My Oh Myocarditis

Diagnosis and Treatment of Viral Myocarditis

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Myocarditis

- inflammatory infiltration of the myocardium with associated necrosis or degeneration, or both.
- WHO 1995 classification: myocarditis with cardiac dysfunction
- Also referred to as inflammatory cardiomyopathy

Clinicopathologic classification

Not widely used.

- Fulminant (17% incidence) outcome: die or recover
- Acute (65%) moderate compromise, LV dysfunction, death.
- Chronic active (11%) mild to moderate CV dysfunction. Can be restrictive. Fibrosis.
- Chronic persistent (7%) no cardiovascular compromise.

Dallas Classification 1986

- Initial biopsy: 1a Myocardial necrosis, degeneration, or both. Absent significant coronary artery disease.
- Adjacent inflammatory infiltrates or fibrosis.
- 1b borderline
- 1c no myocarditis. No inflammatory infiltrates or myocyte damage.
- 2. subsequent biopy
- a. Ongoing persistent myocarditis and/or fibrosis
- B. Resolving healing myocarditis and/or fibrosis
- C. Resolved healed myocarditis and/or fibrosis

The Marburg criteria from World Health Organization 1996

- Minimum of 14 infiltrating leukocytes per millimeter
- preferably T lymphocytes
- + up to 4 macrophages may be included.

Clinical presentation

- May be totally asymptomatic or can manifest with chest pain syndromes
- Mild persistent chest pain and 35% of cases with an acute myopericarditis
- Severe symptoms that can mimic acute myocardial infarction
- Rarely see chest pain associated with coronary artery vasospasm.
- Pericardial involvement may present with the pleuritic chest pain changing with position.
- 1 to 2 weeks prior 60% of patients have arthralgias, malaise, fever, sweats, pharyngitis, tonsillitis, URI or chills consistent with viral infection.
- Hallmark CHF symptoms dyspnea, decreased exercise capacity, fatigue, and edema.
- Diffuse severe myocarditis can **progress rapidly** and result in acute myocardial failure and cardiogenic shock.
- arrhythmia with **syncope**
- palpitations caused by **heart block** (stokes-adams attack)
- **ventricular** tachyarrhythmia
- **WORST CASE SCENARIO : sudden cardiac death**

Physical exam:

- Acute decompensated heart failure: Rales/crackles in the lungs, hypoxic, with S3 gallop (Kentucky)
- Central and peripheral edema
- JVD
- Tachycardia
- May have an Audible pericardial friction rub

Squirrel

- S_3 is thought to be caused by the oscillation of blood back and forth between the walls of the ventricles initiated by the inflow of blood from the atria. The reason the third heart sound does not occur until the middle third of diastole is probably that, during the early part of diastole, the ventricles are not filled sufficiently to create enough tension for reverberation. It may also be a result of tensing of the chordae tendineae during rapid filling and expansion of the ventricle.
- Associated with Rapid ventricular filling. Think mitral regurgitation
- Post MI :Poor LV function. Hypokinetic or akinetic walls relax more slowly so LV filling is relatively too rapid.
- Dilated cardiomyopathy. Ventricular walls become thin and stiff so do not relax well.

Physical Exam Challenge

- Board Fodder: What are the associated exam findings with these diagnoses?
- Sarcoid myocarditis
- Acute rheumatic fever
- Hypersensitivity/eosinophilic myocarditis
- Giant cell myocarditis
- Peripartum cardiomyopathy

- Answers are at end of the presentation

Laboratory Testing

- CBC will show leukocytosis, often lymphocytic unless eosinophilic.
- Acute phase reactants such as ESR or high-sensitivity CRP have low specificity. Good for monitoring clinical progression or response to therapy though.
-
- *Novel inflammatory markers under investigation*: Tumor necrosis factor alpha, interleukins, interferon gamma, serial soluble Fas ligand levels. (worse prognosis).
- Rarely indicated: Serum viral antibody titers: Fourfold increase acutely and gradually drop during convalescence.
- Anti cardiac antibody titers: Low specificity so not indicated. (Only 62% of cases have titers greater than 1:40) examples include: Sarcolemma, myosin, lamina and, ADP/ADT trans-locator, or beta adrenergic receptors

Labs continued… what about Rheumatology?

- Rheumatologic screening: Antinuclear antibodies and rheumatoid factor
- Disease specific testing if following conditions are suspected:
- SLE: Anti-DS DNA with reported positive anti-Ro/SSA and anti-La/SSB in lupus carditis in children
- Polymyositis: Anti-Jo 1
- Wegener's granulomatosis: C ANCA (antineutrophil cytoplasmic antibody)
- Scleroderma: Anti-SCL 70

Show me the Troponin$

- Serum cardiac enzymes are markers of myonecrosis. These include creatine kinase: Myoglobin subfraction elevations and only 7.5% of patients with biopsy-proven myocarditis
- Cardiac troponin I or T elevated and **at least 50%** of patients with biopsy-proven myocarditis
- Notes: 89% to 94% specificity and 34% to 53% sensitivity

Diagnostic Imaging

- EKG:47% sensitivity
- Sinus tachycardia
- Nonspecific ST segment and T wave abnormalities can represent focal or global ischemia
- May include acute myocardial infarction with ST segment elevation
- May manifest in pericarditis-like changes
- Fascicular block or AV conduction disturbances and ventricular tachyarrhythmia may be hemodynamically significant

Echocardiogram: Complete.

- Standard operative procedure.

You want to exclude alternative causes of CHF, detect intracardiac thrombi, associated valvular disease, and quantify LV dysfunction.

- Monitor response to therapy.
- Focal wall motion abnormalities and pericardial effusion may prompt further work-up or intervention
- Fulminant often characterized by near normal diastolic dimensions and increased septal wall thickness. Contrasted with acute has increased diastolic dimensions but normal septal wall thickness
- RV dysfunction was a powerful predictor of death or need for cardiac transplant in biopsy-proven myocarditis.

Diagnostic Imaging: Echo

- Echocardiogram: Complete.
- Standard operative procedure.
- You want to exclude alternative causes of CHF, detect intracardiac thrombi, associated valvular disease, and quantify LV dysfunction.
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Endangered species: Cardiac MRI

- Anti-myosin scintigraphy (indium 3 monoclonal anti-myosin antibody)
  - Provides identification of myocardial inflammation with a high-sensitivity 91 to 100% and negative predictive value 93 to 100% below specificity 28 to 33%
- Gallium scanning: Identifies severe myocardial cellular infiltration with high specificity (98%) but low sensitivity 36%
- Gadolinium enhanced magnetic resonance imaging **(MRI)** is being used more frequently for diagnosis based on small observational studies and found up to 100 for sensitivity and specificity depending on the protocol.
- Help to guide biopsy to areas of focal increased uptake of gadolinium in patients with clinically suspected myocarditis with significantly higher diagnostic yield compared to those who did not have enhancing areas with which to guide the bioptome.

Activate the Cath Lab

- Coronary angiography is often indicated to rule out CAD as the cause of new onset CHF because the clinical presentation of myocarditis may mimic MI in a pseudo-infarct pattern, especially if there are focal wall motion abnormalities and localizing EKG changes.
- So the coronary arteries will be normal.

Why? Etiology

- Idiopathic: 50% of all cases may not have a clear underlying cause
- We breakdown into infectious and noninfectious causes
- Infectious causes include viruses, Rickettsia, fungi, protozoa (Chagas), helminths, bacteria, and spirochetes
- Noninfectious include hypersensitivity reactions, cardiotoxic drugs, collagen vascular diseases, systemic illnesses, acute rheumatic fever, bites and stings, chemicals, physical injury, childbirth, and allo antigens

VIRAL (bolded terms are preventable by vaccines)

Influenza virus
Poliovirus
Mumps
Rubella
Rubeola
Hepatitis B

Hepatitis C

HIV (1.6%)
Epstein-Barr virus
Cytomegalovirus

Herpes viruses
Adenovirus

Enterovirus
Coxsackie A and B
Echovirus
Parvovirus B19 (Fifth's disease rash), polyarthropathy syndrome, severe anemia. *Not same as dog version that we have a vaccine for.*

NEW IN 2020! Coronavirus. SARS2 Covid 19

HIV

- HIV: Important because of dilated cardiomyopathy with an estimated incidence of 1.6%
- HIV type I virions infect myocardial cells in patchy distributions, leading to cytokine activation and progressive tissue damage.
- Cardiac autoimmunity, nutritional deficiencies, and drug toxicities such as mitochondrial damage from zidovudine and vasculitis or CAD associated with highly active antiretroviral therapy regimens might contribute.
- Opportunistic viral infections: CMV, EBV, coxsackie virus B have been isolated from endomyocardial biopsy specimens of HIV-positive patients with myocarditis in conjunction with HIV nucleic acid sequences

Treatment

- DRUGS:
- Diuretics
- Beta-blockers
- Aldosterone antagonists
- ACE inhibitors* or ARB/ARNI
- Statins. Monitor liver enzymes
- Avoid digoxin due to proarrhythmic properties
- If they have an apical aneurysm with thrombus, prior embolic episodes, or atrial fibrillation, anticoagulate to prevent thromboembolic events.
- Inotropes reserved for severe hemodynamic compromised such as fulminant

Is There a Role For Statin Therapy in Acute Viral Infections?

Mar 18, 2020

Cardiology Magazine

Doctor the patient is in a wide complex tachycardia

- Antiarrhythmics are first-line therapy including beta-blockers, amiodarone, and sotalol
- ICD is for patient stabilized in chronic phase with persistent low EF or with malignant arrhythmias refractory to medical therapy
- Permanent pacemaker is in heart block or bradycardia arrhythmias
- It's inflammation so I can fix it with a NSAID, Right? Wrong
- No benefits have been established for antiviral regimens or NSAIDs
- Refractory disease or biopsy-proven giant cell myocarditis (GCM): Immunosuppressive therapy

Treatment continued

- NON-DRUGS
- Aggressive mechanical circulatory support and surgical intervention
- Intra-aortic balloon counterpulsation for hemodynamic support and afterload reduction
- Mechanical assistive left ventricular assist device
- Extracorporeal membrane oxygen
- Consider early for transplant in patients with biopsy-proven giant cell myocarditis or peripartum cardiomyopathy. Unfortunately their rejection rate and survival is reduced compared with people who do not have myocarditis. Recurrent disease can affect the allograft.

Don’t run… Walk to your Cardiologist

- Abstain from vigorous exercise for up to 6 months or longer after onset of symptoms. Lift restriction once LV recovers (repeat echo with normal EF)
- Animal models demonstrated a theoretical increased risk of myocardial inflammation and necrosis, cardiac remodeling, and death.
- Close clinical follow-up with cardiology because persistent chronic inflammation may lead to dilated cardiomyopathy. Usually 1 to 3-month intervals for drug and physical activity rate titration
- Serial echoes of ventricular structure and function with disagreement on frequency post myocarditis.

To biopsy or not to biopsy?

- EMB = endomyocardial biopsy
- High false-negative rates. 50% in 4 or 5 biopsies because of small number of lymphocytes and difficulties in distinguishing cell types with wide interobserver variability.
- Consider this for patients to deteriorate rapidly for idiopathic reasons who do not respond to standard medical therapy
- Incidence of biopsy-proven myocarditis and recent onset unexplained heart failure is as low as 8 to 10%.
- You might have noticed the Dallas criteria is kind of old. Recent trials exploring immunosuppressive therapy or using supplemental pathologic criteria to assess myocarditis:
- Up regulation of human leukocyte antigen, presence of virus, and anti-cardiac antibodies.
- When it is going to impact your prognosis and or therapeutic possibility
- Approximately 12 to 50% of patients with acute or chronic myocarditis have persistent viral mRNA detected in biopsy samples

Treasure hunt:

- Identify markers that predict favorable response to immunosuppressive regimens.
- Acute lymphocytic myocarditis: In the study of 112 patients with biopsy-proven who did not respond to conventional therapy.
- Prednisone and azathioprine use resulted in one half of treatment group improving with EF rising from 26% to 47% and improvement in biopsy findings. Statistically significant sleep more likely positive cardiac antibodies (90% versus 0%) and less likely to have viral persistence when compared with nonresponders (14% versus 85%)

Prognosis

- The first hurdle is to get over the acute phase.
- Second you can have a full recovery with a 12.8% recurrence rate with idiopathic dilated cardiomyopathy
- Chronic active myocarditis less favorable prognosis
- IABP or ECMO patients can still have a full spontaneous recovery.
- Myocarditis treatment trial: 1 year mortality rate was 20%. 4-year mortality rate 56%. Neutral findings regarding routine immunosuppressive therapy
- 11-year survival rate of 93% for fulminant and 45% for non-fulminant based on in-hospital case series
- Up to 50% of patients with myocarditis developed subsequent cardiomyopathy over 3 months to 13 years.
- Histologic evidence seen in 4 to 10% of endomyocardial biopsies of patients with idiopathic dilated cardiomyopathy
- 1% developed severe heart block requiring permanent pacemaker placement

Morbidity and mortality predictors

- Unfavorable: Extremes of age, EKG abnormalities such as QRS alteration, A. fib, low voltages, syncope.
- In nonviral: Peripartum cardiomyopathy and giant cell cardiomyopathy

- CORONAVIRUS: Mortality in patients with underlying cardiovascular disease approaching 70% versus 40% in patients without it

Coronavirus COVID 19

- Viral infection with SARS-CoV-2, the causative agent of COVID-19, has been proposed to impact cardiac function via at least three distinct mechanisms.
- LATE PHASE: Associated with a profound systemic inflammatory response resulting in cytokines released which trigger cardio myocyte dysfunction and cardiac depression.
  - This phenomenon has been well described in other inflammatory conditions such as sepsis, where TNFα and IL-1ß/ß directly suppress cardiomyocyte contractility
- Direct infection: Sars/Cov–2 can directly infect the heart leading to immune cell recruitment and myocarditis. heart expresses the SARS-CoV-2 receptor ACE2 and MRI-based imaging and ECG findings of myocardial involvement have been reported
  - related virus SARS-CoV-1, which also uses ACE2 for cell entry, demonstrated the presence of viral RNA in 35% of hearts at autopsy. more macrophage infiltration. insubstantial T-cell response
- MICROVASCULAR DYSFUNCTION : Impacting the microvasculature via effects on ACE 2 could trigger microvascular dysfunction and tissue ischemia leading to ventricular dysfunction and/or arrhythmias.

What is driving the troponin?

- Mechanisms underlying troponin elevations in COVID-19 patients may include direct viral infection of myocytes, inflammatory cytokine signaling in myocytes, hypotension, and/or ischemia.
- SO HOW DO WE TELL IF IT'S A HEART ATTACK?
- It is important to note that elevated troponin levels or evidence of cardiac dysfunction rarely occurs in the absence of severe pulmonary disease, which suggests that isolated myocardial involvement is unlikely to occur with SARS-CoV-2.
- In addition, C-reactive protein (CRP), ferritin, D-dimer, IL-6, and LDH are markedly elevated in patients with profound systemic inflammation in response to SARS-CoV-2. These inflammatory biomarkers are also associated with poor prognosis

Other diagnostic considerations

- **ECG**
- ECG findings with COVID-19 can include diffuse ST-elevations as seen in myopericarditis, nonspecific ST changes, low voltage in the limb leads, and PVCs.[9]
- Although outside the scope of this discussion, patients can also present with STEMI in the setting of COVID-19 and often without evidence of coronary obstruction, perhaps secondary to myocarditis or direct cardiac injury from the virum.
- use of point-of-care ultrasound (POCUS) can provide useful information about cardiac function while limiting the number of people that are exposed to an infected patient.
- At present, there is minimal role for transesophageal echocardiography and MRI, both of which pose significant risk of aerosolization to the imaging team.

Pulmonary Artery Catheter Assessment

- Pulmonary artery catheters (PAC) provide information about hemodynamic status and cardiac filling pressures. Although these data may be useful to direct inotropic and mechanical support in cardiogenic shock, the potential risk of exposure to providers during COVID-19 limits the routine utility of this approach.
- BEST TO USE WHEN THINKING ABOUT ECMO because inotropes and pressors aren't working.

Coronavirus investigational drugs

- In vitro and preliminary clinical research have suggested that hydroxychloroquine alone and in combination with azithromycin could prove to be an effective treatment for COVID-19.
- Based on a small study in France enrolling 26 treated patients and 16 non-randomized controls showed that hydroxychloroquine alone or in combination with azithromycin shortened the time to resolution of viral shedding of COVID-19, clinicians in many countries have prescribed these in clinical practice with multiple randomized trials currently underway.
- However, chloroquine, hydroxychloroquine and azithromycin all prolong QT interval, raising concerns about the risk of arrhythmic death from individual or concurrent use of these medications.

Joint statement from ACC, American Heart Association and Heart Rhythm Society leadership outlines critical cardiovascular considerations in the use of hydroxychloroquine and azithromycin for the treatment of COVID-19

- In order to minimize risk, approaches outlined in the statement include:
- 1) electrocardiographic/QT interval monitoring, with guidance for drug withdrawal;
- 2) correction of hypokalemia >4 mEq/L and hypomagnesemia >2 mg/dL; and 3) avoiding other drugs that prolong QTc when feasible. The statement also includes a table rating potential adverse cardiac events of medications currently being repurposed for COVID-19 treatment, such as chloroquine and lopinavir/ritonavir.
- If used outside of a clinical trial, it should be at the direction of an infectious disease or COVID-19 expert, with cardiology input for QT monitoring. This guidance reviews the arrhythmogenicity of hydroxychloroquine and azithromycin, providing tables for a risk score of drug-associated QTc prolongation and risk levels.

Arrhythmogenicity of Hydroxychloroquine and Azithromycin

- Drug-induced QT prolongation has long served as a surrogate indicator for increased risk of drug-associated torsades de pointes (TdP), a potentially lethal polymorphic ventricular tachycardia.
- The risk of TdP is not a linear function of QT duration nor the extent of change; some drugs which prolong QTc are not associated with increased arrhythmic death.[2,3]
- The duration of use for these medications for COVID-19 infection is short (5 to 10 days for acute illness).
- Azithromycin, a frequently used macrolide antibiotics lacks strong pharmacodynamic evidence of iKr inhibition
- Chloroquine, and its more contemporary derivative hydroxychloroquine, have remained in clinical use for more than a half-century as an effective therapy for treatment of some malarias, lupus, and rheumatoid arthritis. Data show inhibition of iKr and resultant mild QT prolongation associated with both agents.

Inpatient EKG QTc monitoring

- Baseline
  - Discontinue and avoid all other non-critical QT prolonging agents.
  - Assess a baseline ECG, renal function, hepatic function, serum potassium and serum magnesium.
  - When possible, have an experienced cardiologist/electrophysiologist measure QTc, and seek pharmacist input in the setting of acute renal or hepatic failure.
- Relative contraindications (subject to modification based on potential benefits of therapy)
  - History of long QT syndrome, or
  - Baseline QTc >500 msec (or >530-550 msec in patients with QRS greater than >120 msec)
- Ongoing monitoring, dose adjustment and drug discontinuation
  - Place on telemetry prior to start of therapy.
  - Monitor and optimize serum potassium daily.
  - Acquire an ECG 2-3 hours after the second dose of hydroxychloroquine, and daily thereafter.
  - If QTc increases by >60 msec or absolute QTc >500msec (or >530-550 msec if QRS >120 msec), discontinue azithromycin (if used) and/or reduce dose of hydroxychloroquine and repeat ECG daily.
  - If QTc remains increased >60 msec and/or absolute QTc >500 msec (or >530-550 msec if QRS >120 msec), reevaluate the risk/benefit of ongoing therapy, consider consultation with an electrophysiologist, and consider discontinuation of hydroxychloroquine.

Outpatient…first weigh risk of infection against benefit of EKG/Qtc risk

- Baseline
  - Discontinue and avoid all other non-critical QT prolonging agents.
  - Assess a baseline ECG, renal function, hepatic function, serum potassium and serum magnesium.
  - When possible, have an experienced cardiologist/electrophysiologist measure QTc.
  - Avoid outpatient initiation in the setting of acute renal or hepatic failure.
- Relative contraindications (subject to modification based on potential benefits of therapy)
  - History of long QT syndrome, or
  - Baseline QTc >480 msec (or >510-530 msec if QRS >120 msec), or
  - Tisdale risk score ≥11
- Ongoing monitoring, dose adjustment and drug discontinuation
  - If quarantine or resource constraints are prohibitive, consider no further ECG / telemetry assessment if Tisdale risk score ≤6. Also consider use of alternative mechanisms of QT and arrhythmia assessment outlined below.
  - Otherwise, repeat ECG 2-3 hours after dosing on day 3 of therapy. If QTc increases by >30-60 msec or absolute QTc >500msec (or >530-550 msec if QRS >120 msec), consider discontinuing therapy.

Tisdale Risk score for QTc Prolongation

- A risk score has been derived and validated by Tisdale et al., for prediction of drug-associated QT prolongation among cardiac-care-unit-hospitalized patients

If otherwise ready for discharge, patients who have had QT intervals that are well within normal range and have had no concerning arrhythmias on telemetry should not be held in the hospital exclusively for the purpose of hydroxychloroquine-related arrhythmia monitoring.

Table 1. Risk Score For Drug-Associated QTc Prolongation[9]

Risk Factors	Points
Age ≥68 y	1
Female sex	1
Loop diuretic	1
Serum K+ ≤3.5 mEq/L	2
Admission QTc ≥450 ms	2
Acute MI	2
≥2 QTc-prolonging drugs	3
sepsis	3
Heart failure	3
One QTc-prolonging drug	3
Maximum Risk Score	21
K+ indicates potassium; and MI, myocardial infarction.	

A Tisdale score of ≤ 6 predicts low risk, 7-10 medium risk, and ≥ 11 high risk of drug-associated QT prolongation (Table 2).

Table 2. Risk Levels For Drug-Associated QT Prolongation[9]

Low risk = ≤6 points
Moderate risk = 7-10 points
High-risk = ≥11 points

Coronavirus

- VA Study just released. Non-blinded. Univ of VA assisted.
- Hyroxychloroquine in 368 VA patients
- **CONCLUSIONS:**
- In this study, we found no evidence that use of hydroxychloroquine, either with or without
- azithromycin, reduced the risk of mechanical ventilation in patients hospitalized with Covid-19.
- An association of increased overall mortality was identified in patients treated with
- hydroxychloroquine alone. These findings highlight the importance of awaiting the results of ongoing prospective, randomized, controlled studies before widespread adoption of these drugs.

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2020

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
Influenza inactivated (IIV) or **Influenza recombinant** (RIV)	1 dose annually			
or	or			
Influenza live, attenuated (LAIV)	1 dose annually			
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			
Varicella (VAR)	2 doses (if born in 1980 or later)		2 doses	
Zoster recombinant (RZV) *(preferred)*			2 doses	
or			or	
Zoster live (ZVL)			1 dose	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal conjugate (PCV13)	1 dose			65 years and older
Pneumococcal polysaccharide (PPSV23)	1 or 2 doses depending on indication			1 dose
Hepatitis A (HepA)	2 or 3 doses depending on vaccine			
Hepatitis B (HepB)	2 or 3 doses depending on vaccine			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, see notes for booster recommendations			
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations			
	19 through 23 years			
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication			

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No recommendation/ Not applicable

TABLE 11.1 Causes of Myocarditis

Cause	Examples
	Infectious Causes
Viruses	Enteroviruses, coxsackievirus A and B, echovirus, influenza virus, poliovirus, herpesviruses, adenovirus, mumps, rubella, rubeola, hepatitis B or C virus, human immunodeficiency virus, Epstein–Barr virus, cytomegalovirus, and parvovirus B19
Rickettsia	Rocky Mountain spotted fever
Fungi	Cryptococcosis, aspergillosis, coccidioidomycosis, and histoplasmosis
Protozoa	*Trypanosoma cruzi* (Chagas disease) and *Toxoplasmosis gondii*
Helminths	Trichinosis and schistosomiasis
Bacteria	*Legionella*, *Clostridium*, streptococci, staphylococci, *Salmonella*, and *Shigella*
Spirochetes	*Borrelia burgdorferi* (Lyme disease)
	Noninfectious Causes
Hypersensitive reaction	Eosinophilic myocarditis
Cardiotoxic drugs	Catecholamines, amphetamines, cocaine, chemotherapeutic drugs (e.g., anthracyclines, fluorouracil, streptomycin, cyclophosphamide, interleukin-2, trastuzumab [Herceptin]), and smallpox vaccine
Collagen vascular diseases	Systemic lupus erythematosus (i.e., lupus carditis), Wegener granulomatosis or Churg–Strauss syndrome, dermatomyositis or polymyositis, and scleroderma
Systemic illnesses	Sarcoidosis, giant cell myocarditis, Kawasaki disease, large-vessel vasculitis (e.g., polyarteritis nodosa and Takayasu arteritis), and inflammatory bowel diseases (e.g., ulcerative colitis and Crohn disease)
Acute rheumatic fever	
Bites and stings	Venoms of scorpions, snakes, wasps, and black widow spiders
Chemicals	Hydrocarbons, carbon monoxide, thallium, lead, arsenic, and cobalt
Physical injury	Irradiation, heat stroke, and hypothermia
Childbirth	Peripartum cardiomyopathy
Alloantigens	Posttransplantation cellular rejection

TABLE 11.2 Relevant ACC/AHA Recommendations for the Role of Endomyocardial Biopsy Scenario

	Class of Recommendation
New-onset heart failure of <2-wk duration associated with a normal-sized or dilated left ventricle and hemodynamic compromise	I
New-onset heart failure of 2-wk to 3-mo duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1–2 wk	I
Heart failure of >3-mo duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1–2 wk	IIa
Heart failure associated with a dilated cardiomyopathy of any duration associated with suspected allergic reaction and/or eosinophilia	IIa
New-onset heart failure of 2-wk to 3-mo duration associated with a dilated left ventricle, without new ventricular arrhythmias, or second- or third-degree heart block that responds to usual care within 1–2 wk	IIb
Heart failure of >3-mo duration associated with a dilated left ventricle, without new ventricular arrhythmias, or second- or third-degree heart block that responds to usual care within 1–2 wk	IIb
Unexplained ventricular arrhythmias	IIb

Adapted from Cooper LT, Baughman KL, Feldman AM, et al. The role of endomyocardial biopsy in the management of cardiovascular disease. *Circulation*. 2007;116:2216–2233; American Heart Association, Inc.

Statin thoughts…

- emphasize continuation and adherence to statin therapy in patients with clinical atherosclerotic cardiovascular disease (ASCVD), diabetes, or those at high-risk of ASCVD.
- This is important as the case-fatality rates with COVID-19 infection are extremely high in those with established cardiovascular disease (10.8%) and diabetes (7.3%).[9]
- Furthermore, statin therapy should be continued in patients with suspected COVID-19 infection as acute cardiac injury has been described in these patients.
- Place High-risk primary prevention patients on guideline-directed statin therapy in the outpatient setting.
- This will help mitigate some of the increased risk of cardiovascular events associated with COVID-19 infection.
- In patients with active COVID-19 infection who may develop severe rhabdomyolysis (frequency unknown at this time), it may be prudent to withhold statin therapy for a short period of time.

Physical exam challenge

- 1. Sarcoid myocarditis
- 2. Acute rheumatic fever
- 3. Hypersensitivity/eosinophilic myocarditis
- 4 Giant cell myocarditis
- 5 Peripartum cardiomyopathy

1. Lymphadenopathy with arrhythmias and involvement in other organs up to 70%

2. Usually affects the heart (50 to 90% of cases) associated with erythema marginatum, polyarthralgia, Chorea, and subcutaneous nodules. Jones criteria

3. Pruritic maculopapular rash and history of onset temporally related to initiation of potential culprit medications

4. Sustained ventricular tachycardia and rapidly progressive heart failure

5. CHF developing in the last month of gestation or within 5 months after delivery

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