Cardiomyopathies

1) Dilated Cardiomyopathy:	
General characteristics:	- Most common type of cardiomyopathy - characterized by ventricular dilation and impaired contractile performance, which may involve the left or both ventricles - many die within 5 years of the onset of symptoms - Pathobiology: Systolic dysfunction may result from: - Altered hemodynamic parameters ➡ ⬇ stroke volume & ⬆ chamber pressures ➡ trigger neurohumoral changes of heart failure ➡insult to myocyte integrity and cell death -50 to 60% of such patients have familial disease that trigger immune-mediated pathogenesis, and disease-causing mutations currently can be identified in 10 to 20% of such families and disease causing mutations currently can be identified in 10 to 20% of such families, Mutations in genes encoding important structural proteins (Sarcomeric genes 10% and lamin A/C 5%), 1/3 of probands and family members develop low-titer, organ-specific autoantibodies to cardiac α-myosin. - Insidious progression leads to ventricular remodeling and that is the rule in inherited dilated cardiomyopathy and is also seen with viral persistence, anthracycline toxicity, and autoimmune dilated cardiomyopathy
Causes:	-Up to 50% of cases are idiopathic -Other causes include: 1. CAD (with prior MI) is a common cause 2. Toxic: Alcohol, doxorubicin, Adriamycin 3. Metabolic: Thiamine or selenium deficiency, hypophosphatemia, uremia 4. Infectious: Viral, Chagas disease, Lyme disease, HIV 5. Thyroid disease: Hyperthyroidism or hypothyroidism 6. Peripartum cardiomyopathy 7. Collagen vascular disease: SLE, scleroderma 8. Prolonged, uncontrolled tachycardia 9. Catecholamine induced: Pheochromocytoma, cocaine 10. Familial/genetic
Clinical features:	- Symptoms and signs of left- and right-sided CHF develop. - S3, S4, and murmurs of mitral or tricuspid insufficiency may be present. - Cardiomegaly is commonly seen. - Many patients with DCM will have a coexisting arrhythmia (atrial or ventricular) related to the dilated ventricle. - Sudden death.
Diagnosis:	- An early diagnosis of dilated cardiomyopathy requires consideration of the commonly recognized causes: systemic hypertension, valvular heart disease, associated systemic disorders, high-output states, and the muscular dystrophies - ECG, CXR, and Echocardiogram results consistent with CHF. - The changes in ECG of early disease are not specific and may include: left axis deviation and T wave abnormalities - Genetic testing may be warranted if there is a family history of DCM and no other cause can be identified - With progressive and advanced disease conduction abnormalities develop: 1)PR prolongation,2) QRS widening, 3) left bundle branch block - Echocardiogram used as a baseline and for serial assessment to monitor disease progression and the effect of treatment - MRI: by utilizing Gadolinium-enhanced magnetic resonance imaging may be very helpful in differentiating segmental wall motion abnormalities in dilated cardiomyopathy from previous myocardial infarction

	- Biopsy, occasionally should be considered in patients with potential unexplained myocarditis.
Treatment:	- Similar to treatment of CHF: Digoxin, diuretics, vasodilators, and cardiac transplantation. - Remove the offending agent if possible. (Sodium and fluid restriction, Avoidance of alcohol and other toxins) - Anticoagulation should be considered because patients are at increased risk of embolization.

2) Hypertrophic Cardiomyopathy:	
General characteristics :	-Most cases are inherited as an autosomal-dominant trait. -However, spontaneous mutations may account for some cases. - -Abnormalities in sarcomeric contractile protein genes account for approximately 50 to 60% of cases -Defined clinically by the presence of unexplained left ventricular hypertrophy -Pathologically by the presence of myocyte disarray surrounding increased areas of loose connective tissue, with cells forming in whorls around foci of connective tissue
Causes:	Pathophysiology: - The main problem is diastolic dysfunction due to a stiff, hypertrophied ventricle with elevated diastolic filling pressures. - - These pressures increase further with factors that increase HR and contractility (such as exercise) or decrease left ventricular filling (e.g., the Valsalva maneuver). - - Patients may also have a dynamic outflow obstruction due to asymmetric hypertrophy of the interventricular septum.
Clinical features:	- Symptoms a. Dyspnea on exertion b. Chest pain (angina) c. Syncope (or dizziness) after exertion or the Valsalva maneuver d. Palpitations e. Arrhythmias (AFib, ventricular arrhythmias)—due to persistently elevated atrial pressures f. Cardiac failure due to increased diastolic stiffness g. Sudden death—sometimes seen in a young athlete; may be the first manifestation of disease h. Some patients may remain asymptomatic for many years - Signs i. Sustained PMI j. Loud S4 k. Systolic ejection murmur outflow obstruction) increases the outflow obstruction) decreased gradient across aortic valve) ▯▯ l. Rapidly increasing carotid pulse with two upstrokes (bisferious pulse)
Diagnosis:	-Echocardiogram establishes the diagnosis(Differential Diagnosis: Causes of left ventricular hypertrophy)Long-standing systemic hypertension, Aortic Stenosis, Highly trained athletes)
Treatment:	1- Asymptomatic patients generally do not need treatment, but this is controversial. No studies have shown any alteration in the prognosis with therapy, so treatment generally focuses on reducing symptoms . 2- All patients should avoid strenuous exercise, including competitive athletics. 3- Symptomatic patients : a. beta Blockers should be the initial drug used in symptomatic patients; they reduce symptoms by improving diastolic filling (as HR decreases, duration in diastole increases), and also reduce myocardial contractility and thus oxygen consumption. b. Calcium channel blockers (verapamil). -can be used in patients not responding to beta blockers - reduce symptoms by the same mechanism as beta blocker c. Diuretics can be used if fluid retention occurs. d. If AFib is present, treat accordingly e. Surgery -myomectomy has a high success rate for relieving symptoms it involves excision of part of the myocardial septum. It is reserved for patients with severe disease. ▯▯ f. Pacemaker implantation has had variable results.

3) Restrictive Cardiomyopathy:	
General characteristics:	-Infiltration of the myocardium results in impaired diastolic ventricular filling due to decreased ventricular compliance. -Systolic dysfunction is variable and usually occurs in advanced disease. -Less common than dilated and hypertrophic cardiomyopathies.
Causes:	1) Amyloidosis 2)Sarcoidosis 3)Hemochromatosis 4)Scleroderma 5)Carcinoid syndrome 6) Chemotherapy or radiation induced
Clinical features:	- Elevated filling pressures cause dyspnea and exercise intolerance. - Right-sided signs and symptoms are present for the same reason.
Diagnosis:	- Echocardiogram: A. Thickened myocardium and possible systolic ventricular dysfunction B. Increased right atrium (RA) and LA size with normal LV and RV size C. In amyloidosis, myocardium appears brighter or may have a sparkled appearance -ECG: Low voltages or conduction abnormalities, arrhythmias, AFib -Endomyocardial biopsy may be diagnostic
Treatment:	1-Treat underlying disorder - A. Hemochromatosis: Phlebotomy or deferoxamine B. Sarcoidosis: Glucocorticoids C. Amyloidosis: No treatment available *Give digoxin if systolic dysfunction is present (except in patients with cardiac amyloidosis, who have increased incidence of digoxin toxicity) 2-Use diuretics and vasodilators (for pulmonary and peripheral edema) cautiously, because a decrease in preload may compromise cardiac output

4) Arrhythmogenic Right Ventricular Cardiomyopathy:	
General characteristics:	- A genetically determined heart muscle disorder characterized by fibrofatty replacement of right ventricular myocardium. - Associated with arrhythmia, heart failure, and premature sudden death. - Inherited as an autosomal dominant disease, usually with incomplete penetrance - Recessive forms with cutaneous manifestations have been recognized - Recognized mutations account for approximately 40% of cases
Clinical features:	•In the early phase, patients are usually asymptomatic •Resuscitated cardiac arrest and sudden death may be the initial manifestations •The overt arrhythmic phase most often first occurs in adolescents and young adults, when patients note palpitations or syncope •The third phase, characterized by diffuse right ventricular disease, usually is recognized in the middle and later decades. •Patients may present with right-sided heart failure despite relatively preserved left ventricular function •In the advanced stage, obvious left ventricular involvement and biventricular heart failure are seen
Treatment:	- Intracardiac defibrillator with supplemental antiarrhythmic agents

Unclassified Cardiomyopathies	General characteristics
Alcoholic Cardiomyopathy	- Alcohol and its metabolite, acetaldehyde, are cardiotoxins acutely and chronically. - Myocardial depression is initially reversible but, if sustained, can lead to irreversible vacuolization, mitochondrial abnormalities, and fibrosis - The amount of alcohol necessary to produce symptomatic cardiomyopathy in susceptible individuals is not known - Abstinence leads to improvement in at least 50% of patients with severe symptoms, some of whom normalize their left ventricular ejection fractions
Chemotherapy	- Doxorubicin (Adriamycin) cardiotoxicity causes characteristic histologic changes on Endomyocardial biopsy, with overt heart failure in 5 to 10% of patients who receive doses greater than or equal to 450 mg/m2 of body surface area - Cyclophosphamide and ifosfamide can cause acute severe heart failure and malignant ventricular arrhythmias - 5-Fluorouracil can cause coronary artery spasm and depressed left ventricular contractility. - Trastuzumab has been associated with an increased incidence of heart failure
Metabolic	- Excess catecholamines, as in pheochromocytoma, Cocaine increases synaptic concentrations of catecholamines by inhibiting reuptake at nerve terminals; the result may be an acute coronary syndrome or chronic cardiomyopathy - Thiamine deficiency can cause beriberi heart disease, with vasodilation and high cardiac output followed by low output. - Calcium deficiency resulting from hypoparathyroidism, gastrointestinal abnormalities, or chelation directly compromises myocardial contractility. - Hypophosphatemia which may occur in alcoholism, during recovery from malnutrition, and in hyperalimentation, also reduces myocardial contractility. - Patients with magnesium depletion owing to impaired absorption or increased renal excretion also may present with left ventricular dysfunction
Skeletal Myopathies	- Duchenne's muscular dystrophy and Becker's X-linked skeletal muscle dystrophy typically include cardiac dysfunction - Maternally transmitted mitochondrial myopathies such as Kearns-Sayre syndrome frequently cause cardiac myopathic changes
Peripartum Cardiomyopathy	- Peripartum cardiomyopathy appears in the last month of pregnancy or in the first 5 months after delivery in the absence of preexisting cardiac disease - Lymphocytic myocarditis, found in 30 to 50% of biopsy specimens, suggests an immune component - The prognosis is improvement to normal or near-normal ejection fraction during the next 6 months in more than 50% of patients.