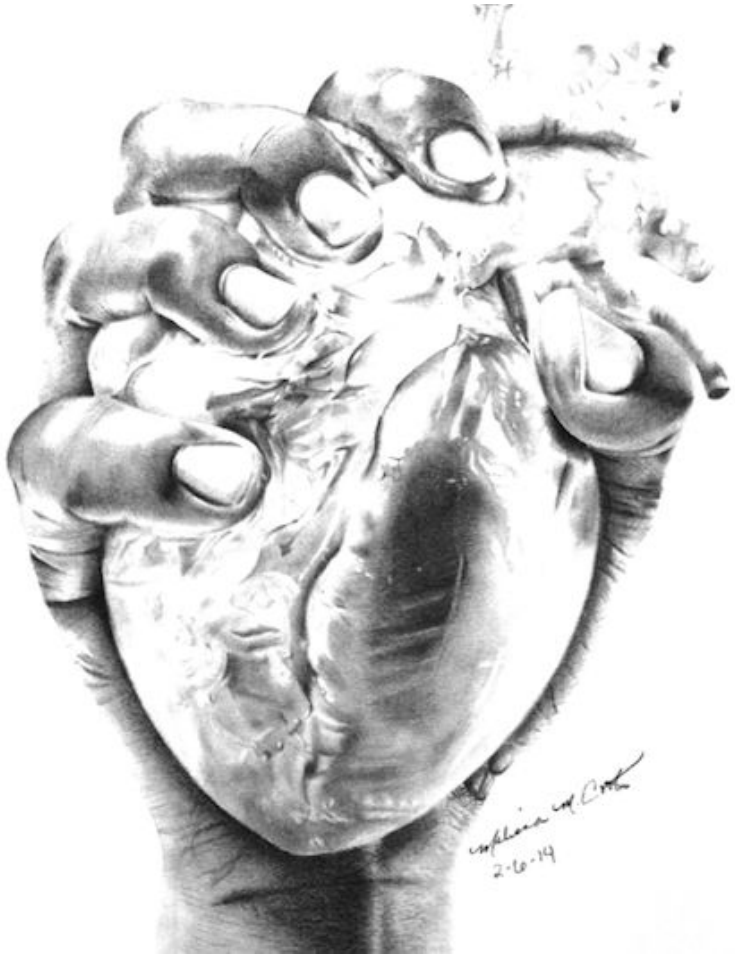
Microbiology

435's Teamwork
Cardiovascular Block



- Please contact the team leaders for any suggestion, question or correction.
- Pay attention to the statements highlighted in **bold** and\or red.
- **Footnotes color code:** General | Females | Males.

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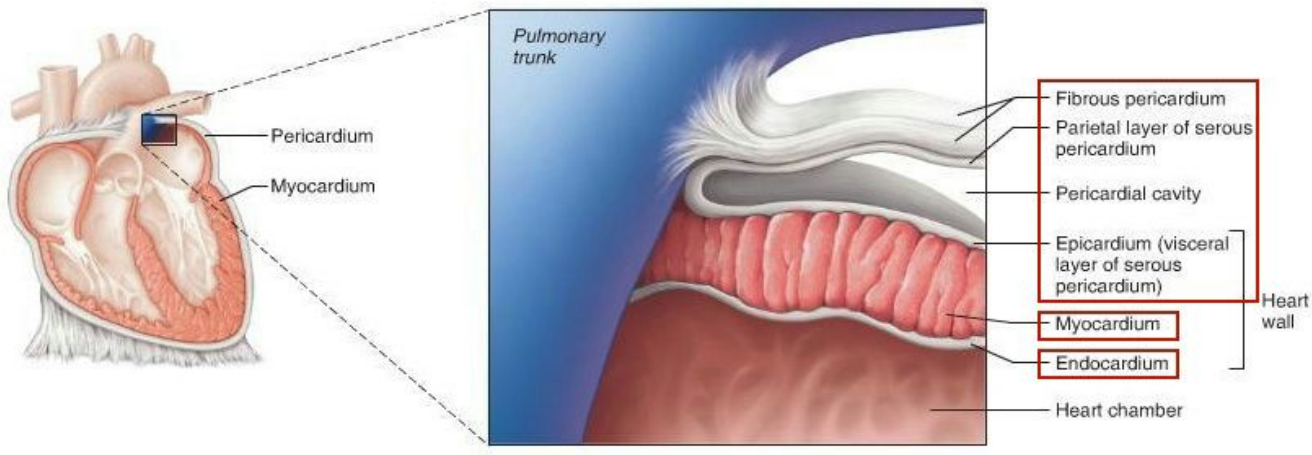
Myocarditis, Pericarditis and Endocarditis

- Lectures One and Two -

Learning Objectives:

- Know their epidemiology, etiology and risk factors.
- Explain their pathogenesis.
- Differentiate between their various types.
- Describe their clinical presentation and differential diagnosis.
- Discuss their microbiological and non microbiological methods of diagnosis.
- Explain their management methods, complications and prognosis.

حينما نتطرق للحديث عن القلب، فنحن نشير إلى الوحدة المركزية لتغذية الحياة في جسم الانسان، بالتالي، يكون الخلل فيه بمثابة خلل خزان الوقود في سياراتكم، أو عطب البطاريات التي تغذي أجهزتكم المحمولة. من هذا المنطلق، وعيًنا كطلبة بمدى خطورة الأمراض القلبية من أهم المعارف وأحد أكثرها حساسية فيما يتعلق بالممارسة الطبية. سنناقش في هذا البلوك التهابات القلب المتعلقة بالمخلوقات المجهرية المسببة للمرض، وهي مقسمة لثلاثة أقسام (ندرسها على محاضرتين بإذن الله) بناءً على الطبقة المتضررة من النسيج القلبي، وهم كالتالي:



Myocarditis	التهاب عضلة القلب	Inflammation of the myocardium, the heart's muscular layer.
Pericarditis	التهاب غشاء القلب	Inflammation of the pericardium, the double-walled sac.
Endocarditis	التهاب الشغاف (بطانة القلب)	Inflammation of the innermost layer of the heart.

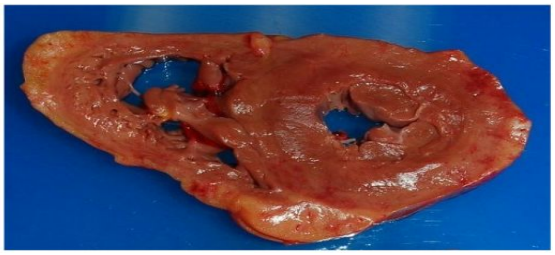
Myocarditis

Robbins Basic Pathology P. 401

(Myocarditis - From Causes to Followup)

Introduction:

Myocarditis is an **inflammatory disease** of the heart muscle **(myocardium)**. It can be **mild** and **self-limiting with few symptoms**, or **severe** with **progressions** such as **congestive heart failure**[1] or dilation of the cardiac muscle. It can also vary in location, as it may be localized or diffused.



Epidemiology:

There is no accurate estimate of incidence because many cases are mild, and therefore, diagnosis is **not easily made.** Although the exact incidence of myocarditis is not known, some sources estimated that several thousand patients per year are diagnosed. Myocarditis usually attacks healthy people. It is believed that 20% of all cases of sudden death in young adults are due to myocarditis.

Giant cell myocarditis:

A complicated type of myocarditis that is characterized by multinucleated giant cells.

Occurs due to:

1. Thymoma[2] **2.** SLE[3] **3.** Thyrotoxicosis[4]

Etiology:

Myocarditis can be due to a **variety of infectious** and noninfectious causes.

Viral infections are the most common causes, meanwhile other causative agents like environmental toxins, drugs and hypersensitivity immune responses (autoimmune diseases) are less common.

(Details next page)

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[1] Weakness of the heart that leads to a buildup of fluid in the lungs and surrounding body tissues.

[2] Benign tumor arising from thymus.

[3] Systemic Lupus Erythematosus.

[4] Hyperthyroidism.

Infectious	Noninfectious
Viral[5]	**Systemic Diseases**
Coxsackievirus B[6] is the most common cause of myocarditis. **Other viral causes include:** Coxsackievirus A, Echoviruses, Adenoviruses, Influenza, Rubella, Varicella, Mumps, Rabies, Hepatitis viruses, EBV, HIV.	Sarcoidosis[7] Celiac disease[8] Vasculitis (Wegener's disease)[9] SLE[10]
Bacterial[11]	**Neoplastic Infiltration**
Corynebacterium diphtheriae (Diphtheria) *Treponema pallidum* (Syphilis)[12] *Borrelia burgdorferi* (Lyme disease)[13] As a complication of bacterial endocarditis[14]	-
Parasitic	**Drugs and Toxins**
Trypanosoma cruzi (Chagas diseases)[15] *Trichinella spiralis* *Toxoplasma gondii* *Echinococcus*	Ethanol Cocaine Radiation
Other Organisms	**Chemotherapeutic agents**
Fungi, *Rickettsiae*, *Chlamydia*, Enteric pathogens, *Legionella* or *M. tuberculosis*[16]	Doxorubicin[17]

[5] The most common cause of myocarditis.
[6] **Coxsackie B** is the name of a group of six serotypes of Coxsackievirus, a pathogenic enterovirus, that trigger illness from mild GIT distress to full-fledged pericarditis and myocarditis. MORE
[7] Abnormal collections of granulomas that can form as nodules in multiple organs. MORE.
[8] A disease in which the small intestine is hypersensitive to gluten, leading to difficulty in digesting.
[9] Inflammation of blood vessels that affects small- and medium-size vessels. MORE.
[10] Systemic Lupus Erythematosus. MORE.
[11] من الضروري معرفة اسم المرض المذكور لأن المايوكاردايتس يكون غالبًا مصاحبًا له، بالتالي تشخيصنا للمرض الأول يترتب عليه تشخيصنا للثاني.
[12] A disease contracted by infection during sexual intercourse usually happens at a late stage. MORE.
[13] Myocarditis occurs in approximately 5% of patients with Lyme disease. MORE.
[14] Addressed next lecture.
[15] Has myocardial involvement in most people who are suffering from it. MORE.
[16] M. TB is more common in pericarditis than in myocarditis.
[17] Bacterial antibiotic that is used to treat leukemia and various other forms of cancer.

Clinical presentation:

- The clinical spectrum of myocarditis is broad and **highly variable.**
- It takes days to weeks after the onset of acute febrile illness.[18]
- Heart failure may occur without any antecedent symptoms.[19]

Patients may be present with chest pain, palpitation, heart block, arrhythmias, sweating, fatigue, congestive heart failure, fever, headache, muscle aches, diarrhea, sore throat and rashes.[20]

Differential diagnosis:

Based on the clinical presentation, what would you possibly think about?

1. Acute Myocarditis.
2. Vasculitis.
3. Cardiomyopathy[21] (due to drugs or radiation).

Methods of detection[22]	
WBC's, ESR, Troponin[23] and CK-MB[24]	Usually elevated[25]
ECG	Nonspecific ST-T changes and conduction delays
Blood cultures[26]	Positive if the patient has septicemia
Viral serology	IgM (acute stage) and IgG (late chronic stage) are elevated
Specific tests	Lyme disease, diphtheria and Chagas disease. May be indicated on a case by case basis[27]
Chest X-rays	Show cardiomegaly[28]
MRI and Echocardiogram[29]	May give a hint of an abnormality in the heart muscle
Heart muscle biopsy[30]	Inflammatory response (lymphocytic)

[18] Febrile illness is when the patient has fever, but the cause is unknown or not certain.

[19] يحصل لديهم cardiac failure مفاجئة بلا أية أعراض لأمراض قلبية سابقة.

[20] Signs are similar to any regular viral infection.

[21] Chronic disease of the heart muscle.

[22] We start with the less invasive (serology tests) to the more invasive (Biopsy and fluid aspiration).

[23] A protein that is released when the heart muscle has been damaged. MORE.

[24] A cardiac marker used to assist diagnoses of an acute myocardial infarction. MORE.

[25] This indicates acute heart disease.

[26] Usually in cases of bacterial infections.

[27] Case by case bases means decisions that are made separately, each according to its own facts.

[28] Abnormal enlargement of the heart.

[29] Type of ultrasound test that uses high-pitched sound waves.

[30] This happens at the end, when the clinician is confused and is not sure whether it's a virus, autoimmune disease, or a malignancy. He does it in order to give the patient the correct treatment and when the patient is deteriorating.

Endomyocardial biopsy (EMB):

Pathologic exam may reveal lymphocytic inflammatory response with necrosis, but this is not sensitive because of the patchy[31] areas of distribution.

1. **"Dallas" criteria[32] for histopathologic diagnosis.**
2. **"Giant cells" may be seen.**

Management:

One third of the patients are **left with lifelong complications**, ranging from **mild** conduction defects to **severe heart failure**. They should be followed regularly every 1-3 months.

Management is often supportive, no direct treatment had been found.

- **Most** cases of viral myocarditis are **self limited**[33].
- Restricted physical activity in heart failure.
- Specific antimicrobial therapy is indicated when an infecting agent is identified.
- Treatment of heart failure arrhythmia.
- Other life supporting drugs indicated in special situations like anticoagulants, **NSAIDs**, **steroids** or immunosuppressive immunomodulatory agents.
- Heart transplant in hopeless, severe cases.

Sudden death may be the presentation of myocarditis in about 10% of cases.

Further Read

Wikipedia | Medscape | Text book for cardiology | Myocarditis foundation | Medical Dictionary

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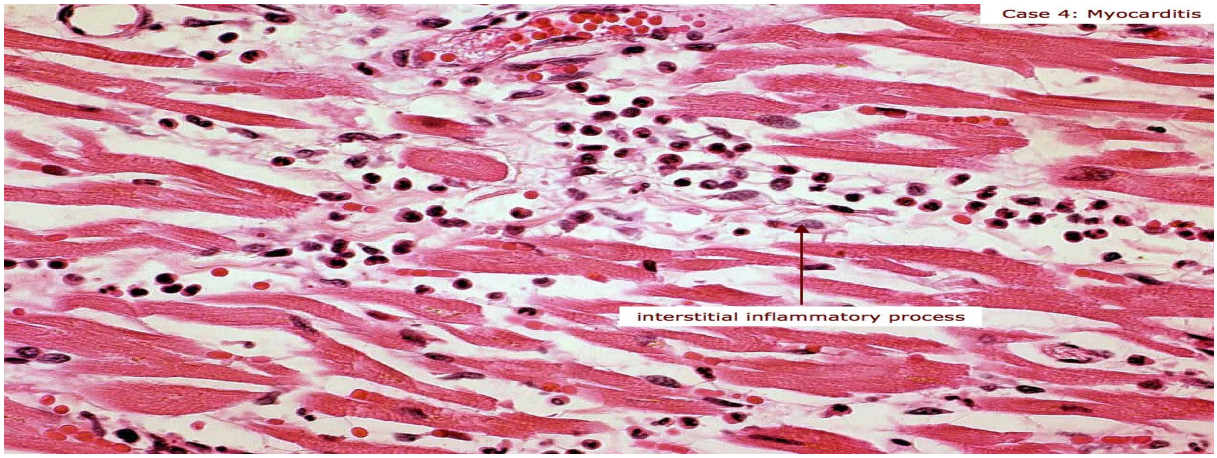
[31] Existing in small, isolated areas.

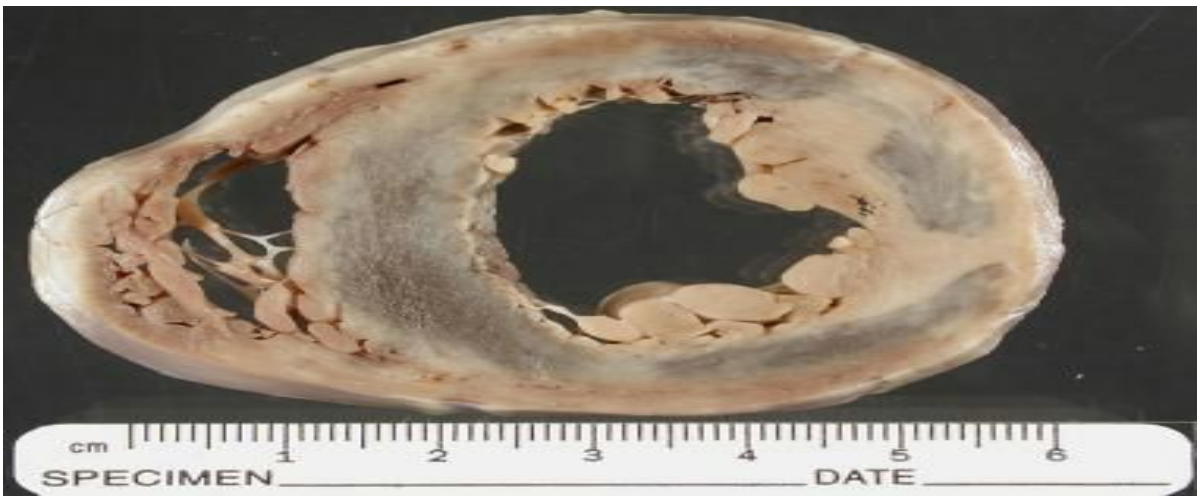
[32] The presence of an inflammatory infiltrate of the myocardium.

[33] لان غالبيتها عن طريق فيروسات.

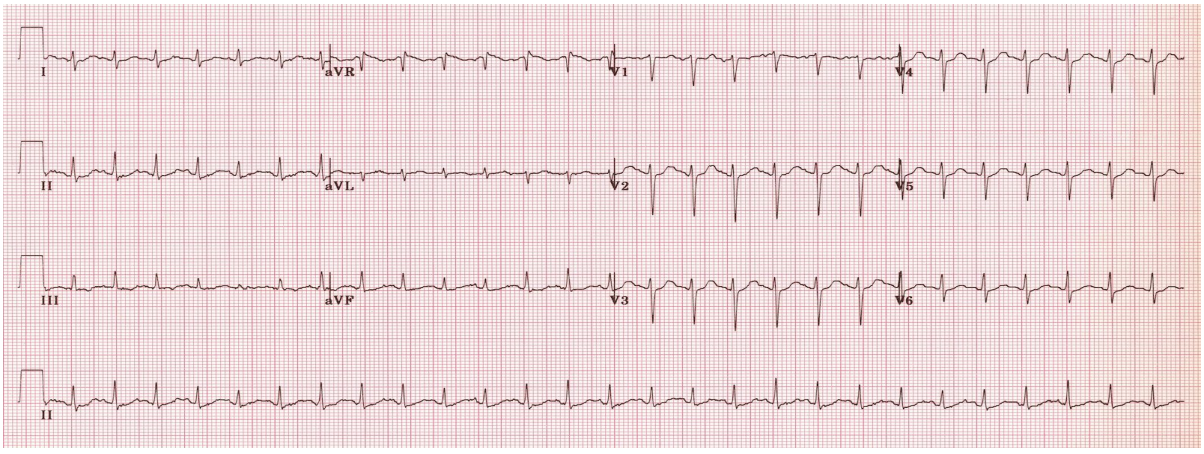
EXTRA INFORMATION



Myocardial biopsy showing inflammatory cells, edema and myocyte injury



Gross view of a myocarditic dead patient's heart (dilated)



ECG of a patient suffering from myocarditis

Pericarditis

Robbins Basic Pathology P. 403

(Pericarditis and chest pain)

Introduction:

Pericarditis is an inflammation of the double-walled fibroserous sac surrounding the heart (pericardium) usually of infectious etiology (viral, bacterial, fungal or parasitic).

Epidemiology:

Pericarditis affects approximately one in 1,000 people. The most common form is caused by viral infections. People in their 20s and 30s who have had a recent upper respiratory infection are most likely to be affected, along with men aged 20-50. One out of every four people who have had pericarditis will get it again, but after two years these relapses are less likely.

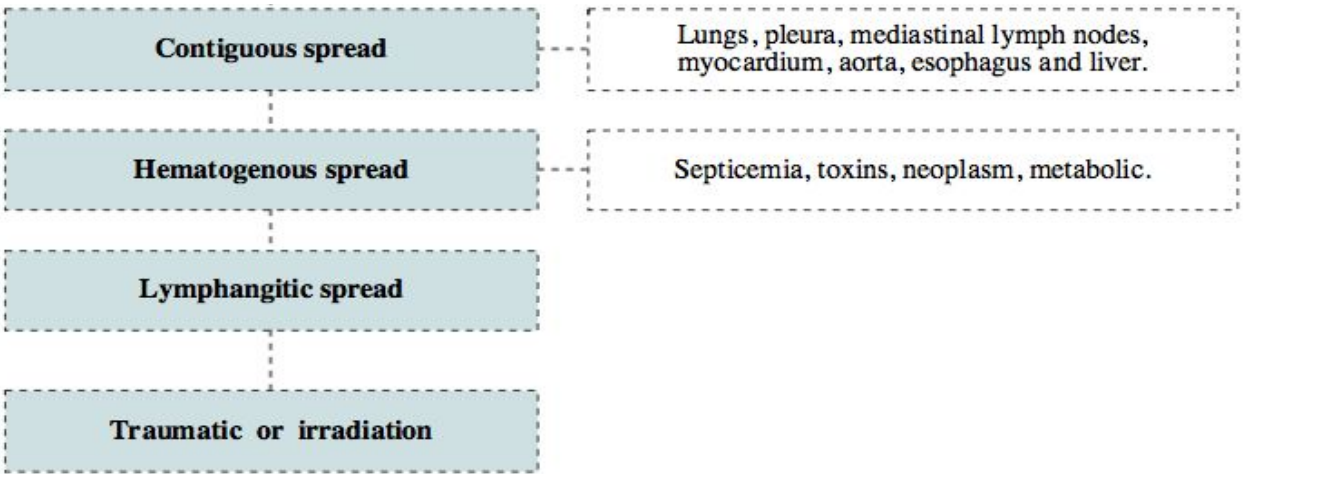
<table>
<tr><th colspan="4">Etiology</th></tr>
<tr><th>Viral[34]</th><th>Bacterial</th><th>fungal[35]</th><th>Parasitic</th></tr>
<tr><td>Most common:
Coxsackievirus A
Coxsackievirus B
Echovirus</td><td>Usually a complication of pulmonary infections (Pneumonia and emphysema)
Streptococcus pneumoniae
Mycobacterium tuberculosis[36]
Staphylococcus aureus
Haemophilus influenzae
Klebsiella pneumoniae
Legionella</td><td>Histoplasma</td><td>Disseminated toxoplasmosis[37]</td></tr>
<tr><td>Other viruses:
Herpes viruses, Hepatitis B, Mumps, Influenza, Adenovirus, Varicella and HIV.</td><td>HIV patients may develop pericardial effusions
Mycobacterium tuberculosis[38]
Mycobacterium avium complex</td><td>Coccidioides</td><td>Contagious[39] spread of Entamoeba histolytica[40]
RARE CAUSES</td></tr>
</table>

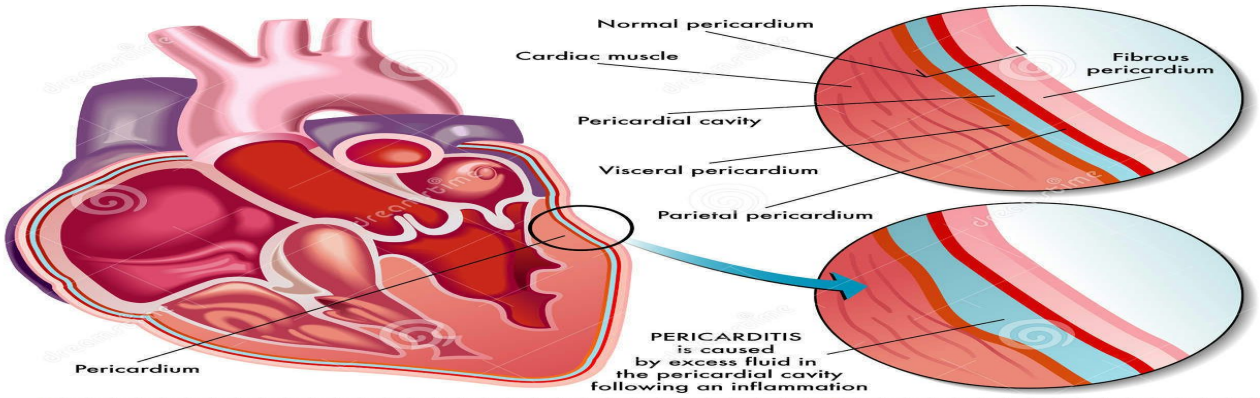
[34] Common worldwide.
[35] Fungal infections mostly affect patients who are immunocompromised.
[36] The most common In Saudi Arabia, even more than viral.
[37] Commonly causes pericarditis in patients who have domestic cats. مربين القطط.
[38] Know that pericarditis can be associated with TB.
[39] Spread from one person or organism to another by direct or indirect contact.
[40] Diarrheal disease, liver disease and may progress to pericarditis.

Pathophysiology:

When microbes are inhaled or ingested, they migrate to the pericardium and cause inflammation. So when these membranes are inflamed, they rub against each other and cause classic sounds of which the patient complains of severe chest pains which increases when the patient lies supine and decreases when in sitting position. This acute inflammation causes accumulation of fluid in the pericardial sac called "pericardial effusion". Inflammation provokes a fibrinous exudate with or without serous effusion. The normal transparent and glistening pericardium is turned into **a dull**, **opaque**, and **"sandy" sac** that can cause pericardial scarring with adhesions and fibrosis.[41] The excessive accumulation of fluid in the sac causes compression of the heart, resulting in decreased venous retain of the heart resulting in ventricular filling and a decrease in stroke volume. These events will eventually lead to cardiac failure, shock and death.

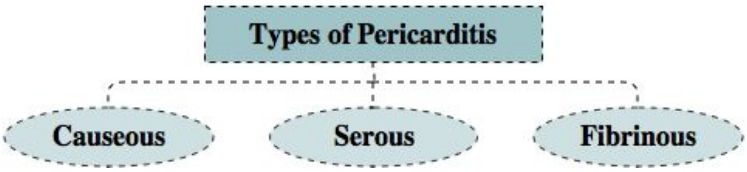
How can such disease be acquired? (IMPORTANT)





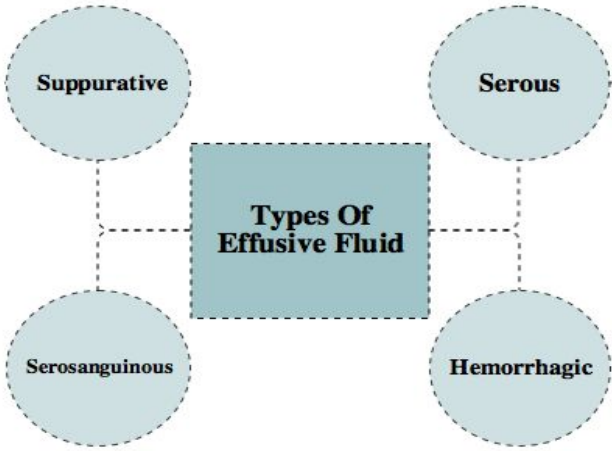
[41] تتغير طبيعة السائل من المادة المائية الملساء إلى المادة القيحية الخشنة.

(This will also cause the thickening of the pericardium, making it unable to move freely. Hence restricting the movement of the heart.)



- **Caseous[42] Pericarditis**: Tuberculous in origin.
- **Serous Pericarditis**: Due to autoimmune diseases (Rheumatoid Arthritis, SLE).
- **Fibrinous Pericarditis[43]**:
  - Chronic.
  - Suppurative.
  - Caseous.
  - Encased in a thick layer of scar tissue.

Inflammation causes accumulation of fluid in the pericardial sac called pericardial effusion. The type of fluid found can indicate the accompanying conditions according to the cause.



- **Serous effusion[44]** is associated with transudates and heart failure.
- **Suppurative effusion[45]** is seen with pyogenic infections which usually show cellular debris and a **large number of leukocytes.**
- **Hemorrhagic effusion[46]** occurs with any type of pericarditis especially with infections and malignancies.
- **Serosanguinous effusion.[47]**

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[42] Causing caseous necrosis because of its association with TB.
[43] Usually bacterial infection.
[44] Pale yellow and transparent fluid that has a benign nature (normally found in the body).
[45] Form or discharge pus.
[46] Whole blood with platelet clumps and leucocytes.
[47] Composed of serum and blood.

Constrictive pericarditis:

It is a medical condition characterized by a thickened, fibrotic pericardium, limiting the heart's ability to function normally. In many cases, the condition continues to be difficult to diagnose and therefore benefits from a good understanding of the underlying cause.

- Bacterial infections or idiopathic.
- Requires radiotherapy, cardiac surgery and dialysis[48].
- Causes connective tissue disorders.

Tuberculous pericarditis[49]:

Pericarditis caused by tuberculosis is difficult to diagnose, because definitive diagnosis requires culturing Mycobacterium tuberculosis from aspirated pericardial fluid or pericardial biopsy, which requires high technical skill and is often not diagnostic.

- Incidence of pericarditis in patients with pulmonary TB ranges from 1–8%.
- **Physical findings[50]:** Fever, pericardial friction rub[51] and hepatomegaly.
- Tuberculin skin test is usually positive.
- Fluid smear for Acid Fast Bacilli is often negative.
- Pericardial biopsy is more definitive.

Clinical Presentation:

- Patients with pericarditis will be present with sudden pleuritic chest pain, fever, dyspnea and a friction rub[52] and stabbing pain.
- Patients with **tuberculous** pericarditis have insidious onset of symptoms.
- **On examination**, exaggerated pulsus, paradoxus JVP[53] and tachycardia can be noticed.[54]
- As the pericardial pressure increases, palpitations, presyncope or syncope[55] may occur.

Differential diagnosis:

Based on the clinical presentation, what would you possibly think about?

- Acute myocardial infarction.
- Pulmonary embolism[56].
- Pneumonia.
- Aortic dissection.

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[48] غسيل الكلى.

[49] Pericarditis can be caused by TB that is why you should ask a patient who has pericarditis if s/he has a history of TB. (Especially here in Saudi Arabia).

[50] اعراض السل العادية مثل خسارة الوزن.

[51] An audible medical sign used in the diagnosis of pericarditis. LISTEN.

[52] This is one of the clinical presentations that differentiate between myocarditis and pericarditis. (very important to know)

[53] Jugular Venous Pressure.

[54] This is typical of pericarditis.

[55] This happens because there is no ejection fraction and no fluid return to the heart, resulting in not enough blood supply reaching the brain hence causing syncope.

[56] Blood clot, fat globule, gas bubble or foreign material in the bloodstream.

Methods of detection	
ECG[57]	ST **elevation**, PR depression and T-wave inversion may occur later
Leukocytosis, ESR and **CBC**	Typically **elevated**[58]
Blood cultures	Positive if the patient has septicemia
Tuberculin skin test	Usually positive in tuberculous pericarditis
Chest X-rays	Show enlarged cardiac shadow or calcified pericardium and CT scan show pericardial thickening >5mm
Pericardial fluid or **pericardial biopsy specimens**	Used for for fungi, antinuclear antibody tests and Histoplasmosis
Complement fixation[59]	Indicated in endemic area
Urea and **creatinine**	Additional tests

Management:

- Management is largely supportive for cases of idiopathic and viral pericarditis including bed rest, **NSAIDS** and Colchicine[60].
- Corticosteroid is controversial and anticoagulants usually contraindicated.

Antibiotics:
Must include activity against *Staphylococcus aureus* and respiratory bacteria.

Antiviral:
Acyclovir for *Herpes simplex Virus* (HSV) or *Varicella*.
Ganciclovir for *Cytomegalovirus* (CMV).
Pericardiocentesis[61] to relieve tamponade[62].

- Patients who recovered should be observed for recurrence.
- Symptoms due to viral pericarditis usually subsided within one month.

Further Read

AlmostDoctor | UTAS | Wikipedia | MedScape | MedicineNet

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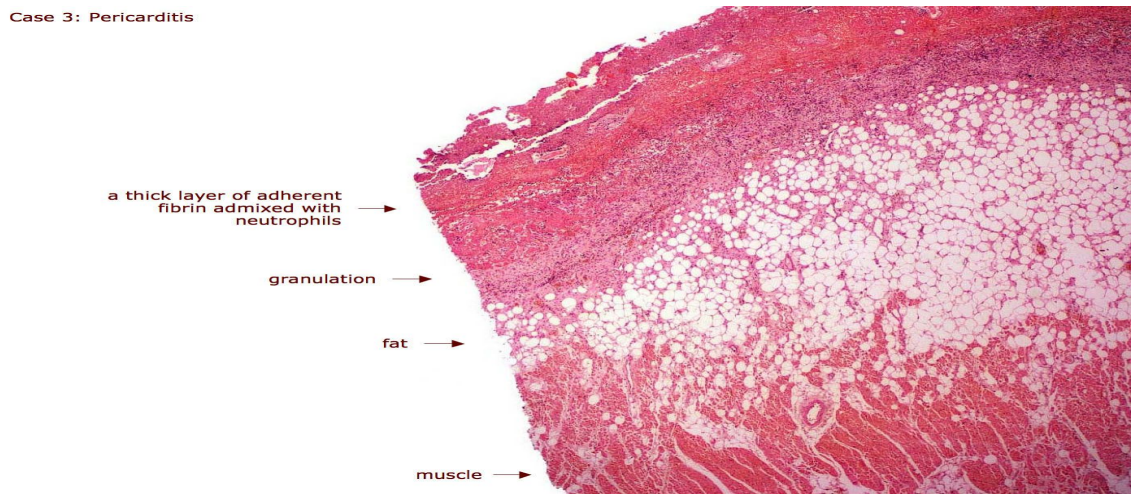
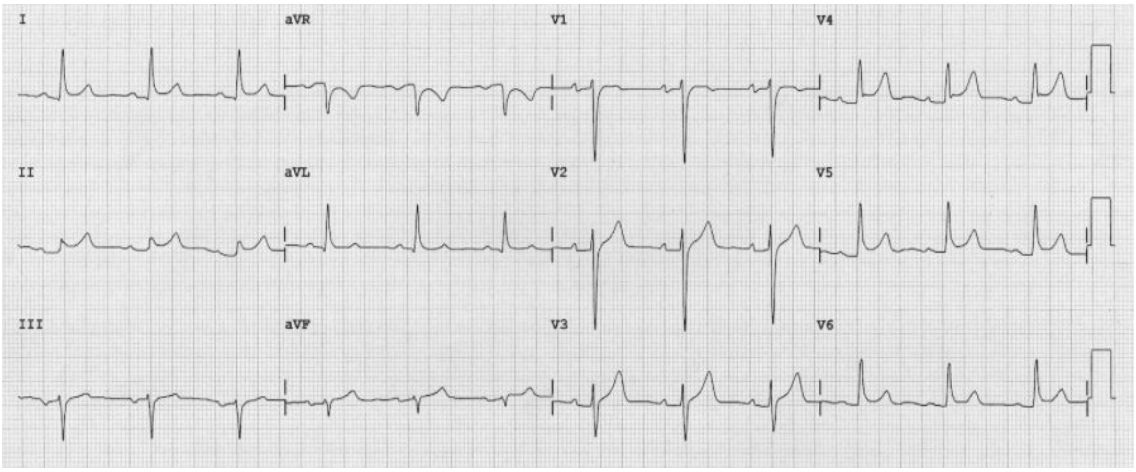
[57] You must know the changes occurring in ECG during pericarditis because they are specific, unlike myocarditis which are non-specific changes.
[58] This indicates an inflammatory response in the body.
[59] Immunological test that can detect the presence of a specific antibody or antigen in a patient's serum.
[60] Strong anti-inflammatory drug that is given for patients with gouty arthritis.
[61] Drainage of accumulated fluid in the pericardial sac.
[62] Compression of the heart by an accumulation of fluid in the pericardial sac.

EXTRA INFORMATION



Histological appearance showing adherent fibrin and neutrophils

Gross view of a dead patient's heart showing pericarditis



ECG of a patient suffering from pericarditis

تمت كتابة الجدول من قبل د. الصميلي في محاضرته

هذا الجدول يعني التلخيص وليس الحصر

" قد يكون مسبب المرض في المايوكاردايتس فيروسي، بالتالي يكون العلاج بالادوية الداعمة للاعضاء فقط، على الكفة الأخرى قد يكون المسبب بكتيري (الدفتيريا مثلًا) ويكون بالتالي علاجه البنسيلين... حتى نتمكن من التشخيص والعلاج الدقيق، يجب علينا الإلمام بكل ما هو وارد"

	Myocarditis	Pericarditis
Epidemiology	- Mild → Sometimes flu like - Moderate → Severe with special signs & symptoms	- Mild → Sometimes flu like - Moderate → Severe with special signs & symptoms
Etiology	Viral, most common (**Coxsackievirus B**) but could be Bacterial,fungal...etc	**Coxsackievirus A & B** *Mycobacterium tuberculosis*
Clinical Features	Chest Pain, palpitation, heart block, fever	Stab pain, JVP (elevated), friction rub
Diagnosis	- WBC & CBC (Always elevated) - ECG & Troponin - Heart muscle biopsy (lymphocytic) - Viral serology(We'll find both IgM & IgG elevated. - X-ray (cardiomegaly)& Blood cultures	- Pericardial fluid or pericardial biopsy specimens. - WBC & CBC (Always elevated) - ECG & Troponin - Blood cultures
Treatment	Usually **supportive** such as **NSAIDs**, **Steroid** after admitted to hospital	Admitted to hospital **Then:** If the patient has M.TB give him RIF+isoniazid..ETC, If viral give him life supporting...ETC

Infective Endocarditis (IE)[63]

Robbins Basic Pathology P. 392
(Medical School - Infective Endocarditis)

Introduction:

Infective endocarditis is an **infection** or **colonization** of the **endocardium** and/or **heart valves** that is associated with low grade bacteremia[64], which causes destruction of the underlying cardiac tissues (or possibly other organs) in addition to the heart. The main causative agents of such condition are congenital defects, bacteria, fungi or *Rickettsiae*[65].

Epidemiology:

Endocarditis -irrespective of underlying **cardiac condition**[66]- is a serious, **life-threatening disease** that was always fatal in the pre-antibiotic era[67] with mortality of approximately 30%.

- Treatment advances (gets better) in antimicrobial therapy.
- Early recognition and management of IE complications are essential.
- Improved surgical technology have reduced the morbidity and mortality of IE.

Risk factors:

Numerous comorbid factors may complicate IE, such as:

1. Old age, diabetes mellitus, **immunosuppressive conditions** or dialysis[68].
2. **Follow-dental** procedures (tooth extraction)[69]:
   - **Rheumatic heart disease.**
   - **Congenital heart disease.**

Source of infection:

- Bacteremia.
- Dental extraction and procedures.
- Cardiac surgery (specially prosthetic valves).
- Intravenous medication or addiction (drug abuse).
- Intracardiac or intravenous catheters.[70]
- Obstetric or gynaecological procedures.[71]

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[63] التهابُ الشَّغاف هو حالةٌ التهابية تصيب شغافَ القلب، أي البطانة الداخلية للقلب. وهو ينتج عادةً عن إصابةٍ جرثومية أو فطريةٍ أو عن أنواع أخرى من الجراثيم. وإذا قامت هذه الجراثيمُ بغزو مجرى الدم، فإنَّها يمكن أن تهاجمَ المناطقَ الشاذَّة في القلب (المزيد هنا).

[64] Presence of bacteria in the blood.

[65] It if related to (Obligate intracellular bacteria): cannot reproduce outside their host cell

[66] بصرف النظر أو بمعزل عن أية أمراض قلبية مصاحبة أخرى.

[67] عصر ما قبل اكتشاف المضادات الحيوية.

[68] غسيل الكلى.

[69] How are dental problems related to heart diseases? HERE.

[70] أجهزة القسطرة.

[71] العمليات التناسلية التوليدية (نساء وولادة).

Classification:

1. Depending upon where the infection is located:

Native Valve[72]	Prosthetic Valve[73]
Intravenous drug abuse	Nosocomial[74]

2. Clinically, based on the severity of the clinical course:

Acute	Subacute
Affects **normal** heart valves.	Affects **damaged** heart valves[75].
Highly virulent organisms.	**Weakly** virulent organisms.
If not treated, usually fatal within **6 weeks**.	If not treated, usually fatal by **one year**.
Rapidly destructive. Metastatic foci[76]. Commonly Staphylococcus species.	Indolent (lazy) nature.

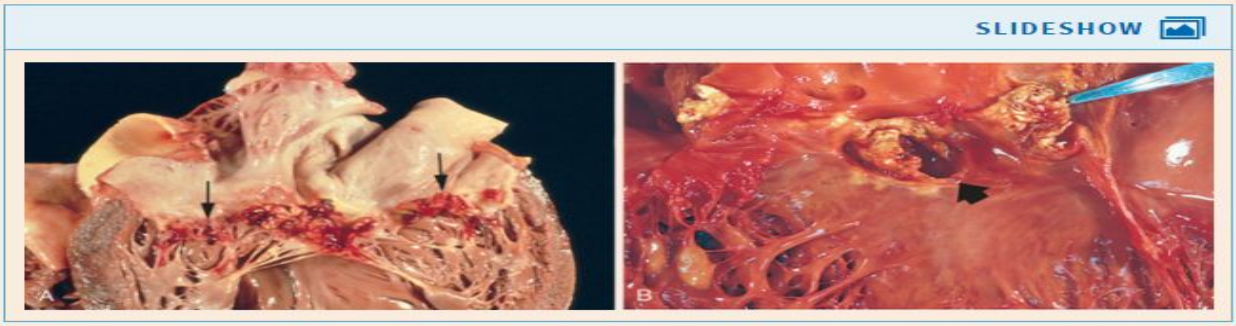


Figure 10–21 Infective endocarditis. **A,** Subacute endocarditis caused by...

Subacute endocarditis typically elicits less valvular destruction than that associated with acute endocarditis. On microscopic examination, the subacute vegetations of infective endocarditis often have granulation tissue at their bases (suggesting chronicity), promoting development of chronic inflammatory infiltrates, fibrosis, and calcification over time.

[72] Local, natural human valve.

[73] صمام صناعي.

[74] مكتسب من المستشفيات.

[75] E.g. Rheumatic Fever.

[76] Explained later on.

Factors affecting severity and outcome:

1. Bacterial factors[77]:

A healthy bloodstream is normally sterile (**does not contain any normal flora**), however, a condition of which the blood becomes infected by virulent bacteria is called "**bacteremia**", and it is one of the most dangerous conditions on this aspect.[78]

2. Host factors:

There are many sources by which the patient's susceptibility may increase for IE.

<table>
<tr><th>Local</th><th>General</th><th>Drugs</th></tr>
<tr><td rowspan="3">Congenital rheumatic heart disease[79]
Prosthetic heart valves
Other cardiovascular disease
Heart surgery</td><td rowspan="3">Underlying disease like Diabetes Mellitus or HIV infection</td><td>Iatrogenic[80]:
Immunosuppressive treatment
Cytotoxic agents</td></tr>
<tr><td>Protective treatment:
Antimicrobial chemotherapy</td></tr>
<tr><td>Self-Inflicted:
Alcoholism
Addiction[81]</td></tr>
</table>

3. Predisposing factors:

Cardiac lesions	Systemic factors
Chronic rheumatic valvular disease Congenital heart disease and defects Atherosclerosis Prosthetic valves[82] (Immediate/Delayed)	Immunosuppressive treatment Immune defects Alcoholism IV Drug abuse

[77] This includes the degree of virulence of the bacteria and the number of bacteria that entered the bloodstream.

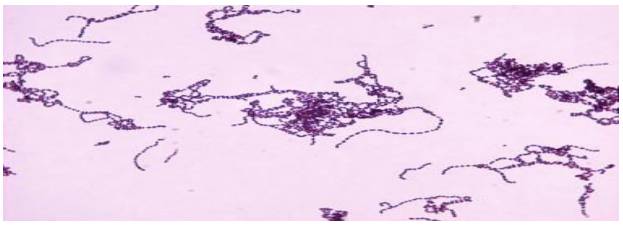
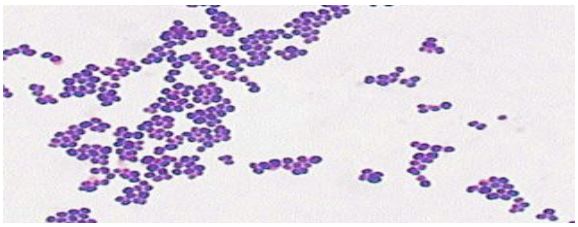
[78] MORE.

[79] ما يسمى بثقب القلب.

[80] An illness that is caused by medical examination or treatment. علاجي المنشأ.

[81] Major problem that may cause endocarditis.

[82] Because it's a foreign body + a susceptible place for bacterial growth.

Causative Organisms[83]	
Streptococcus	***Staphylococcus***
	
Streptococcus ***viridans***[84] Cause (subacute) endocarditis	*Staphylococcus* ***aureus***[85] Cause (acute) endocarditis
Streptococcus ***mutans*** *Streptococcus* ***sanguis*** Produce glucagons → adhere to endocardium	*Staphylococcus* ***epidermidis*** Cause (prosthetic heart valves) endocarditis
Streptococcus ***faecalis*** *Streptococcus* ***faecium*** *Streptococcus* ***pneumoniae***	
Other[86]	
Brucella species[87]*, Actinobacillus, Actinomycetes comitans, Rickettsiae,* Fungi, *Coxiella burnetii* and *Candida albicans.*	

Mechanism of entry:

1. Dental extraction → bleeding → bacteraemia.

Rocking the tooth in the socket has a pumping effect on the vessels of the periodontal ligament[88], that forces bacteria which has been located in the gingival pockets[89] to infect the bloodstream causing 40–80% of bacteraemia cases; the percentage depends upon:

- Sensitivity of blood culture techniques.
- Severity of gingival infection.

2. Oral irrigation device.

---

[83] In order for the heart to get infected by any of these organisms and has endocarditis, it must have abnormal or somewhat damaged heart valves.

[84] Most common cause of subacute endocarditis. It's a normal flora in the mouth and may enter the blood if the person brushes his/her teeth aggressively and cause an injury or during dental extractions.

[85] Although the number of staph. epidermidis in the body is larger than the number of staph. aureus, the infection is usually caused by staph. aureus because it's more virulent.

[86] May cause endocarditis but very rarely.

[87] This means it can be transmitted from animals.

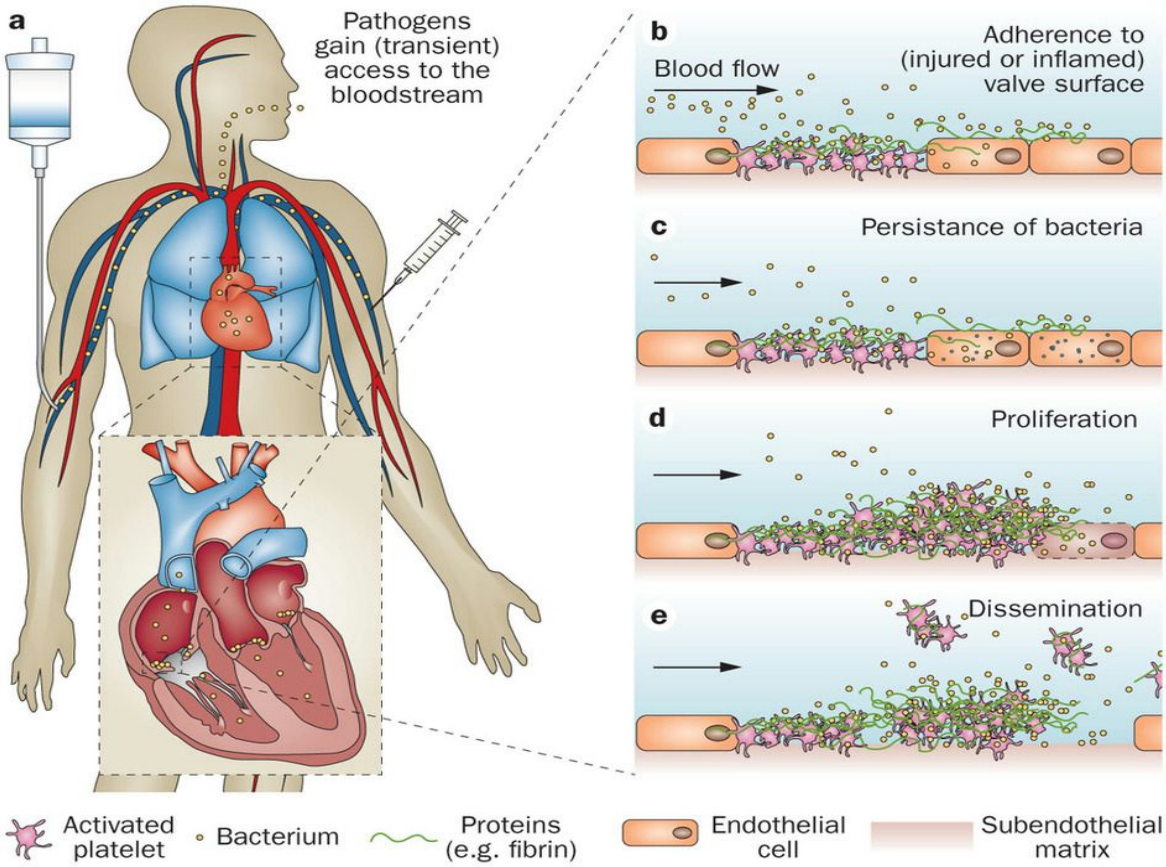
[88] Specialized connective tissue fibers that attach the tooth to the alveolar bone within which it sits.

[89] Dental term indicating the presence of an abnormally deepened gingival sulcus.

Pathogenesis (IMPORTANT):

Infection of the heart → distorted[90] heart shape → "stasis" of the blood flow.
That cause: 1) Settee of bacteria on the endocardium. 2) Formation of vegetation.[91]

Fibrin, platelets "thrombi" and bacterial colonies attach to the heart valves:	
1	Break off → infected emboli → distant organs (kidney, brain)
2	Immune complex formation → glomerular damage → haematuria[92]
3	Valves infection → destruction → heart failure
4	Drug addicts → tricuspid pulmonary valve → lung emboli → pneumonia

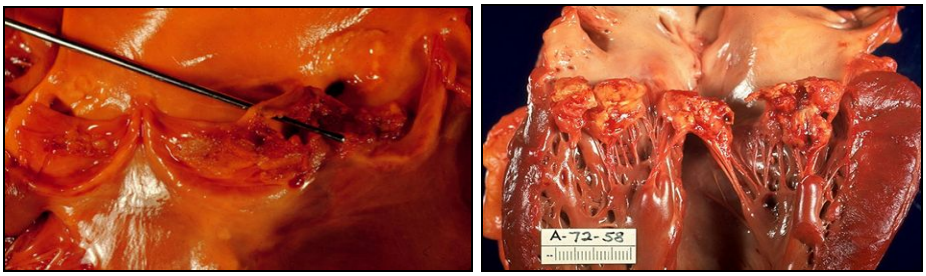


[90] Pulled or twisted out of shape; contorted.
[91] Live or spend a period of time in a dull, inactive, unchallenging way. MORE.
[92] Presence of blood in urine.

Local Spread of Infection:

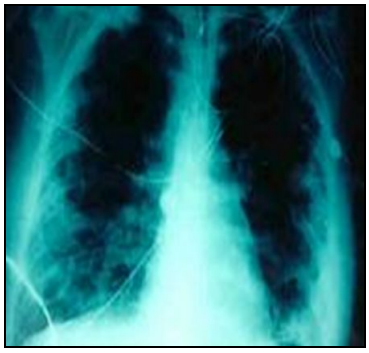
- **Heart failure:**
- Extensive valvular damage.
- **Paravalvular abscess (30-40%):**
- Most common in aortic valve (IVDA and *Staph. aureus* infection)
- May extend into adjacent conduction tissue causing arrhythmias.
- Higher rates of embolization and mortality.
- **Pericarditis.**
- **Fistulous intracardiac connections.**

Left image: Acute *S.aureus* IE with perforation of the aortic valve and aortic valve vegetations.
Right image: Acute *S.aureus* IE with mitral valve ring abscess extending into myocardium.



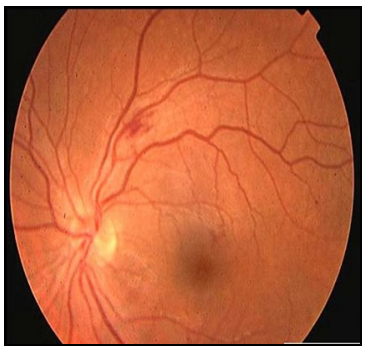
Metastatic Spread of Infection:

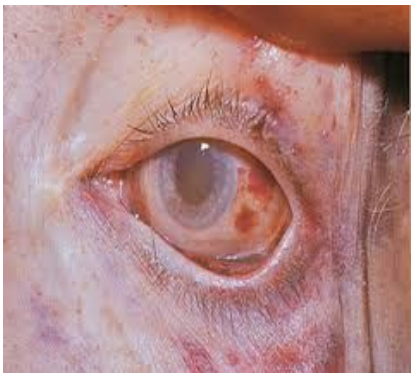
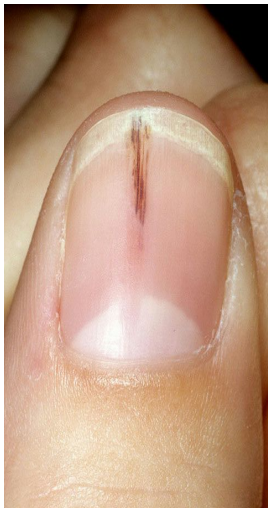
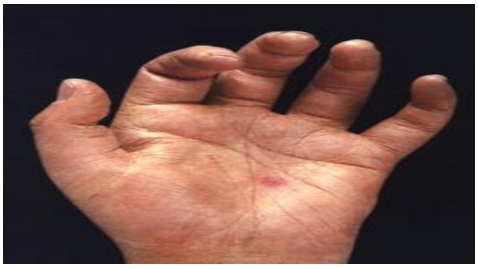
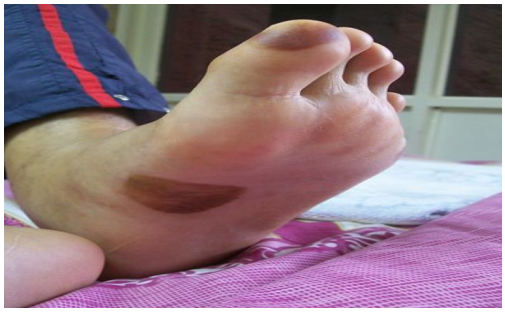
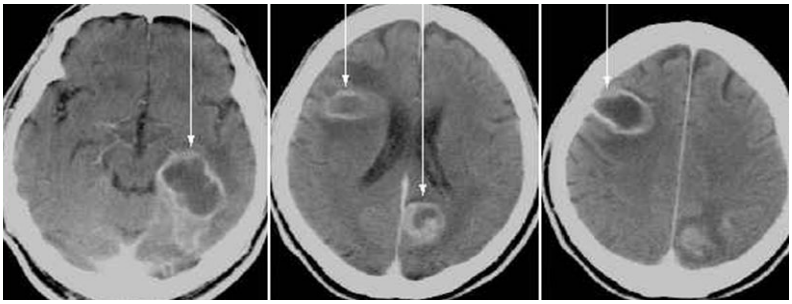
- **Metastatic abscess:**
- Kidneys, spleen, brain and soft tissues.
- **Meningitis and/or encephalitis.**
- **Vertebral osteomyelitis.**
- **Septic arthritis.**



Embolic Complications:

- **Stroke.**
- **Myocardial Infarction.**
- Fragments of valvular vegetation or vegetation-induced stenosis of coronary ostia.
- **Ischemic limbs.**
- **Hypoxia from pulmonary emboli.**
- **Abdominal pain (splenic or renal infarction).**

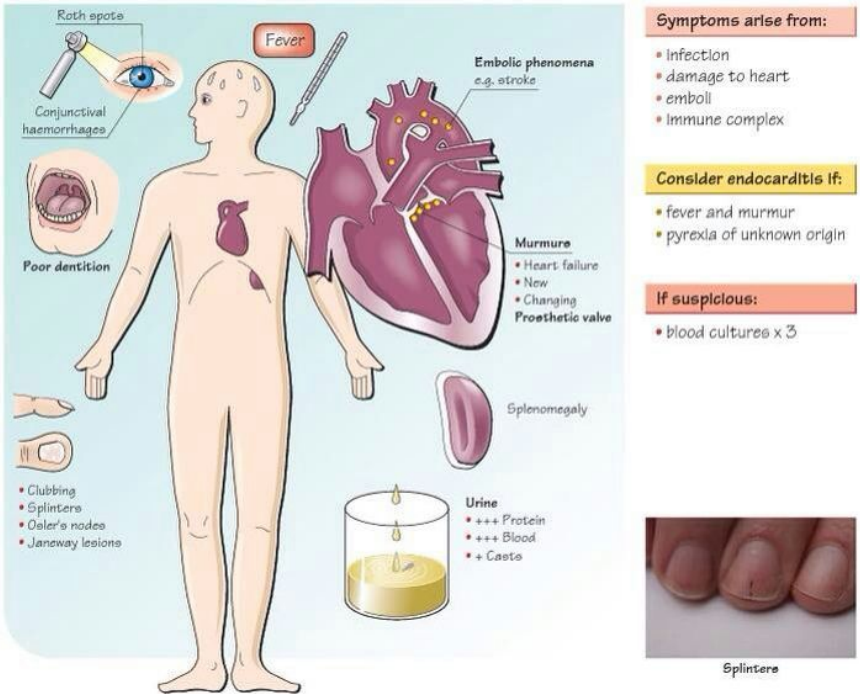


<table>
<tr><th colspan="3">Clinical features</th></tr>
<tr><th>Petechiae[93]</th><th>Splinter haemorrhage[94]</th><th>Osler's Nodes[95]</th></tr>
<tr>
<td>Nonspecific
Often located on extremities or mucous membranes
  </td>
<td>  </td>
<td>More specific
Painful and erythematous nodules
Located on pulp of fingers and toes
More common in subacute IE
  </td>
</tr>
<tr><th>Embolic manifestations of endocarditis</th><th colspan="2">CNS manifestations of endocarditis</th></tr>
<tr>
<td>  </td>
<td colspan="2">  </td>
</tr>
</table>

- Onset is insidious (Subacute Bacterial Endocarditis) – 3 weeks after extraction.
- Fever is mild and prolonged.[96]
- Malaise, weight loss, weakness and changing murmurs.
- Anaemia, leukocytosis and hypergammaglobulinemia[97].
- Microscopic haematuria and splenomegaly[98].

---

[93] A small red or purple spot caused by bleeding into the skin due to the immune complexes which are caused by the infection, not the infection itself.
[94] Tiny blood clots that tend to run vertically under the nails.
[95] Painful, red, raised lesions found on the hands and feet.
[96] Is the most consistent sign of infective endocarditis.
[97] Increased levels of a certain immunoglobulin in the blood serum.
[98] Abnormal enlargement of the spleen.



Laboratory Diagnosis		
Serial blood culture	**Serological tests**	**Sensitivity test**
2-3 sets[99] before starting antibiotic **1.** Test for Aerobic **2.** Test for Anaerobic[100]	CFT (*coxiella burnetii*)	Determines the antibiotic choice
Additional tests		
CBC, ESR and CRP, Complement proteins levels (C3, C4, CH50) and RF/Urinalysis.		
Chest X-ray	**ECG**	**Echocardiography**
Look for multiple focal infiltrates and calcification of heart valves.	Rarely diagnostic. Look for evidence of ischemia conduction delay, and arrhythmias.	The most important. Very sensitive and is a very good tool for diagnosis.

[99] We'll need 3 sets because some organisms (e.g. viridans) are found as normal flora, so if they are found in only one culture it may not be the organism that caused the disease. One set of blood culture cannot be use as a diagnostic tool.

[100] زراعة الدم تتم في حاويتين، الأولى تحتوي بيئة مخصصة لنمو البكتيريا الهوائية، والثانية تحتوي بيئة مخصصة لنمو البكتيريا اللاهوائية، وسبب تعبئة الحاوية المخصصة للهوائية أولا هو احتواء أنبوب سحب الدم على الهواء في المرة الأولى، والذي لا يصلح لنمو النوع اللاهوائي.

Bacteraemia:

There are three clinical patterns of **bacteremia**

Transient	Intermittent	Continuous
Lasts **minutes** to **hours**: **1.** Following manipulation of infected tissues (abscess, furuncle, or during a surgical procedure). **2.** Instrumentation of contaminated mucosal surfaces (dental procedures, cystoscopy, or sigmoidoscopy). **3.** At the onset of bacterial pneumonia, arthritis, osteomyelitis, and meningitis.	Common with undrained abscesses	Reflects an endovascular infection such as endocarditis or endarteritis, suppurative thrombophlebitis, or an infected aneurysm. It also occurs in the first two weeks of typhoid fever and brucellosis.

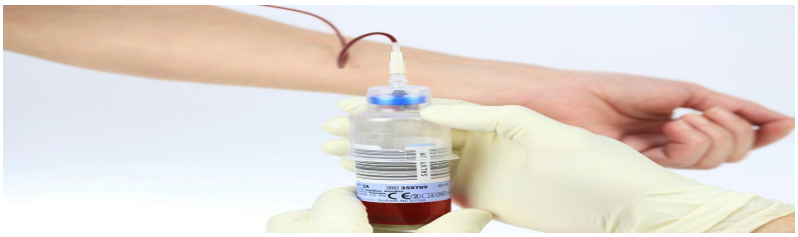
Important notes:

- Bacteraemia may follow scaling, tooth brushing or endodontic therapy[101].
- Lack of clinical effect of many bacteraemia is due to small number or low virulence.
- They are rapidly cleared by normal body defences (leucocytes).
- ***Strep. Faecalis*** may cause endocarditis after genitourinary or gut procedures.

Technique for collection of blood culture (VIDEO):

- Blood culture may be contaminated with normal skin flora like:
  1) ***Staphylococcus epidermidis.***
  2) ***Diphtheroids.***
  3) ***Propionibacteria*** (anaerobic diphtheroides).
- Therefore, we should clean the site first (mainly antecubital fossa) with 70% alcohol, chlorhexidine or iodine and leave it to dry for 1-2 minutes.
- Blood culture by automated machines like “Bactec” or “Bactalert-upto” that take 5 days when the signal is positive.

Specimen → gram stained → reported to clinician → cultured → identified → and tested for antimicrobial susceptibility



[101] What is that? HERE.

Treatment[102]:

- Disk diffusion test[103] (not sufficient).
- MIC[104] and MBC[105] tests should be done.[106]

Criteria of antibiotic choice:

- **Bactericidal[107]**
- **Parenteral[108]**
- **High dose**
- **Prolonged**

***Viridans streptococci* :**

1. Benzylpenicillin (I.V.) every 4 hours for 4 weeks.
2. Penicillin + Gentamicin[109].

Streptococcus faecalis:

Ampicillin + Gentamicin (I.V)

(Recurrence after cure is common in drug addicts and immunodeficient patients)

Antimicrobial prophylaxis (prevention):

- Susceptible patients suffering from rheumatic valvular or congenital heart diseases.
- Before tooth extraction, deep scaling and other operations.
- People who have prosthetic valves.

Give (1) first, then (2) afterwards:

1. Benzylpenicillin (I.M.) 30 minutes before operation.
2. Penicillin-V 500 mg (oral) every 6 hours for 2 days.

If patient is allergic to penicillin:

Vancomycin or Erythromycin lactobionate (I.V.) 30 minutes before operation.

Genitourinary procedures:

Gentamicin + ampicillin (I.V.) 30 minutes before operation.

---

[102] It must be a long term treatment because we're trying to treat the valves which are avascular.

[103] An antibiotic sensitivity test.

[104] Minimal Inhibitory Concentration:Is the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation. The lower the MIC, the more sensitive the organism is to that antibiotic.

[105] Minimum Bactericidal Concentration: the lowest concentration of an antibacterial agent required to kill a particular bacterium.

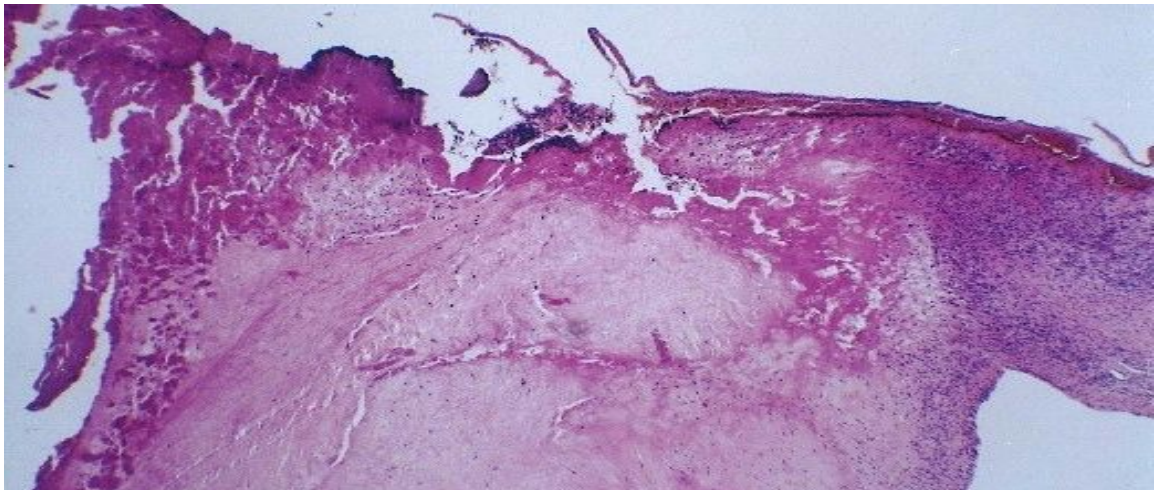
[106] What is the difference? HERE.

[107] We cannot use bacteriostatic drugs!

[108] By injection, because it will not be absorbed if given orally.

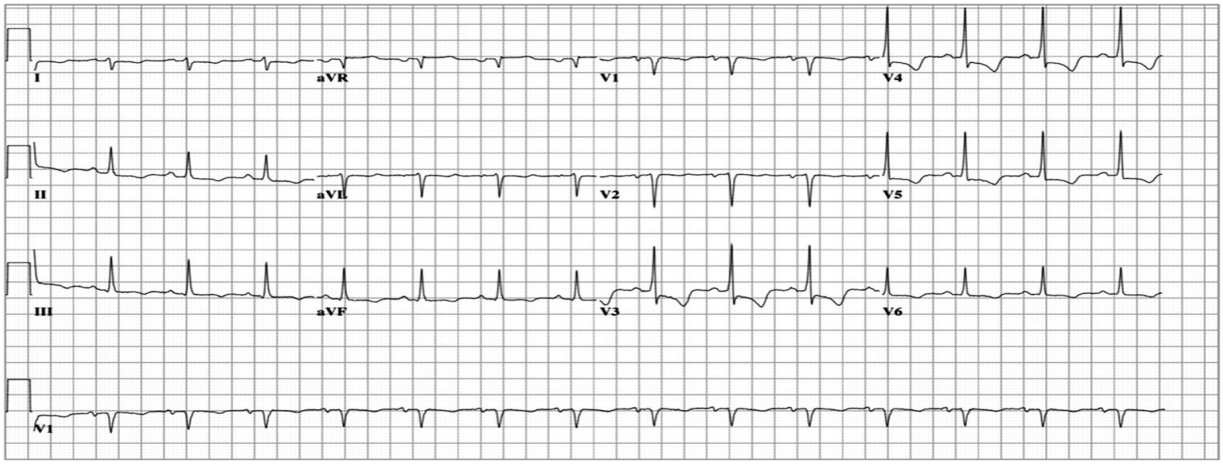
[109] Ampicillin (Beta lactam) + Gentamicin (Aminoglycoside) are used together to achieve synergy. The Beta lactam antibiotics will work on the cell wall of the bacteria while the Aminoglycosides will work on the ribosomes of the organism. So they will work on 2 different structures in the organism and give a better effect in killing it.

EXTRA INFORMATION



Microscopic appearance showing destructed tissue, inflammation and fibrin formation.

Gross view of a dead patient's mitral valve showing endocarditis



ECG of a patient suffering from endocarditis

SUMMARY (WITH EXTRA INFORMATION)

INFECTIVE ENDOCARDITIS (IE) – AETIOLOGY

Native valve
- Viridans group streptococci
- Enterococci
- Other streptococci
- *Staphylococcus aureus*
- Coagulase-negative staphylococci
- Fastidious Gram-negatives

Culture-negative endocarditis
- NB serological diagnosis
- Previous antibiotic therapy
- *Chlamydophila pneumoniae/ Chlamydia psittaci*
- *Coxiella burnetti* (Q fever)
- *Mycoplasma*

Prosthetic valve – Early
- Coagulase-negative staphylococci
- *Staphylococcus aureus*
- Viridans group streptococci
- Enterococci and other streptococci
- Fungi

Late – as for native valve

Right sided
- Nutritionally deficient strains
- *Staphylococcus aureus*
- Mixed infections
- Fungi

IE – PATHOGENESIS

Damage and roughening of endothelium

↓

Fibrin and platelet deposition

↓ Bacteraemia – oropharynx/gut/ urinary tract

Colonization of deposit

↓

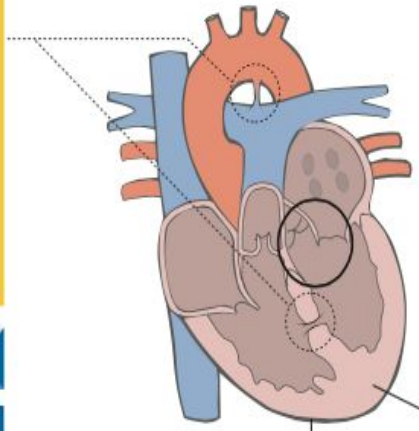
Bacterial multiplication, further fibrin and platelet deposition, immune activation

↓

Systemic signs of infection, development of vegetation, toxic, embolic and immune complex phenomena

IE – PREDISPOSING FACTORS

- Atherosclerosis/ischaemic changes
- Degenerative changes
- Congenital abnormalities, e.g. VSD, coarctation
- Rheumatic fever
- Prosthetic material, e.g. valves, pacing wires, patches/ grafts, central venous lines
- i.v. drug abusers – right sided



PERICARDITIS – AETIOLOGY

- Pneumonia, e.g. Pneumococcus, S. aureus, M. tuberculosis
- Enterovirus
- Influenza
- Mycoplasma

MYOCARDITIS – AETIOLOGY

- Coxsackievirus
- Echovirus
- Adenovirus
- Rubella
- Mycoplasma
- Toxic – septicaemia – diphtheria

N.B. Immune mediated

Pericarditis

Pericarditis is most often secondary to a non-infectious condition, such as myocardial infarction. It may complicate bacteraemia or follow spread of pus from an empyema (*Streptococcus pneumoniae*), or liver abscess (enterococci, *Entamoeba histolytica*). Tuberculosis can cause sub-acute pericarditis. Viral pericarditis is a self-limiting condition featuring fever, 'flu-like symptoms and sharp chest pain. Enteroviruses, especially coxsackie and influenza viruses, are most commonly implicated. The chest pain may vary with posture, swallowing or heartbeat. A pericardial rub may be heard. Cardiographic evidence of pericarditis may be demonstrated.

Patients with suppurative pericarditis present with fever, neutrophilia and signs of the underlying source of infection. Chest pain is severe and a fall in blood pressure may indicate developing tamponade. The ECG shows upward-curving elevated ST segments. Echocardiography will show pericardial thickening or effusion. Infection can be complicated by fibrosis and constrictive pericarditis, leading to congestive cardiac failure. Treatment is directed against the likely causative organism.

Endocarditis

Heart valves may become infected during transient bacteraemia. Congenitally abnormal or damaged valves are at greatest risk. Bacteria may originate from the mouth, urinary tract, intravenous drug misuse or colonized intravascular lines.

Clinical features

- Malaise, fever and variable heart murmurs.
- Arthralgia.
- Classical stigmata (e.g. splinter haemorrhages, Osler's nodes, microhaematuria, retinal infarcts, finger clubbing, *café-au-lait* skin, and Janeway lesions) are only seen in long-standing infection.
- In the later stages, septic emboli may cause a stroke.
- With aggressive organisms (e.g. *Staphylococcus aureus*) disease progresses rapidly and valves may rupture.

Diagnosis

A diagnosis is made if there are two major Duke criteria present or one major and three minor criteria.

The major Duke criteria include: positive blood culture with characteristic organisms (e.g. viridans streptococci); persistently positive blood cultures with any organism; evidence of endocardial involvement demonstrated by echocardiogram; and new valvular regurgitation. Minor criteria include: predisposition; fever >38 °C; immunological signs (e.g. septic pulmonary infarcts); and echocardiographic or microbiological evidence insufficient to be a major criterion.

Complications

- Local progression may lead to aortic root abscess.
- Valve destruction may lead to cardiac decompensation.
- Cerebral or limb infarction may follow septic embolus.
- Nephritis secondary to immune complex deposition can progress rapidly if sepsis is uncontrolled or if antibiotics with renal toxicity are given without care (e.g. aminoglycosides).

Myocarditis

Most myocarditis is caused by viral infection, with enteroviruses being the commonest cause; however, it may complicate systemic viral infections, follow bacteraemia or form part of brucellosis, rickettsial or chronic Chagas infection.

- Presentation is with influenza-like symptoms associated with fatigue, exertional dyspnoea, palpitations and precordial pain.
- Tachycardia, dysrhythmia or cardiac failure may be present.
- The electrocardiogram (ECG) may show T-wave inversion, prolongation of the PR or QRS interval, extrasystoles or heart block.
- Other features include cardiomegaly on chest X-ray and elevated cardiac enzymes.
- The diagnosis is suggested by a temporal relationship between the viral symptoms and cardiological abnormalities.
- Viruses may be detected in faecal, nasopharyngeal and throat specimens (see Chapter 32) by nucleic acid amplification tests (NAATs).
- Treatment is supportive.

Investigation

Echocardiography, either transthoracic or transoesophageal (more sensitive), will demonstrate vegetations on the valves; a plain chest X-ray may show evidence of cardiac failure. At least three sets of blood cultures should be taken, an hour apart, while fever is present. Antibiotic therapy should await the results of blood culture if possible. Serum should be tested for antibodies to *Coxiella, Bartonella* and *Chlamydia psittaci.*

Management

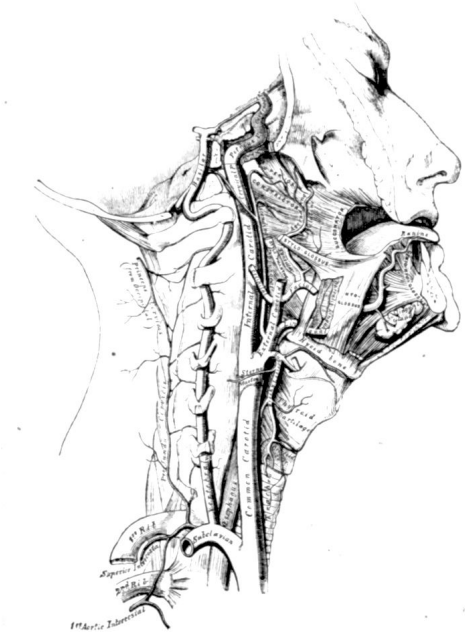
Ideally, antibiotics should not be commenced until the identity and sensitivities of the infecting organism are known; the prognosis of empirically treated, culture-negative endocarditis is poorer than that when the infecting organism is identified. Careful microbiological monitoring of the markers of inflammation (e.g. CRP) is associated with an improved outcome.

Therapy is based on the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of the antibiotics. If gentamicin is used concentrations must be monitored closely. Therapy is continued for 2–6 weeks depending on the organism and its susceptibility. Typical regimens include: benzylpenicillin and gentamicin for viridans streptococci; flucloxacillin and gentamicin for staphylococci; vancomycin and gentamicin for penicillin-allergic patients. National evidence-based guidelines for management should be followed.

Surgical management may be required to deal with the haemodynamic consequences of endocarditis (e.g. valve rupture).

Prevention

Antibiotic prophylaxis is given to patients with damaged valves when they undergo procedures that give rise to significant bacteraemia, such as dental work or urogenital surgery. For procedures that require an anaesthetic, prophylaxis is given at induction followed by subsequent oral doses. There are alternative regimens for penicillin allergy and prosthetic valves laid down by national guidelines.



وَلَقَدْ خَلَقْنَا ٱلْإِنسَٰنَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِۦ نَفْسُهُۥ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ
حَبْلِ ٱلْوَرِيدِ ﴿١٦﴾

Team Leaders

Sara Alenezy **&** **A**li Alzahrani

Heartful thanks to our phenomenal team members

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Fawzan Alotaibi

Ola Alnuhayer

Noura AlTawil
