



Egyptian Society of
CARDIOLOGY

Minia University Suez Canal University Zagazig University

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Myocarditis
How to diagnose and treat ?

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Definition:

Inflammatory disease of the myocardium
diagnosed by established histological,
immunological and immunohistochemical
criteria.

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Incidence:

- The actual incidence of myocarditis is difficult to determine as EMB is used infrequently.
- In North America; more than 2.2 million cases are diagnosed annually with 353,000 deaths.



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Etiology:



Infectious myocarditis



Immune mediated myocarditis



Toxic myocarditis



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Etiology:

1. Infectious myocarditis

Bacterial	Staphylococcus, Streptococcus, Pneumococcus, Meningococcus, Gonococcus, Salmonella, Corynebacterium diphtheriae, Haemophilus influenzae, Mycobacterium (tuberculosis), Mycoplasma pneumoniae, Brucella
Spirochaetal	Borrelia (Lyme disease), Leptospira (Weil disease)
Fungal	Aspergillus, Actinomyces, Blastomyces, Candida, Coccidioides, Cryptococcus, Histoplasma, Mucormycosis, Nocardia, Sporothrix
Protozoal	Trypanosoma cruzi, Toxoplasma gondii, Entamoeba, Leishmania
Parasitic	Trichinella spiralis, Echinococcus granulosus, Toxaria solium
Rickettsial	Coxiella burnetii (Q fever), R. rickettsii (Rocky Mountain spotted fever), R. tsutsugamushi
Viral	RNA viruses: <u>Coxsackieviruses A and B, echoviruses</u> , polioviruses, influenza A and B viruses, respiratory syncytial virus, mumps virus, measles virus, rubella virus, hepatitis C virus, dengue virus, yellow fever virus, Chikungunya virus, Junin virus, Lassa fever virus, rabies virus, human immunodeficiency virus-1 DNA viruses: adenoviruses, parvovirus B19, cytomegalovirus, human herpes virus-6, Epstein-Barr virus, varicella-zoster virus, herpes simplex virus, variola virus, vaccinia virus



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Etiology:

2. Immune-mediated myocarditis

Allergens	Tetanus toxoid, vaccines, serum sickness <u>Drugs:</u> penicillin, cefaclor, colchicine, furosemide, isoniazid, lidocaine, tetracycline, sulfonamides, phenytoin, phenylbutazone, methyldopa, thiazide diuretics, amitriptyline
Alloantigens	Heart transplant rejection
Autoantigens	Infection-negative lymphocytic, infection-negative giant cell Associated with autoimmune or immune-oriented disorders: systemic lupus erythematosus, rheumatoid arthritis, <u>Churg-Strauss syndrome, Kawasaki's disease, inflammatory bowel disease, scleroderma, polymyositis, myasthenia gravis, insulin-dependent diabetes mellitus, thyrotoxicosis, sarcoidosis, Wegener's granulomatosis, rheumatic heart disease (rheumatic fever)</u>

3. Toxic myocarditis

Drugs	Amphetamines, anthracyclines, cocaine, cyclophosphamide, ethanol, fluorouracil, lithium, catecholamines, hemetine, interleukin-2, trastuzumab, clozapine
Heavy metals	Copper, iron, lead (rare, more commonly cause intramyocyte accumulation)
Miscellaneous	Scorpion sting, snake, and spider bites, bee and wasp stings, carbon monoxide, inhalants, phosphorus, arsenic, sodium azide
Hormones	Phaeochromocytoma, vitamins: beri-beri
Physical agents	Radiation, electric shock



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Clinical presentation

Acute coronary syndrome-like

New onset or worsening heart failure

Arrhythmia (life threatening or SCD)




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Clinical presentation

mild symptoms of chest pain and palpitations

life-threatening cardiogenic shock and ventricular arrhythmia



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Clinical presentation:

Features support clinical suspicion of myocarditis:

- Fever $\geq 38^{\circ}$ C at presentation or within the preceding 30 days.
- Peri-partum period.
- Previous myocarditis.
- Personal and/or family history of allergy, extra-cardiac autoimmune disease.
- Family history of DCM.



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Investigations



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Non-invasive assessment:

- ECG.
- Echocardiography.
- Biomarkers.
- CMR imaging.



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ECG:

- Usually abnormal in myocarditis though ECG signs are neither specific nor sensitive.
- Findings:
 - Sinus tachycardia.
 - T wave inversion.
 - Saddle shaped ST elevation.
 - Rhythm abnormalities.
- QRS prolongation is an independent negative predictor for survival.



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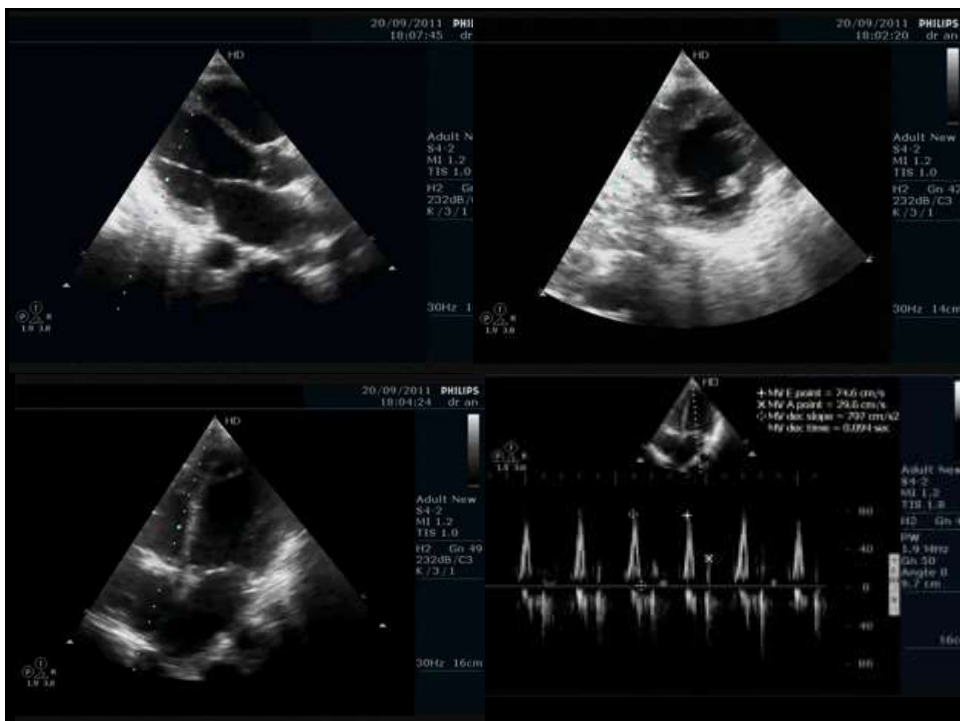
Echocardiography:

- Rule out other non-inflammatory diseases.
- Global ventricular dysfunction & RWMA.
- Fulminant myocarditis: non-dilated, thickened, and impaired LV (interstitial edema).
- Monitor changes in chamber size, wall thickness, ventricular function, and pericardial effusions.



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CMR:

CMR PROTOCOL:

- CINE SSFP: long axis (2ch, 3ch, 4ch) and short axis
- T2-weighted black blood imaging
- Early gadolinium enhancement
- Late gadolinium enhancement: long axis (2ch, 3ch, 4ch) and short axis

* SSFP: Contrast-enhanced steady-state free precession



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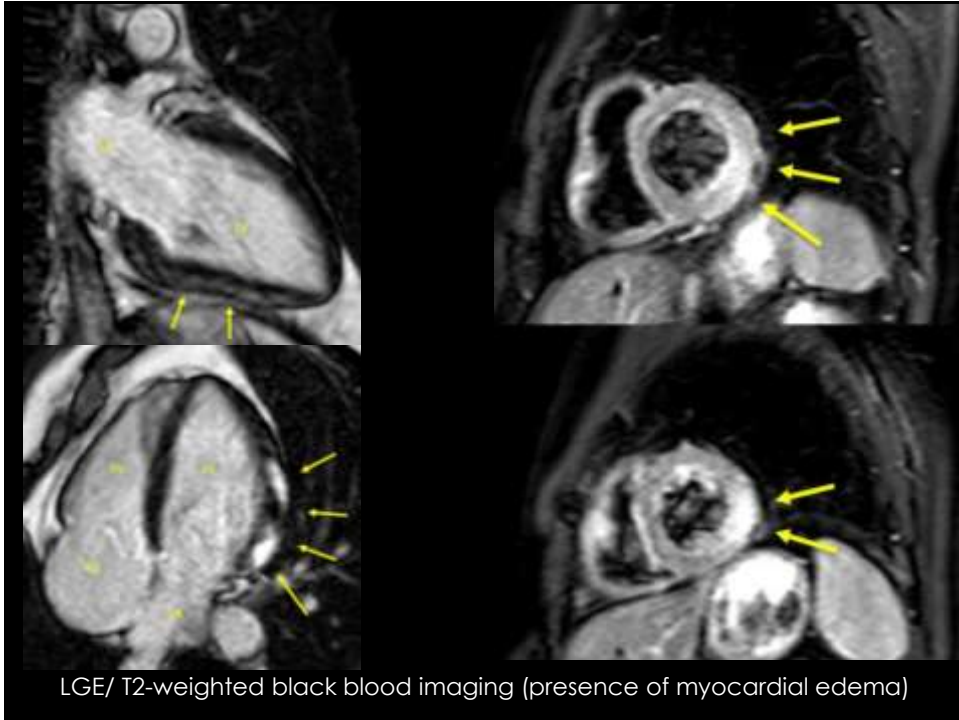
Lake Louise Criteria

at least two:

- Regional or global myocardial signal intensity increase in T2-weighted oedema images
- Increased global myocardial early gadolinium enhancement ratio between myocardium and skeletal muscle in gadolinium-enhanced T1-weighted images
- at least one focal lesion with non-ischemic regional distribution in inversion recovery-prepared gadolinium-enhanced T1-weighted images (late gadolinium enhancement)



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Biomarkers:



- Troponin
- CK (MB)

- BNP

- ESR
- CRP

* normal levels do not exclude myocarditis.

Viral antibodies:

- +ve viral serology \neq myocardial infection (interaction of the peripheral immune system with virus).
- No correlation between virus serology and EMB findings, thus limited diagnostic value.



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Serum cardiac autoantibodies (aabs)

- Aabs are found in myocarditis patients
- Lack of viral genome on EMB with detectable serum aabs suggests immune-mediated myocarditis.



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Diagnosis



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Table 4 Diagnostic criteria for clinically suspected myocarditis

Clinical presentations^a

Acute chest pain, pericarditic, or pseudo-ischaemic

New-onset (days up to 3 months) or worsening of dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs

Subacute/chronic (>3 months) or worsening of dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs

Palpitation, and/or unexplained arrhythmia symptoms and/or syncope, and/or aborted sudden cardiac death

Unexplained cardiogenic shock

Diagnostic criteria

I. ECG/Holter/stress test features

Newly abnormal 12 lead ECG and/or Holter and/or stress testing, any of the following: 1 to III degree atrioventricular block, or bundle branch block, ST/T wave change (ST elevation or non ST elevation, T wave inversion), sinus arrest, ventricular tachycardia or fibrillation and asystole, atrial fibrillation, reduced R wave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature beats, supraventricular tachycardia

II. Myocardial injury markers

Elevated TnT/TnI

III. Functional and structural abnormalities on cardiac imaging (echo/angio/CMR)

New, otherwise unexplained LV and/or RV structure and function abnormality (including incidental finding in apparently asymptomatic subjects): regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without endocavitary thrombi

IV. Tissue characterization by CMR

Oedema and/or LGE of classical myocarditic pattern (see text)

Clinically suspected myocarditis if ≥ 1 clinical presentation and ≥ 1 diagnostic criteria from different categories, in the absence of: (1) angiographically detectable coronary artery disease (coronary stenosis $\geq 50\%$); (2) known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome (e.g. valve disease, congenital heart disease, hyperthyroidism, etc.) (see text). Suspicion is higher with higher number of fulfilled criteria.

If the patient is asymptomatic ≥ 2 diagnostic criteria should be met.



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Diagnosis:

- 1 or more of the clinical presentations and 1 or more of the diagnostic criteria from different categories.
- If the patient is asymptomatic, 2 or more diagnostic criteria from different categories.



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Invasive assessment:

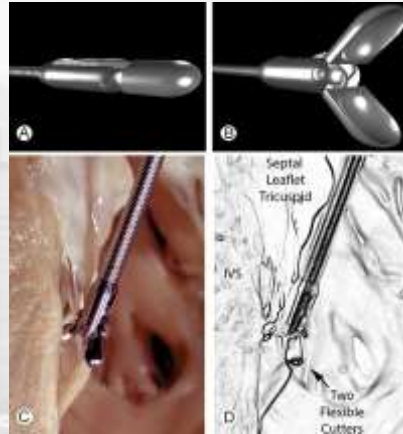
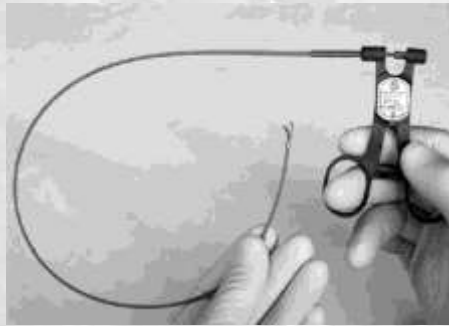
- **Coronary angiography.**
- **EMB**



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Endomyocardial biopsy



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Endomyocardial biopsy

- Confirms the diagnosis (gold standard).
- Identifies Etiology and type of inflammation (e.g. giant cell & sarcoidosis) → treatment and prognosis.
- 3 samples, 1–2 mm in size, (RV or LV).
- Histology, immunohistochemistry, and viral PCR.



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Dallas criteria

Based on **EMB** specimens

- 1. Active Myocarditis:** if light microscopy revealed infiltrating lymphocytes and myocytolysis
- 2. Borderline or on going Myocarditis** if lymphocyte infiltration and NO myocytolysis
- 3. Negative for Myocarditis** if no lymphocytic infiltrate and no myocytolysis



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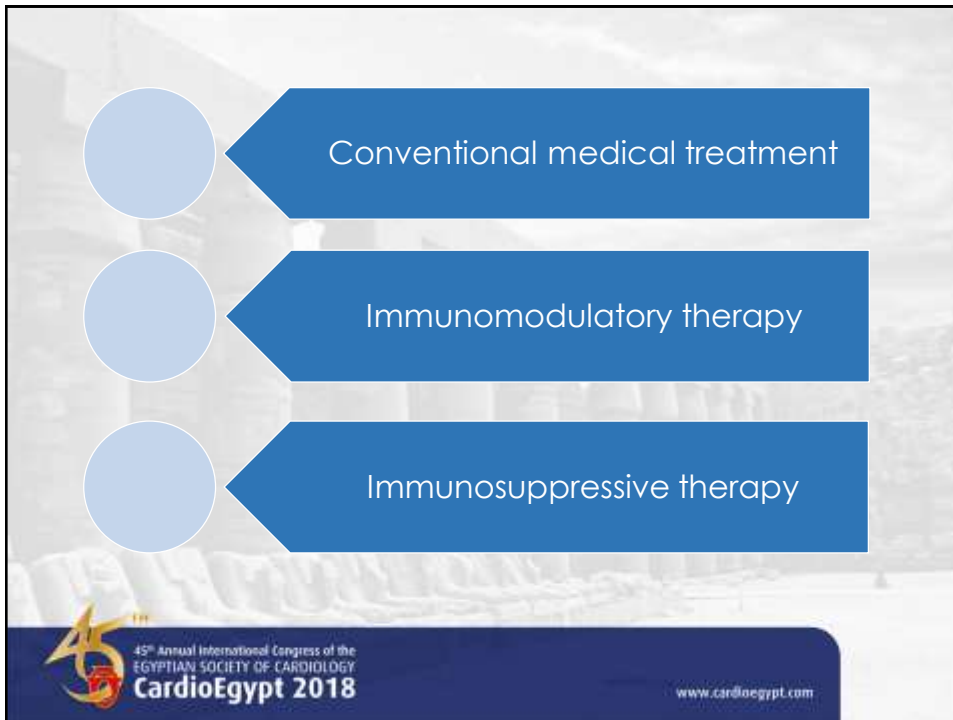
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Management



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Conventional medical treatment

- Principles:
 - Arrhythmia management.
 - Heart failure management.
 - Etiology-targeted therapy (If supported by evidence).

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Hemodynamically **unstable** patients

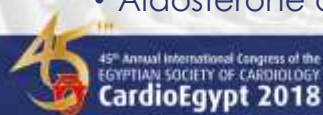
- Units with hemodynamic monitoring, cardiac catheterization, and expertise in EMB.
- Mechanical cardio-pulmonary assist device (e.g. ECMO) may be needed as a bridge to recovery.
- Cardiac transplantation should be deferred in the acute phase (to be considered for patients who cannot be stabilized e.g. giant cell myocarditis).



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Hemodynamically **stable** patients

- Hospital admission as rapid deterioration may occur.
- Hemodynamically stable heart failure:
 - Diuretics
 - ACEIs/ ARBs
 - BB
 - Aldosterone antagonists.



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Arrhythmia

- No specific recommendations for the management of arrhythmia in myocarditis.
- Temporary pacing (AV block).
- ICD implantation should be deferred until resolution of the acute episode.



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Avoidance of exercise

- Physical activity should be restricted during the acute phase of myocarditis until the disease has completely resolved.
- Athletes should be temporarily excluded from sport activity (6 m)



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Immunomodulatory therapy

- Anti-viral therapies.
- High dose intravenous immunoglobulin.
- Immunoabsorption (IA).



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Antiviral therapies:

- Acyclovir/Ribavirin: their efficacy is unproven in myocarditis.
- Interferon β may eliminate enteroviral and adenoviral genomes in patients with LV dysfunction and improves NYHA functional class.



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High dose intravenous immunoglobulin (IVIg)

- IVIG was ineffective in recent-onset DCM in which only 15% of patients had biopsy-proven myocarditis of non-specified cause.



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Immunoabsorption (IA)

- IA is a treatment options for autoimmune myocarditis.
- Larger randomized trial is currently underway, IA is not yet recommended.



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Immunosuppressive therapy

- Steroids
- Azathioprine and steroids
- Cyclosporine A, azathioprine and steroids



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Immunosuppressive therapy

- Response to therapy is reported mainly in
 - Chronic virus-negative forms
 - Giant cell myocarditis
 - Active autoimmune myocarditis defined as virus-negative and autoantibody positive.
 - cardiac sarcoidosis
 - Myocarditis associated with known extra-cardiac autoimmune disease



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Immunosuppressive therapy

- Immunosuppression should be started only after ruling out active infection on EMB by PCR.
- Follow-up EMB may be required to guide the intensity and the length of immunosuppression



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Prognosis:

- Varies according to the underlying etiology.
- The majority of cases of acute myocarditis have a benign course (~ 50% Complete resolution).
- 25% will develop persistent cardiac dysfunction
- Survival rates in giant-cell myocarditis are markedly worse.



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Prognosis:

- Myocarditis may relapse many years after the first episode.
- Relapses should be managed similarly to the index episode.
- In patients who do not resolve, disease may continue subclinically and lead to DCM.



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Follow up

- All patients with myocarditis should be followed up with:
 - Clinical assessment.
 - ECG.
 - Echocardiography.
- Long-term follow-up for patients that have experienced myocarditis is recommended.



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Take Home message:

- Myocarditis is not rare, and may be fatal.
- Diagnosis could be made based on Lab, Echocardiography and CMR. EMB may be needed in many cases.
- Treatment is mainly supportive with some etiology specific therapies.
- Outcome is related to severity of presentation and etiology.



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Thank You