Pericardial Diseases
(Diagnosis and Management of)

The Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology
Task Force members

Chairperson: Bernhard Maisch, Marburg, Germany

- Yehuda Adler
  (Tel Hashomer, Israel)
- Raimund Erbel
  (Essen, Germany)
- Reiner Rienmüller
  (Graz, Austria)
- Arsen D. Ristic
  (Belgrade, Serbia and Montenegro)
- Petar M. Seferovic
  (Belgrade, Serbia and Montenegro)
- Gaetano Thiene
  (Padua, Italy)
- Witold Z. Tomkowski
  (Warsaw, Poland)
- Magdi H. Yacoub
  (Harefield, UK.)
Guidelines on the Diagnosis and Management of Pericardial Diseases

ESC Committee for Practice Guidelines (CPG)
Chairperson: Silvia G. Priori, Italy

Maria Angeles Alonso Garcia, Spain; Jean-Jacques Blanc, France;
Andrzej Budaj, Poland; Martin Cowie, UK; Veronica Dean, France;
Jaap Deckers, The Netherlands; Enrique Fernandez Burgos, Spain;
John Lekakis, Greece; Bertil Lindahl, Sweden; Gianfranco Mazzotta,
Italy; João Morais, Portugal; Ali Oto, Turkey; Otto A. Smiseth,
Norway

Document Reviewers

CPG Review Coordinator: Gianfranco Mazzotta, Italy

Jean Acar, France; Eloisa Arbustini, Italy; Anton E. Becker, The
Netherlands; Giacomo Chiaranda, Italy; Yonathan Hasin, Israel; Rolf
Jenni, Switzerland; Werner Klein, Austria; Irene Lang, Austria;
Thomas F. Lüscher, Switzerland; Fausto J. Pinto, Portugal; Ralph
Shabetai, USA; Maarten L. Simoons, The Netherlands; Jordi Soler
Soler, Spain; David H. Spodick, USA.
Main Topics

- Acute pericarditis
- Pericardial effusion and cardiac tamponade
- Constrictive pericarditis
- Viral pericarditis
- Bacterial pericarditis
- Pericarditis in renal failure
- Autoreactive pericarditis and pericardial involvement in systemic autoimmune diseases
- The post-cardiac injury syndrome
- Postinfarction pericarditis
- Traumatic pericardial effusion
- Haemopericardium in aortic dissection
- Neoplastic pericarditis
- Pericardial effusion in pregnancy
- Drug- and toxin-related pericardial disease
Level of Evidence

- Level of evidence A: Multiple randomized clinical trials or meta-analyses.
- Level of evidence B: A single randomized trial or large non-randomized studies.
- Level of evidence C: Consensus opinion of the experts.
Classes of Recommendations

- **Class I**: evidence and/or general agreement that a given procedure or treatment is useful and effective.

- **Class II**: conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
  - **Class IIa**: Weight of evidence/opinion is in favour of usefulness/efficacy.
  - **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.

- **Class III**: evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.
**Pericardial Diseases Guidelines Slide-Set © 2004 European Society of Cardiology**

**ACUTE PERICARDITIS**

- **ECHOCARDIOGRAPHY**
  - **TAMPONADE or PE > 20 ml in diastole**
    - Suspected purulent, TBC or neoplastic effusion
      - **PERICARDIOCENTESIS PERICARDIAL DRAINAGE**
        - **PERICARDIOSCOPY AND PERICARDIAL/EPICARDIAL BIOPSY**
          - **INTRAPERICARDIAL THERAPY**
            - **CHRONIC PERICARDIAL EFFUSION**
              - If symptomatic for >2 years
                - **CARDIAC CATHETERISATION**
      - **SUBXIPHOID PERICARDIOTOMY AND DRAINAGE**
        - **FOLLOW-UP ECHOCARDIOGRAPHY**
          - **CONSTRUCTIVE PERICARDITIS**
            - **EFFUSIVE - CONSTRUCTIVE PERICARDITIS**
              - **RECURRENT PERICARDITIS**
                - **PERCUtANEOUS BALLOON PERICARDIOTOMY**
          - **PERICARDIOTOMY**
  - **NO TAMPONADE PE 10 - 20 ml in diastole**
    - **FOLLOW-UP ECHOCARDIOGRAPHY**
      - **PERCUtANEOUS BALLOON PERICARDIOTOMY**
  - **NO TAMPONADE PE < 10 ml in diastole**
    - **Symptomatic management**
      - Hospitalisation and exercise restriction
      - Pain management
        - **ibuprofen** 300-800 mg tid or qid
        - **Colchicine**, 0.5 mg bid

Acute Pericarditis

Diagnostic pathway and sequence of performance
(level of evidence B for all procedures)

Technique
Obligatory (class I)
• Auscultation
• ECG
• Echocardiography
• Blood analyses
• Chest X-ray
Acute Pericarditis

Diagnostic pathway and sequence of performance
(level of evidence B for all procedures)

Mandatory in Tamponade (class I)
Optional in large/recurrent effusions of if previous tests
inconclusive (class IIa) in small effusions (class IIb):
Pericardocentesis and drainage

Optional or if previous tests inconclusive (class IIa)
CT
MRI
Pericardioscopy, Pericardial biopsy
Diagnosis of Cardiac Tamponade

Diagnostic Procedure
- Clinical presentation
- Precipitating factors
- ECG
- Chest X-ray
- M-mode/2D echocardiogram
- Doppler
- M-mode colour Doppler
- Cardiac catheterisation
- RV/LV angiography
- Coronary angiography
- Computer tomography
Acute Pericarditis

Symptomatic management

- Exercise restriction
- Hospitalisation to determine the aetiology and observe for tamponade and the effect of treatment.
- Pain management
  - NSAIDs are the mainstay (level of evidence B, class I)
  - Ibuprofen is preferred for its rare side-effects, favourable impact on the coronary flow, and the large dose range (300-800 mg every 6-8 h)
  - Aspirin 300-600 mg every 4-6 h
  - Indomethacin should be avoided in elderly patients (flow reduction in the coronaries).
  - Gastrointestinal protection must be provided.
Recurrent Pericarditis

Treatment and prevention of recurrences

- **Colchicine** (0.5 mg bid) added to an NSAID or as monotherapy is well tolerated with fewer side effects than NSAIDs (level of evidence B, class IIa).

- **Percutaneous balloon pericardiectomy** - in recurrences resistant to medical treatment (level of evidence B, class IIb).

- **Corticosteroids** should be used only in patients with poor general condition or in frequent crises (level of evidence C, class IIa). The recommended regimen is: prednisone 1-1.5 mg/kg, for at least one month. If patients do not respond adequately, azathioprine (75-100 mg/day) or cyclophosphamide can be added.

- **Pericardiectomy** - only in frequent and highly symptomatic recurrences resistant to medical treatment (level of evidence B, class IIa).
Pericardial Effusion and Cardiac Tamponade

Indications for Pericardiocentesis

Class I
- Cardiac tamponade
- Effusions >20 mm in echocardiography (diastole)
- Suspected purulent or tuberculous pericardial effusion

Class IIa
- Effusions 10-20 ml in echocardiography in diastole for diagnostic purposes other than purulent pericarditis or tuberculosis (pericardial fluid and tissue analyses, pericardioscopy, and epicardial/pericardial biopsy)
- Suspected neoplastic pericardial effusion
Pericardial Effusion and Cardiac Tamponade

Indications for Pericardiocentesis

Class Iib

- Effusions <10 ml in echocardiography in diastole for diagnostic purposes other than purulent, neoplastic or tuberculous pericarditis.

Class III (contraindications)

- Aortic dissection
- Relative contraindications include uncorrected coagulopathy, anticoagulant therapy, thrombocytopenia <50000/mm³, small, posterior, and loculated effusions.
- If the diagnosis can be made otherwise or the effusions are small and resolving under anti-inflammatory treatment.
Pericardial Effusion and Cardiac Tamponade

How to Perform Pericardiocentesis

- Obtain current and reliable echocardiography findings before the procedure.
- Pericardiocentesis guided by fluoroscopy is performed in the cardiac catheterization laboratory in local anaesthesia.
- The subxiphoid approach has been used most commonly, with a long needle directed towards the left shoulder at a 30° angle to the skin.
Pericardial Effusion and Cardiac Tamponade

How to Perform Pericardiocentesis

Pericardiocentesis guided by echocardiography is performed in intensive care unit or in operating theatre.

- Echocardiography should identify the shortest route where the pericardium can be entered intercostally (usually in the sixth or seventh rib space in the anterior axillary line).
- Intercostal arteries should be avoided.
Pericardial Effusion and Cardiac Tamponade

How to Perform Pericardiocentesis

- Strict aseptic conditions, ECG, and blood pressure monitoring have to be provided.
- Direct ECG monitoring from the puncturing needle is not an adequate safeguard.
- Right-heart catheterization can be performed simultaneously, allowing exclusion of constriction.
Pericardial Effusion and Cardiac Tamponade

How to Perform Pericardiocentesis

- The needle approaches pericardium slowly.
- Steady manual aspiration is essential.
- Stop the needle as soon as the effusion is aspirated.
- Exchange for soft J-tip guidewire and after dilatation for a multi-holed pigtail catheter.
- Drain the fluid in <1 l steps to avoid the acute right-ventricular dilatation.
- Perform prolonged pericardial drainage (several days) until <25 ml/day.
Pericardial Effusion Analyses

Should be ordered according to the clinical presentation

CLASS I

• Suspected malignant effusion: CYTOLOGY

• Suspected tuberculous effusion: ACID-FAST BACILLI STAINING, mycobacterium CULTURE (preferably with radiometric growth detection e.g., BACTEC-460), adenosine deaminase, IFN-gamma, pericardial lysozyme, PCR analyses.

• Suspected bacterial infection: at least three cultures of pericardial fluid for aerobes and anaerobes as well as three blood cultures. Positive cultures should be followed by sensitivity tests for antibiotics.
Pericardial Effusion Analyses

Should be ordered according to the clinical presentation

**CLASS IIa**

- **Viral vs. autoreactive pericarditis:** PCR analyses for cardiotropic viruses.

- **Suspected neoplastic pericarditis:** Tumour markers (CEA, AFP, CA 125, CA 72-4, CA 15-3, CA 19-9, CD-30, CD-25...).

- **Benign reactive mesothelial cells vs. adenocarcinoma:** Combination of epithelial membrane antigen, CEA, and vimentin immunocytochemical staining.
Pericardial Effusion Analyses

Should be ordered according to the clinical presentation

CLASS IIb

Exudate vs transudate:

- Pericardial fluid specific gravity (>1015)
- Protein level (>3.0 g/dl; fluid/serum ratio >0.5)
- LDH (>200mg/dl; serum/fluid >0.6), and
- Glucose (exudates vs. transudates = 77.9±41.9 vs. 96.1±50.7 mg/dl)
Constrictive pericarditis vs. Restrictive cardiomyopathy

Diagnostic Procedure

- Clinical presentation
- ECG
- Chest X-ray
- M-mode/2D echocardiogram
- Doppler
- TEE
- CT/MRI
- Cardiac catheterization
- RV/LV angiography
- Coronary angiography
Constrictive pericarditis vs. Restrictive cardiomyopathy

Methods

- Physical findings
- ECG
- Chest radiography
- 2D-echocardiography
- Doppler studies

Mitral inflow, pulmonary vein, tricuspid inflow, hepatic veins, inferior vena cava, colour M-mode, mitral annular motion

- Tissue Doppler, echocardiography
- Cardiac catheterization
- EMB
- CT/MRI
Management of Constrictive Pericarditis

- Pericardiectomy is the only treatment for permanent constriction.

- The indications are based upon clinical symptoms, echocardiography findings, CT/MRI, and heart catheterization.

- Antero-lateral thoracotomy

- Median sternotomy (faster access to the aorta and right atrium for extracorporeal circulation).

- Primary installation of cardiopulmonary bypass is not recommended (diffuse bleeding following systemic heparinisation).

- Areas of strong calcification or dense scarring may be left as islands to avoid major bleeding.
Pericardiectomy for Constrictive Pericarditis

Major complications

- Acute perioperative cardiac insufficiency (should be treated by fluid substitution and catecholamines, high doses of digitalis, and intraaortic balloon pump in most severe cases).
- Ventricular wall rupture.
- Mortality (in properly selected cases 6-12%, but >40% in unselected patients).

Long term results

- If indication for surgery was established early, long-term survival after pericardiectomy corresponds to that of the general population.
Pathoanatomical forms of Constrictive Pericarditis

- Cardiac mortality and morbidity at pericardiectomy is mainly caused by the pre-surgically unrecognised presence of myocardial atrophy or myocardial fibrosis.

- Exclusion of patients with extensive myocardial fibrosis and/or atrophy significantly reduce the mortality rate for pericardiectomy.
Diagnosis of Viral Pericarditis

- The diagnosis of viral pericarditis is not possible without the evaluation of pericardial effusion and/or pericardial/epicardial tissue, preferably by PCR or in-situ hybridisation (level of evidence B, class IIa).

- A four-fold rise in serum antibody levels (two samples within 3-4 weeks) is suggestive but not diagnostic for viral pericarditis (level of evidence B, class IIb).
Management of Viral Pericarditis

- In most cases the disease is self-limiting and no specific treatment is necessary.
- Symptomatic treatment for chest pain, and eventual rhythm disorders and congestive heart failure is indicated.
- In patients with chronic or recurrent symptomatic pericardial effusion and confirmed viral infection the following specific treatment is under investigation:
  - **CMV pericarditis**: hyperimmunoglobulin - 1 time per day 4ml/kg on day 0, 4, and 8; 2 ml/kg on day 12 and 16;
  - **Coxsackie B pericarditis**: Interferon alpha or beta 2,5 Mio. IU/m² surface area s.c. 3 x per week;
  - **Adenovirus and parvovirus B19 pericarditis**: immunoglobulin treatment: 10 g intravenously at day 1 and 3 for 6-8 hours.
Management of Viral Pericarditis

- Treatment is symptomatic, while in large effusions and cardiac tamponade pericardiocentesis is necessary.
- Persons with HIV infection and tuberculosis usually can be treated with standard anti-tuberculous regimens with good results, although in some cases, prolonged therapy may be warranted.
- Since treatment of HIV may require protease inhibitors or non-nucleoside reverse transcriptase inhibitors use of rifampicin may be precluded.
- The use of corticoid therapy as an adjunct to tuberculostatic treatment is allowed (level of evidence A, class I).
Diagnosis of Bacterial Pericarditis

- Percutaneous pericardiocentesis must be promptly performed if bacterial pericarditis is suspected.
- Pericardial fluid should undergo Gram, acid-fast, and fungal staining, followed by cultures for aerobes, anaerobes, and M. tuberculosis (preferably with radiometric growth detection).
- Drug sensitivity testing is essential for treatment selection.
- PCR analyses, increased levels of adenosine deaminase (>40 IU/L), interferon-gamma (>200 pg/L), or pericardial lysozyme (>6.5 microg/dL) are highly sensitive and specific for diagnosis of tuberculous effusion, but are cost-effective only if the pre-test probability is high (populations with high incidence of tuberculosis).
Management of Bacterial Pericarditis

- Urgent pericardial drainage, combined with intravenous antibiotic therapy (e.g. vancomycin 1 g bid, ceftriaxone 1-2 g bid, and ciprofloxacin 400 mg/day) is mandatory in purulent pericarditis.

- In selecting antimicrobial therapy the ability of potential agents to kill the causative organism as well as the minimum inhibitory concentration (MIC - the lowest concentration that inhibits growth) and minimum bactericidal concentration (MBC - the lowest concentration that decreases a standard inoculum of organisms 99.9% during 24 hours) need to be considered.

- Irrigation with urokinase or streptokinase, using large catheters, may liquefy the purulent exudate, but open surgical drainage is preferable.
Management of Tuberculous Pericarditis

• The initial treatment:
  - Isoniazid 300 mg/day
  - Rifampicin 600 mg/day
  - Pyrazinamide 15-30 mg/kg/day
  - Ethambutol 15-25 mg/kg/day
  - Prednisone (1-2 mg/kg/day) may be given simultaneously with antituberculous therapy for 5-7 days and progressively reduced to discontinuation in 6-8 weeks.

• After two months most patients can be switched to two-drug regimen (isoniazid and rifampicin) for the total of six months.
Management of Tuberculous Pericarditis

- **Respiratory isolation** if active pulmonary or laryngeal tuberculosis is also suspected.

- Patients are considered to be noninfectious if they have a clinical response to anti-tuberculous chemotherapy and three consecutive smear-negative sputum samples that were collected on different days.

- **Pericardiectomy** is reserved for recurrent effusions or continued elevation of central venous pressure after 4-6 weeks of antituberculous and corticosteroid therapy.
Pericarditis in Renal Failure

Diagnosis

Chest pain, pericardial friction rub and pericardial effusion in a patient with advanced renal failure (acute or chronic) before dialysis has been instituted or in patients on maintenance chronic haemodialysis or peritoneal dialysis.

- Due to autonomic impairment in uremic patients, heart rate may remain slow (60–80 beats/min) during tamponade, despite fever and hypotension.

- The ECG does not show the typical diffuse ST/T wave elevations observed with other causes of acute pericarditis due to the lack of the myocardial inflammation.
Pericarditis in Renal Failure

Management
Frequent (heparin-free) haemodialyses.

- Peritoneal dialysis, which does not require heparinisation, may be therapeutic in pericarditis resistant to haemodialysis, or if heparin-free haemodialysis cannot be performed.

- NSAIDs and systemic corticosteroids have limited success when intensive dialysis is ineffective.

- Cardiac tamponade and large chronic effusions resistant to dialysis must be treated with pericardiocentesis (level of evidence B, class IIa).

- Large, non-resolving symptomatic effusions should be treated with intrapericardial instillation of corticosteroids (triamcinolone hexacetonide 50 mg every 6 hours for 2 to 3 days).

- Pericardiectomy is indicated only in refractory, severely symptomatic patients.
Autoreactive Pericarditis

Diagnosis

Pericardial effusion with $>5000/\text{mm}^3$ lymphocytes and mononuclear cells (autoreactive lymphocytic), or antibodies against heart muscle tissue (autoreactive antibody-mediated).

- **Inflammation** in epicardial/endomyocardial biopsies by $\geq 14 \text{ cells/mm}^2$.
- **Exclusion of active viral infection** both in pericardial effusion and endomyocardial/epimyocardial biopsies (no virus isolation, no IgM-titer against cardiotropic viruses in pericardial effusion, and negative PCR for major cardiotropic viruses).
- TBC, B. burgdorferi, C. pneumoniae, and other **bacterial infection excluded** by PCR and/or cultures.
- Neoplastic infiltration **absent** in pericardial effusion and biopsy samples.
- Exclusion of systemic, metabolic disorders, and renal failure.
Autoreactive Pericarditis and Pericardial Involvement in Systemic Autoimmune Diseases

Management

- Intrapericardial treatment with triamcinolone plus colchicine per os 0.5 mg bid for six months is highly efficient with rare side effects (level of evidence B, class IIa).
- In systemic autoimmune diseases intensified treatment of the underlying disease and symptomatic management are indicated (evidence level B, class I).
- For tapering of prednisone, ibuprofen or colchicin should be introduced early.
Postpericardiotomy Syndrome

Diagnosis
- Chest pain, pericardial friction rub, ECG changes, PE within days to months after cardiac, pericardial injury or both.

Management
- Symptomatic treatment as in acute pericarditis.
- In refractory forms long term (3-6 months) oral corticoids or preferably pericardiocentesis and intrapericardial instillation of triamcinolone (300 mg/m²).
- redo surgery and pericardiectomy are very rarely needed.
- Primary prevention with short-term perioperative steroid treatment or colchicine is under investigation.
- Warfarin administration in pts with early postoperative PE imposes greatest risk.
Postinfarction Pericarditis

(Pericarditis epistenocardica and Dressler’s syndrome)

Diagnosis

• Detection of PE after acute myocardial infarction.

• ECG changes are often overshadowed by myocardial infarction changes.

• Postinfarction PE >10 mm is most frequently associated with haemopericardium, and two thirds of these patients may develop tamponade/free wall cardiac rupture.
Postinfarction Pericarditis

(Pericarditis epistenocardica and Dressler's syndrome)

Management

- Hospitalisation to observe for tamponade, differential diagnosis, and adjustments of treatment is needed.
- Ibuprofen, which increases coronary flow, is the agent of choice.
- Aspirin, up to 650 mg every 4 hours for 2 to 5 days has also been successfully applied (other nonsteroidal agents risk thinning the infarction zone).
- Corticosteroid therapy can be used for refractory symptoms only but could delay myocardial infarction healing.
- In cardiac rupture, urgent surgical treatment is life saving. However, if the immediate surgery is not possible pericardiocentesis and intrapericardial fibrin-glue instillation could be an alternative.
Traumatic Pericardial Effusion

Management

- Urgent echocardiography, if available TEE
- Rescue pericardiocentesis
- Autotransfusion
- Urgent thoracotomy and surgical repair
Haemopericardium in Aortic Dissection

Diagnosis

- Echocardiography (both TTE and TEE)
- CT or MRI in complex cases
- Angiography (only in stable patients)
Management

- Pericardiocentesis is contraindicated, due to the risk of intensified bleeding and extension of the dissection.

- Surgery should be performed immediately (evidence level B, class I).
Neoplastic Pericarditis

Diagnosis

- Confirmation of the malignant infiltration within the pericardium (cytology, histology, if available tumour markers) (level of evidence B, class I).

- Of note, in up to 2/3 of the patients with documented malignancy pericardial effusion is caused by non-malignant diseases, e.g. radiation pericarditis, or opportunistic infections.
Neoplastic Pericarditis

Management

- **Systemic antineoplastic therapy** whenever possible (prevents recurrences in up to 67% of cases).

- **Pericardiocentesis** to relieve symptoms and establish diagnosis (level of evidence B, class IIa).

- **Intrapericardial instillation of a cytostatic/sclerosing agent** (level of evidence B, class IIa).
  - **Cisplatin** (single instillation of 30 mg/m2) is preferred for pericardial metastases of the lung cancer and
  - Intrapericardial instillation of **thiotepa** (15 mg on days 1, 3, and 5) for breast cancer.
Neoplastic Pericarditis

Management (cont.)

- Prolonged pericardial drainage is recommended, in all patients with large effusions because of the high recurrence rate (40-70%) (level of evidence B, class I).

- In resistant cases percutaneous balloon pericardiectomy or rarely pericardiectomy may be indicated (repeated pericardiocentesis and/or intrapericardial therapy were not successful).

- Radiation therapy is very effective (93%) in controlling malignant effusion (level of evidence B, class IIa) in patients with radiosensitive tumours (e.g. lymphomas and leukemias). However, radiotherapy of the heart can cause myocarditis and pericarditis by itself.
Pericardial Effusion in Pregnancy

Diagnosis

- Many pregnant women develop a minimal to moderate clinically silent hydropericardium by the third trimester. Cardiac compression is rare.

- ECG changes of acute pericarditis in pregnancy should be distinguished from the slight ST-segment depressions and T-wave changes seen in normal pregnancy.

- Occult constriction becomes manifest in pregnancy due to the increased blood volume.
Pericardial Effusion in Pregnancy

Procedures
- Pulsus paradoxicus
- Electrocardiogram
- Chest radiography
- Echocardiography
- Magnetic resonance imaging
- Swan-Ganz catheterization
- Cardiac catheterization
- Pericardiocentesis
- Pericardioscopy and epicardial/pericardial biopsy
Pericardial Effusion in Pregnancy

Management

- Most pericardial disorders are managed as in nonpregnant.
- Caution is necessary while high-dose aspirin may prematurely close the ductus arteriosus.
- Calcineurin is contraindicated in pregnancy.
- Pericardiotomy and pericardiectomy can be safely performed if necessary and do not impose a risk for subsequent pregnancies.
Foetal Pericardial Effusion

- Foetal pericardial fluid can be detected by echocardiography after 20 weeks' gestation and is normally 2 mm or less in depth.

- More fluid should raise questions of hydrops foetalis, Rh disease, hypoalbuminemia, and immunopathy or maternally transmitted mycoplasmal or other infections, and neoplasia.
Drug- and Toxin-related Pericardial Disease

**A. Drug-induced lupus erythematosus**
- Procainamide
- Tocainide
- Hydralazine
- Methyldopa
- Mesalazine
- Reserpine
- Isoniazid
- Hydantoins

**B. Hypersensitivity reaction**
- Penicillins
- Tryptophan
- Cromolyn sodium

**C. Idiosyncratic reaction or hypersensitivity**
- Methysergide
- Minoxidil
- Practolol
- Bromocriptine
- Psicofuranine
- Polymer fume inhalation (Teflon)
- Cytarabine
- Phenylbutazone
- Amiodarone
- Streptokinase
- p-Aminosalicylic acid
- Thiazides
- Streptomycin
- Thiouracils
- Sulfas drugs
- Cyclophosphamide
- Cyclosporine
- Mesalazine
- 5-Fluorouracil
- Vaccines (Smallpox, Yellow fever)
- GM-CSF

**D. Anthracyclines**
- Doxorubicin
- Daunorubicin

**E. Serum sickness**
- Foreign antisera (e.g., antitetanus)
- Blood products

**F. Venom**
- Scorpion fish sting

**G. Foreign-substance reactions (direct pericardial application)**
- Talc (Mg silicate)
- Silicones
- Tetracycline/other sclerosants
- Asbestos
- Iron in β-thalassemia

**H. Haemopericardium**
- Anticoagulants
- Thrombolytic agents