Acute Pericarditis

**Definition:**

- Pericarditis is an inflammation of the pericardium, which is the sac that surrounds the heart. The pericardium normally functions to protect the heart and reduce friction between the heart and surrounding organs.
- Pericarditis may be accompanied by pericardial effusion, which is fluid accumulation in the pericardial sac. If a large amount of fluid accumulates in the pericardium, it may squeeze or constrict the heart; this is called cardiac tamponade. Cardiac tamponade is a serious condition that can be life-threatening if not recognized and treated promptly.
- Most cases of acute pericarditis are idiopathic but other causes include infections, metabolic disorders, myocardial infarction, autoimmune disorders, postprocedural cardiac injury (such as after cardiac surgery or ablation), and neoplasms.
- The initial episode of pericarditis may be followed by relapsing or recurrent pericarditis in about one-quarter of patients.
- Myopericarditis, characterized by inflammation of both pericardium and myocardium, may be present in some patients.

**Signs and symptoms:**

-Acute pericarditis can present with a variety of nonspecific signs and symptoms, depending on the underlying etiology. The major clinical manifestations of acute pericarditis include:
1. Chest pain: It begins suddenly usually worsened when taking a deep breath.
2. Pericardial friction rub
3. Electrocardiogram (ECG) changes
4. Pericardial effusion
## Diagnosis:

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG is recommended in all patients with suspected acute pericarditis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Transthoracic echocardiography is recommended in all patients with suspected acute pericarditis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Chest X-ray is recommended in all patients with suspected acute pericarditis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Assessment of markers of inflammation (i.e. CRP) and myocardial injury (i.e. CK, troponin) is recommended in patients with suspected acute pericarditis</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

CK = creatine kinase; CRP = C-reactive protein; ECG = electrocardiogram.

*Class of recommendation.

*bLevel of evidence.
Initial history and physical examination:
This evaluation should consider disorders that are known to involve the pericardium, such as prior malignancy, autoimmune disorders, uremia, recent MI, and prior cardiac surgery. The examination should pay particular attention to auscultation for a pericardial friction rub and the signs associated with cardiac tamponade.

Initial testing in all suspected cases:
• An ECG.
• Chest radiography: To determine if pericardial effusion is present.
• Complete blood count, troponin level, erythrocyte sedimentation rate, and serum C-reactive protein level
• Echocardiography, with urgent echocardiography if cardiac tamponade is suspected. Even a small effusion can be helpful in confirming the diagnosis of pericarditis, although the absence of an effusion does not exclude the diagnosis.

Selected additional testing:
• Blood cultures if fever higher than 38°C (100.4°F), signs of sepsis, or a documented, concomitant bacterial infection (eg, pneumonia)
• Antinuclear antibody (ANA) titer in selected cases
• Tuberculin skin test or an interferon-gamma release assay if not recently performed.
• Multimodality imaging.
Treatment:

- The goals of therapy are:
  - The relief of pain
  - Resolution of inflammation (and, if present, pericardial effusion)
  - Prevention of recurrence.

Algorithm 1:

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**Initial treatment of acute pericarditis in adults**

<table>
<thead>
<tr>
<th>Are any of the following high-risk markers present?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever &gt;38°C (100.4°F)</td>
</tr>
<tr>
<td>Subacute course (without acute onset of chest pain)</td>
</tr>
<tr>
<td>Hemodynamic compromise suggesting cardiac tamponade</td>
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<tr>
<td>Large pericardial effusion seen by echocardiography</td>
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<tr>
<td>Immunosuppression or immunodepressed patient</td>
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<tr>
<td>Treatment with vitamin K antagonist or novel oral anticoagulant</td>
</tr>
<tr>
<td>Acute trauma</td>
</tr>
<tr>
<td>Elevated troponin suggesting myopericarditis</td>
</tr>
</tbody>
</table>

- **Yes**
  - Admit to hospital for inpatient diagnostic evaluation and therapy
  - Initiate treatment
    - NSAIDs*
    - Colchicine
    - Restriction from strenuous activity
  - Is patient responding to therapy? |
    - **Yes**
      - Taper NSAIDs
      - Complete three months of colchicine therapy
      - Outpatient follow up
    - **No**

* NSAIDs: nonsteroidal antiinflammatory drugs.

* NSAIDs are the preferred antiinflammatory for nearly all patients with acute idiopathic or viral pericarditis. Glucocorticoids should be used for initial treatment of acute pericarditis only in patients with contraindications to NSAIDs or for specific indications (ie, systemic inflammatory diseases, pregnancy, renal failure), and should be used at the lowest effective dose. Refer to the UpToDate topic on treatment of acute pericarditis for glucocorticoid dosing information.

Response to therapy includes improvement/resolution of symptoms within 1 to 2 weeks of initiation of therapy and normalization of C-reactive protein level (if measured).

Δ Refer to UpToDate content on recurrent/refractory pericarditis for therapeutic approach to patients who are not showing clinical improvement.
# Recommendations for the treatment of acute pericarditis

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin or NSAIDs are recommended as first-line therapy for acute pericarditis</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>with gastroprotection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colchicine is recommended as first-line therapy for acute pericarditis as an</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>adjunct to aspirin/NSAID therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum CRP should be considered to guide the treatment length and assess the</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>response to therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-dose corticosteroids(^d) should be considered for acute pericarditis in</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>cases of contraindication/failure of aspirin/NSAID and colchicine, and when an</td>
<td></td>
<td></td>
</tr>
<tr>
<td>infectious cause has been excluded, or when there is a specific indication such</td>
<td></td>
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<tr>
<td>as autoimmune disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise restriction should be considered for non-athletes with acute</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>pericarditis until resolution of symptoms and normalization of CRP, ECG and</td>
<td></td>
<td></td>
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<tr>
<td>echocardiogram</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For athletes, the duration of exercise restriction should be considered until</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>resolution of symptoms and normalization of CRP, ECG and echocardiogram—at least</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months is recommended</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids are not recommended as first-line therapy for acute pericarditis</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

CRP = C-reactive protein; ECG = electrocardiogram; NSAIDs = non-steroidal anti-inflammatory drugs.

*Class of recommendation.

\(^d\)Level of evidence.

Reference(s) supporting recommendations.

\(^a\)Added to colchicine.
A) Non Pharmacological treatment:

- Activity restriction:
  - Patients should be instructed to restrict strenuous physical activity until symptoms have resolved and biomarkers have normalized.
  - Noncompetitive athletes should restrict activity until the resolution of symptoms and normalization of biomarkers.
  - Competitive athletes should not participate in competitive sports for at least three months following the resolution of symptoms and normalization of biomarkers, and should be re-evaluated by a clinician prior to resuming training and competition. In patients with milder symptoms which promptly resolve with treatment, a shorter period or activity restriction (a minimum of one month) may be reasonable on a case-by-case basis.
  - In cases of myopericarditis, we recommend withdrawal from competitive sports for six months and return to play only after normalization of laboratory data (eg, markers of inflammation, electrocardiogram [ECG], and echocardiogram.)
### R) Pharmacological treatment:

#### Drug therapy in acute and recurrent pericarditis for adult patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Antiinflammatory dose</th>
<th>Duration of initial or maintenance dose</th>
<th>Tapering regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line therapy for most patients</strong>&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin&lt;sup&gt;*&lt;/sup&gt;</td>
<td>650 to 1000 mg orally 3 times daily</td>
<td>1 to 2 weeks</td>
<td>Decrease dose by about 250 mg per week</td>
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<tr>
<td>OR</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ibuprofen&lt;sup&gt;†&lt;/sup&gt;</td>
<td>600 to 800 mg orally 3 times daily&lt;sup&gt;§&lt;/sup&gt;</td>
<td>1 to 2 weeks</td>
<td>Decrease dose by 200 mg per week</td>
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<tr>
<td>OR</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Indomethacin&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>25 to 50 mg orally 3 times daily</td>
<td>1 to 2 weeks</td>
<td>Decrease dose by 25 mg per week</td>
</tr>
<tr>
<td><strong>PLUS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colchicine&lt;sup&gt;**&lt;/sup&gt;</td>
<td>0.5 to 0.6 mg orally 2 times daily</td>
<td>3 months (acute)</td>
<td>Usually not tapered</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 months or more (recurrent)</td>
<td></td>
</tr>
<tr>
<td><strong>Second-line therapy (for refractory cases or patients with a contraindication to NSAID therapy):</strong></td>
<td></td>
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</tr>
<tr>
<td>Prednisone</td>
<td>0.2 to 0.5 mg/kg daily</td>
<td>1 to 2 weeks (acute)</td>
<td>Gradual tapering over 2 to 3 months; refer to UpToDate topic review of treatment of acute pericarditis, section on glucocorticoids</td>
</tr>
<tr>
<td><strong>PLUS</strong></td>
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<tr>
<td></td>
<td></td>
<td>6 months or more (recurrent)</td>
<td></td>
</tr>
<tr>
<td><strong>Third-line therapy:</strong> Second-line therapy plus aspirin dosed as for first-line therapy</td>
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<tr>
<td><strong>Fourth-line therapy:</strong> One of the following agents (or pericardectomy)</td>
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<tr>
<td>Rilonacepl</td>
<td>Loading dose of 320 mg delivered as 2 SC doses of 160 mg on the same day at 2 different sites</td>
<td>160 mg SC weekly for several months</td>
<td>Slow taper over 3 months or more</td>
</tr>
<tr>
<td>Anakinra</td>
<td>1 to 2 mg/kg daily (maximum dose 100 mg daily)</td>
<td>Several months</td>
<td>Slow taper over 3 months or more</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>1 mg/kg/day increasing to 2 to 3 mg/kg/day (maximum dose 150 mg daily)</td>
<td>Several months</td>
<td>Not tapered</td>
</tr>
<tr>
<td>IVIG</td>
<td>400 to 500 mg/kg IV daily</td>
<td>5 days (may repeat after 1 month)</td>
<td>Not tapered</td>
</tr>
</tbody>
</table>

NSAID: nonsteroidal antiinflammatory drug; SC: subcutaneous injection; IVIG: intravenous immunoglobulin; IV: intravenous; CRP: C-reactive protein.

<sup>*</sup> This column describes the typical duration of full-dose therapy for symptom control. Except for colchicine, the duration of full-dose therapy and subsequent tapering should be tailored according to resolution of symptoms and normalization of markers of inflammation; refer to topic reviews for approach.

<sup>†</sup> Tapering is begun once symptoms have resolved for at least 24 hours and CRP level has normalized. Tapering is continued only if the patient remains asymptomatic with normal CRP levels.

<sup>Δ</sup> For patients with perifarction pericarditis (pericarditis associated with acute myocardial infarction), NSAIDs (such as ibuprofen and indomethacin) and glucocorticoids are avoided. Refer to UpToDate content on pericardial complications of myocardial infarction.

<sup>‡</sup> Proton pump inhibitor (e.g., omeprazole) gastrointestinal protection may be indicated.

<sup>§</sup> Some patients may require ibuprofen every 6 hours (4 times daily), in which case the dose should not exceed 600 mg every 6 hours.

<sup>**</sup> 0.5 mg colchicine is not available in the United States. It is widely available elsewhere.

<sup>**</sup> Colchicine dose should be reduced to 0.5 to 0.6 mg once daily in patients <70 kg. Refer to UpToDate content on colchicine dosing for other indications for dosage reduction.

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Data from:
1) NSAIDS

- For nearly all patients with acute idiopathic or viral pericarditis, we recommend NSAIDs (in combination with colchicine) as the initial treatment (algorithm 1).

- Duration of treatment is based upon the resolution of symptoms and normalization of C-reactive protein (CRP). In this approach, CRP is assessed at presentation and then weekly, using the anti-inflammatory dose of NSAIDs until complete resolution of symptoms and normalization of CRP, which usually occurs in two weeks or less, with tapering once the patient is symptom-free for at least 24 hours.

- In symptomatic pericarditis occurring within days after an acute myocardial infarction, we suggest aspirin plus colchicine rather than another NSAID plus colchicine. The use of NSAIDs other than aspirin should be avoided, since anti-inflammatory therapy may impair scar formation. Aspirin may also be the first choice in patients who require concomitant antiplatelet therapy for any reason.

**NSAID dosing:**

- Ibuprofen (600 to 800 mg three times per day) – Ibuprofen should be given three times.
- Following the resolution of symptoms, we taper the ibuprofen dose weekly for two to four weeks in an attempt to reduce the subsequent recurrence rate.
- Aspirin (650 to 1000 mg three times per day)
  - Aspirin should be given every six to eight hours
- Following the resolution of symptoms, we taper the aspirin dose weekly over two to four weeks in an attempt to reduce the subsequent recurrence rate.
- Indomethacin (25 to 50 mg three times per day)
  - Indomethacin should be given three times daily
**Gastrointestinal protection with NSAIDs:**

**NSAIDs can lead to gastrointestinal toxicity** (ie, gastritis, ulcers, etc), particularly when used in high doses or for prolonged periods of time, patient-related factors associated with a higher risk of gastrointestinal toxicity include:

- History of peptic ulcer disease
- Age greater than 65 years
- Concurrent use of aspirin, corticosteroids, or anticoagulants
- Patients considered at risk of gastrointestinal toxicity related to NSAID treatment should be treated:
  1. With NSAIDs for the shortest interval possible.
  2. Receive concomitant gastroprotective therapy while taking NSAIDs. Proton pump inhibitors (eg, omeprazole, pantoprazole) are generally preferred for prevention of gastrointestinal toxicity due to their efficacy and favorable safety profile

**Bleeding risk of NSAIDs combined with other antithrombotic:**

- Patients with acute pericarditis treated with NSAIDs may also have an indication for an additional antiplatelet or anticoagulant in which case the overall risk of bleeding should be assessed. Because NSAIDs (especially aspirin) can impact the metabolism of vitamin K antagonists, patients will typically require close monitoring and dose adjustments for the duration of treatment for acute pericarditis

**2) Colchicine:**

- We recommend that colchicine be added to anti-inflammatory therapy (either NSAIDs or glucocorticoids) Glucocorticoids should be used for initial treatment of acute pericarditis only in patients with contraindications to NSAID
- Colchicine is generally efficacious for pericarditis caused by systemic inflammatory diseases and post-cardiac injury syndromes. However, for patients with diagnosed bacterial pericarditis, colchicine has not been proven efficacious. Additionally, colchicine is also not proven to be efficacious in malignancy-related pericarditis and pericardial effusion.
• colchicine, when used as an adjunct to NSAID therapy, reduces symptoms, decreases the rate of recurrent pericarditis, and is generally well tolerated

❖ **Colchicine dosing:**

Colchicine may be given with or without a loading dose. When a loading dose is chosen, the loading dose is typically 0.5 to 1 mg (or 0.6 to 1.2 mg) twice daily on day 1, depending upon the patient’s body weight. The daily maintenance dose of colchicine is weight-based:

- Patients weighing ≥70 kg should receive 0.5 to 0.6 mg twice daily
- Patients weighing <70 kg should receive 0.5 to 0.6 mg once daily

❖ **Colchicine side effects:**

- Is typically well tolerated
- Most commonly gastrointestinal side effects (eg, diarrhea, nausea, vomiting)

❖ **Glucocorticoids:**

It is considered as second line therapy should be used for initial treatment of acute pericarditis only in patients with contraindications to NSAIDs, or for specific indications (ie, systemic inflammatory diseases, pregnancy, and possibly renal failure), and should be used at the lowest effective dose because chronic use of systemic glucocorticoids is associated with a number of potentially significant side effects

- NSAIDs and colchicine remain the preferred treatment options for acute pericarditis, a minority of patients will have refractory symptoms requiring treatment with systemic steroid therapy.

❖ **Glucocorticoid dosing:**

- We suggest the use of moderate initial dosing (eg, 0.2 to 0.5 mg/kg/day of prednisone) followed by a slow taper. rather than high doses with a rapid taper.
- We add colchicine during glucocorticoid therapy and continue colchicine for three months for initial cases of acute pericarditis
• We introduce aspirin or another NSAID toward the end of tapering or in case of recurrences instead of increasing the dose of the glucocorticoids
• We usually begin tapering glucocorticoids at two to four weeks after resolution of symptoms and CRP normalization. Each decrement in prednisone dose should proceed only if the patient is asymptomatic and CRP remains normalized, particularly for doses lower than 25 mg/day. A proposed tapering scheme follows:
  1. Daily dose >50 mg – Taper 10 mg/day every one to two weeks
  2. Daily dose 25 to 50 mg – Taper 5 to 10 mg/day every one to two weeks
  3. Daily dose 15 to 25 mg – Taper 2.5 mg/day every two to four weeks
  4. Daily dose <15 mg – Taper 1.25 to 2.5 mg/day every two to six weeks

❖ **systemic steroid therapy be restricted to patients with the following conditions:**
  1. Patients with symptoms refractory to standard therapy
  2. Acute pericarditis due to connective tissue disease
  3. Uremic pericarditis

❖ **Adjunctive therapies:**
Most patients with uncomplicated low risk acute pericarditis are managed effectively with medical therapy alone. On occasion, however, patients may require adjunctive therapies for:
• A moderate to large pericardial effusion, particularly if hemodynamically significant and causing cardiac tamponade or symptomatic and refractory to medical therapy
• Suspicion of a neoplastic or bacterial etiology and moderate to large pericardial effusion
• Frequent, highly symptomatic recurrences of acute pericarditis with pericardial effusion
• Evidence of constrictive pericarditis (a late occurrence when present)

- **Percutaneous and surgical techniques may be considered for such patients.**
Which patients require hospitalization?

High-risk patients with acute pericarditis should be admitted to the hospital in order to initiate appropriate therapy and expedite a thorough initial evaluation. Conversely, patients with uncomplicated (ie, low-risk) acute pericarditis can usually be evaluated and sent home, with outpatient follow-up to assess the efficacy of treatment.

![Recommendations for the management of acute pericarditis](image_url)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class &lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level &lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission is recommended for high-risk patients with acute pericarditis (at least one risk factor&lt;sup&gt;d&lt;/sup&gt;)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Outpatient management is recommended for low-risk patients with acute pericarditis</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Evaluation of response to anti-inflammatory therapy is recommended after 1 week</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.
References:


-Done by Pharm D students:
Lana Ibrahim Khanfar
Malak Mufeed Momani

- Supervised by clinical pharmacist : Eshraq Al-abweeny