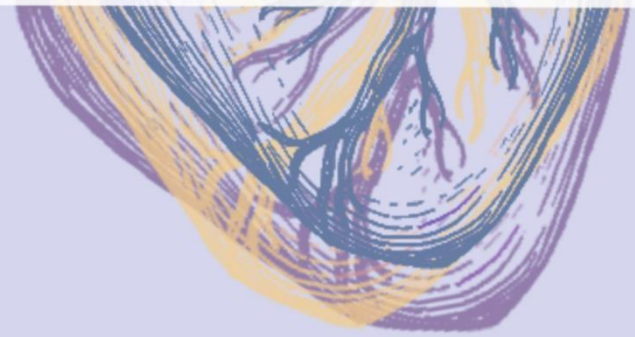
Cardio-Vascular System

9
&
10

Pathology



UBDATED BY 019

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Normally, the heart has four chambers and four valves that separate these chambers. Blood enters the heart through two large veins, the inferior and superior vena cava, emptying oxygen-poor venous blood from the body into the right atrium, then it travels to the right ventricle through the tricuspid valve, and from there, it goes through the pulmonary valve to the pulmonary arteries which route it to the lungs for oxygenation.

The highly oxygenated blood (also called systemic or arterial blood) travels through the pulmonary veins into the left atrium, and then, from the left atrium into the left ventricle through the mitral valve, to be pumped out of the left ventricle through the aortic valve into the systemic circulation.
*A murmur means abnormal heart sound(abnormal valve)

Valve stenosis and valve regurgitation

Valve stenosis occurs when the valve does not open appropriately. This is usually due to a chronic process (e.g. a chronic inflammation or scarring of the affected valve).
**Consequence of the mitral valve stenosis?? 1-Cardiac output decreases 2-left atrium dilates → thrombosis 3-conduction problems(arrythmias)
**Stenosis could happen because of 1-inflammation → scarring 2-calcifications as a regenerative process

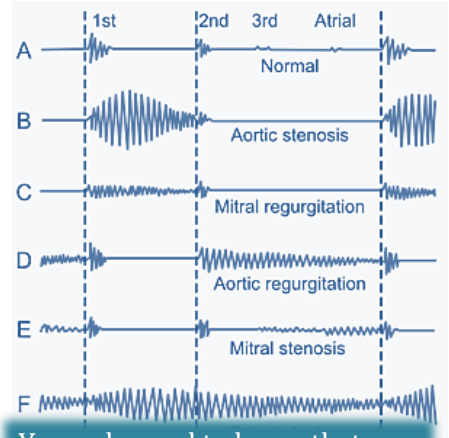
On the other hand, *valve regurgitation* refers to a valve that does not close properly. Other terms that describe valve regurgitation include **(1)** valve incompetence and **(2)** valve insufficiency.
**Consequences: 1-vascular collapse because of the back of blood instead of proceeding 2-decreased cardiac output

Valve regurgitation may develop either due to **(1)** cusps abnormalities (Infection for instance) or **(2)** abnormalities that affect the supporting structures of the valve (e.g. mitral annulus, chordae tendineae, papillary muscles…etc.). It may occur due to **(1)** an acute process(e.g. chordal rupture) or **(2)** a chronic process (e.g. scarring).

Clinical signs of any valve disease include having heart *murmurs* which are defined as abnormal (long) heart sounds.

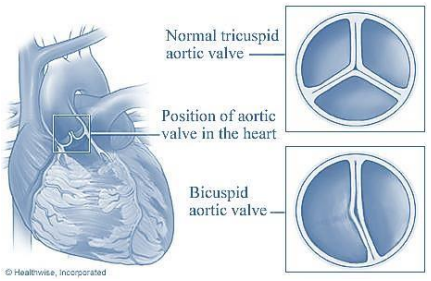
We know that -normally- two heart sounds are present andheard through a stethoscope, these are called *S1* ***lup*** and *S2* ***dup*** heart sounds, however, in certain pathological conditions, abnormal sounds (murmurs) are found, either during systole or diastole.

When the heart murmur is so loud that it can be palpated, we call it a cardiac thrill *(you can actually feel a rumbling ifyou put your hand on the person's chest!)*.Definitely, in addition to murmurs and thrills, valvular diseases (or valve diseases) cause specific clinical signs depending on the involved valves.



You only need to know that there are different types of murmurs that can be heard according to the affected valve and its related condition.

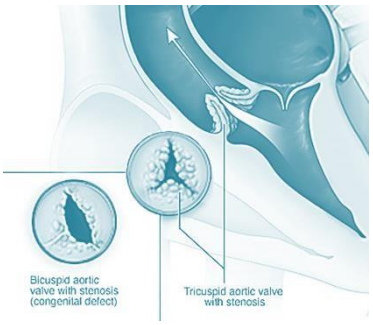
Valve diseases can be either congenital or acquired (e.g. infective endocarditis and rheumatic fever). The most common congenital abnormality is the *bicuspid aortic valve disease (BAVD)*, and the most important cause of acquired valve diseases is *rheumatic fever.* *We'll discuss these two diseases in addition to infective endocarditis.*



Bicuspid aortic valve disease (BAVD) refers to the abnormal presence of two cusps (instead of the normal three cusps) in the semilunar aortic valve. This condition affects 1-2% of all live births. It can be a single isolated abnormality, or associated with other congenital anomalies.

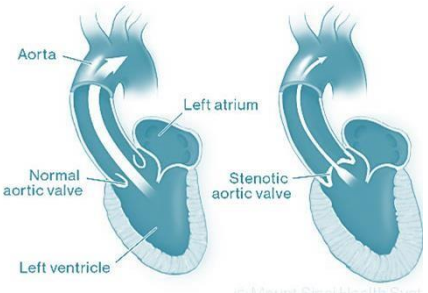
**The main problem of having 2 instead of 3 cusps is making the load heavier on a single cusp

During early life, this condition is usually asymptomatic, but later on, at the age of 50, some patients develop progressive degenerative calcification and fibrosis of the aortic valve, which usually lead to *aortic stenosis.* Unfortunately, there aremany serious consequences of *aortic valve stenosis*, the majortwo are:



1. Diminished heart ability to eject enough blood from the left ventricle to the aorta, and this reduces the cardiac output significantly.

2. Increased load on the left ventricle which might lead to *left ventricular hypertrophy* → heart failure



Acquired valve diseases

Again, the most common cause of acquired valvular diseases is the post-inflammatory scarring of *rheumatic fever* which may affect up to 2/3^{rds} of all cases.

The *mitral valve* is considered to be the most common targetof acquired valvular diseases. (2 cusps with high blood flow

Rheumatic fever (also called rheumatic cardiac disease or rheumatic valve disease) is an immune-mediated inflammatory condition that follows infection caused by group A beta-hemolytic streptococci (for example, streptococcal skin infection, or streptococcal pharyngitis (more common)).

The incidence of this condition has dropped in western world; thanks to the improved socio-economic status , the rapid diagnosis, and the treatment of streptococcal pharyngitis by antibiotics. However, this condition is still an important public health problem in the developing countries.

Streptococcal pharyngitis usually affects children (80%), and in order to protect these poor children from the risk of developing *rheumatic fever*, you should treat them with antibiotic injections early at this stage (penicillin, usually).

What happens in rheumatic fever is that there's some kind of hypersensitivity reactions due to the presence of auto-antibodies against group A streptococcal antigens, these auto-antibodies cross-react with certain host antigens, these self-antigens are distributed in several organs, including the **(1)** heart, **(2)** brain, **(3)** joints, and **(4)** skin.

Keep in mind that this condition immunogenic; meaning that it's caused by the immune system and not by the bacteria; the immune system forms antibodies against group A streptococcal antigens, and in some patients these antibodies cross-react with the host antigens. The manifestations of rheumatic fever may be seen a few weeks (10-14 days) following pharyngitis or skin infection (producing antibodies needs time)

This condition has two major phases; **(1)** an acute phase(80% children) and **(2)** a chronic phase. The acute phase is characterized by (1) fever, (2) migratory polyarthritis (joints pain), (3) carditis, (4) central nervous system symptoms (chorea), and (5) skin rashes. The chronic phase involves thecardiac valve disease.

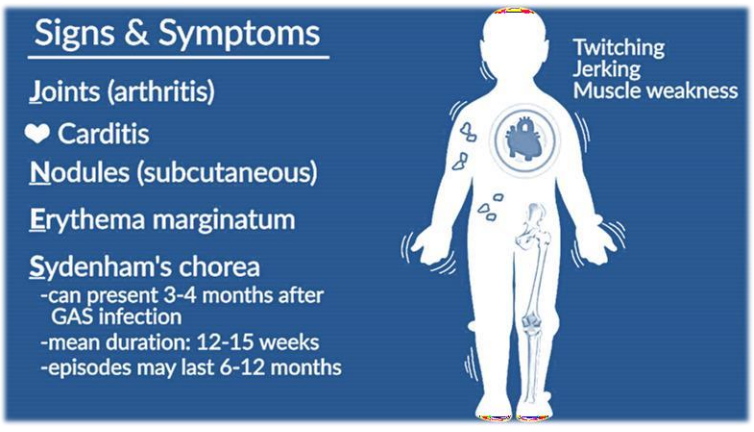
The word "carditis" refers to the clinical detection of the presence of (1) arrhythmias, (2) signs and symptoms of myocarditis, (3) cardiac dilation, (4) functional mitral insufficiency, and possibly (5) congestive heart failure (CHF).

For the diagnosis of this condition we need an evidence of a previous streptococcal infection, just like high serum titers of *anti-Streptolysin O* or *anti-DNAase. (antigens)*

Culture of Streptococci is negative at the time of symptoms onset, because the infection itself would have been spontaneously resolved or treated.

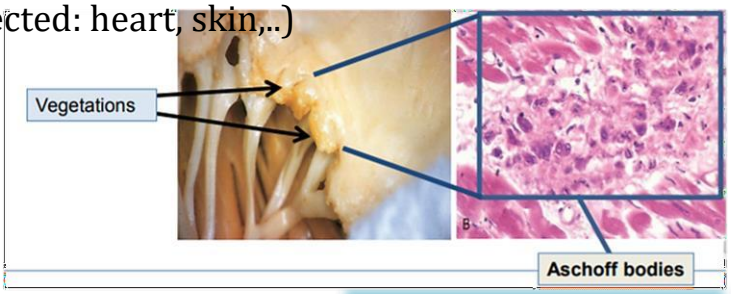
The clinical manifestations of the acute phase of *rheumatic fever* have been lumped together in *jones criteria*, the word "j❤nes" comes from the first letters of the main clinical signs of the disease.

The letter J indicates joints' involvement (arthritis), the ❤ (the letter O) represents carditis, the N is for subcutaneous Nodules, the E is for Erythema marginatum (a skin rash that characterizes this condition), and the S stands for Sydenham chorea (abnormal twitching, jerking, and muscle weakness).



Acute RHD histological analyses

The cardiac manifestations of rheumatic fever are in the form of focal inflammatory involvement in all 3 layers of the heart (*pancarditis*). The pathognomonic feature of pancarditis in the case of *rheumatic heart disease* is the presence of *Aschoff bodies*, which are granulomatous structures consisting of T lymphocytes, plasma cells, and activated macrophages.(in any organ affected: heart, skin,..)

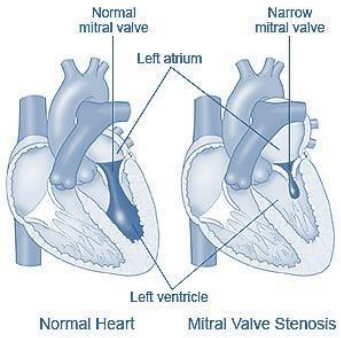


Recall that the endocardium covers the four cardiac valves, thus, its involvement might lead to the formation of *valve vegetations* (thrombi overlying the valves).

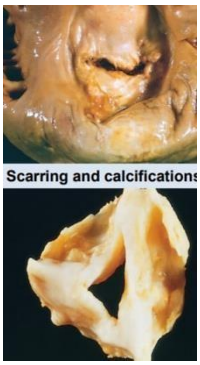
The diagnosis of acute rheumatic fever can be made when two of the major criteria (that constitute the word "*jones*"), *or* only one major criterion *plus* two minor criteria, are present along *with* evidence of streptococcal infection (elevated anti-Streptolysin O titer or anti-DNAase). (you don't have to know the minor criteria)

The minor criteria include (1) arthralgia, (2) fever, (3) raised ESR levels, (4) raised C-reactive protein levels, (5) prolonged PR interval, (6) anamnesis of rheumatism,(7) and leukocytosis.

Following the acute phase of rheumatic fever, and possibly years or even decades after the initial acute episode, rheumatic fever can cause permanent damage to the heart especially if not treated(now the condition is called rheumatic heart disease, chronic phase of rheumatic fever, or rheumatic carditis). During this phase, the chronic inflammation that has been present over the valve formany years will lead to scarring, fibrosis, calcification, and consequently, *mitral valve stenosis*. (rarely regurgitation)



As mentioned above, there are many consequences of *valve stenosis.* For example, the patient may develop cardiac *murmurs*, congestive heart failure (*CHF*), arrhythmias (e.g. *atrial fibrillation*), and even *mural thrombi* inside the left atrium.



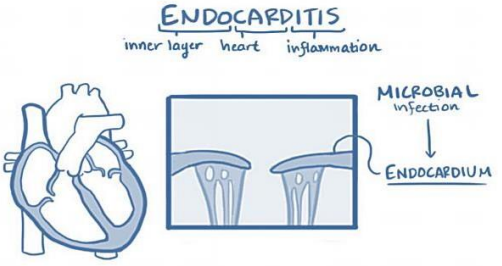
The prognosis of the chronic rheumatic fever is variable; it depends on the **(1)** severity and **(2)** the exact location of the damage inside the heart.

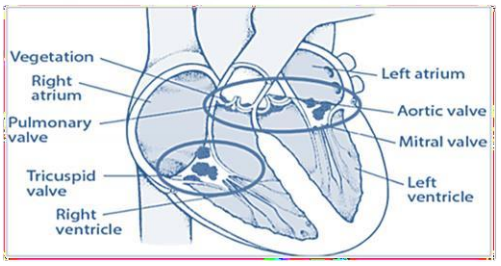
The management would be either **(1)**

surgical repair of the affected valve oreven **(2)** complete replacement of the diseased valve.

- Aschoff bodies are rarely seen in the chronic rheumatic fever.
- All heart valves can be affected by rheumatic fever, but the mitral valve is the most commonly affected one, followed by the aortic valve, tricuspidvalve, and then, the pulmonary valve (rarely).

Infective endocarditis (an acquired valvular disease)

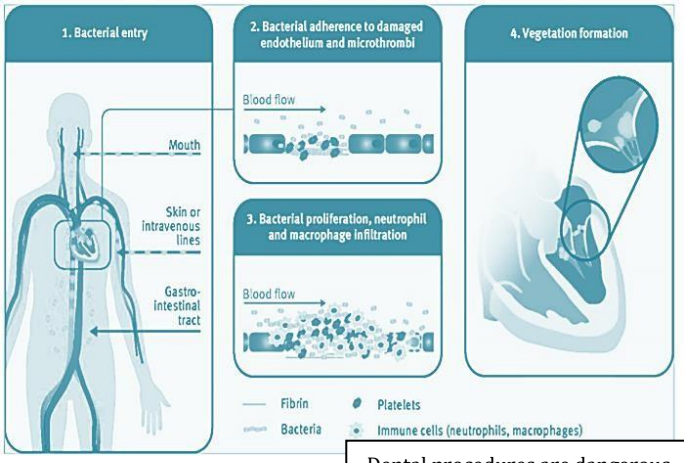




Endocarditis is a life-threatening inflammation of the inner lining of the heart's chambers and -most importantly- valves (endocardium). It is usually caused by a microbial infection. This infection of the heart valves leads to the formation of large bulky friable vegetations which
are made of (1) fibrin and platelets (the constituents of a thrombus), (2) colonies of the infectious microorganism, and (3) necrotic debris.

Endocarditis occurs when germs, usually bacteria, enter the bloodstream (hematogenous pathway) (septicemia) through (1) the mouth, (2) the gastrointestinal tract, (3) the skin (e.g. intravenous vascular lesions or intravenousinjections), or (4) the genitourinary system, and travel to the heart valves and the endocardium.(extra examples from 018)

The problem starts when the bacteria reach the endocardium (the endothelium) inside the heart, damage the endothelial cells, and illicit an inflammatory response (neutrophils and macrophages). As we know, injury to endothelium is accompanied by loss of protective molecules and expression of adhesive and pro-coagulant molecules, leading to development of *thrombosis* over the rapidly growing bacterial colonies (*vegetations*).



Extra: It appears that circulating bacteria do not readily adhere to normal endothelial surfaces. Theremust be a defective surface, susceptible to colonization by circulating bacteria.

Dental procedures are dangerous for those who are at high risk to develop infective endocarditis; this is due to the access of microbes to the blood, as well as the mouth is a place where normal flora exist, so once it gets in the blood, it is infective

Prothesis valves are risky for developing endocarditis because they're not a viable tissue where immune system can get into, and some bacteria like to adhere to these prosthetic valves

Risk factors for infective endocarditis

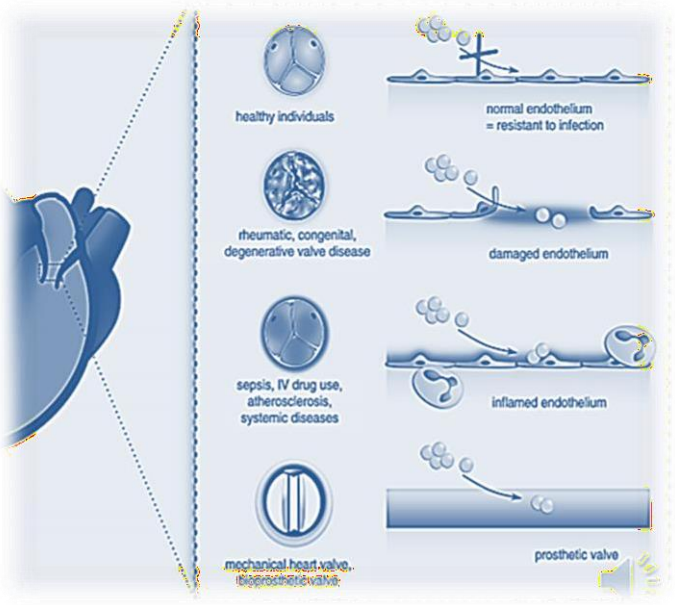
1. Congenital heart disease of any type.(abnormal valves)
2. Acquired heart diseases (especially rheumatic fever).(abnormal valves)
3. Indwelling vascular catheters.
4. Intra-cardiac devices and prosthesis.
5. Immunodeficiency of any kind.(HIV for instance)
6. IV drug use or abuse (access for infective organisms)
7. Septicemia

Damaged valves are more vulnerable to be infected

What about dental procedures?

Dental procedures in patients withany of the risk factors we have discussed before are said to be at ahigh risk to develop infective endocarditis, that's why they needto take antibiotic therapy prior to any dental procedure (especially dental extractions).

As you can see in this picture, the healthy individual, having normal endothelium, and not having any one of those risk factors, is resistant to infective endocarditis. On the other hand, another person, having rheumatic fever or any type of valve diseases that damages the endothelium, is at a higher risk of developing this kind of infection because the endothelial injury would make it easy for microorganisms to adhere and induce inflammation and *thrombosis*.



Now infective endocarditis and its clinical course can be classified into two types: **(1)** acute infective endocarditis, and **(2)** sub-acute infective endocarditis. The classification is based on two things; the first one is **(1)** the *virulence* of the microorganism, and the second is **(2)** the presence of any underlying cardiac disease. *Please memorize the table very well.*

- The word *virulence* means the tendency of the microorganism to cause damage and infection; microorganisms with high virulence are said to be causing acute infective endocarditis instead of sub-acute, while low-virulence microorganisms are usually associated with sub-acute forms of infective endocarditis.

Feature	Acute endocarditis	Subacute endocarditis
Virulence	highly virulent organism	low virulent organism
Most common organism	Staph. aureus	Streptococcus viridans
Underlying cardiac disease	previously normal valve	previously abnormal valve (scarred or deformed)
Clinical course Duration	rapidly developing Few days	Insidious disease Weeks (slow progression)
Outcome	High morbidity and mortality	most patients recover after appropriate antibiotic therapy

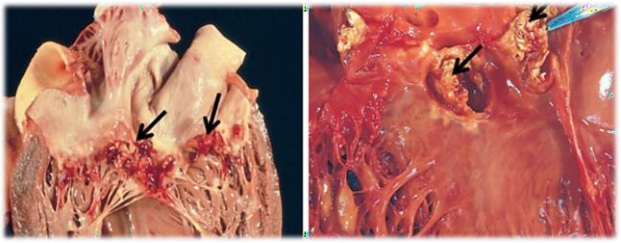
- *Viridans streptococci* are part of the normal oral flora and generally gain access to the bloodstream through breaches in the oral mucosa.

- It's written that having normal and healthy valves is associated with acute endocarditis, well, this is because the highly virulent microorganisms like *Staph. aureus* are capable of infecting –even- the previously normal valves, while other low-virulence microorganism like *Strep. viridans* cannot –usually- infect normal valves or patients with normal immune-status, so previously abnormal, scarred, or deformed valves or valves had rheumatic fever before are needed for a low-virulence microorganism to cause a sub-acuteendocarditis.

Keep in mind that there are other causative microorganisms, like rickettsiae, chlamydia, and fungi.

The patient usually comes with fever, chills, weakness, and cardiac manifestations (especially, cardiac murmurs).

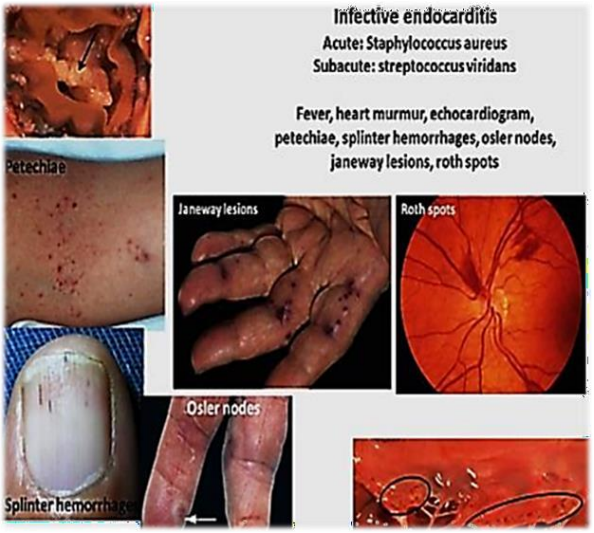
The *valve vegetations* can send pieces of the thrombus leading to the formation of emboli; these emboli are said to be *septic* (emboli that are infected with bacteria), and they can target different body tissues.



Regarding the *valvular involvement;* the most commonly affected valves are the aortic and the mitral valves. However, it depends on the exact clinical picture or the exact risk factor that led to the infection; for example, the **tri**cuspid valve is the one most commonly affected in people who use IV drug medications and IV drug abusers (don't **tri** IV drugs). (IntraVENOUS means that organisms seed venous circulation → right side of the heart → tricuspid valve involvement)

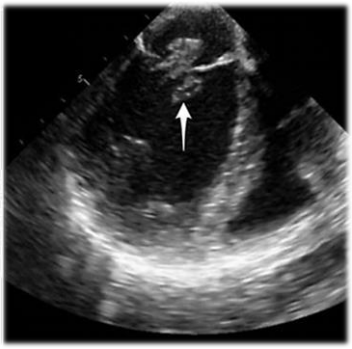
Complications of infective endocarditis (associated with emboli formation):

1. Emboli.
2. Septic infarcts (the embolism can causeocclusion in any part of the body).
3. Abscesses within blood vessels.
4. They can lead to *mycotic aneurysm* (a dilation of an artery due to damage of thevessel wall by an infection)
5. Also, it could cause regurgitation of the valve



Treatment includes long-term (≥6 weeks) intravenous antibiotic therapy (depending on the genus of the infective organism) and/or valve replacement, so the treatment is prolonged and oral therapy is not sufficient.

The diagnosis depends on **(1)** the clinical picture (the suspicion of this condition), **(2)** a positive blood culture for the offending microorganism to decide what antibiotic to use, and **(3)** the presence of echocardiographic findings → *(an imaging tool that is used to examine the heart, the blood flow through the heart chambers, and the major blood vessels)*.



The Duke criteria are a set of clinical criteria set forward for the diagnosis of infective endocarditis.

We're not supposed to memorize the Duke criteria, but we should understand how difficult it is to diagnose infective endocarditis; multiple criteria and a constellation of findings are involved; it's not easyat all and needs a high clinical index of suspicion.

These two squares summarize the most important points regarding the two lectures (9 & 10)

Rheumatic fever

A consequence of pharyngeal infection with group A B-hemolytic streptococci.

Late sequelae include rheumatic heart disease, which affects heart valves.

Valvular involvement:

Mitral > Aortic >> Tricuspid (RheuMATic fever)

Associated with Aschoff bodies (granuloma with giant cells)

High anti-streptolysin O (ASO) and anti-DNase titers

Immune mediated (hypersensitivity), not a direct effect of bacteria

Antibodies to bacterial antigens cross-react with self-antigens

Treatment/prophylaxis: penicillin injections.

Infective endocarditis

May be non-bacterial

Symptoms: fever (most common), new murmur, Requires multiple blood cultures for diagnosis.

Valvular involvement: Mitral valve and Aortic valves are most frequently involved. Tricuspid valve endocarditis is associated with IV drug abuse (don't tri IV drugs).

Associated with septic arterial or pulmonary emboli.

Treatment is prolonged and oral therapy is not sufficient (IV).

(1) Acute-S aureus (high virulence)

It causes large vegetations on previously normal valves, and has a rapid onset.

(2) Subacute-viridans streptococci (low virulence)

They cause smaller vegetations on congenitally abnormal or diseased valves. It's associated with dental procedures, and has a gradual onset.

Test your-self

The myocardial lesions shown in the figure were observed at autopsy examination of a pediatric patient who died after a short illness. During life, which of the following was most likely a manifestations of his illness?

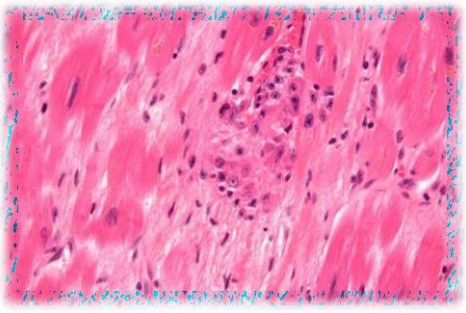
(A) Systemic lupus erythematosus

(B) Systemic embolization

(C) Chorea

(D) Unstable angina

(E) Wasting diseases



Good luCk