

# **ENDOCARDITIS AND PERICARDITIS.**

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A. **Endocarditis** is an inflammation of the inner lining of the heart, or endocardium. It usually involves an infection of the heart valves. Most of them are characterized by the presence of vegetation of verrucae which have distinct features summarized in table

## Distinguishing Features of Vegetations in Major Forms of Endocarditis.

FEATURE	RHEUMATIC	LIBMAN-SACKS	NON-BACTERIAL THROMBOTIC	BACTERIAL
1. <i>Valves commonly affected</i>	Mitral alone; mitral and aortic combined	Mitral, tricuspid	Mainly mitral; less often aortic and tricuspid	Mitral; aortic; combined mitral and aortic
2. <i>Location on valve cusps or leaflets</i>	Occur along the line of closure, atrial surface of atrio-ventricular valves and ventricular surface of semilunar valves	Occur on both surfaces of valve leaflets or cusps, in the valve pockets	Occur along the line of closure	SABE more often on diseased valves; ABE on previously normal valves; location same as in RHD
3. <i>Macroscopy</i>	Small, multiple, warty, grey brown, translucent, firmly attached, generally produce permanent valvular deformity	Medium-sized, multiple, generally do not produce significant valvular deformity	Small but larger than those of rheumatic, single or multiple, brownish, firm, but more friable than those of rheumatic	Often large, grey-tawny to greenish, irregular, single or multiple, typically friable
4. <i>Microscopy</i>	Composed of fibrin with superimposed platelet thrombi and no bacteria, Adjacent and underlying endocardium shows oedema, proliferation of capillaries, mononuclear inflammatory infiltrate and occasional Aschoff bodies.	Composed of fibrinoid material with superimposed fibrin and platelet thrombi and no bacteria. The underlying endocardium shows fibrinoid necrosis, proliferation of capillaries and acute and chronic inflammatory infiltrate including the haematoxylin bodies of Gross.	Composed of degenerated valvular tissue, fibrin-platelets thrombi and no bacteria. The underlying valve shows swelling of collagen, fibrinoid change, proliferation of capillaries but no significant inflammatory cell infiltrate.	Composed of outer eosinophilic zone of fibrin and platelets, covering colonies of bacteria and deeper zone of non-specific acute and chronic inflammatory cells. The underlying endocardium may show abscesses in ABE and inflammatory granulation tissue in the SABE.

## **Bacterial Endocarditis**

**Definition:-** Bacterial endocarditis (BE) is serious infection of the valvular and mural endocardium caused by different forms of bacteria (other than tubercle bacilli and non-bacterial microorganisms) and is characterized by typical infected and friable vegetations. Depending upon the severity of infection, BE is subdivided into 2 clinical forms.

1. **Acute bacterial endocarditis (ABE)** is the fulminant and destructive acute infection of the endocardium by highly virulent bacteria in a previously normal heart and almost invariably runs a rapidly fatal course in a period of 2-6 weeks.
2. **Subacute bacterial endocarditis (SABE) or endocarditis lenta** (lenta = slow) is caused by less virulent bacteria in a previously diseased heart and has a gradual downhill course in a period of 6 weeks to a few months and sometimes years.

Although classification of bacterial endocarditis into acute and subacute forms has been largely discarded because the clinical course is altered by antibiotic treatment, still a few important distinguishing features are worth describing. However, characteristic of the vegetations in the two forms of BE are difficult to distinguish.

**Incidence.** Introduction of antibiotic drugs has helped greatly in lowering the incidence of BE as compared with its incidence in the pre-antibiotic era. Though BE may occur at any age, most cases of ABE as well as SABE occur over 50 years of age. Males are affected more often than females.

**Etiology.** All cases of BE are caused by infection with microorganisms in patients having certain predisposing factors.

**A. Infective agents.** About 90% cases of BE are caused by streptococci and staphylococci.

- In ABE, the most common causative organisms are virulent strains of staphylococci, chiefly *Staphylococcus aureus*. Others are pneumococci, gonococci,  $\beta$ -streptococci and enterococci.
- In SABE, the commonest causative organisms are the streptococci with low virulence, predominantly *Streptococcus Viridans*, which forms part of normal flora of the mouth and pharynx. Other less common etiologic agents include other strains of streptococci and staphylococci (e.g. *Streptococcus bovis* which is the normal inhabitant of gastrointestinal tract, *Streptococcus pneumoniae*, and *Staphylococcus epidermidis* which is a commensal of the skin), gram-negative enteric bacilli (e.g. *E. coli*, *Klebsiella*, *Pseudomonas* and *Salmonella*), pneumococci, gonococci and *Haemophilus influenzae*.

## Distinguishing Features of Acute and Subacute Bacterial Endocarditis.

FEATURE	ACUTE	SUBACUTE
1. Duration	<6 weeks	>6 weeks
2. Most common organisms	<i>Staph. aureus</i> , $\beta$ -streptococci	<i>Streptococcus viridans</i>
3. Virulence of organisms	Highly virulent	Less virulent
4. Previous condition of valves	Usually previously normal	Usually previously damaged
5. Lesion on valves	Invasive, destructive, suppurative	Usually not invasive or suppurative
6. Clinical features	Features of acute systemic infection	Splenomegaly, clubbing of fingers, petechiae

**B. Predisposing factors.** There are 3 main factors which predispose to the development of both forms of BE:

1. conditions initiating transient bacteraemia, septicaemia and pyaemia;
2. underlying heart disease; and
3. impaired host defenses.

1. Bacteraemia, septicaemia and pyaemia: Bacteria gain entrance to the bloodstream causing transient and clinically silent bacteraemia in a variety of day-to-day procedures as well as from other sources of infection. Some of the common examples are:
  - i. Peridontal infections such as trauma from vigorous brushing of teeth, hard chewing, tooth extraction and other dental procedures.
  - ii. Infections of the genitourinary tract such as in catheterization, cystoscopy, obstetrical procedures including normal delivery and abortions.
  - iii. Infections of the gastrointestinal and biliary tract.
  - iv. Surgery of the bowel, biliary tract and genitourinary tract.
  - v. Skin infections such as boils, carbuncles and abscesses.
  - vi. Upper and lower respiratory tract infections including bacterial pneumonias.
  - vii. Intravenous drug abuse.
  - viii. Cardiac catheterization and cardiac surgery for implantation of prosthetic valves.

2. Underlying heart disease: SABE occurs much more frequently in previously diseased heart valves, whereas the ABE is common in previously normal heart. Amongst the commonly associated underlying heart diseases are the following:

- i. Chronic rheumatic valvular disease in about 50% cases.
- ii. Congenital heart diseases in about 20% cases. These include VSD, subaortic stenosis, pulmonary stenosis, bicuspid aortic valve, coarctation of the aorta, and PDA.
- iii. Other causes are syphilitic aortic valve disease, atherosclerotic valvular disease, floppy mitral valve, and prosthetic heart valves.

3. Impaired host defenses: All conditions in which there is depression of specific immunity, deficiency of complement and defective phagocytic function, predispose to BE. Following are some of the examples of such conditions:

i. Impaired specific immunity in lymphoma.

ii. Leukaemias.

iii. Cytotoxic therapy for various forms of cancers and transplant patients.

iv. Deficient functions of neutrophils and macrophages.

**Pathogenesis.** Bacteria on entering the bloodstream from any of the above-mentioned routes are implanted on the cardiac valves or mural endocardium. There are different hypotheses to explain the occurrence of bacterial implants on the valves:

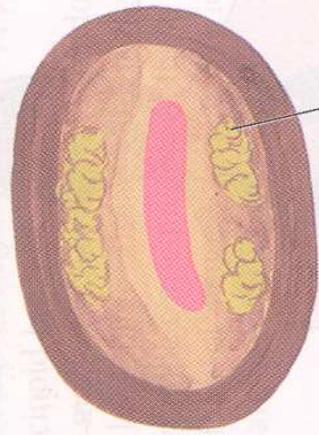
1. The circulating bacteria are lodged much more frequently on previously damaged valves from diseases, chiefly RHD and congenital heart diseases, than on healthy valves.
2. Conditions producing haemodynamic stress on the valves are liable to cause damage to the endothelium, favouring the formation of platelet thrombi which get infected from circulating bacteria.
3. Another alternative hypothesis is the occurrence of non-bacterial thrombotic endocarditis from prolonged stress which is followed by bacterial contamination.

**Pathologic changes.** The characteristic pathologic feature in both ABE and SABE is the presence of typical vegetations or verrucae on the valve cusps or leaflets, and less often, on mural endocardium.

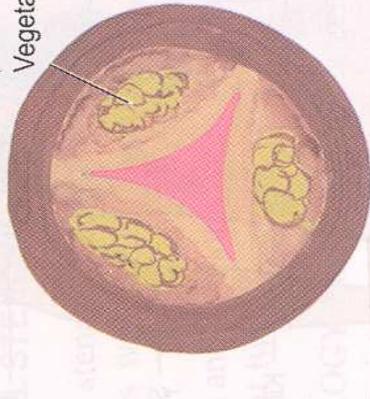
**Microscopically,** the lesions are found commonly on the valves of the left heart, most frequently on the mitral, followed in descending frequency, by the aortic, simultaneous involvement of both mitral and aortic valves, and quite rarely on the valves of the right heart. The vegetations in SABE are more often seen on previously diseased valves, whereas the vegetations of ABE are often found on previously normal valves. Like in RHD, the vegetations are often located on the atrial surface of atrioventricular valves and ventricular surface of the semilunar valves. They begin from the contact areas of the valve and may extend along the surface of the valves and on to the adjacent endocardium.

The vegetations of BE vary in size from a few millimeters to several centimeters, grey-tawny to greenish, irregular, single or multiple, and typically friable. They may appear flat, filiform, fungating or polypoid. The vegetations in ABE tend to be bulkier and globular than those of SABE and are located more often on previously normal valves, may cause ulceration or perforation of the underlying valve leaflet, or may produce myocardial abscesses.

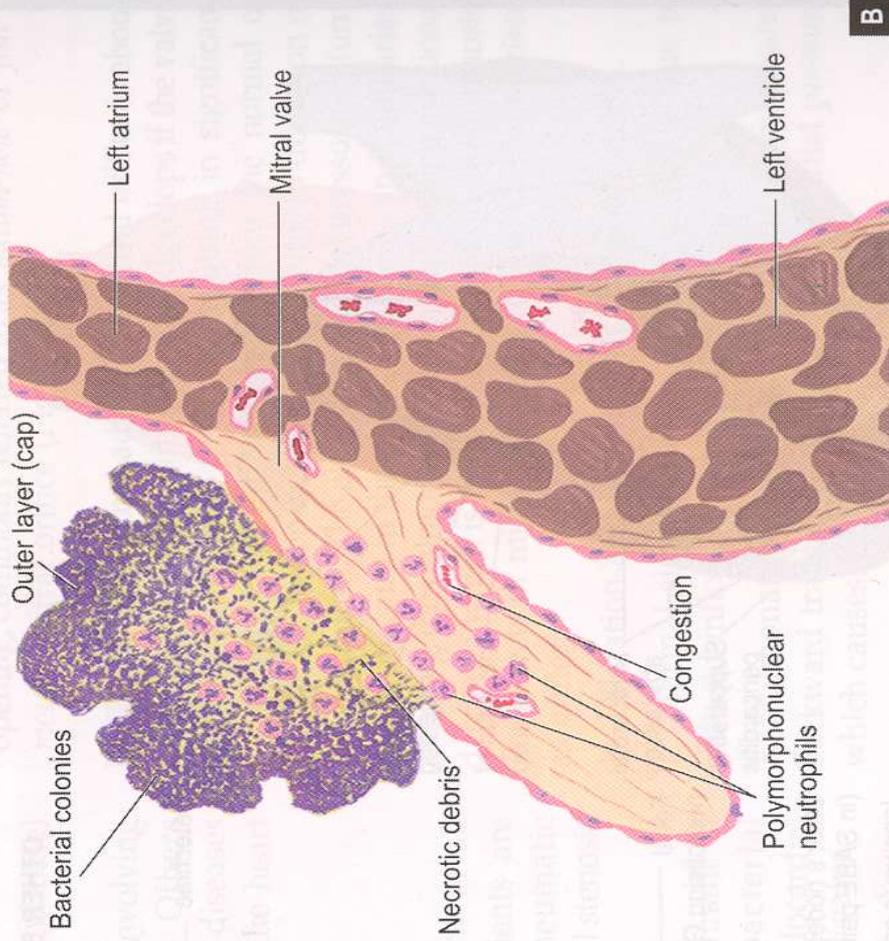
### MITRAL VALVE (ATRIAL SURFACE)



Vegetations in BE



### AORTIC VALVE (VENTRICULAR SURFACE)



**B**

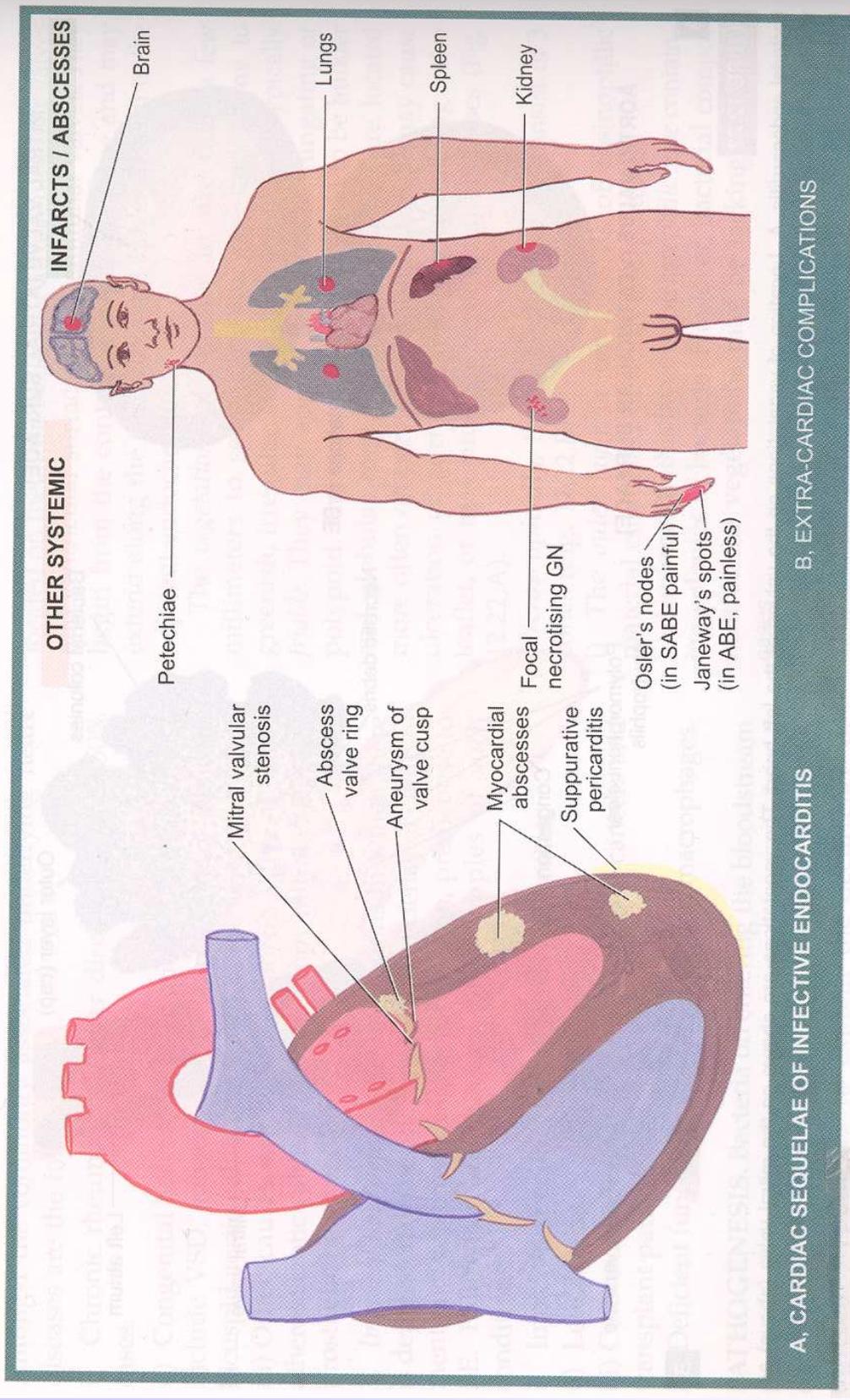
Bacterial endocarditis. A, Location of vegetations on the valves of the left heart. The vegetations are shown on the mitral valve (above) as viewed from the left atrium, while those on the aortic valve (below) are shown as seen from the left ventricle. B, Microscopic structure of a vegetation of BE on the surface of mitral valve in sagittal section.

**Microscopically**, the vegetations of BE consist of 3 zones.

- i. The outer layer or cap consists of eosinophilic material composed of fibrin and platelets.
- ii. Underneath this layer is the basophilic zone containing colonies of bacteria. However, bacterial component of the vegetations may be lacking in treated cases.
- iii. The deeper zone consists of non-specific inflammatory reaction in the cusp itself, and in the case of SABE there may be evidence of repair.

In the acute fulminant form of the disease, the inflammatory cell infiltrate chiefly consists of neutrophils and is accompanied with tissue necrosis and abscesses in the valve rings and in the myocardium. In the subacute form, there is healing by granulation tissue, mononuclear inflammatory cell infiltration and fibroblastic proliferation. Histological evidence of pre-existing valvular disease such as RHD may be present in SABE.

**Complications and Sequelae.** Most cases of BE present with fever. The acute form of BE is characterized by high grade fever, chills, weakness and malaise while the subacute form of the disease has non-specific manifestations like slight fever, fatigue, loss of weight and flu-like symptoms. In the early stage, the lesions are confined to the heart, while subsequent progression of the disease leads to involvement of extracardiac organs. In general, severe complications develop early in ABE than in SABE. Complications and sequelae of BE are divided into cardiac and extracardiac.



Complications and sequelae of infective endocarditis.

**A. Cardiac complications.** These include the following:

- i) Valvular stenosis or insufficiency.
- ii) Perforation, rupture, and aneurysm of valve leaflets
- iii) Abscesses in the valve ring.
- iv) Myocardial abscesses.
- v) Suppurative pericarditis.
- vi) Cardiac failure from one or more of the foregoing complications.

**B. Extracardiac complications.** Since the vegetations in BE are typically friable, they tend to get dislodged due to rapid stream of blood and give rise to embolism which is responsible for very common and serious extra-cardiac complications. These are as under:

- i) Emboli originating from the left side of the heart and entering the systemic circulation affect organs like the spleen, kidneys, and brain causing infarcts, abscesses and mycotic aneurysms.
- ii) Emboli arising from right side of the heart enter the pulmonary circulation and produce pulmonary abscesses.
- iii) Petechiae may be seen in the skin and conjunctiva due to either emboli or toxic damaged to the capillaries.

- iv) In SABE, there are painful, tender nodules on the finger tips of hands and feet called Osler's nodes, while in ABE there is appearance of painless, non-tender subcutaneous maculopapular lesions on the pulp of the fingers called Janeway's spot. In either case, their origin is due to toxic or allergic inflammation of the vessel wall.
- v) Focal necrotizing glomerulonephritis is seen more commonly in SABE than in ABE. Occasionally diffuse glomerulonephritis may occur. Both these have their pathogenesis in circulating immune complexes (hypersensitivity phenomenon).

Treatment of BE with antibiotics in adequate dosage kills the bacteria but complications and sequelae of healed endocardial lesions may occur even after successful therapy. The causes of death are cardiac failure, persistent infection, embolism to vital organs, renal failure and rupture of mycotic aneurysm of cerebral arteries.

## Other infective endocarditis

Besides BE, various other microorganisms may occasionally produce infective endocarditis. These include the following:

1. **Tuberculous endocarditis.** Though tubercle bacilli are bacteria, tuberculous endocarditis is described separately from the bacterial endocarditis due to specific granulomatous inflammation found in tuberculosis. It is characterized by presence of typical tubercles on the valvular as well as mural endocardium and may form tuberculous thromboemboli.
2. **Syphilitic endocarditis.** The endocardial lesions in syphilis have already been described in relation to syphilitic aortitis. The severest manifestation of cardiovascular syphilis is aortic valvular incompetence.
3. **Fungal endocarditis.** Rarely, endocardium may be infected with fungi such as from candida albicans, Histoplasma capsulatum, Aspergillus, Mucor, coccidioidomycosis, Cryptococcosis, Blastomycosis and actinomycosis. Opportunistic fungal infections like candidiasis and aspergillosis are seen more commonly in patients receiving long-term antibiotic therapy, intravenous drug abusers and after prosthetic valve replacement.
4. **Viral endocarditis.** There is only experimental evidence of existence of this entity.

- 5. rickettsial endocarditis.** Another rare cause of endocarditis is from infection with rickettsiae in Q fever.
- (a) The underlying cause of the valvular heart includes mitral valve prolapse (currently most common), rheumatic heart disease (previously most common), congenital heart disease, degenerative (calcific) lesions of the aortic and mitral valves, previous cardiac surgery and intravenous drug abuse.
  - (b) It appears that endothelial damage, typically on the surface of a damaged valve, leads to the formation of sterile platelet fibrin thrombi (called non-bacterial thrombotic endocarditis). When these foci are colonized by circulating bacteria, subacute bacterial endocarditis results. Vegetations developing at sites where a regurgitant jet of blood strikes and damages the endothelium of a cardiac chamber are called **jet lesions**.

(2) **Acute endocarditis** typically occurs on a normal valve in the setting of well-defined bacteremia (the source of infection).

(a) Persons at risk for acute endocarditis include those with debilitating illness, immunocompromised patients, and chronic alcoholics.

(b) The toxic agents of acute endocarditis are responsible for the initial damage to the heart valves. Once damaged, the valves are predisposed to thrombus formation and subsequent infection as in subacute cases.

d] **Complications and prognosis**

(1) Patients may develop signs of septic emboli, which originate from the valvular vegetation and which may result in septic infarct in the brain, heart, kidneys, and spleen.

Embolization to the extremities may result in gangrene. Mycotic aneurysms may result. Other complications include focal glomerulitis or diffuse proliferative glomerulonephritis, which probably results from immune complex deposition.

(2) **Infective endocarditis** always is fatal if not treated. Bacteriologic cure can be achieved in most patients with bacterial endocarditis. This statement is not true, however, in the uncommon cases involving resistant gram-negative bacilli or fungi. In spite of bacteriologic cure, the 5-year survival is only 60% to 70% because of valvular damage occurring prior to treatment.

## 2] **Noninfective endocarditis**

### a] **Nonbacterial thrombotic endocarditis** (i.e., marantic endocarditis).

- (1) This form of endocarditis is characterized by small (1 to 5 mm) sterile, fibrin-platelet vegetations randomly distributed along the line of valve closure; the mitral, aortic or rarely tricuspid valve may be involved.
- (2) Nonbacterial thrombotic endocarditis typically is found in patients with disorders associated with a hypercoagulable state, most frequently disseminated intravascular coagulation or carcinoma (particularly adenocarcinoma).

b] **Nonbacterial verrucous endocarditis** (i.e. Libman-Sacks disease)

(1) This form of endocarditis is characterized by the presence of one or more small, warty vegetations on the surfaces of any of the cardiac valves in a patient with systemic lupus erythematosus.

B. **Pericarditis** represents an inflammatory disorder of the visceral or parietal pericardium, with or without associated myocardial disease.

1] **Etiology**

- a] Similar to myocarditis, pericarditis is of varied etiology. It may be of infectious or noninfectious etiology (including that due to metastatic neoplasms) or it may be idiopathic. Most frequently, pericarditis is secondary to extracardiac disease (e.g. direct spread from adjacent pulmonary infection), represents a component of a systemic illness (e.g. lupus) or is idiopathic.
- b] Currently in the United States and Western Europe, the most severe type of pericarditis: **Constrictive pericarditis** usually is idiopathic or is due to neoplastic infiltration, radiotherapy, trauma or a connective tissue disease. Tuberculosis and pyogenic bacterial infection also can cause constrictive pericarditis, however, these disorders are less frequent causes than in the past.
- 2] **Clinical features.** Although pericarditis often is only an incidental autopsy finding, it can cause severe chest pain that stimulates a myocardial infarction. A pericardial friction rub is a pathognomonic clinical sign but is not always present.

### 3] Pathology

a] **Acute pericarditis** often is classified by the morphologic pattern of inflammation.

(1) **Fibrinous inflammation** is characterized by shaggy, granular fibrin deposits (“bread and butter” pericarditis) and suggests acute rheumatic fever, uremia, or lupus as a cause among others.

(2) **Purulent inflammation** suggests bacteria (e.g. staphylococci) or fungi as a cause.

(3) **Caseating granuloma** suggests tuberculosis.

- (4) **Prominent hemorrhage** typically is associated with malignant cells that have metastasized to the pericardium.
- b] Occasionally, accumulation of fluid in the pericardial sac, or **pericardial effusion**, is so massive that it impedes (interfere with) venous return to the heart, resulting in cardiac tamponade.
  - c] In most cases, acute pericarditis resolves completely or develops into mild fibrosis, which may cause the pericardium to adhere to adjacent structures (adhesive pericarditis).
  - d] Diffuse organization may lead to dense fibrous thickening and sometimes calcification of the pericardium, a condition known as **constrictive pericarditis**. The pericardial fibrosis impairs ventricular filling in diastole, resulting in decreased output. Both atria have elevated filling pressures, which results in congestion of both the pulmonary and systemic venous circulations.