A few comments about pericarditis and other pericardial diseases in relation to primary care

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Faculty/Presenter Disclosure

- **Faculty:** Andrew L. Morris, M.D.

- **Relationships with commercial interests: None**
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  - **Other:** Employee of XXY Hospital Group

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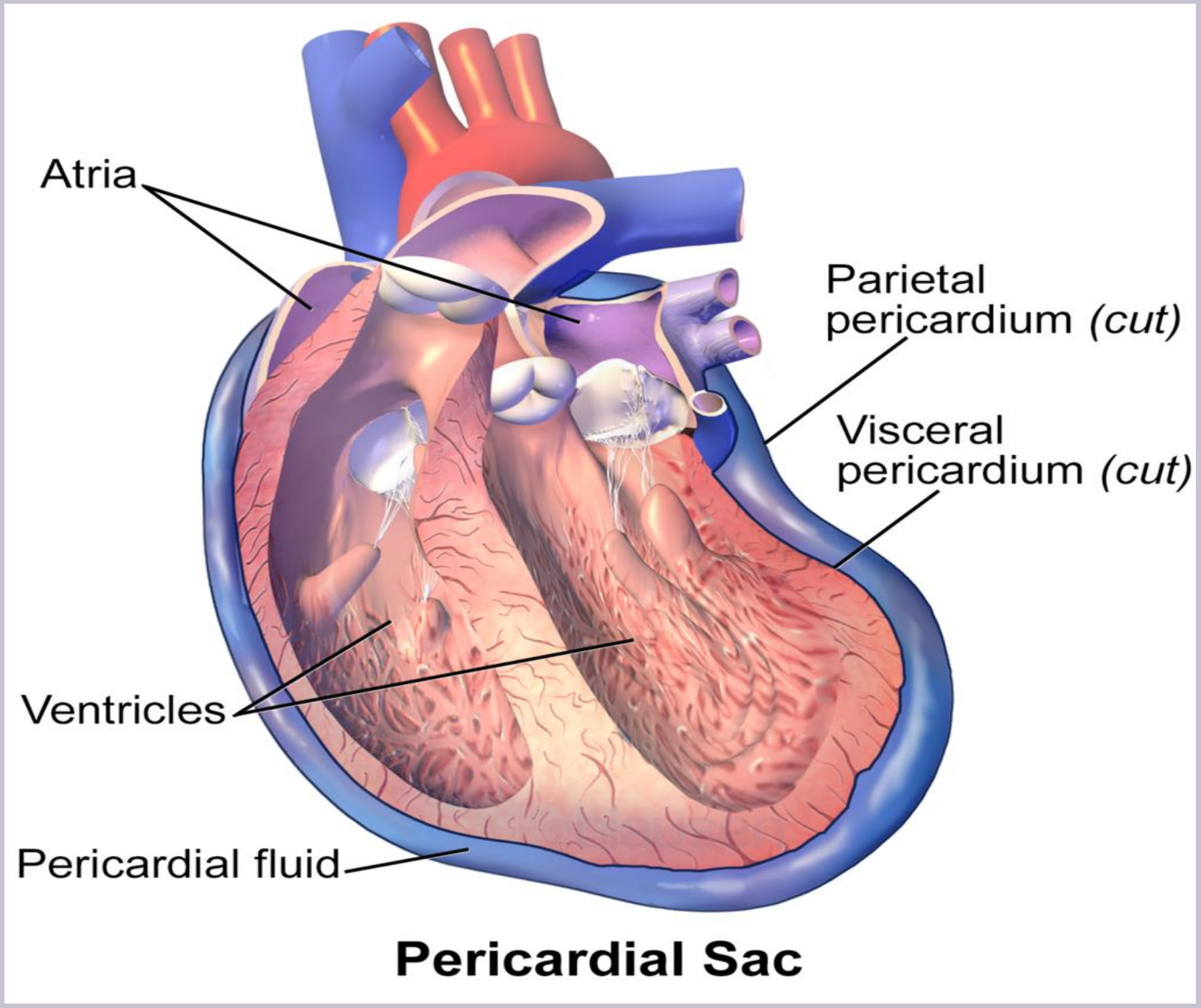
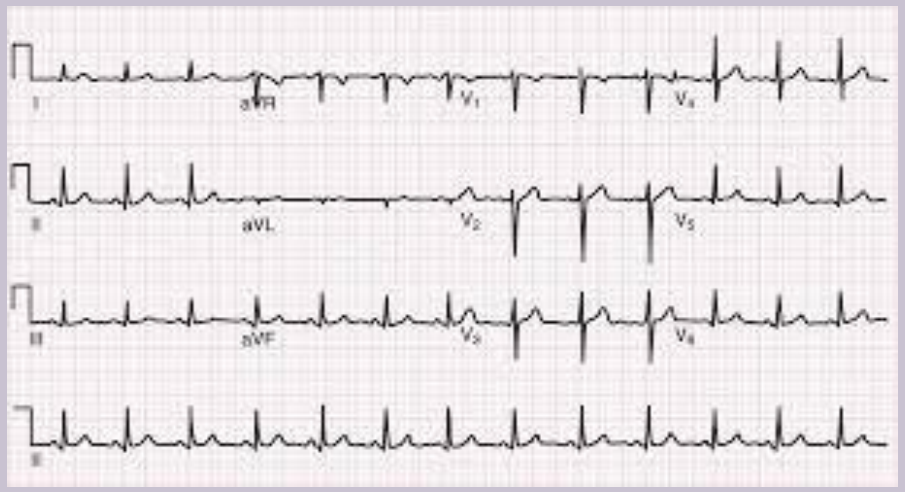


Pericardial Sac

Pericardial diseases you might see in your office practice

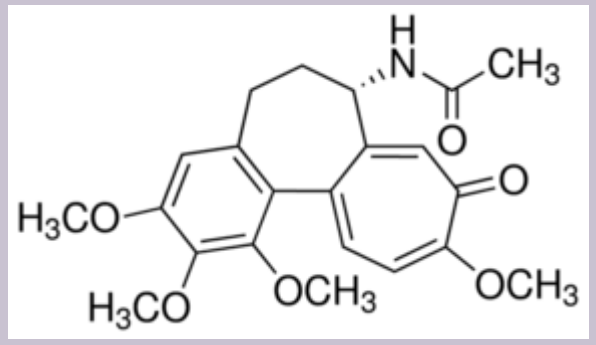
1) **Idiopathic pericarditis-acute & recurrent**
2) Idiopathic pericardial effusion-may be chronic or of uncertain duration
3) Pericardial effusion of known cause
4) Effusive-constrictive pericardial disease
5) Constrictive pericardial disease
6) **Purulent pericarditis**
7) Malignant pericardial effusion (not really "pericarditis" since it is not inflammatory)

Which EKG is typical of pericarditis?



Colchicine as adjunctive therapy to NSAIDs in idiopathic pericarditis

Meadow saffron



$C_{22}H_{25}NO_6$

A 'potpourri' of conditions in which colchicine has been studied

- Gout, familial Mediterranean fever (familial paroxysmal polyserositis), primary biliary cirrhosis, **recurrent pericarditis**, psoriasis, psoriatic arthritis, generalized pustular psoriasis, palmo-plantar pustulosis, Behcet's disease, primary antederma, dermatitis herpetoformis, recurrent aphthous stomatitits, linear IgA dermatosis, relapsing polychrondritis, necrotizing vasculitis, Sweet's syndrome, scleroderma, amyloidosis, idiopathic pulm. fibrosis, leukocytoclastic vasculitis, acquired epidermolysis bullosa, dermatomyositis.

Bhat A et al. Annals N.Y. Acad. Sci. Sept. 1, 2009;1173;766

Fowler NO, Harbin AD III: Recurrent acute pericarditis: Follow-up study of 31 patients

J Am Coll Cardiol 1986;7:300

Population: 31 pts. Followed for from 2 to 19 years

Etiology: 24, idiopathic; 4 post-op/post-traumatic; 2 post-MI; 1 anticoagulant-related

Remissions: Symptom-free interval between attacks

≥6 months: 23/31; >6 Mo to 1 yr: 3; ≥1 yr, 8, ≥2 years, 5.

Symptom-free intervals: 4 yr, one; 6 yr, three, 8 yr, two.

Frequent (16 of 31) continuous or intermittent symptoms of active pericarditis up to 15 years after the acute event!

Fowler NO. JACC 1986;7:300

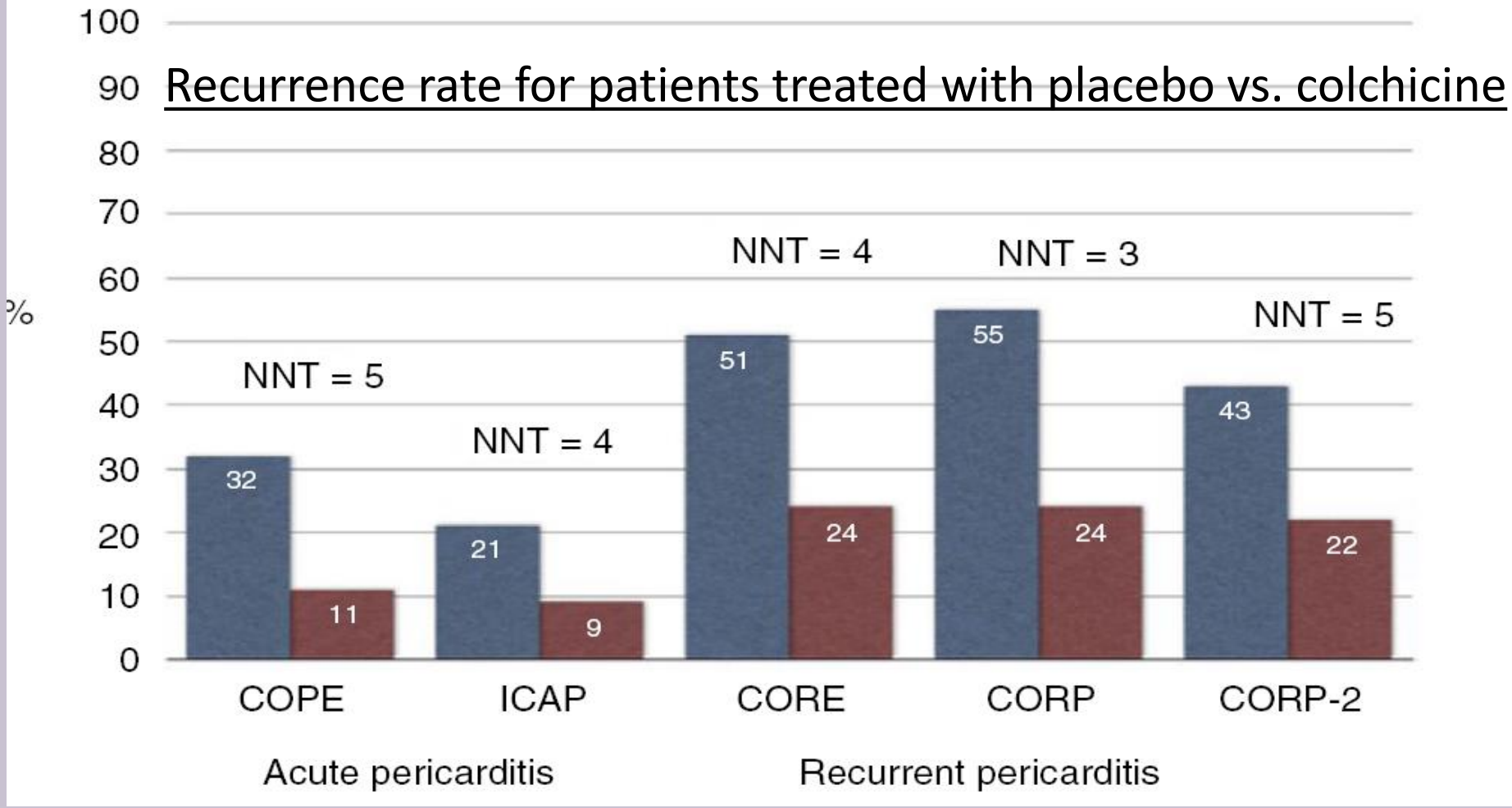
Editorial Comment*:

Old Drugs With New Uses

Colchicine for Treatment of Recurrent Pericarditis. Robert J. Adolph, M.D. University of Cincinnati

Circulation 1990;82:1505-1506

*Guindo J, Rodriguez de la Serna A, Ramio J, de Miguel Diaz MA, Subirana MT, Perez Ayuso MJ, Cosin J, Bayes de Luna A: Recurrent pericarditis: Relief with colchicine. Circulation 1990;82:1117-1120



All received NSAIDs

Figure 1. Main trials on colchicine for the prevention of pericarditis in acute and recurrent cases. When colchicine is added on top of standard anti-inflammatory therapy (red bars) the recurrence rate is halved (at least) and the NNT is 3 to 5, meaning that only 3 to 5 patients with pericarditis need to be treated to prevent 1 recurrence. NNT, number needed to treat.

All clinical trials have M. Imazio, Italy, as the lead author

Meta-analysis for the value of colchicine for the therapy of pericarditis and of postpericardiotomy syndrome

Lutschinger LL[1], Rigopoulos AG[2], Schlattmann P[3], Matiakis M[2], Sedding D[2], Schulze C[1], Noutsias M[4,5]

BMC Cardiovasc Disord. 2019 Sep 2;19(1):207. doi: 10.1186/s12872-019-1190-4.

CONCLUSIONS:

Our meta-analysis confirms that colchicine is efficacious and safe for prevention of recurrent pericarditis and PPS, while it reduces rehospitalizations and symptom duration in pericarditis. The clinical use of colchicine for the setting of PPS and postoperative PE after heart surgery should be investigated in further multicenter RCT.

BMC Cardiovasc Disord. 2019 Sep 2;19(1):207. doi: 10.1186/s12872-019-1190-4.

ESC Guidelines-Pericarditis

ESC 2015 guidelines for acute and recurrent pericarditis:

a. *Colchicine 0.5 mgm po od or bid for <70 kg.*

b. Continue for 3 months (acute) or 6 months (recurrent).

Class IA ESC recommendation

A small Spanish multicenter study with contrary results

- Barcelona
- Tarragona
- Palma de Mallorca

Colchicine administered in the first episode of acute idiopathic pericarditis: a randomized multicenter open-label study

- A. Sambola et al (Jaume Sagrista-Sauleda)-Barcelona
- 3 Spanish tertiary teaching centers
- 110 patients who received no steroids.
  - ASA or NSAIDs plus colchicine 1 mgm/12 hr for >70 kg. or 0.5 mgm/12 hr. for <70 kg. for 3 months. The colchicine dose was reduced by 50% for diarrhea.
  - ASA 1 gm q 6-8 hrs., ibuprofen 600 mgm q 8 hrs or indomethacin 50 mgm q 8 hrs for 2 to 10 days with tapering over 3 to 4 weeks.

Rev. Esp. Cardiol. 2018, in press. https://doi.org/10.1016/j.rec.2018.11.016

Main outcomes: colchicine vs. no colchicine in steroid-naïve patients

	Overall N=110	Colchicine N=59	No colchicine N-51	P
Recurrent pericarditis	12 (10.9%)	8 (13.5)	4 (7.8)	0.34
Time to 1st recurrence	9.1 ± 9.0	9.6 ± 9.0	8.3 ± 10.5	0.80
Episode duration, days	7.2 ± 4.8	6.3 ± 2.9	9.1 ± 3.4	0.40
Follow-up, mo	30.2 ± 17.0	28.4 ± 15.3	30.5 ± 18.7	0.54

Rev. Esp. Cardiol. 2018, in press. https://doi.org/10.1016/j.rec.2018.11.016

- “The main finding of our study is that the incidence of recurrence was very low after a first episode of AIP in patients who had not received corticosteroids, and was no different in patients who received colchicine in addition to conventional anti-inflammatory treatment compared to patients who only receive conventional anti-inflammatory treatment.”

Rev. Esp. Cardiol. 2018, in press. https://doi.org/10.1016/j.rec.2018.11.016

Non-steroidal medications for the treatment of acute pericarditis

Table 1. Dosing of the most commonly prescribed anti-inflammatory therapy for acute pericarditis.

Drugs	Usual dosing	Treatment duration	Tapering*
Aspirin	750-1,000 mg every 8 hrs	1-2 weeks	Decrease doses by 250-500 mg every 1-2 weeks
Ibuprofen	600 mg every 8 hrs	1-2 weeks	Decrease doses by 200-400 mg every 1-2 weeks
Colchicine	0.5 mg once (<70 kg) or 0.5 mg twice daily (>70 kg)	3 months	Not mandatory, alternatively 0.5 mg every other day (<70 kg) or 0.5 mg once (>70 kg) in the last weeks

E-Journal of Cardiology Practice. 2017; 15(16)

2015 ESC Guidelines

Web Table 1A **Aspirin and commonly used NSAIDs in pericardial diseases; main regimens in adults (for children see Web Table 7; for concomitant use of anti-platelets and anticoagulant therapy see Web box)**

Drug	Usual initial dose (with possible range)	Length of treatment	Tapering
Aspirin	500–1000 mg every 6–8 hours (1,5–4 g/day).	FIRST uncomplicated episode: 1–2 weeks.	Decrease the total daily dose by 250–500 mg every 1–2 weeks.
Ibuprofen	600 mg every 8 hours (range 1200–2400 mg).	RECURRENCES: 2–4 weeks up to several months. The optimal length of treatment is debatable, and CRP should be considered as a marker of disease in activity to guide management and treatment length. The need for gradual tapering (every 1–2 weeks and only if the patient is asymptomatic and CRP is normal) is recommended by this Task Force.	Decrease the total daily dose by 200–400 mg every 1–2 weeks.
Indomethacin	25–50 mg every 8 hours: start at lower end of dosing range and titrate upward to avoid headache and dizziness.		Decrease the total daily dose by 25 mg every 1–2 weeks.
Naproxen	500–1000 mg daily every 12 hours; if tolerated well and clinically indicated, may increase to 1500 mg daily of naproxen base for limited time period (<6 months). Dosage expressed as naproxen base; 200 mg naproxen base is equivalent to 220 mg naproxen sodium.		Decrease the total daily dose by 125–250 mg every 1–2 weeks.

CrCl = creatinine clearance; NSAIDs = non-steroidal anti-inflammatory drugs.
Start at lower end of dosing range and titrate upward.
According to local availability of the different agents, consider intravenous use of NSAIDs in hospitalized symptomatic patients.
Dosing: geriatric refer to adult dosing. Use lowest recommended dose and frequency
Dosing: renal impairment CrCl <30 mL/min: NSAIDs use is not recommended (for aspirin: use is not recommended if CrCl <10 mL/min)
Dosing: hepatic impairment use with caution; dose adjustment may be required.

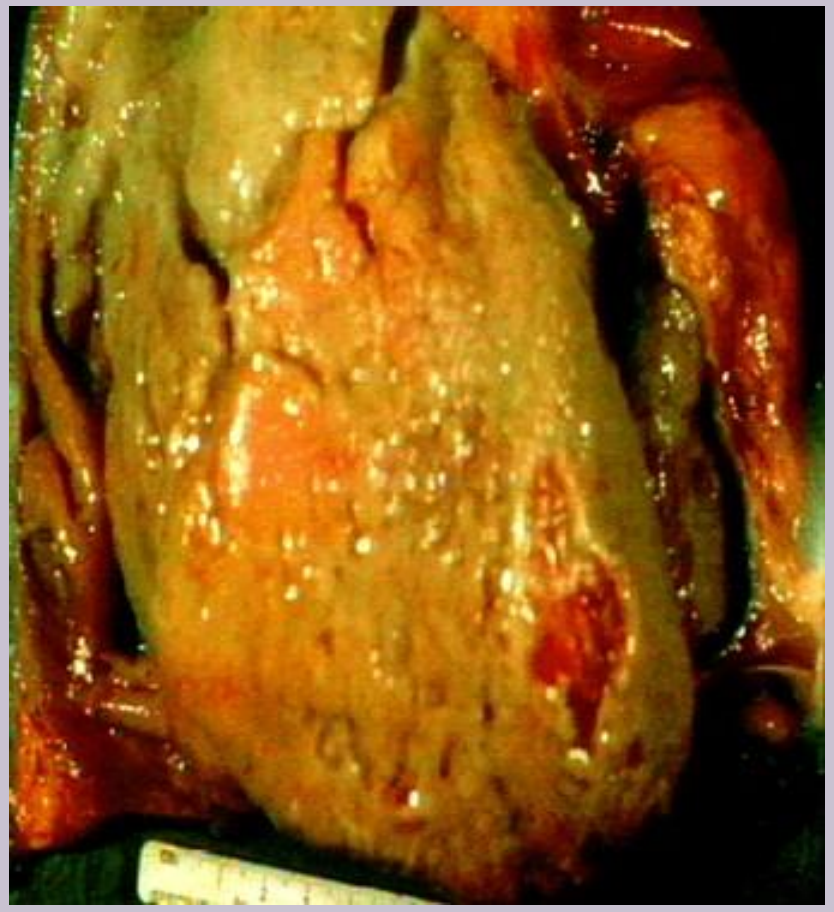
European Heart Journaldoi:10.1093/eurheartj/ehv31

A very sick patient who looks toxic probably is!

Patient you sent to the ER because of severe pain and fever who looked very unwell

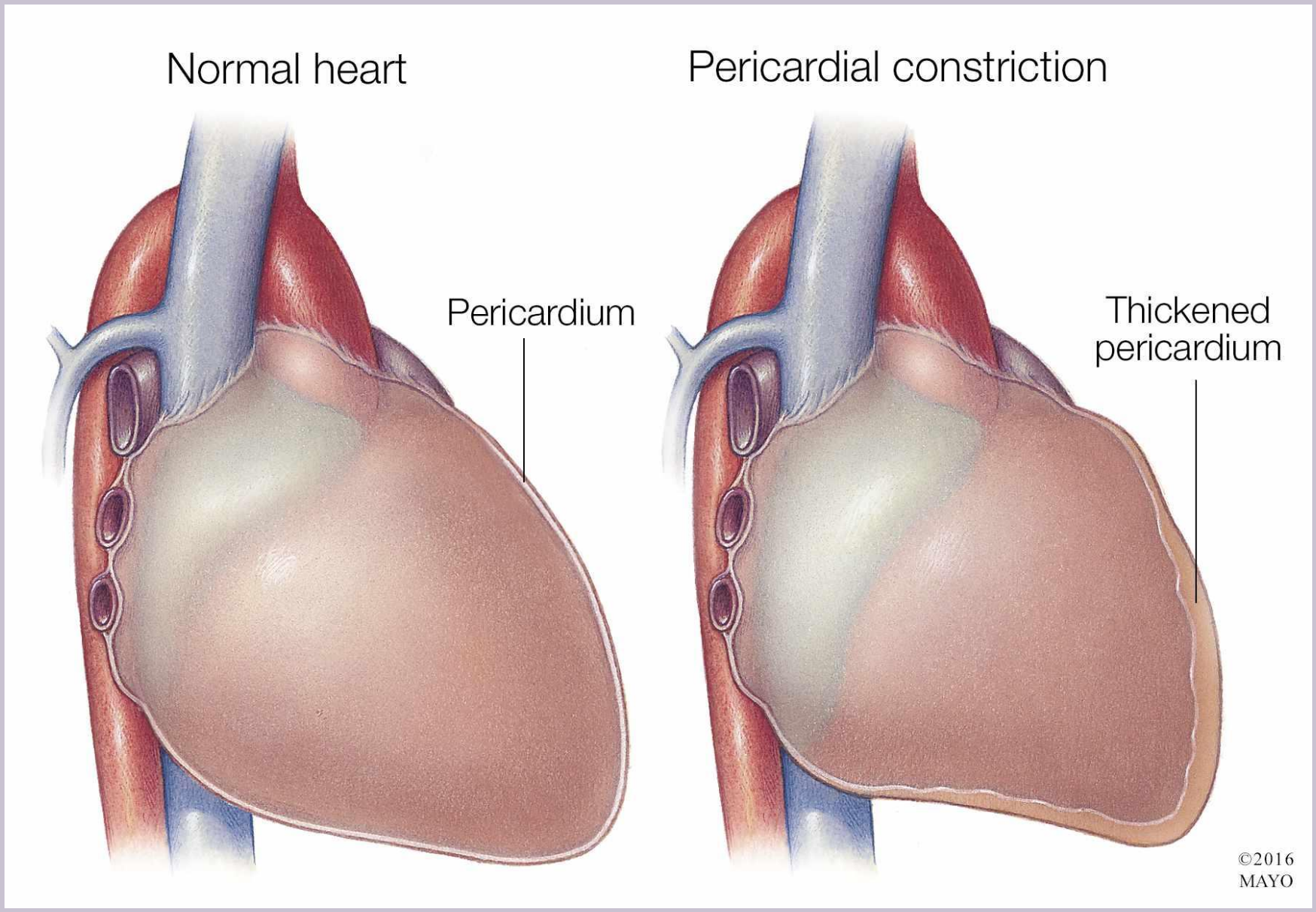
- Temperature 41C.
- Heart rate 140 per minute.
- X-ray: cardiac enlargement and possible “pneumonia”
- Elevated JVP
- Echo: Next slide
- Pericardiocentesis: Next slide

Pericardial effusion with image of aspirated material



Constrictive pericardial disease

- Typical case:
  - You are called about a young patient with ascites and no previous medical history.
  - Your first question is, “What’s the JVP?”
  - Answer: “Oh, I don’t usually check that.”
  - Your second question is, “What’s the heart size on chest x-ray?”
  - Answer: “Oh, the chest x-ray is normal.”
  - Your comment: “If the JVP is elevated this is likely constriction. If the JVP is not elevated this may be nephrosis. Can someone check?


Normal heart
Pericardial constriction
Pericardium
Thickened pericardium
©2016 MAYO

What is constrictive pericardial disease?

- May be acute, subacute, or chronic
- May present as unexplained anasarca, often chronic.
- The JVP distinguishes between a cardiac (i.e. elevated) and a non-cardiac (i.e. not elevated) cause of “right heart failure.”
- Chronic constrictive disease may be associated with varying degrees of elevation of cardiac filling pressures and is partially responsive to diuretics.
- Surgery is not a simple matter and complete normalization of filling pressures should not be expected in all cases.

Summary: Pericardial diseases

- You will see patients with pericarditis and with pericardial effusions in your office.
- Not all such patients need to be referred to the ER. Most patients are seen in the ER because of concern about ACS, etc., and/or for pain control.
- No “routine” tests are usually needed. An EKG, a chest x-ray, and a CBC are usually helpful.
- Idiopathic pericarditis can be well-treated with NSAIDs and colchicine. Recurrent pericarditis is a chronic problem.

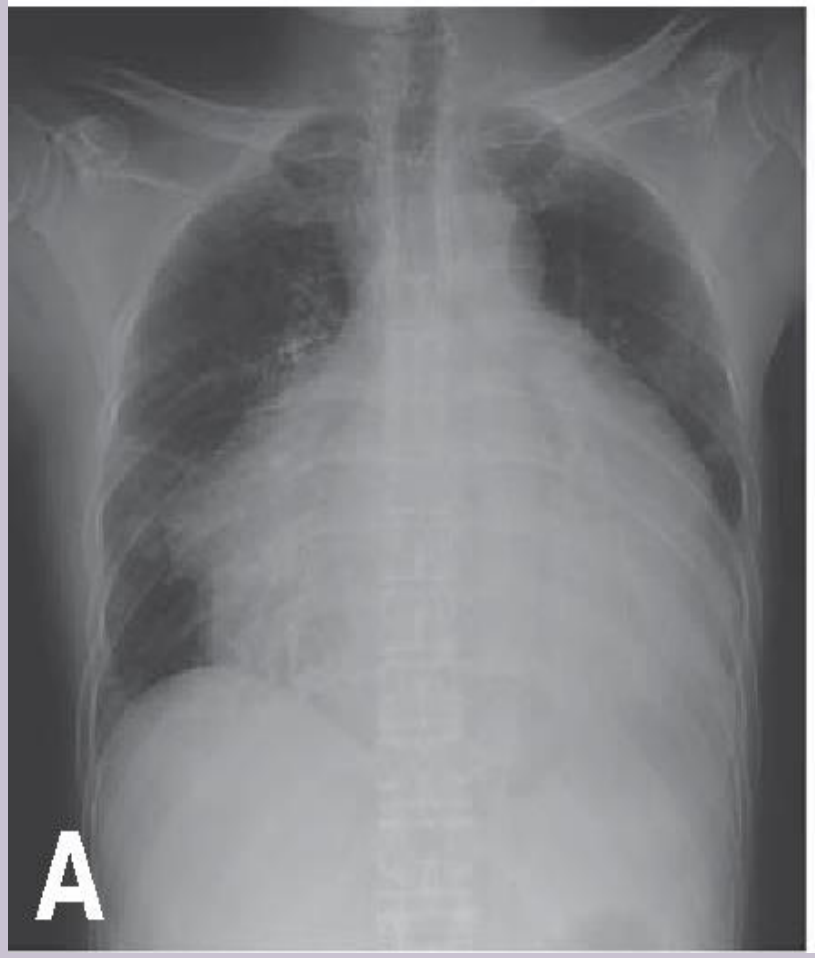

Q&A

Malignant pericardial effusions

- May complicate known malignancies
- May be the initial presentation of previously undetected malignancies.

A large effusion in a patient with dyspnea of recent onset and no chest pain

- Frequently someone who's been well with no history of disease.
- Painless gradual onset of dyspnea.
- Chest x-ray shows enlargement of the cardiac silhouette.
- CT scan-may or may not show malignancy
- Pericardiocentesis-send for cytology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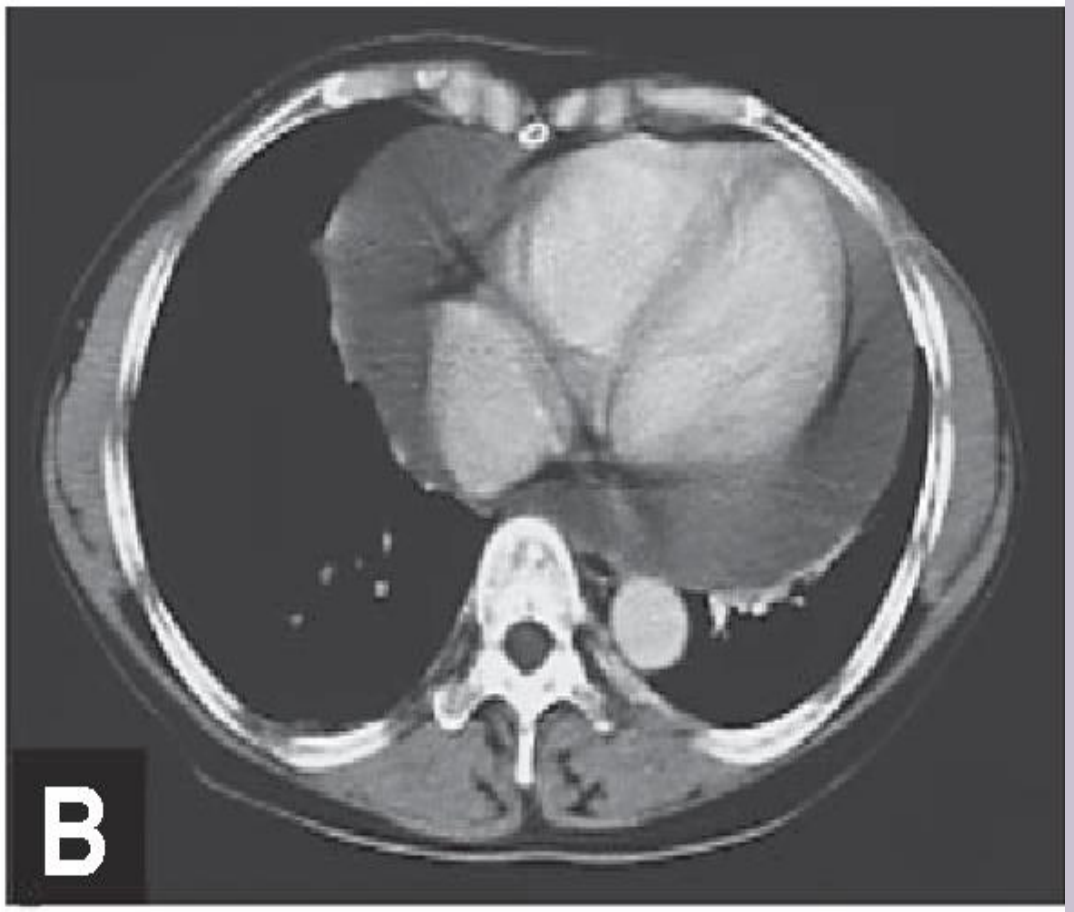
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Approach to malignant pericardial effusions

1. Diagnosis-Is the effusion due to a malignancy?
2. Does the effusion need drainage? Tap for diagnosis?
3. What's the best route of drainage?
   - Percutaneous? From which site?
   - Surgical?
4. Do chemotherapeutic agents need to be instilled into the pericardium at the time of drainage?
5. What's the prognosis for patients with malignant pericardial effusions?

Paul C. Cremer, Arnav Kumar, Apostolos Kontzias, Carmela D. Tan, E. Rene Rodriguez, Massimo Imazio, Allan L. Klein

- P.C. Cremer, A. Kumar, A. Kontizas, *et al.* Complicated pericarditis. J Am Coll Cardiol, 68 (2016), pp. 2311-2328

Do we have some understanding of the etiology of this “idiopathic” disorder?

- B. Maisch, H. Rupp, A. Ristic, *et al.* Pericardioscopy and epi- and pericardial biopsy- a new window to the heart improving etiological diagnoses and permitting targeted intra-pericardial therapy Heart Fail Rev, 18 (2013), pp. 317-328
- M. Imazio, A. Brucato, A. Doria, *et al.* Antinuclear antibodies in recurrent idiopathic pericarditis: prevalence and clinical significance. Int J Cardiol, 136 (2009), pp. 289-293

- A.L. Caforio, A. Brucato, M. Imazio, *et al.* Anti-heart and anti-intercalated disk autoanti-bodies: evidence for autoimmunity in idiopathic recurrent acute pericarditis. Heart, 96 (2010), pp. 779-784
- A. Brucato, M. Imazio, M. Gattorno, *et al.* Effect of anakinra on recurrent pericarditis among patients with colchicine resistance and corticosteroid dependence. JAMA, 31 (2016), pp. 1906-1912

Current Rheumatology Reports 2019 Mar 9;21(5):18. doi: 10.1007/s11926-019-0820-2.

Idiopathic Pericarditis-an Autoinflammatory Disease? Blank N, Lorenz HM. Heidelberg, Germany

Activation of the innate immune system in pericarditis suggests that autoinflammation contributes to acute and recurrent pericarditis. The efficacy of colchicine and anti-IL1β-targeted medication in clinical trials indicates that acute and recurrent pericarditis should be regarded as an autoinflammatory disease. Therefore, idiopathic pericarditis should be considered as an autoinflammatory disease.

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- Nature Reviews Cardiology 2016 Feb;13(2):99-105. doi: 10.1038/nrcardio.2015.115. Epub 2015 Aug 11.

Recurrent pericarditis: new and emerging therapeutic options. Imazio M, Lazaros G, Brucato A, Gaita F. Italy & Greece.

Bedtime reading list: Colchicine and pericarditis
Articles from 2005 to 2019-Imazio: 7 of 9 papers

1. Sambola A, Roca Luque I, Mercé J, et al. Colchicine Administered in the First Episode of Acute Idiopathic Pericarditis: A Randomized Multicenter Open-label Study. *Rev Esp Cardiol.* 2019. http://dx.doi.org/10.1016/j.rec.2018.11.016.
2. Adler Y, Charron P, Imazio M, et al. ESC Scientific Document Group. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2015;36:2921–2964.
3. Bayes-Genis A, Adler Y, de Luna AB, Imazio M. Colchicine in Pericarditis. *Eur Heart J.* 2017;38:1706–1709.
4. Imazio M, Bobbio M, Cecchi E, et al. Colchicine in addition to conventional therapy for acute pericarditis: results of the COlchicine for acute PEricarditis (COPE) trial. *Circulation.* 2005;112:2012–2016.
5. Imazio M, Bobbio M, Cecchi E, et al. Colchicine as first-choice therapy for recurrent pericarditis: results of the CORE (COlchicine for REcurrent pericarditis) trial. *Arch Intern Med.* 2005;165:1987–1991.
6. Imazio M, Brucato A, Cemin R, et al. ICAP Investigators. A randomized trial of colchicine for acute pericarditis. *N Engl J Med.* 2013;369:1522–1528.
7. Imazio M, Brucato A, Cemin R, et al. CORP (COlchicine for Recurrent Pericarditis) Investigators. Colchicine for recurrent pericarditis (CORP): a randomized trial. *Ann Intern Med.* 2011;155:409–414.
8. Imazio M, Belli R, Brucato A, et al. Efficacy and safety of colchicine for treatment of multiple recurrences of pericarditis (CORP-2): a multicentre, double-blind, placebo-controlled, randomised trial. *Lancet.* 2014;383:2232–2237.
9. Li YL, Qiao SB, Wang JY, Chen YM, Luo J, Zhang HF. Colchicine in addition to conventional therapy for pericarditis recurrence: An update meta-analysis. *Herz.* 2016;41:630–638.

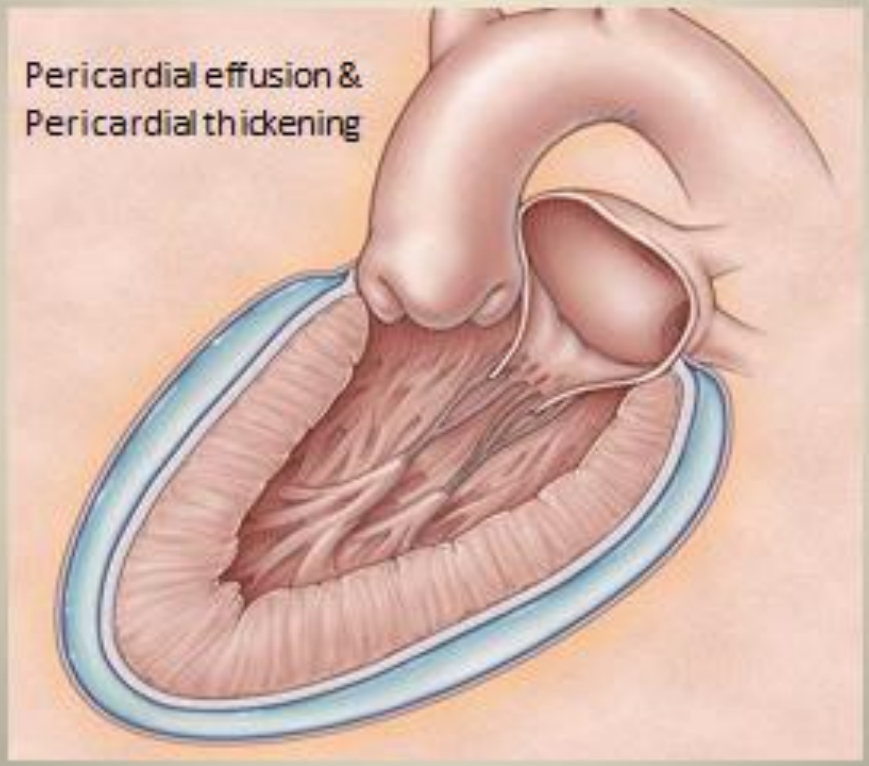
Rev. Esp. Cardiol. 2018……

Effusive-constrictive pericarditis? What's this? Who cares?

- What does the term mean?
- How often does the phenomenon occur?
- What can be done about it?

A Clearer View of Effusive–Constrictive Pericarditis

E. William Hancock, M.D.



NEJM 2004 Jan 29;350(5):435

Frequency of effusive-constrictive pericarditis

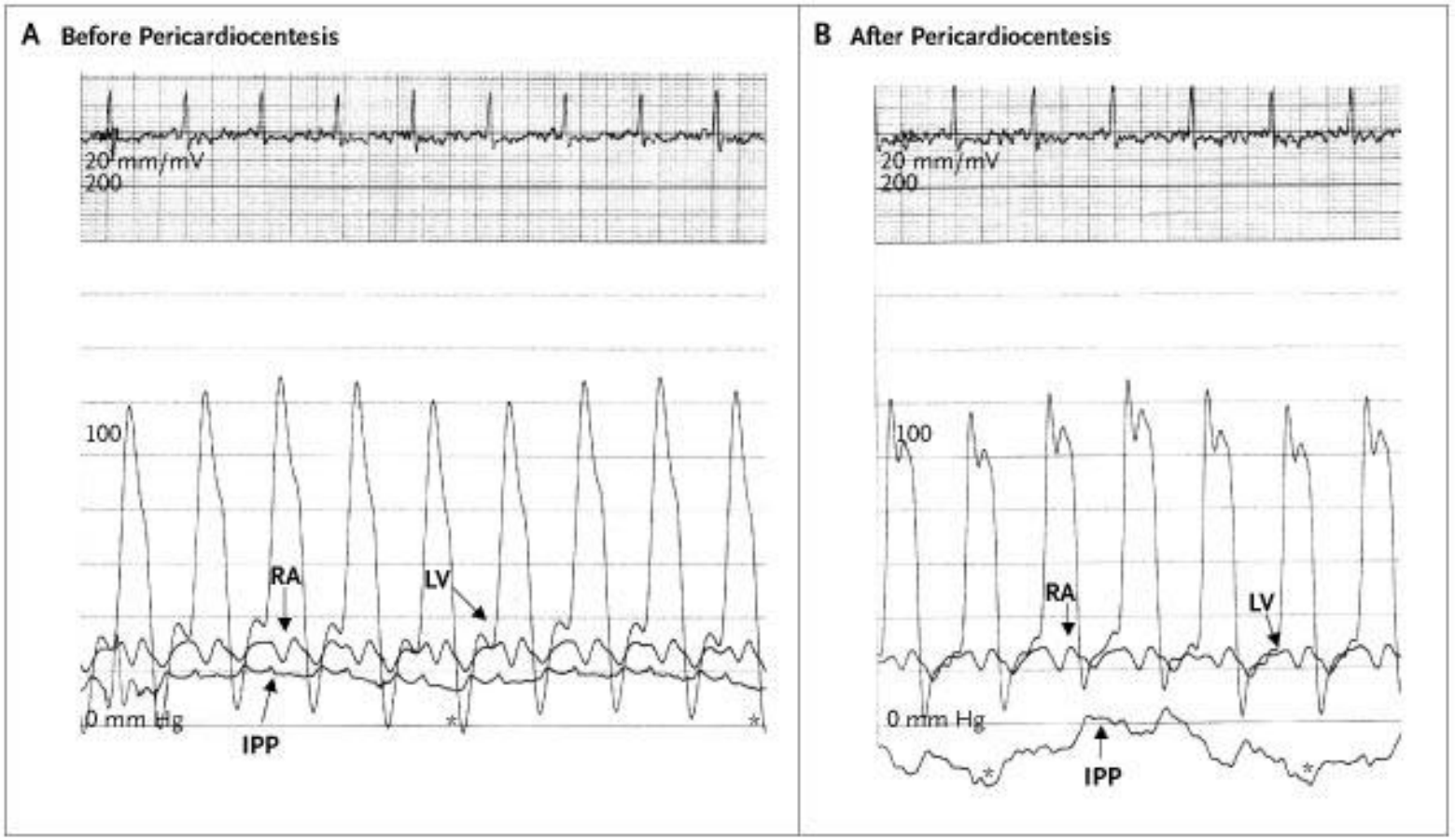
Table 2. Causes of 1184 Cases of Pericarditis of Any Type from 1986 to 2001 and the Number of Cases of Effusive–Constrictive Pericarditis.

Cause of Pericarditis	No. of Patients	No. with Effusive–Constrictive Pericarditis
Idiopathic	401	7
Neoplastic	44	4
Postsurgical	125	1
Uremia	85	0
Purulent and tuberculous	55	1
Radiation	7	2
Miscellaneous	467	0

Effusive-Constrictive Pericardial Disease

- Looks like a pericardial effusion with elevated filling pressures.
- The echocardiogram often suggests both a liquid and a more solid-layered appearance.
- Pericardiocentesis, is successful for fluid removal, but fails to reduce the systemic venous pressure.
- The effusion in this disease is not the major hemodynamic culprit.

Findings at Catheterization during Two Spontaneous Respiratory Cycles in Patient 13 before and after Pericardiocentesis



Sagrista-Sauleda, J. et al. N Engl J Med 2004;350:469-475

Barcelona group: 2004

The NEW ENGLAND JOURNAL of MEDICINE