4.2.2

Rheumatic Heart Disease

Rheumatic Fever (RF)

Rheumatic Fever (RF) is an immune-mediated, multi-system inflammatory disease that involves the heart, skin, joints, and central nervous system. Rheumatic fever can be manifest as an acute, recurrent, or chronic disorder. Because the disease can affect several body systems, it can manifest as rheumatic carditis, polyarthritis, erythema marginatum (pink to red rings of rash on the body), chorea (abnormal and involuntary movements), and affect the mitral and aortic valves of the heart.

Rheumatic fever may follow a **group A *Streptococcus pyogenes* (GAS)** infection of the upper respiratory tract (commonly referred to as strep throat). GAS infections are much more common in children and young adults. RF is rare in developed countries, but in underdeveloped countries it is a major health issue.

It is very important that a GAS infection be quickly diagnosed and treated in order to avoid RF and its negative effects. The gold standard for detecting a GAS infection is a throat culture. However the **"rapid test for GAS"** is more commonly used because it can be applied right in the doctor's office. It involves taking a swab to collect a sample of mucus from the throat. This mucus is then exposed to a reagent containing antibodies that will bind antigens specific to the GAS bacteria. This test is highly specific, but is limited in sensitivity. This means that a patient may have a negative test result when they do indeed have a streptococcal infection. Because of this limitation, a negative antigen test should always be followed up with a throat culture when streptococcal infection is suspected. During the acute phase of RF, patients should be prescribed antibiotics. Patients with cardiac valve pathology may receive low-dose antibiotic prophylaxis.

Rheumatic Heart Disease and RF

Rheumatic Heart Disease (RHD) is the cardiac manifestation of RF. Chronic deformity and impairment of one or more of the heart valves is the most important consequence of RHD. RHD following a GAS infection occurs in up to 3% of infected individuals and is much more likely in strep throat infections that are left untreated. However, the pathogenesis of RHD is not due to the direct bacterial infection of the heart. Rather, it is due to an autoimmune reaction triggered by the presence of the bacteria. There is a surface protein on group A *Streptococcus pyogenes* called an **M protein**. This protein appears to provide additional virulence to the bacteria because it decreases the immune response by impairing activation of the complement system. B-cells of the immune system are capable of producing antibodies that recognize and bind the M protein. However, natural body tissues can also end up subject to this antibody attack because the M proteins share structural homology with glycoproteins of the heart valves. The idea that similarities between foreign and self-peptides can result in cross activation of the specific immune system is called **molecular mimicry**. The immune system then mistakenly attacks these tissues in the heart in an autoimmune process that causes inflammation. The joints, skin and nervous system may be involved because of autoimmune reactions against antigens in these tissues and/or because of the deposition of immune complexes.

Distinctive inflammatory lesions/granulomas called **Aschoff bodies** are found in the heart of individuals with RHD. They consist of T-cells, plasma cells, and enlarged macrophages called **Anitschkow cells** (also known as "caterpillar cells"

due to their appearance). Anitschkow cells are pathognomonic (meaning “characteristic of” or “indicative of”) for rheumatic fever and rheumatic heart disease.

Diagnosis of RHD can be done by performing a serologic test (a test on blood serum) which checks for antibodies against streptococcus such as **antistreptolysin O** and **antideoxyribonuclease B**. Presence of these antibodies in a patient’s serum is indicative of a recent streptococcal infection. Laboratory markers of acute inflammation are also used. They include elevated erythrocyte sedimentation rate (ESR is the rate at which RBCs in anticoagulated blood descend in a tube over an hour), elevated leukocyte count, and elevated C-reactive protein (CRP plays a role in immunity). Echocardiography is also useful for assessing changes in the heart valves and sizes of the heart chambers. To aid in diagnosis, the **Jones criteria** is used to separate clinical features into major and minor categories (see table). The Jones criteria states that if an individual has two major signs or one major sign and two minor signs along with evidence of previous group A strep infection (obtained through a positive serologic test or positive throat culture for GAS), the likelihood of RF is high.

THE JONES CRITERIA:	
Major Category Symptoms:	• Carditis (heart inflammation) • Polyarthritis (arthritis of many joints) • Chorea • Erythema marginatum • Subcutaneous nodules
Minor Category Symptoms:	• Arthralgia (joint pain) • Fever • Elevated ESR • Elevated CRP • Elevated leukocyte count • Prolonged PR interval on ECG
Diagnosis:	If an individual has 2 major signs or 1 major sign + 2 minor signs and evidence of a GAS infection has been obtained, likelihood of RF is high.

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