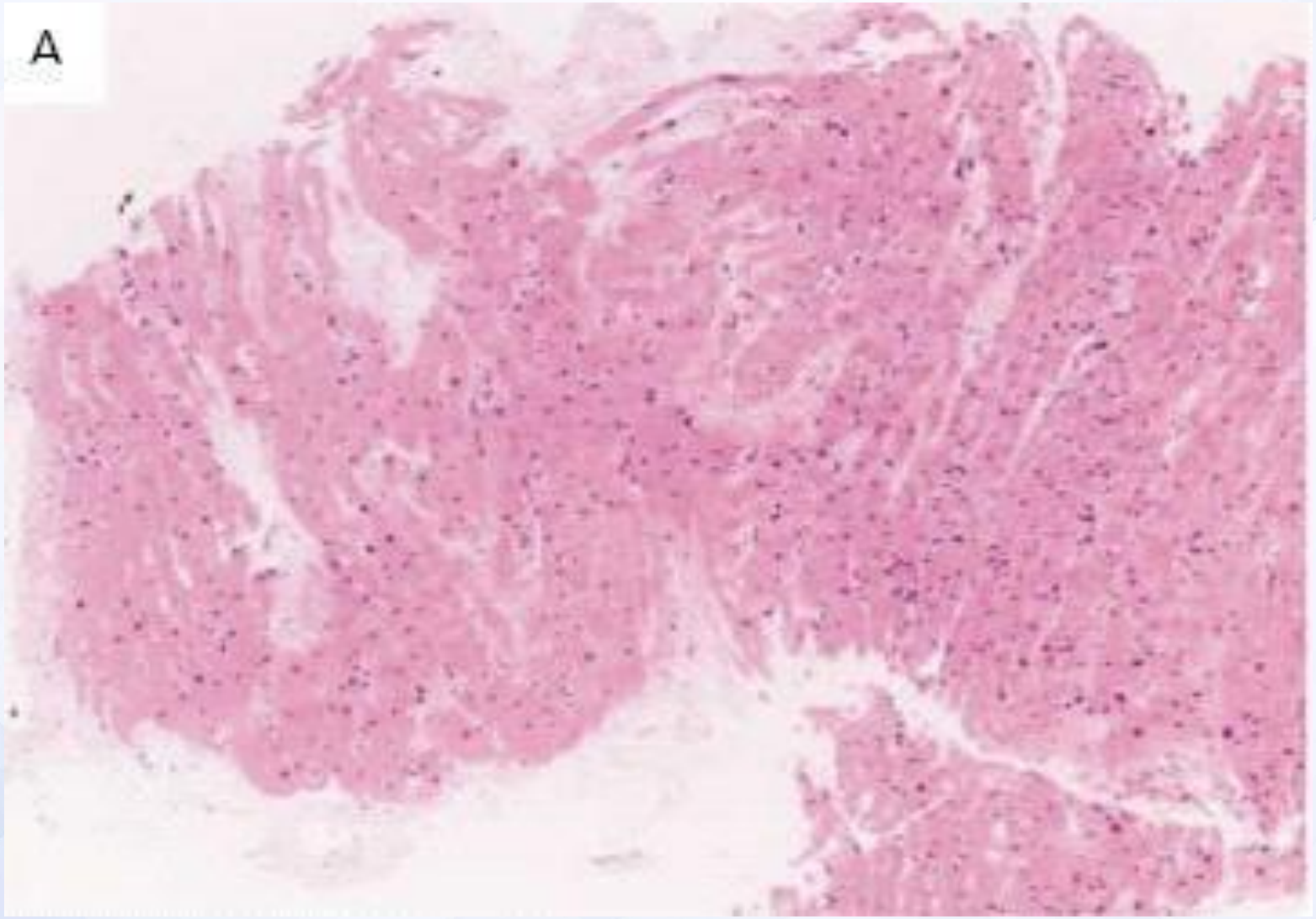
Dallas Classification (1987)

Initial Biopsy

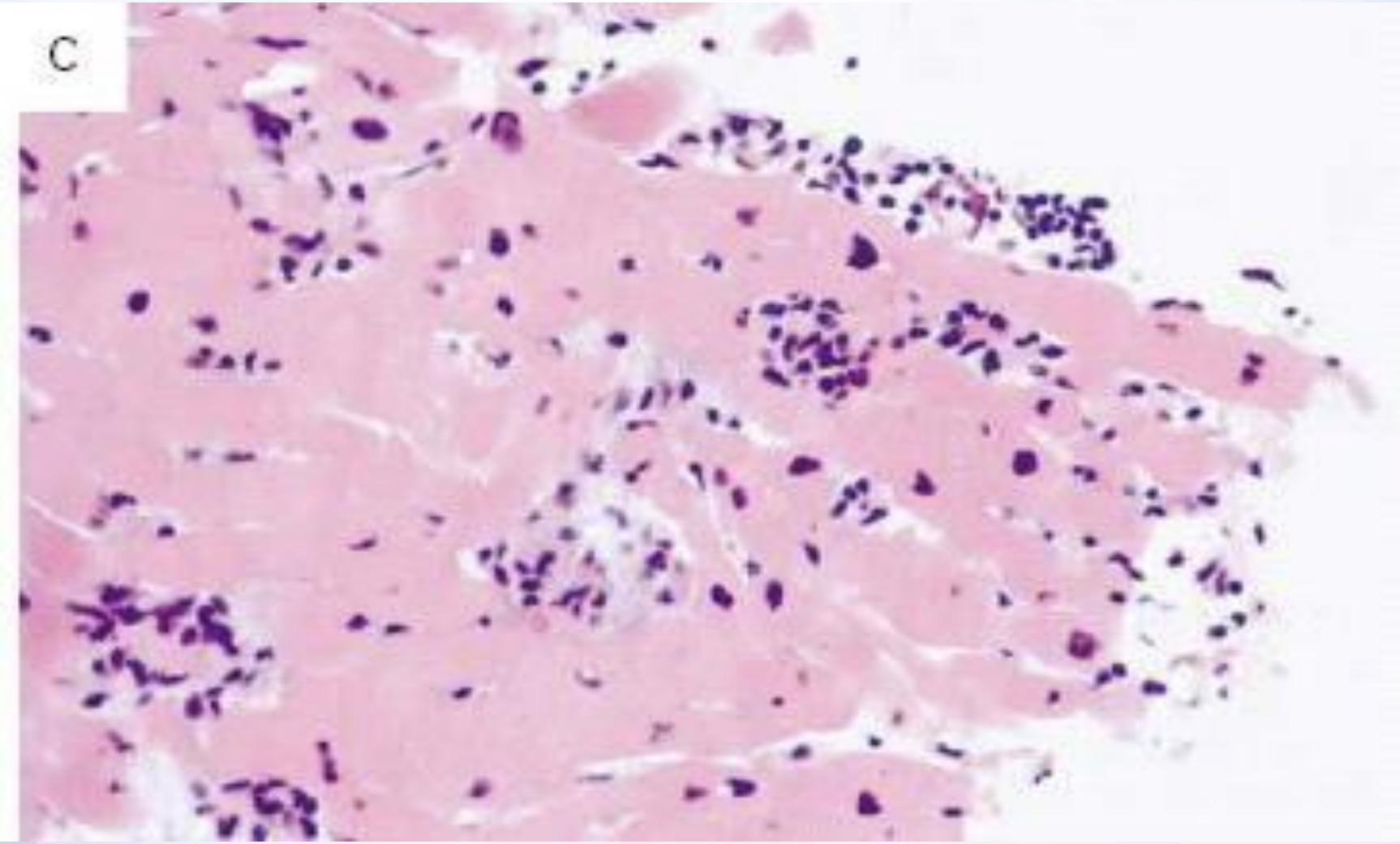
- Myocarditis: Myocardial necrosis, degeneration, or both, in the absence of significant coronary artery disease with adjacent inflammatory infiltrate with or without fibrosis.
- Borderline myocarditis: Inflammatory infiltrate too sparse or myocyte damage not apparent.
- No myocarditis
- **Subsequent Biopsies**
- Ongoing (persistent) myocarditis with or without fibrosis.
- Resolving (healing) myocarditis with or without fibrosis.
- Resolved (healed) myocarditis with or without fibrosis.



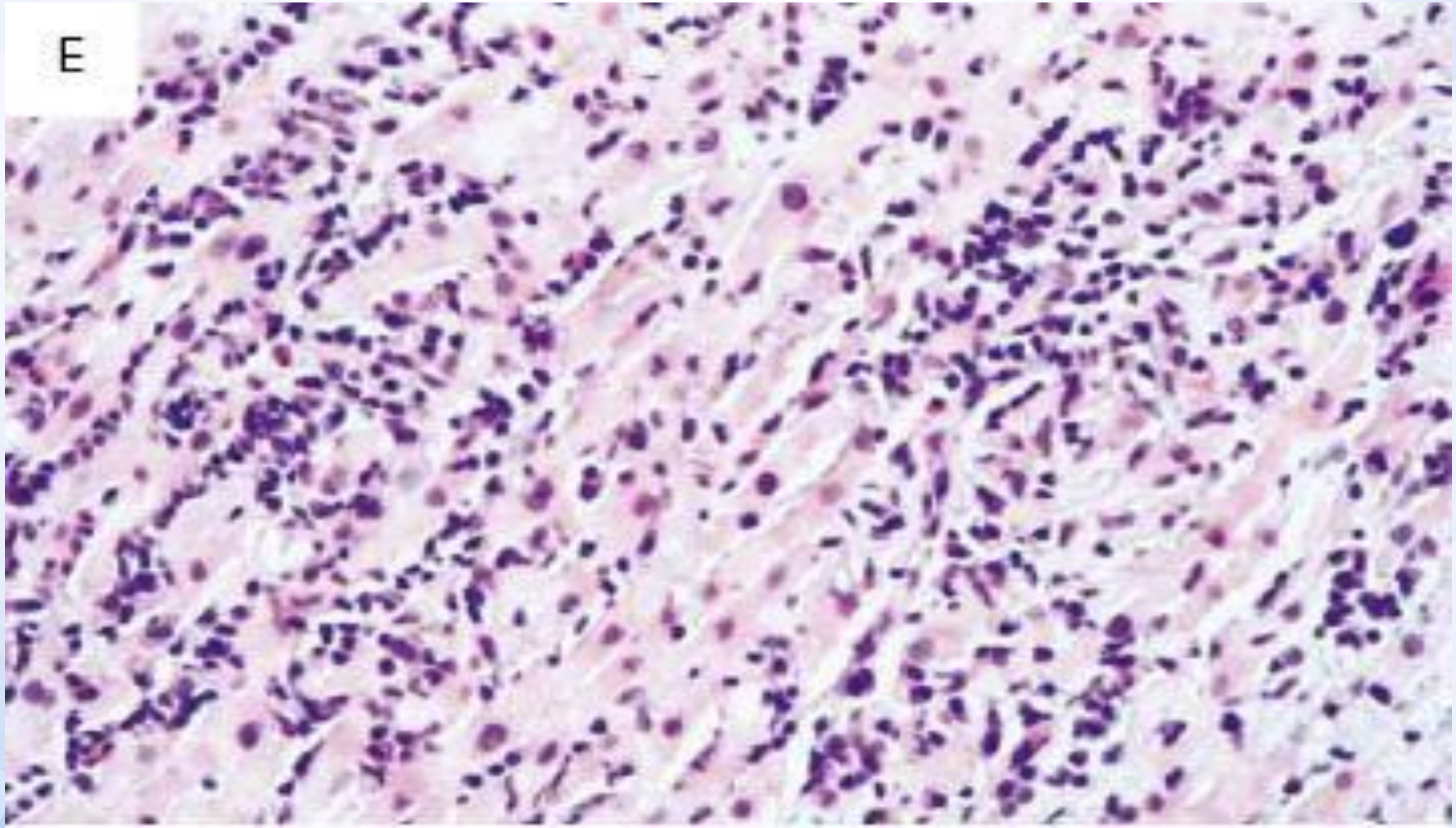
Normal Myocardium



Borderline Myocarditis



Active Myocarditis



Treatment

Non-pharmacological treatment

- Bed rest
- Reducing salt and liquids intake
- No training for athletes – 6 months

Therapeutic options

- treatment of heart failure
- treatment of arrhythmias
- Immunomodulators, immunosuppression, and antiviral therapy

Treatment of heart failure

- Angiotensin Converting Enzyme inhibitors (enalapril, captopril) or Angiotensin Receptor Blockers (valsartan, losartan)
- Diuretics (furosemide)
- Mineralocorticoid receptor antagonists (spironolactone, eplerenone)
- Beta-blockers (metoprolol, bisoprolol, carvedilol)
- Drugs with positive inotropic effect (dopamine, dobutamine, milrinone)

Antiviral Therapy

As a viral infection is thought to be the cause of the majority of myocarditis, antivirals have been proposed as a therapeutic option in patients with an identified causative agent.

But patients are also often thought to present too late in the disease process for antiviral therapy to affect the inflammatory process and cardiac damage

Immunomodulators and Immunosuppressants

As myocarditis is known to involve both inflammatory- and autoimmune-mediated cellular damage, various immunomodulator therapies have been used in the treatment of myocarditis.

IVIG has known anti-inflammatory and immunomodulatory effects through multiple but not completely understood mechanisms, with indications for use in a variety of autoimmune and inflammatory diseases, although has no definite effect.
It is the main medication of myocarditis in children.

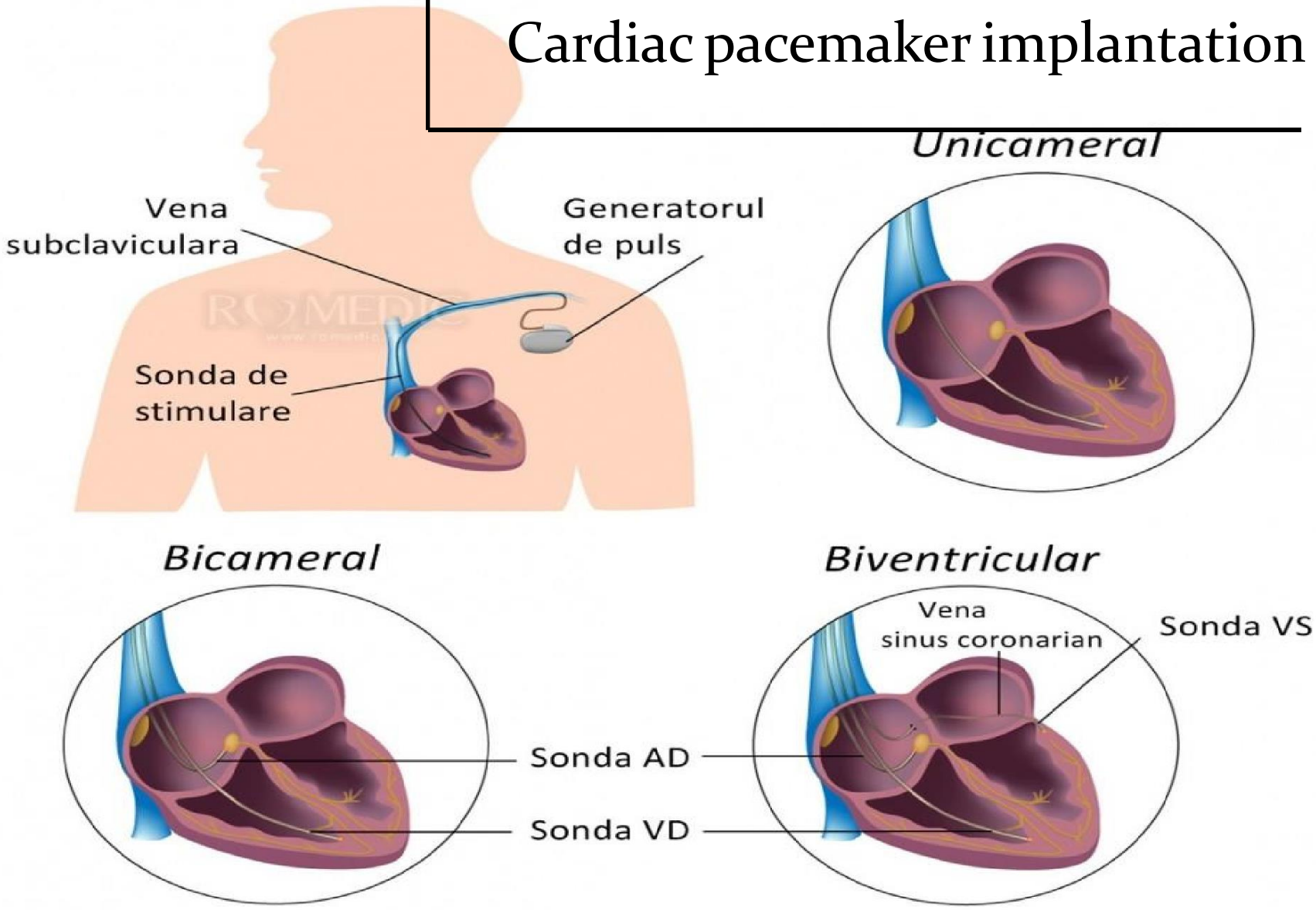
Therapeutic options

- Antibiotics in bacterial myocarditis
- Anti-lymphocyte monoclonal antibodies-debatable
- Glucocorticoids and azathioprine – debatable
- NSAIDs are contraindicated in the ACUTE PHASE (increase cardiomyocyte lesion and necrosis).

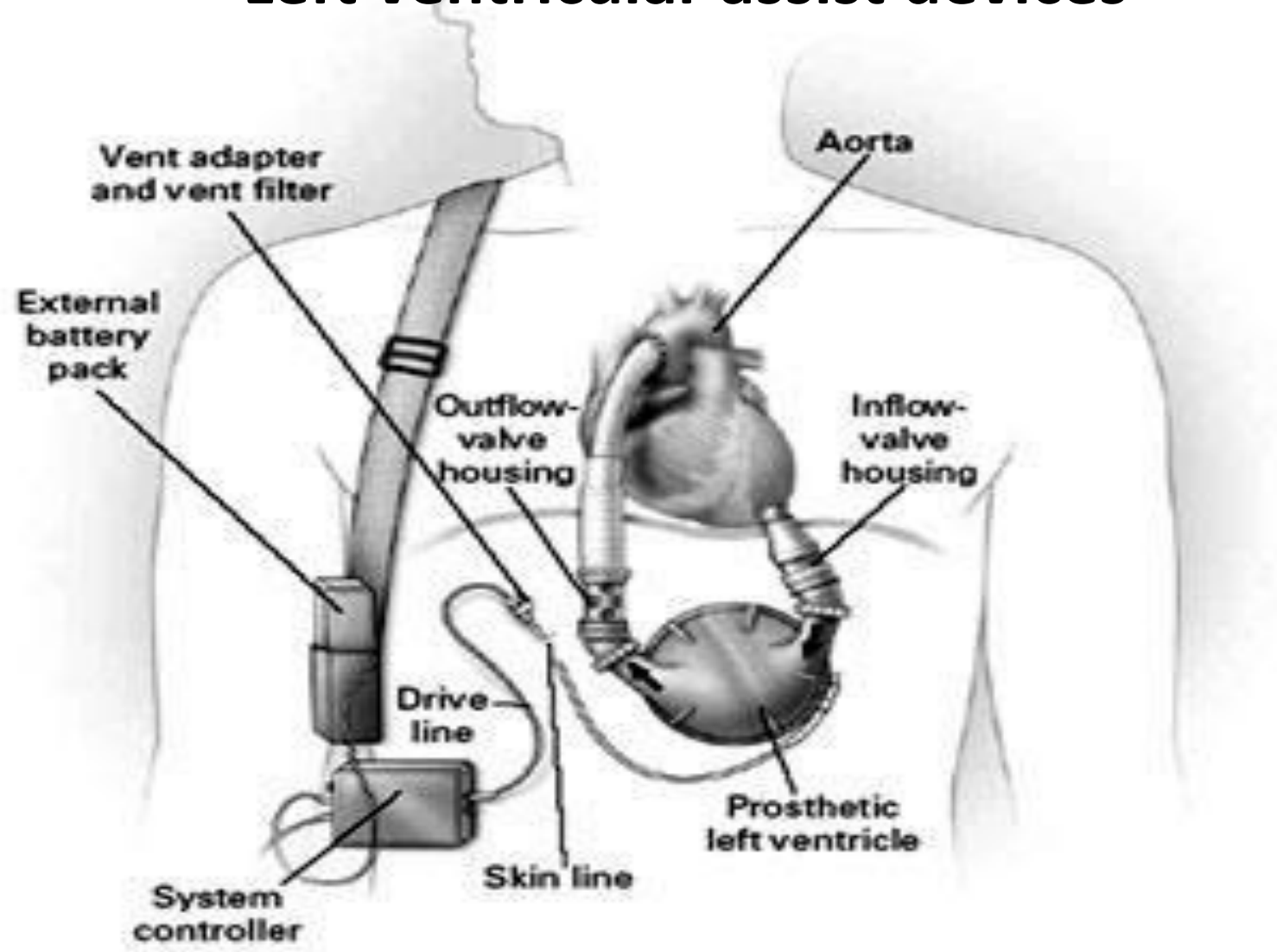
Surgical and interventional treatment in Myocarditis

- Implantation of pacemaker in patients with complete heart block
- Cardiac transplantation
- Left ventricular assist devices

Cardiac pacemaker implantation



Left ventricular assist devices



Complications

- Sudden death
- Heart failure
- Arrhythmias
- Progression to dilated cardiomyopathy

Thank you very much