

Management of Idiopathic Pericarditis: Old Drugs with New Tricks

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Walter P. Scheffe 2019 CPE Series

Financial Disclosure and Resolution

Under guidelines established by the Accreditation Council for Pharmacy Education (ACPE), disclosure must be made regarding financial relationships with commercial interests within the last 12 months.

- I have **no** relevant financial relationships or affiliations with commercial interests to disclose.
- **I will be** discussing experimental or off-label drugs, therapies and/or devices that have not been approved by the FDA.
- None of the medications that I will be discussing today have FDA-approved indications for the treatment of pericarditis.
- I will make clinical recommendations during this presentation.

Learning Objectives

At the completion of this activity, pharmacists will be able to:

1. Select appropriate anti-inflammatory therapy based on patient-specific factors.
2. Outline a tapering schedule for anti-inflammatory therapies.
3. Identify drug interactions associated with colchicine.
4. List monitoring parameters for colchicine, anti-inflammatory therapy, and corticosteroids.
5. Describe an empiric pharmacotherapy plan for a patient with acute or recurrent idiopathic pericarditis.

Pre-Assessment Question 1

- Which of the following medications increases the risk of recurrence in acute idiopathic (viral) pericarditis?
 - A. Aspirin
 - B. Colchicine
 - C. Prednisone
 - D. Anakinra

Pre-Assessment Question 2

- Which of the following is an appropriate anti-inflammatory regimen for an adult patient diagnosed with acute idiopathic (viral) pericarditis?
 - A. Aspirin 325 mg PO daily for 1 month, then taper
 - B. Ibuprofen 800 mg PO TID for 6 months
 - C. Indomethacin 50 mg PO TID for 1 week, then taper
 - D. Ketorolac 15 mg PO daily for 3 weeks, then taper

Pre-Assessment Question 3

- Which of the following medications increases the plasma concentration of colchicine?
 - A. Carvedilol
 - B. Rifampin
 - C. Pravastatin
 - D. Levothyroxine

Pre-Assessment Question 4

- Which of the following parameters would be appropriate for monitoring the safety of colchicine?
 - A. Creatine phosphokinase
 - B. Blood glucose
 - C. INR
 - D. Fasting lipid panel

What is Pericarditis?

- Pericarditis – inflammation of the pericardium
- Most common form of pericardial disease
- Can “look” like other serious cardiovascular disorders
 - Acute myocardial infarction
 - Aortic dissection
 - Pulmonary embolism
 - Myocarditis

Importance of the Pericardium

- Pericardium functions to
 - lubricate the heart
 - anchor heart to mediastinum
 - prevent overfilling of heart
 - protect heart from infection
- Pericardium is comprised of two layers
- Contains upwards of 50 mL of pericardial fluid to help lubricate the two layers of the pericardium

Prog Cardiovasc Dis. 2017;59:341-348.

Pathophysiology of Pericarditis

- Inflammatory disease involving the pericardium
- Visceral and parietal layers can rub together to produce inflammation and potentially pain
- Thought to be caused by autoinflammatory or autoimmune mechanisms
 - Interleukin-1
 - Type 1 interferon

Eur Heart J 2015; 36: 2921-2964.
Curr Cardiol Rep. 2017;19:60.

Epidemiology of Pericarditis

- Incidence rate of hospitalization for acute pericarditis occurs in 3.32 per 100,000 person-years.
- Majority of patients with pericarditis present within the fifth decade of life.
- Care related to pericarditis is associated with high cost and healthcare burden, with a length of stay of approximately 4 days

N Engl J Med. 2013;369:1522-1528. *Lancet.* 2014;383:2232-2237.
Cardiology. 2016; 135: 27-35. *Ann Intern Med.* 2011;155:409-414.
Circulation. 2014; 130: 1601-1606. *Circulation.* 2005;112:2012-2016. *Arch Intern Med.* 2005;165:1987-1991.

Outcomes Associated with Pericarditis

- Incessance
- Recurrence
- Impaired quality of life
- Adverse effects secondary to prolonged use of corticosteroids
- Procedural care
 - Pericardiectomy
 - Pericardial window
 - Pericardiotomy
- Constrictive pericarditis
- Cardiac tamponade

Eur Heart J 2015; 36: 2921-2964.

Relevance of Pericarditis to Pharmacy Practice

- Pharmacotherapy is a mainstay of treatment for certain etiologies of pericarditis.
- Pharmacotherapy used to treat such etiologies are associated with potentially significant adverse effects and requires diligent monitoring.
- Pericarditis is associated with significant morbidity related to certain medications.
- Pharmacists in **every practice area** can potentially influence patient-related outcomes associated with pericarditis.

J Pharm Pract. 2019;1-8.

Diagnosis of Pericarditis

- Pericarditic chest pain
- Electrocardiogram (ECG) changes
- New or worsening pericardial effusion
- Pericardial friction rub
- Elevated inflammatory markers
 - C-reactive protein (CRP)
 - High sensitivity (hs)-CRP
 - White blood cell (WBC) count
 - Erythrocyte sedimentation rate (ESR)
- Evidence of pericardial inflammation by an imaging technique

Eur Heart J 2015; 36: 2921-2964

Important Definitions Related to Pericarditis

- **Subacute**
- **Acute pericarditis**
- **Recurrent pericarditis**
- **Incessant pericarditis**
- **Chronic pericarditis**
- **Constrictive pericarditis**

Eur Heart J 2015; 36: 2921-2964.

Etiologies of Pericarditis

- **Idiopathic**
- **Infectious**
 - **Viral**
 - **Bacterial**
 - **Fungal**
- **Autoimmune**
- **Traumatic/Iatrogenic**
- **Neoplastic**
- **Metabolic**
- **Amyloidosis**
- **Pulmonary arterial hypertension**
- **Aortic dissection**
- **Chronic heart failure**
- **Medications...**

Eur Heart J 2015; 36: 2921-2964.

Drug-Induced Pericarditis

- Lupus-like syndrome
 - Procainamide
 - Hydralazine
 - Methyldopa
 - Isoniazid
 - Phenytoin
- Minoxidil
- Anthracyclines
- Clozapine
- Anti-TNF α agents

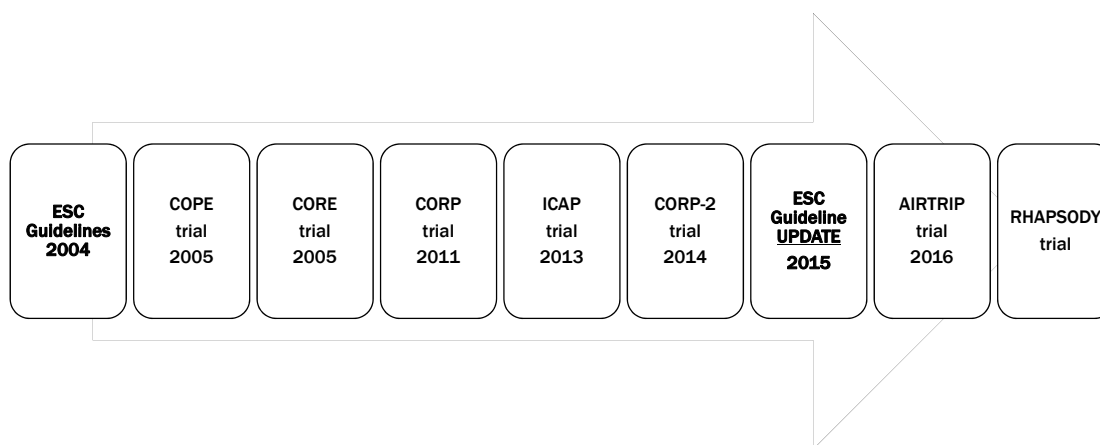
Eur Heart J 2015; 36: 2921-2964.

Idiopathic (Viral) Pericarditis

- Most common type of pericarditis in the Western hemisphere
- Associated with inflammatory sequelae
- The majority of patients studied in landmark pharmacotherapy studies include *idiopathic or viral etiologies* of pericarditis
- Recurrence is the most common complication associated with *idiopathic or viral etiologies* pericarditis

Eur Heart J 2015; 36: 2921-2964.

Timeline of Literature/Guideline Updates



Negative Prognostic Factors Associated with Idiopathic (Viral) Pericarditis

Major

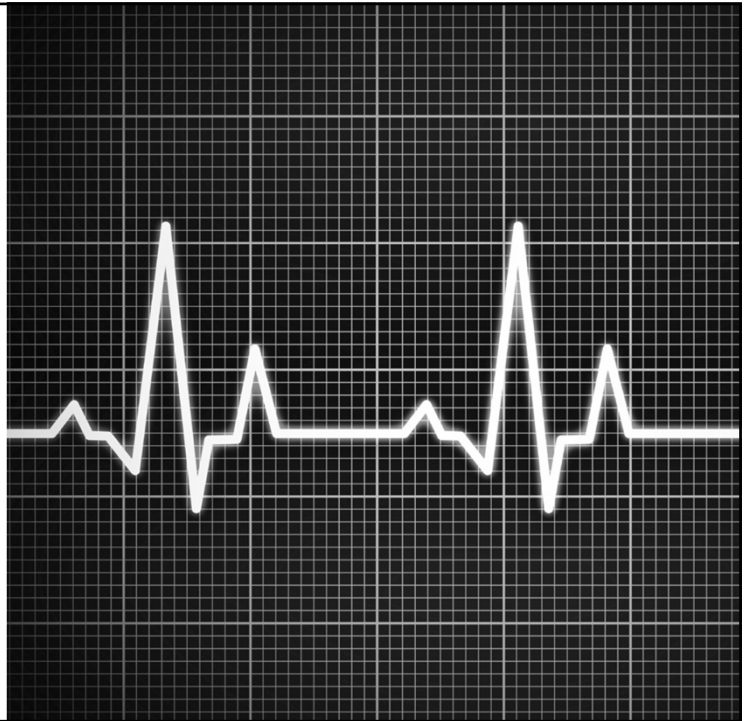
- Fever $>38^{\circ}\text{C}$
- Subacute onset
- Large pericardial effusion
- Cardiac tamponade
- **Lack of response to aspirin (ASA) or non steroidal anti-inflammatory drugs (NSAIDs) after at least 1 week of therapy**

Minor

- Myopericarditis
- **Immunosuppression**
- Trauma
- **Oral anticoagulant therapy**

Circulation 2007; 115: 2739-2744.
Eur Heart J 2015; 36: 2921-2964.

**Check-Point:
QUESTIONS?**



Management of Pericarditis

2015 ESC Guideline Recommendations for the Treatment of Acute Pericarditis

Recommendation	Class	Level
ASA or NSAIDs are recommended as first-line therapy for acute pericarditis with gastroprotection.	I	A
Colchicine is recommended as first-line therapy for acute pericarditis as an adjunct to ASA/NSAID therapy.	I	A
Serum CRP should be considered to guide the treatment length and assess the response to therapy.	IIa	C
Low-dose corticosteroids should be considered for acute pericarditis in cases of contraindication/failure of aspirin/NSAIDs and colchicine, and when an infectious cause has been excluded.	IIa	C
Corticosteroids are not recommended as first-line therapy for acute pericarditis.	III	C

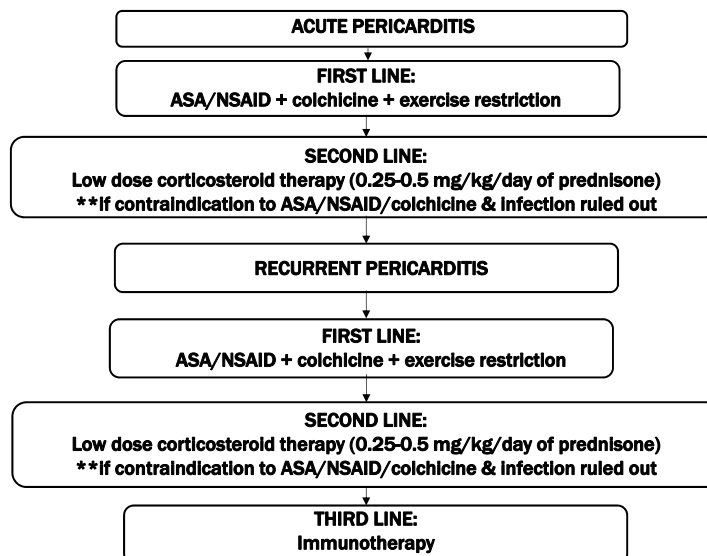
Eur Heart J 2015; 36: 2921-2964.

2015 ESC Guideline Recommendations for the Treatment of Recurrent Pericarditis

Recommendation	Class	Level
ASA and NSAIDs are mainstays of treatment and are recommended at full doses, if tolerated, until complete symptom resolution.	I	A
Colchicine (0.5 mg twice daily or 0.5 mg daily for patients < 70 kg or intolerant to higher doses); use for 6 months is recommended as an adjunct to aspirin/NSAIDs.	I	A
CRP dosage should be considered to guide the treatment duration and assess the response to therapy.	IIa	C
After CRP normalization, a gradual tapering of therapies should be considered, tailored to symptoms and CRP, stopping a single class of drugs at a time.	IIa	C
Drugs such as intravenous (IV) immunoglobulin (IG), anakinra and azathioprine may be considered in cases of corticosteroid-dependent recurrent pericarditis in patients not responsive to colchicine.	IIb	C

Eur Heart J 2015; 36: 2921-2964.

Idiopathic (Viral) Pericarditis Treatment



Eur Heart J 2015; 36: 2921-2964.

Benefits of Combination Therapy in the Treatment of Idiopathic (Viral) Pericarditis

- **Acute Pericarditis**
 - Combination of ASA PLUS Colchicine decreased rate of recurrence compared to ASA monotherapy (11.7% vs. 33%, p=0.009, respectively.)
 - Combination of ASA/IBU PLUS Colchicine decreased rate of recurrence compared to ASA monotherapy (16.7% vs. 37.5%, p < 0.001, respectively.)

ASA – Aspirin
IBU - ibuprofen

Circulation. 2005;112:2012-2016.
N Engl J Med. 2013;369:1522-1528.

Benefits of Combination Therapy in the Treatment of Idiopathic (Viral) Pericarditis

- **Recurrent Pericarditis**
 - **First episode of recurrence**
 - Combination of ASA PLUS Colchicine decreased rate of future recurrence compared to ASA monotherapy (24% vs. 50.6%, p=0.02, respectively.)
 - Combination of ASA/IBU PLUS Colchicine decreased rate of future recurrence compared to ASA monotherapy (24% vs. 55%, p < 0.001, respectively.)
 - **Multiple recurrences**
 - Combination of ASA,IBU, or indomethacin PLUS Colchicine decreased rate of future recurrence compared to ASA monotherapy (21.6% vs. 42.5%, p = 0.0009, respectively.)

Ann Intern Med. 2011;155:409-414.
Arch Intern Med. 2005;165:1987-1991.
Lancet. 2014;383:2232-2237.

ASA and NSAIDs

- **First line - used to treat pericarditic chest pain**
- **Mechanism of Action**
 - Inhibits prostaglandin synthesis
- ***Obtain baseline hs-CRP before initiating ASA or NSAID***
- **Initial high doses needed to elicit anti-inflammatory effects**
 - “Attack dosing” for 7-10 days
- **Ensure tapering over 3 - 4 weeks**
 - When patient is asymptomatic **and** hs-CRP has normalized

Pharmaceuticals. 2016;9:1-18.

ASA and NSAIDs

Agent	Common Attack Dose (Dose Range)	Tapering (Every 1-2 weeks)
ASA	800-1,000 mg PO every 6- 8 hours (2-4 g/day)	Decrease dose by 250-500 mg q. 1-2 weeks
Ibuprofen	600 mg PO every 8 hours (1,600-3,200 mg/day)	Decrease dose by 200-400 mg q. 1-2 weeks
Indomethacin	50 mg PO three times daily (750-150 mg/day)	Decrease doses by 25 mg q. 1-2 weeks

Pharmaceuticals. 2016;9:1-18.

ASA and NSAIDs

- Examples of Attack Dosing Tapering Regimens
 - ASA
 - 975 mg every 8 hours for 1 week
 - 650 mg every 8 hours for 2 weeks
 - 325 mg every 8 hours for 1 week
 - Ibuprofen
 - 600 mg every 8 hours for 1 week
 - 400 mg every 8 hours for 1 week
 - 200 mg every 8 hours for 1-2 weeks
 - Indomethacin
 - 50 mg every 8 hours for 1 week
 - 25 mg every 8 hours for 1-2 weeks
 - 25 mg every 12 hours for 1 week

ASA and NSAIDs

- Ketorolac tromethamine
 - 10-90 mg IV or IM
 - Controls symptoms in 1-2 hours
 - Maximum dose of 120 mg/day
 - Oral therapy is only indicated as continuation treatment following IV or IM administration
 - 20 mg followed by 10 mg every 4-6 hours
 - Maximum dose of 40 mg/day

Am Heart J. 1993;125:1455-8.
Pharmaceuticals. 2016;9:1-18.

ASA and NSAIDs

- Ketorolac tromethamine
 - **Maximum treatment duration of 5 days**
 - Dose adjustment
 - ≥ 65 years of age
 - Low body weight
 - Renal impairment

Am Heart J. 1993;125:1455-8.
Pharmaceuticals. 2016;9:1-18.

ASA and NSAIDs

- Adverse Effects
 - Dyspepsia
 - GI bleeding
 - Peptic ulcer disease
 - CNS-related
 - Acute kidney injury

Pharmaceuticals. 2016;9:1-18.

ASA and NSAIDs

- Gastroprotection for duration of high-dose ASA or NSAID therapy
 - Proton pump inhibitor (PPI)
 - H₂ receptor blocker
 - Misoprostol
- Choice of class is dictated by
 - Drug-disease interactions
 - Hypertension
 - Coronary artery disease
 - Heart failure
 - Renal disease
 - Tolerability
 - Cost
 - Drug-drug interactions

Pharmaceuticals. 2016;9:1-18.

ASA and NSAIDs

- **Role of the Pharmacist**
 - **Inpatient Pharmacists**
 - Ensure affordability and access to care
 - Devise taper schedule with team
 - Ensure patients understand their taper schedule
 - Educate patients on the role of ASA/NSAIDs for the treatment of pericarditis.
 - Counsel patients regarding use of ASA/NSAID, including the potential adverse effects and to use their gastroprotection for the duration of high-dose ASA or NSAID therapy
 - Check for drug-drug and drug-disease interactions
 - Monitoring
 - Transitions of care

J Pharm Pract. 2019;1-8.

ASA and NSAIDs

- **Role of the Pharmacist**
 - **Community or Ambulatory Care Pharmacists**
 - Educate patients on the role of ASA/NSAIDs for the treatment of pericarditis
 - Counsel patients regarding use of ASA/NSAID, including the potential adverse effects and to use their gastroprotection for the duration of high-dose ASA or NSAID therapy
 - Ensure patients understand their taper schedule
 - Check for drug-drug and drug-disease interactions
 - Medication therapy management (MTM)
 - Monitoring and follow-up
 - Transitions of care

J Pharm Pract. 2019;1-8.

Colchicine

- **First line** - combination of colchicine **PLUS** ASA/NSAID, decreases:
 - recurrence rates
 - rate of symptom persistence at 72 hours from treatment onset
 - time to remission within a week
 - incessance rate
- Mechanisms of action
 - inhibits NLRP-3 inflammasome
 - inhibits chemostasis of leucocytes to pericardium

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

- May administer an “attack dose” then maintenance dosing
- Preferentially use twice daily dosing
- Treatment duration:
 - Acute: 3 months
 - Recurrent: 6-12 months
- Narrow therapeutic index
 - Wide volume of distribution
 - Hepatic metabolism
 - Renal elimination

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

	COPE trial	CORE trial	CORP trial	ICAP trial	CORP-2 trial	U.S. tablet dosing
AD	1-2 mg	1-2 mg	2 mg	—	—	1.2-1.8 mg
MD	0.5 mg -1 mg/day	0.5 mg -1 mg/day	1 mg/day	1 mg/day	0.5 mg BID	0.3-0.6 mg daily or BID

*In patients who weigh < 70 kg or experience adverse effects, consider dose adjustment as follows: attack dose 1.2 mg; maintenance dose 0.6 mg daily

Proposed dosing regimen was not exclusively studied in patients with pericarditis, drug-drug interactions, or drug-disease interactions.

AD = attack dose

MD = maintenance dose

Arch Intern Med. 2005;165:1987-1991. Am J Cardiovasc Drugs. 2015;15:295-306. Ann Intern Med. 2011;155:409-414. Circulation. 2005;112:2012-2016. Lancet. 2014;383:2232-2237. N Engl J Med. 2013;369:1522-1528.

Colchicine

- Formulations
 - 0.6 mg oral tablet
 - Scored
 - 0.6 mg oral capsule
 - Maximum daily dose of 1.2 mg/day
 - 0.6 mg/5 mL oral solution
 - Maximum daily dose of 1.2 mg/day

J Pharm Pract. 2019;1-8.

Colchicine

Adverse Effects

- **Gastrointestinal**
 - Can be ameliorated by dose adjustment
 - Diarrhea
 - Nausea
 - Vomiting

Adverse Effects

- **Blood dyscrasias**
 - Decrease dose or temporarily discontinue
 - Present within 24-72 hours of treatment
 - Myelosuppression
 - Thrombocytopenia
 - Aplastic anemia

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

- **Adverse Effects**
 - **Neuromuscular toxicity**
 - May present as rhabdomyolysis and is associated with chronic use
 - Myopathy
 - Proximal muscle weakness
 - Elevated creatine phosphokinase (CPK) levels
 - **Increased incidence when combined with**
 - Statins
 - Fibrates
 - Cyclosporine

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

- **Dose Adjustment**
 - **Drug-drug interactions**
 - CYP 3A4 and P-glycoprotein (p-gp)
 - Statins
 - **Drug-disease interactions**
 - Renal impairment
 - Hepatic impairment
 - **Adverse effects**
 - **Weight < 70 kg**
 - **Elderly > 70 years of age**

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

Drug-Drug Interactions

CYP 3A4

- **Statins**
- **Amiodarone**
- **Cyclosporine**
- **Grapefruit juice**
- **Verapamil**
- **Diltiazem**
- **Protease inhibitors**

Drug-Drug Interactions

CYP 3A4

- **Antiretroviral-boosting agents**
- **Clarithromycin**
- **Itraconazole**
- **Nefazadone**
- **Erythromycin**
- **Fluconazole**
- **Azithromycin**

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

Drug-Drug Interactions

P-glycoprotein

- Azithromycin
- Itraconazole
- Clarithromycin
- Erythromycin
- Grapefruit juice

Drug-Drug Interactions

P-glycoprotein

- Amiodarone
- Ranolazine
- Verapamil
- Cyclosporine
- Digoxin
- Carvedilol

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

Drug-Disease Interactions

Renal Impairment

- Dose adjustment not required in patients with mild-moderate impairment*
- Patients with a serum creatinine of > 2.5 mg/dL were excluded from the landmark studies
- Concurrent use of colchicine and P-gp or strong CYP3A4 inhibitors is contraindicated in renal impairment.

Drug-Disease Interactions

Hepatic Impairment

- Dose adjustment not required in patients with mild-moderate impairment*
- Patients with liver function tests > 1.5 times the upper limit of normal were excluded from the landmark trials
- Concurrent use of colchicine and P-gp or strong CYP3A4 inhibitors is contraindicated in hepatic impairment.

Am J Cardiovasc Drugs. 2015;15:295-306.

Colchicine

- **Role of the Pharmacist**
 - **Inpatient Pharmacists**
 - Ensure affordability and access to care
 - Devise dosing regimen with team
 - Check for drug-drug and drug-disease interactions
 - Educate patients on the role of colchicine for the treatment of pericarditis
 - Counsel patients regarding use of colchicine, the potential adverse effects and to promptly report new onset of diarrhea
 - Monitoring
 - Transitions of care

J Pharm Pract. 2019;1-8.

Colchicine

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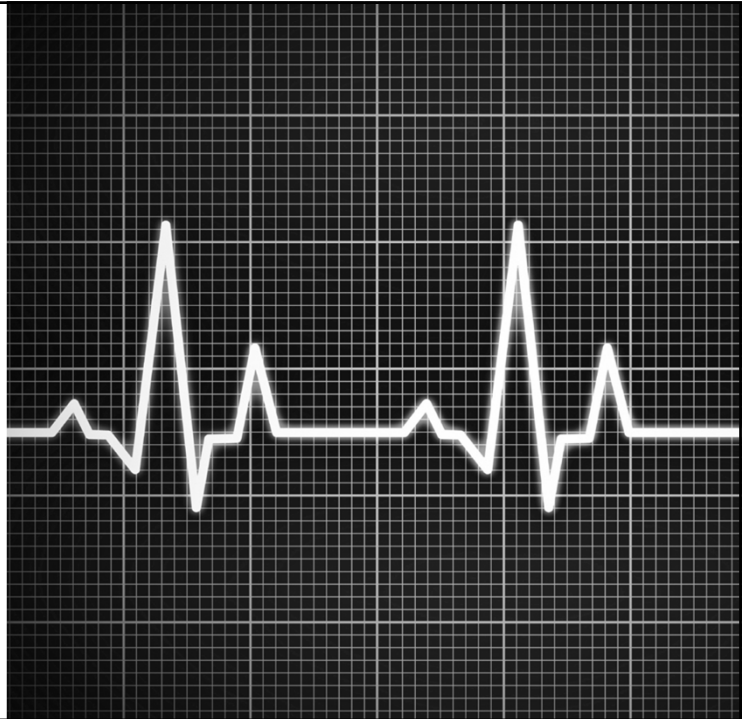
J Pharm Pract. 2019;1-8.

Colchicine

- **Role of the Pharmacist**
 - **Managed Care Pharmacists**
 - Access to medicine
 - Prior Authorizations
 - Formulary
 - Tier placement
 - Drug utilization review (DUR)
 - Medication therapy management (MTM)

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**Check-Point:
QUESTIONS?**



Corticosteroids

- Provide rapid symptom control and initial remission of symptoms
- Mechanism of action
 - Inhibit inflammatory cytokines
- Glucocorticoids are most commonly studied
 - Prednisone 0.2-0.5 mg/kg/day
 - Prednisolone in children or in patients with hepatic impairment

Pharmacotherapy. 2015;35:99-111.

Corticosteroids

- **Not to be used first-line for the treatment of acute or recurrent pericarditis**
 - **Associated with higher rates of recurrence**
- Used in the setting of acute or recurrent pericarditis that is refractory to ASA/NSAID plus colchicine OR if there is a contraindication to ASA/NSAID/colchicine.
- Must rule-out infection prior to initiation
- May attenuate colchicine response

*Eur Heart J. 2005; 26: 723-727.
Eur Heart J. 2015; 6: 2921-2964.*

Corticosteroids

- High doses (prednisone 1.0 mg/kg/day) compared to low doses (prednisone 0.2 to 0.5 mg/kg/day) in patients with recurrent pericarditis
 - Compared to lower doses, high doses of prednisone associated with
 - higher rate of severe side effects
 - (23.5% versus 2.0%; p = 0.002)
 - higher recurrence rate
 - (64.7% versus 32.6%; p = 0.002)
 - higher rate of disease-related hospitalizations
 - (31.4% versus 8.2%; p = 0.005)

Circulation. 2008; 118: 667-671.

Corticosteroids

- Draw baseline hs-CRP
- Start tapering when:
 - patient is asymptomatic **AND** hs-CRP is normal

Prednisone daily dose	Tapering Schedule
> 50 mg	10 mg/day q. 1-2 weeks
50-25 mg	5-10 mg/day q. 1-2 weeks
25-15 mg	2.5 mg/day q. 2-4 weeks
< 15 mg	1.25-2.5 mg/day q. 2-6 weeks

Circulation. 2008; 118: 667-671.

Corticosteroids

Short-Term Adverse Effects

- Hypertension
- Hyperglycemia
- Hypokalemia
- Mood disturbances
- Insomnia
- Edema
- Increased appetite
- Weight gain
- Peptic ulcer disease

Long-Term Adverse Effects

- Dyslipidemia
- Osteoporosis
- Immunosuppression
- Thinning of skin
- Impaired wound healing
- Mania
- Cushingoid appearance
- Myopathy

Circulation. 2008; 118: 667-671.

Corticosteroids

- **Role of the Pharmacist**
 - **Inpatient Pharmacists**
 - Ensure affordability and access to care
 - Devise dosing regimen with team
 - Ensure patients understand how to take corticosteroid
 - Educate patients on the role of corticosteroids for the treatment of pericarditis
 - Counsel patients regarding use of corticosteroids, including the potential short-term and long-term adverse effects
 - Check for drug-drug and drug-disease interactions
 - Monitoring
 - Transitions of care

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Corticosteroids

- **Role of the Pharmacist**
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J Pharm Pract. 2019;1-8.

Corticosteroids

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J Pharm Pract. 2019;1-8.

Immunotherapies

- Evidence limited to weak study designs and type of studies
- Many of these agents are very toxic
 - Require diligent monitoring!
- Anakinra
- IV-IG
- Azathioprine
- Methotrexate
- Cyclophosphamide

Pharmacotherapy. 2017; 37:305-318.

Immunotherapies

- Anakinra
 - Mechanism of action
 - Interleukin-1 (IL-1) receptor antagonist
 - Usually reserved for patients with recurrent pericarditis who are receiving colchicine, ASA/NSAIDs, and cannot be successfully weaned off of corticosteroids
 - Associated with resolution of symptoms and prevention of relapses or recurrences

JAMA. 2016; 316:1906-1912.

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **Anakinra**
 - Dosed 100 mg SQ daily
 - Extend interval to every other day in moderate to severe renal impairment
 - Avoid in patients with hypersensitivity to *E. coli*
 - Adverse Effects
 - Injection-site reaction
 - Headache
 - Arthralgia
 - Neutropenia

JAMA. 2016; 316:1906-1912.

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **IV IG**
 - Mechanism of action
 - Comprised of opsonizing and neutralizing IG antibodies
 - Usually reserved for patients with recurrent pericarditis who are receiving colchicine, ASA/NSAIDs, and cannot be successfully weaned off of corticosteroids
 - Associated with resolution of symptoms and prevention of relapses or recurrences

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **IV IG**
 - Dosed by cycles
 - 500 mg/kg/day for 5 consecutive days = 1 cycle
 - Adverse Effects
 - Infusion-related reactions
 - Thrombosis
 - Renal impairment

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **Azathioprine**
 - Mechanism of action
 - Anti-metabolite that incorporates itself into replicating DNA
 - subsequently blocks the production of purine
 - Usually initiated in patients with pericarditis that is refractory to corticosteroid use
 - Associated with a relatively longer time to remission of pericarditis signs, symptoms, and recurrence

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **Azathioprine**
 - Initiated at 100-200 mg daily
 - Dose-adjust in renal and hepatic impairment
 - Drug-drug interaction with allopurinol
 - Adverse effects
 - GI-related
 - Myelosuppression

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **Alternative Immunotherapies**
 - Anecdotally used
 - Cyclophosphamide
 - Methotrexate
 - Use if patient cannot tolerate, fails, or has contraindications to previously mentioned immunotherapies
 - Monitor diligently!

Pharmacotherapy. 2017;37:305-318.

Immunotherapies

- **RHAPSODY study**
 - **Rilonacept Treatment in Subjects With Recurrent Pericarditis**
 - Phase 3, global, multicenter, double-blind, placebo-controlled, randomized withdrawal study with open-label extension
 - Assessing the efficacy and safety of rilonacept in patients with recurrent pericarditis

Immunotherapies

- **Role of the Pharmacist**
 - **Inpatient Pharmacists**
 - Ensure affordability and access to care
 - Devise dosing regimen with team
 - Check for drug-drug and drug-disease interactions
 - Ensure patients understand how to administer
 - Educate patients on the role of corticosteroids for the treatment of pericarditis
 - Counsel patients regarding use of immunotherapies, including the potential adverse effects
 - Monitoring
 - Transitions of care

Immunotherapies

- **Role of the Pharmacist**
 - **Community or Ambulatory Care Pharmacists**
 - Ensure access to medication
 - Facilitate and follow-up with prior authorizations
 - Check for drug-drug and drug-disease interactions
 - Ensure patients understand how to administer
 - Educate patients on the role of immunotherapies for the treatment of pericarditis
 - Counsel patients regarding use of immunotherapies, including the potential adverse effects
 - Medication therapy management (MTM)
 - Monitoring and follow-up
 - Transitions of care

J Pharm Pract. 2019;1-8.

Immunotherapies

- **Role of the Pharmacist**
 - **Managed Care Pharmacists**
 - Access to medicine
 - Prior Authorizations
 - Formulary
 - Tier placement
 - Drug utilization review (DUR)
 - Medication therapy management (MTM)

J Pharm Pract. 2019;1-8.

Exercise Restriction

- **Athletes**
 - cease participation in competitive sports during the acute phase of pericarditis for approximately 3 months
 - resume participation in sports after complete resolution of clinical and laboratory manifestations of the disease
- **Non-athletes**
 - exercise restriction should be recommended until resolution of clinical and normalization of laboratory manifestations

Eur Heart J. 2019; 40:19-33.

2015 ESC Guideline Recommendations for the Treatment of Acute Pericarditis

Recommendation	Class	Level
Aspirin or NSAIDs are recommended as first-line therapy for acute pericarditis with gastroprotection.	I	A
Colchicine is recommended as first-line therapy for acute pericarditis as an adjunct to aspirin/NSAID therapy.	I	A
Serum CRP should be considered to guide the treatment length and assess the response to therapy.	IIa	C
Low-dose corticosteroids should be considered for acute pericarditis in cases of contraindication/failure of aspirin/NSAIDs and colchicine, and when an infectious cause has been excluded.	IIa	C
Corticosteroids are not recommended as first-line therapy for acute pericarditis.	III	C

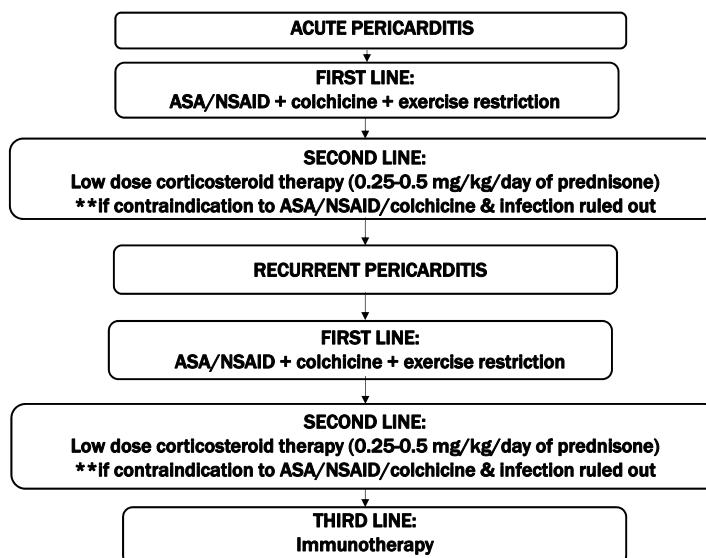
Eur Heart J. 2015; 36: 2921-2964.

2015 ESC Guideline Recommendations for the Treatment of Recurrent Pericarditis

Recommendation	Class	Level
Aspirin and NSAIDs are mainstays of treatment and are recommended at full doses, if tolerated, until complete symptom resolution.	I	A
Colchicine (0.5 mg twice daily or 0.5 mg daily for patients < 70 kg or intolerant to higher doses); use for 6 months is recommended as an adjunct to aspirin/NSAIDs.	I	A
CRP dosage should be considered to guide the treatment duration and assess the response to therapy.	IIa	C
After CRP normalization, a gradual tapering of therapies should be considered, tailored to symptoms and CRP, stopping a single class of drugs at a time.	IIa	C
Drugs such as IVIG, anakinra and azathioprine may be considered in cases of corticosteroid-dependent recurrent pericarditis in patients not responsive to colchicine.	IIb	C

Eur Heart J. 2015; 36: 2921-2964.

Idiopathic (Viral) Pericarditis Treatment



Eur Heart J 2015; 36: 2921-2964.

Post-Assessment Question 1

- Which of the following medications increases the risk of recurrence in acute idiopathic (viral) pericarditis?
 - A. Aspirin
 - B. Colchicine
 - C. Prednisone
 - D. Anakinra

Post-Assessment Question 2

- Which of the following is an appropriate anti-inflammatory regimen for an adult patient diagnosed with acute idiopathic (viral) pericarditis?
 - A. Aspirin 325 mg PO daily for 1 month, then taper
 - B. Ibuprofen 800 mg PO TID for 6 months
 - C. Indomethacin 50 mg PO TID for 1 week, then taper
 - D. Ketorolac 15 mg PO daily for 3 weeks, then taper

Post-Assessment Question 3

- Which of the following medications increases the plasma concentration of colchicine?
 - A. Carvedilol
 - B. Rifampin
 - C. Pravastatin
 - D. Levothyroxine

Post-Assessment Question 4

- Which of the following parameters would be appropriate for monitoring the safety of colchicine?
 - A. Creatine phosphokinase
 - B. Blood glucose
 - C. INR
 - D. Fasting lipid panel

Conclusions and Clinical Pearls

- Recurrence of pericarditis is relatively common, especially in patients with idiopathic (viral) pericarditis, who are not treated with optimal pharmacotherapy.
- ASA/NSAIDs in combination with colchicine should be used as first line, for the treatment for acute or recurrent idiopathic (viral) pericarditis.
- Corticosteroids should not be used as first-line therapy for the treatment of idiopathic (viral) pericarditis.

Conclusions and Clinical Pearls

- hs-CRP monitoring should be considered in order to guide efficacy of therapy.
- U.S. formulations of colchicine should be extrapolated **carefully** when creating a dosing regimen.
- More robust U.S. literature is needed to more appropriately guide therapy and improve outcomes in patients with idiopathic (viral) pericarditis.

Management of Idiopathic Pericarditis: Old Drugs with New Tricks

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