Acute Rheumatic Fever

:Objectives

1. Define rheumatic fever and its pathology.
2. Recognise the causes of rheuatic fever.
3. Describe clincal manifestations of rheumatic fever.
4. Describe the major and minor criteria of rheumatic fever.
5. Identify the investigations for diagnosis of rheumatic fever.
6. Explain the management of rheumatic fever.
7. Identify the complications of rheumatic fever.

Acute rheumatic fever (RF) occurs as a result of a complex interaction between group A streptococcus (GAS), a susceptible host, and the environment. An abnormal immune response to GAS infection leads to an acute inflammatory illness that most commonly affects the joints, brain, heart, or skin. Although the other manifestations are self-limiting and resolve without sequelae, carditis may result in significant morbidity and mortality.

Causes

Acute rheumatic fever is believed to be an immunologic response. 1 that occurs as a delayed sequelae of group A streptococcal infection of the pharynx but not of the skin. The attack rate of acute rheumatic fever after streptococcal infection varies with the .severity of the infection, ranging from 0.3% to 3%

Important predisposing factors include family history of. 2 rheumatic fever, low socioeconomic status (poverty, poor hygiene, medical deprivation), and age between 6 and 15 years (with a peak .incidence at 8 years of age)

Pathology

1. The inflammatory lesion is found in many parts of the body, most notably in the heart, brain, joints, and skin.

2. Rheumatic carditis was considered to be pancarditis, with myocarditis being the most important element. It is now recognized that the valvular component may be as important as or much more important than myocardial and pericardial involvement.

3. Valvular damage most frequently and most severely involves the mitral, less commonly the aortic, and rarely the tricuspid and pulmonary valves.

4. Aschoff bodies in the atrial myocardium are believed to be characteristic of rheumatic fever.

These consist of inflammatory lesions associated with swelling, fragmentation of collagen fibers, and surrounded by or infiltrated by large multinucleated cells.

Clinical Manifestations

Acute rheumatic fever is diagnosed by the use of revised Jones criteria. The criteria are three groups of important clinical and laboratory findings: (1) five major manifestations, (2) four minor manifestations, and (3) supporting evidence of an .antecedent group A streptococcal infection

History

History of streptococcal pharyngitis, 1 to 5 weeks (average, 3. 1 weeks) before the onset of symptoms, is common. The latent period may be as long as 2 to 6 months (average, 4 months) in .cases of isolated chorea

Pallor, malaise; easy fatigability; and other history, such as. 2 .epistaxis (5%–10%) and abdominal pain, may be present

Major criteria	Minor criteria
Carditis	Fever
Chorea	Arthralgia
Polyarthritis	Elevated Acute-Phase Reactants
Erythema marginatum	Erythrocyte sedimentation rate
Subcutaneous nodules	C-reactive protein
	Prolonged PR interval (ECG)

Supporting evidence of antecedent group A streptococcal pharyngeal infection

Positive throat culture or rapid streptococcal test

Elevated or rising streptococcal antibody titer

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:Criteria for diagnosis of

Primary episode of RF	major *or* 1 major plus 2 minor *plus* 2 evidence	of preceding strep infection
RF recurrence in a patient without RHD	major *or* 1 major plus 2 minor *plus* 2 evidence	of preceding strep infection
RF recurrence in a patient with RHD	minor *plus* evidence of preceding strep 2 infection	
Chorea or indolent carditis	No other criteria or evidence of preceding strep	infection needed

Major Manifestations

.Five major criteria of acute rheumatic fever are discussed below

Arthritis

Arthritis, the most common manifestation of acute rheumatic fever (70% of cases), usually involves large joints (e.g., knees, .ankles, elbows, wrists)

Often more than one joint is involved, either simultaneously or in succession, with a characteristic migratory nature of the arthritis. Swelling, heat, redness, severe pain, tenderness, and limitation of motion are common. If the patient was given salicylate-containing analgesics, these signs of inflammation may be mild. The arthritis responds dramatically to salicylate therapy; if patients treated with salicylates (with documented therapeutic levels) do not improve in 48 hours, the diagnosis of acute rheumatic fever probably is .incorrect

Carditis

Carditis occurs in 50% of patients. Signs of carditis include some or all .of the following

Tachycardia (out of proportion to the degree of fever) is common;. 1 its .absence makes the diagnosis of myocarditis unlikely

A heart murmur of mitral regurgitation (MR) or aortic regurgitation. 2 (AR) (or both) is almost always present. Mitral regurgitation, the dominant cardiac abnormality in patients with RF, occurs in approximately 95% of cases with acute rheumatic carditis

Significant echocardiographic abnormalities may be present in the absence of heart murmur. Aortic regurgitation occurs in approximately 20% to 25% of patients with acute rheumatic carditis, usually in combination with mitral regurgitation. Isolated aortic regurgitation occurs in approximately 5% of patients with acute rheumatic carditis

Echocardiographic examination can determine the severity of cardiac enlargement, the presence and degree of MR and AR, and the presence of pericardial effusion more objectively than auscultation

Other abnormal echocardiographic findings may include pericardial effusion, increased left ventricular (LV) .dimension, or impaired LV function

Pericarditis (with friction rub, pericardial effusion, chest pain, and. 3 electrocardiographic [ECG] changes) may be present. Pericarditis does not occur without mitral valve involvement in rheumatic fever. Pericardial effusion is usually of small amount and almost never causes cardiac tamponade

Cardiomegaly on chest radiograph is indicative of severity of. 4 .rheumatic carditis (or valvulitis) or congestive heart failure (CHF)

Signs of CHF (gallop rhythm, distant heart sounds, cardiomegaly). 5 .are indications of severe cardiac dysfunction

Sydenham's Chorea

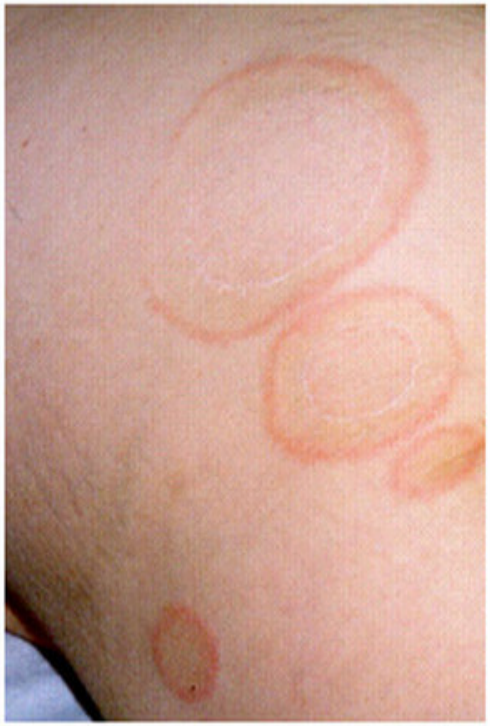
Sydenham's chorea is found in 15% of patients with acute rheumatic fever. It is now known that the clinical manifestations of Sydenham chorea occur because of neuropathologic changes and inflammation in the basal ganglia, cerebral cortex, and the cerebellum It occurs more often in prepubertal girls (8–12 years) than in boys. It is a neuropsychiatric disorder consisting of both neurologic signs (choretic movement involuntary, purposeless movements and hypotonia) and psychiatric signs (e.g., emotional lability, hyperactivity, separation anxiety, obsessions, and .compulsions)

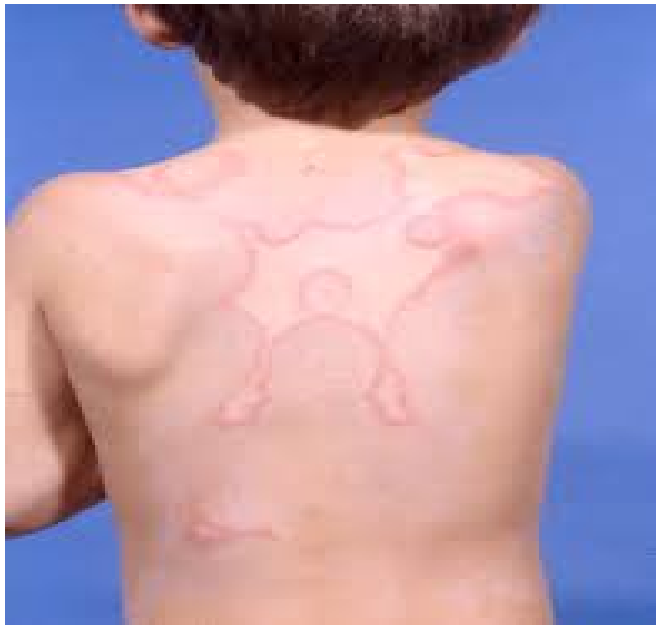
The adventitious movements, weakness, and hypotonia continue for an average of 7 months (up to 17 months) before slowly waning in severity. These findings suggest that chorea may be related to .dysfunction of basal ganglia and cortical neuronal components

Erythema Marginatum

Erythema marginatum occurs in fewer than 10% of patients with acute rheumatic fever. The characteristic nonpruritic serpiginous or annular erythematous rashes are most prominent on the trunk and the inner proximal portions of .the extremities; they are never seen on the face

The rashes are evanescent, disappearing on exposure to cold and reappearing after a hot shower or when the patient is covered with a warm blanket. They seldom are .detected in air-conditioned rooms





Subcutaneous Nodules

Subcutaneous nodules are found in 2% to 10% of patients, particularly in cases with recurrences; it is almost never present as a .sole manifestation of rheumatic fever

They are hard, painless, nonpruritic, freely movable, swelling, and .0.2 to 2 cm in diameter

They usually are found symmetrically, singly or in clusters, on the extensor surfaces of both large and small joints, over the scalp, or ,along the spine. They are not transient, lasting for weeks and have a significant association with carditis. Subcutaneous nodules are not exclusive to rheumatic fever. They occur in 10% of children with rheumatoid arthritis, and benign subcutaneous nodules have been described in children and adults. In adults, they occur with rheumatoid arthritis, systemic lupus erythematosus (SLE), .and other diseases

Minor Manifestations

The following are four minor criteria for the diagnosis of acute .rheumatic fever

Arthralgia refers to joint pain without the objective changes of. 1 arthritis. It must not be considered a minor manifestation when arthritis is used as a major manifestation in making the diagnosis of .rheumatic fever

Fever (usually with a temperature of at least 102°F [38.8°C]) is. 2 .present early in the course of untreated rheumatic fever

In laboratory findings, elevated acute-phase reactants (elevated C-. 3 reactive protein [CRP] levels and elevated erythrocyte sedimentation .rate [ESR]) are objective evidence of an inflammatory process

A prolonged PR interval on the ECG is neither specific for acute. 4 .rheumatic fever nor an indication of active carditis

Evidence of Antecedent Group A Streptococcal Infection

A history of sore throat or of scarlet fever unsubstantiated by. 1 laboratory data is not adequate evidence of recent group A .streptococcal infection

Positive throat cultures or rapid streptococcal antigen tests for. 2 group A streptococci are less reliable than antibody tests because they do not distinguish between recent infection and chronic .pharyngeal carriage

Streptococcal antibody tests are the most reliable laboratory. 3 evidence of antecedent streptococcal infection capable of producing acute rheumatic fever. The onset of the clinical manifestations of acute rheumatic fever coincides with the peak of .the streptococcal antibody response

a. Antistreptolysin O(ASO) titer is well standardized and therefore is the most widely used test. It is elevated in 80% of patients with acute rheumatic fever. ASO titers of at least 333 Todd units in children and 250 Todd units in adults are considered elevated. A .single low ASO titer does not exclude acute rheumatic fever ,If three antistreptococcal antibody tests (antistreptolysin O antideoxyribonuclease B, and antihyaluronidase tests) are obtained, a titer for at least one antibody test is elevated in more .than 95% of patients

b. The antideoxyribonuclease B titers of 240 Todd units or greater in children and 120 Todd units or greater in adults are considered .elevated

c. A slide agglutination test (Streptozyme test, Wampole Laboratories, Cranbury, NJ) that detects antibodies, is a relatively simple slide agglutination test, but it is less standardized and less .reproducible than infection

Other Clinical Features

Abdominal pain, a rapid sleeping heart rate, tachycardia out. 1 of proportion to fever, malaise, anemia, epistaxis, and precordial .pain are relatively common but not specific

A positive family history of rheumatic fever also may heighten. 2 .the suspicion

Diagnosis

A diagnosis of acute rheumatic fever is highly probable. 1
when either two major manifestations or one major and two minor manifestations, plus evidence of antecedent streptococcal infection, arepresent. The absence of supporting evidence of a previous group A streptococcal infection makes the diagnosis doubtful

:The following tips help in applying the Jones criteria. 2

a. Two major manifestations are always stronger than one major .plus two minor manifestations

b. Arthralgia or a prolonged PR interval cannot be used as a minor manifestation when using arthritis and carditis, respectively, as .major manifestations

c. The absence of evidence of an antecedent group A streptococcal infection is a warning that acute rheumatic fever is unlikely (except when chorea is present)

d. The vibratory innocent (Still's) murmur is often misinterpreted as a murmur of MR and thereby is a frequent cause of misdiagnosis (or overdiagnosis) of acute rheumatic fever. The murmur of MR is a *regurgitant-type* systolic murmur (pansystolic murmur)starting with the S1 caused by MR, but the innocent murmur is low pitched and .an *ejection* type

e. The possibility of the early suppression of full clinical manifestations should be sought during the history taking. Subtherapeutic doses of aspirin or salicylate-containing analgesics (e. .g., Bufferin, Anacin) may suppress full manifestations

Exceptions to the Jones criteria include the following. 3 :three specific situations

a. Chorea may occur as the only manifestation of rheumatic .fever

b. Indolent carditis may be the only manifestation in patients who come to medical attention months after the .onset of rheumatic fever

c. Occasionally, patients with rheumatic fever recurrences .may not fulfill the Jones criteria

Differential Diagnosis

Juvenile rheumatoid arthritis is often misdiagnosed as acute. 1
rheumatic fever. The following findings suggest juvenile rheumatoid arthritis rather than acute rheumatic fever: involvement of peripheral small joints, symmetrical involvement of large joints without migratory arthritis, pallor of the involved joints, a more indolent course, no evidence of preceding streptococcal infection, and the absence of prompt response to salicylate therapy within 24 to 48 .hours

Other collagen vascular diseases (SLE, mixed connective tissue. 2
disease); reactive arthritis, including poststreptococcal arthritis; serum sickness; and infectious arthritis (such as gonococcal) .occasionally require differentiation

Virus-associated acute arthritis (rubella, parvovirus, hepatitis B. 3
virus,herpesviruses, enteroviruses) is much more common in adults

Hematologic disorders, such as sickle cell anemia and leukemia. 4

Clinical Course

Only carditis can cause permanent cardiac damage. Signs of. 1
mild carditis disappear rapidly in weeks, but those of severe
.carditis may last for 2 to 6 months

Arthritis subsides within a few days to several weeks, even. 2
.without treatment, and does not cause permanent damage

Chorea gradually subsides in 6 to 7 months or longer and. 3
.usually does not cause permanent neurologic sequelae

Management

When acute rheumatic fever is suggested by history and physical. 1
examination, one should obtain the following laboratory studies: complete blood count, acute-phase reactants (ESR and CRP), throat culture, ASO titer (and a second antibody titer, particularly with .chorea), chest radiographs, and ECG

Cardiology consultation is indicated to clarify whether there is cardiac involvement; two-dimensional echocardiographic and Doppler .studies are usually performed at that time

Benzathine penicillin G, 0.6 to 1.2 million units intramuscularly, is. 2
.given to eradicate streptococci

In patients who are allergic to penicillin,erythromycin, 40 mg/kg per .day in two to four doses for 10 days, may be substituted for penicillin

Antiinflammatory or suppressive therapy with salicylates or. 3
.steroids must not be started until a definite diagnosis is made

When the diagnosis of acute rheumatic fever is confirmed, one. 4 must educate the patient and parents about the need to prevent subsequent streptococcal infection through continuous antibiotic prophylaxis

Bed rest of varying duration is recommended. The duration. 5 depends on the type and severity of the manifestations and may range from 1 week (for isolated arthritis) to several weeks for severe .carditis

Bed rest is followed by a period of indoor ambulation of varying duration before the child is allowed to return to school. The ESR is a helpful guide to the rheumatic activity and therefore to the duration .of restriction of activities

Full activity is allowed when the ESR has returned to normal, except .in children with significant cardiac involvement

Therapy with antiinflammatory agents should be started as soon as. 6 .acute rheumatic fever has been diagnosed

a. For mild to moderate carditis, aspirin alone is recommended in a dose of 90 to 100 mg/kg per day in four to six divided doses. An adequate blood level of salicylates is 20 to 25 mg/100 mL. This dose is continued for 4 to 8 weeks, depending on the clinical response. After improvement, the therapy is withdrawn gradually over 4 to 6 weeks

b. For arthritis, aspirin therapy is continued for 2 weeks and gradually withdrawn over the following 2 to 3 weeks. Rapid resolution of join symptoms with aspirin within 24 to 36 hours is supportive evidence of .the arthritis of acute rheumatic fever

c. Prednisone (2 mg/kg per day in four divided doses for 2 to 6 weeks) .is indicated only in cases of severe carditis

Treatment of CHF includes the following. 7

a. Complete bed rest with orthopneic position and moist, cool oxygen

.b. Prednisone for severe carditis of recent onset

c. Digoxin is used with caution, beginning with half the usual recommended dose, because some patients with rheumatic carditis are supersensitive to digitalis

.d. Furosemide, 1 mg/kg every 6 to 12 hours

:Management of Sydenham's chorea. 8

a. Reduce physical and emotional stress and use protective .measures as indicated to prevent physical injuries

b. Give benzathine penicillin G, 1.2 million units, initially for eradication of streptococci and every 28 days for prevention of recurrence, just as in patients with other rheumatic manifestations. Without the prophylaxis, about 25% of patients with isolated chorea (without carditis) develop rheumatic valvular heart disease .in 20 year follow-up

c. Antiinflammatory agents are not needed in patients with isolated .chorea

d. For severe cases, any of the following drugs may be used: phenobarbital (15–30 mg every 6–8 hours), haloperidol (starting at 0.5 mg and increasing every 8 hours to 2 g), valproic acid, .chlorpromazine and diazepam (Valium), or steroids

RECOMMENDED DURATION OF PROPHYLAXIS FOR RHEUMATIC FEVER

Category	**Duration**
Rheumatic fever without carditis	At least for 5 years or until age 21 years, whichever is longer.1
Rheumatic fever with carditis but without residual heart disease (no valvular disease)	At least for 10 years or well into adulthood, whichever is longer.2
Rheumatic fever with carditis and residual heart disease (persistent valvular disease)	At least 10 years since last episode and at least until age 40 years; sometimes lifelong prophylaxis.3

Prevention

Primary Prevention

Primary prevention of rheumatic fever is possible with a 10-day course of penicillin therapy for streptococcal pharyngitis. However, primary prevention is not possible in all patients because about 30% of the patients develop subclinical pharyngitis .and therefore do not seek medical treatment

Secondary Prevention

?Who should receive prophylaxis. 1

Patients with documented histories of rheumatic fever, including those with isolated chorea and those without evidence of rheumatic .heart disease, must receive prophylaxis

?For how long. 2

Ideally, patients should receive prophylaxis indefinitely. For patients who had acute rheumatic fever without carditis, the prophylaxis should continue for at least 5 years or until the person is 21 years of .age, whichever is longer

,For patients who are in a high-risk occupation (e.g., schoolteachers physicians, nurses), prophylaxis should be continued for a longer period of time. The chance of recurrence is highest in the first 5 years after acute rheumatic fever. If the patient had rheumatic carditis or residual valvular disease as a result of rheumatic fever, the duration of .prophylaxis should be longer

Method of prophylaxis. 3

The method of choice for secondary prevention is benzathine penicillin G, 1.2million units given intramuscularly every 28 days .(not once a month)

:Alternative methods, although not as effective, are the following

a. Oral penicillin V, 250 mg, twice daily

b. Oral sulfadiazine 1 g or sulfisoxazole 0.5 g once daily

c. Oral erythromycin ethyl succinate, 250 mg, twice daily

Complications

Inflammation caused by rheumatic fever can last a few weeks to several months. In some cases, the inflammation .causes long-term complications

Rheumatic heart disease is permanent damage to the heart caused by rheumatic fever. It usually occurs 10 to 20 :years after the original illness. damage can result in

Valve stenosis. This narrowing of the valve decreases .blood flow

Valve regurgitation. This leak in the valve allows blood to .flow in the wrong direction

Damage to heart muscle. The inflammation associated with rheumatic fever can weaken the heart .muscle, affecting its ability to pump

Damage to the mitral valve, other heart valves or other heart tissues can cause problems with the heart :later in life. Resulting conditions can include

An irregular and chaotic beating of the upper chambers of the heart (atrial fibrillation)

An inability of the heart to pump enough blood to the body (heart failure)

Chronic Rheumatic Heart Disease

Mitral Regurgitation

Chronic mitral regurgitation is the most common form of RHD in children and young adults ,whereas mitral stenosis is increasingly common in patients in the fourth to sixth decade of life . In contrast to the chordal elongation and annular dilation that occur with acute rheumatic mitral valvulitis and regurgitation, leaflet shortening, leaflet coaptation and chronic rheumatic mitral regurgitation. In addition, left ventricular dilation may alter the position and orientation of the mitral valve papillary muscles, further impairing leaflet coaptation and resulting rigidity, deformation, and retraction, often associated with chordal fusion and shortening, result in abnormal leaflet in a larger regurgitant orifice and regurgitant volume .

Chronic mitral regurgitation results in compensatory dilation of the left ventricle, allowing for an increased total stroke volume that maintains forward flow. The combination of compensatory dilation of the left ventricle and the left atrium initially prevents a rise in left ventricular filling and left atrial and pulmonary venous pressure

Symptoms, most commonly exertional dyspnea or decreased exercise tolerance, may develop prior to .or with the onset of ventricular dysfunction
In the setting of chronic mitral regurgitation, precordial activity is increased and the apical impulse is displaced because of ventricular dilation. The first heart sound is often softer than normal, and the second heart sound may be widely split because of shortened left ventricular ejection and .earlier aortic valve closure

Aortic Regurgitation

Chronic rheumatic aortic regurgitation occurs because of leaflet thickening, fibrosis, and leaflet contracture, resulting in abnormal leaflet coaptation and a regurgitant orifice. This regurgitation leads to both volume and pressure overload of the left ventricle . During a compensatory phase, ventricular dilation occurs to maintain forward stroke volume and cardiac output, and ejection fraction remains normal. Similar to patients with chronic mitral regurgitation, patients with chronic severe aortic regurgitation may remain asymptomatic for years . Over time, decompensation may occur, resulting in decreased left ventricular function and/or symptoms, most commonly dyspnea on exertion or .decreased exercise tolerance

On examination, significant chronic aortic regurgitation results in a wide pulse pressure (elevated systolic and low diastolic pressures) and bounding pulses. Precordial activity is increased, and the apical impulse is displaced laterally owing to the dilated left ventricle. The typical diastolic murmur of aortic regurgitation is a relatively high-pitched, decrescendo and heard best along the left sternal border with the patient leaning forward at end-expiration. The duration of the murmur rather than the intensity correlates with the severity of regurgitation. A short systolic ejection murmur may be heard at the midleft or upper right sternal border from increased flow across the left ventricular outflow tract or associated aortic valve stenosis. A low-pitched mid- to late-diastolic rumbling murmur in the absence of organic mitral stenosis (Austin Flint murmur) may be audible in .patients with moderate-to-severe aortic regurgitation

Mitral Stenosis

Rheumatic fever resulting in chronic RHD is the most common cause of mitral stenosis. Mitral stenosis does not occur with acute initial carditis. In industrialized countries, the interval between the occurrence of RF and the onset of symptoms from mitral stenosis is usually 15 to 40 years, resulting in presentation in the third to fifth decade of life . In contrast, symptomatic rheumatic mitral stenosis may occur as early as the second decade of life in children from developing countries of the world . Although both greater severity of cardiac involvement with the initial illness and multiple recurrences of RF likely contribute to the development of this more aggressive form of chronic RHD, it is also possible that the disease process itself is different in developing countries of the world . Pure mitral stenosis occurs in about 25% of adults with RHD, and another 40% have combined mitral stenosis and regurgitation . Women are .more likely than men to develop rheumatic mitral stenosis

Aortic Stenosis

Like mitral stenosis, aortic valve stenosis is a form of chronic rather than acute RHD and occurs 20 to 40 years after the acute illness as adhesions, leaflet thickening, fibrosis, commissural fusion, and calcific nodules may develop over time. These changes lead to decreased leaflet mobility, decreased aortic orifice size, and obstruction to flow. Rheumatic aortic stenosis and regurgitation often occur concurrently, usually along with rheumatic mitral valve disease. The increase in stenosis is gradual, allowing for ventricular compensation and the absence of symptoms. With time, compensation fails and symptoms develop (including angina, syncope, dyspnea on exertion, and heart failure), most often in the fifth to . sixth decade of life

Right Heart Involvement

In patients with chronic RHD, tricuspid and/or pulmonary valve involvement may be functional (related to the pulmonary hypertension that may occur with significant left heart disease) or organic (chronic rheumatic changes) . The tricuspid valve is affected more often than the pulmonary valve by the rheumatic process, but clinically significant involvement of either valve is uncommon. Rheumatic tricuspid valve disease (stenosis and/or regurgitation) virtually always occurs with significant mitral or aortic valve disease. Although histologic evidence of rheumatic tricuspid valve involvement may be detectable in 15% to 40% of patients with RHD , significant tricuspid valve disease is detectable by echocardiography in only 7% to 9% and is clinically apparent in 3% to 5% of patients with RHD

HEART DISEASE

- General medical management
- Serial evaluation
- Recognition of progression, symptoms
- Echocardiography: valvular function, chamber sizes, ventricular function, pulmonary pressures
- Education: early recognition of symptoms, prevent complications
- Secondary prophylaxis
- Infective endocarditis prophylaxis
- Activity restrictions based on severity of valvular disease

Mitral regurgitation (MR) (severe) •

Specific medical management: none; no defined role for • .afterload reduction

Indications for surgery: symptoms, ventricular dysfunction, marked ventricular enlargement (possible intervention for severe MR in asymptomatic patients with preserved ventricular function if valve repair likely)

Aortic regurgitation (severe)

Specific medical management: afterload reduction (nifedipine, angiotensin-converting enzyme inhibitors) for asymptomatic patients with preserved ventricular function

Indications for surgery: symptoms, ventricular dysfunction, marked ventricular enlargement

Mitral stenosis

Specific medical management: anticoagulation if history of thromboembolic event and/or atrial fibrillation; possible role for rate control in selected cases

Indications for mechanical intervention (catheter-based or surgical): symptoms, pulmonary hypertension

Percutaneous balloon valvotomy: best results for those with echocardiographic evidence of noncalcified and pliable leaflets, without severe thickening or subvalvular pathology

Surgery (open commissurotomy if possible; valve replacement) in patients not candidates for percutaneous intervention

Aortic stenosis

Specific medical management: none

Indications for surgery (no role for percutaneous balloon valvotomy unless surgery contraindicated): symptoms, ventricular dysfunction, abnormal exercise study