

Rheumatic Heart Disease

History of Presenting Illness

- Dyspnoea on exertion or at rest
- Nocturnal dyspnoea
- Orthopnoea
- Swollen ankles
- "mitral facies"
- Palpitations
- Chest pain

Differential Diagnoses

Aortic Stenosis, Valvar	Human Immunodeficiency Virus Infection
Aortic Valve Insufficiency	Kawasaki Disease
Aortic Valve, Bicuspid	Mitral Stenosis, Congenital
Appendicitis	Mitral Valve Insufficiency
Arthritis, Septic	Mitral Valve Prolapse
Cardiac Tumors	Myocarditis, Viral
Cardiomyopathy, Dilated	Pericardial Effusion, Malignant
Carnitine Deficiency	Pericarditis, Bacterial
Coccidioidomycosis	Pericarditis, Viral
Endocarditis, Bacterial	Sarcoidosis
Heart Failure, Congestive	Systemic Lupus Erythematosus
Histoplasmosis	Transient Synovitis

How is this diagnosis made?

The Jones criteria require the presence of 2 major or 1 major and 2 minor criteria

major diagnostic criteria

- Carditis
- Polyarthritis
- Chorea
- subcutaneous nodules
- erythema marginatum

minor diagnostic criteria

- fever
- arthralgia
- prolonged PR interval on ECG
- elevated ESR or CRP
- leukocytosis

Additional evidence of previous group A streptococcal pharyngitis is required

- Positive throat culture or rapid streptococcal antigen test
- Elevated or rising streptococcal antibody titer
- History of previous rheumatic fever or rheumatic heart disease

Pertinent Findings on History

- **PAST HISTORY OF RHEUMATIC HEART DISEASE:** most important.
- **CHILDHOOD STREP THROAT:** school age (peak 5-15years)

Findings on Examination

CARDIAC MANIFESTATIONS:

Rapid irregular pulse!! → AF

- Pancarditis is the most serious and second most common complication of rheumatic fever (50%). In advanced cases, patients may complain of dyspnea, mild-to-moderate chest discomfort, pleuritic chest pain, edema, cough, or orthopnea.
- **carditis** is most commonly detected by a new murmur and tachycardia out of proportion to fever.
- **Apical pansystolic murmur** is a high-pitched, blowing-quality murmur of mitral regurgitation that radiates to the left axilla. The murmur is unaffected by respiration or position. Intensity varies but is grade 2/6 or greater. The mitral insufficiency is related to dysfunction of the valve, chordae, and papillary muscles.

- **Apical diastolic murmur** = active carditis = severe mitral insufficiency; It is related to relative mitral stenosis, = is low pitched, rumbling, and resembles the roll of a distant drum.
- **Basal diastolic murmur** is an early diastolic murmur of aortic regurgitation and is high-pitched, blowing, decrescendo, and heard best along the right upper sternal border after deep expiration while the patient is leaning forward.

Congestive heart failure:

- tachypnea, orthopnea, jugular venous distention, rales, hepatomegaly, a gallop rhythm, and peripheral swelling and edema.
 - **MITRAL STENOSIS:** On auscultation, S₁ is initially accentuated but becomes reduced as the leaflets thicken.
 - P₂ becomes accentuated, and the splitting of S₂ decreases as pulmonary hypertension develops.
 - **An opening snap** of the mitral valve often is heard at the apex, where a diastolic filling murmur also is heard.

NON-CARDIAC MANIFESTATIONS:

- **Polyarthritis** = the earliest manifestation of acute rheumatic fever (70-75%).
 - Characteristically, the arthritis begins @ knees and ankles
 - Migrates to other large joints in the lower or upper extremities (elbows and wrists). Affected joints are painful, swollen, warm, erythematous, and limited in their range
 - **The pain is out of proportion to clinical findings.**
 - The arthritis reaches maximum severity in 12-24 hours, persists for 2-6 days (rarely more than 3 wk) at each site, and **responds rapidly to aspirin.**
 - Aspirin improves symptoms in affected joints and prevents further migration of the arthritis. Polyarthritis is more common and more severe in teenagers and young adults than in younger children.
- **Sydenham chorea** occurs in 10-30% of patients with rheumatic fever
 - = difficulty writing, involuntary grimacing, purposeless (choreiform) movements of the arms and legs, speech impairment, generalized weakness, and emotional lability.
 - Physical findings include hyperextended joints, hypotonia, diminished deep tendon reflexes, tongue fasciculations ("bag of worms"), and a "milk sign" or relapsing grip demonstrated by alternate increases and decreases in tension when the patient grips the examiner's hand.
 - **In the absence of a family history of Huntington chorea, the diagnosis of acute rheumatic fever is almost certain.**
Onset = 1-6 months after streptococcal pharyngitis
- **Erythema marginatum**, also known as erythema annulare, is **a characteristic rash that occurs in 5-13% of patients with acute rheumatic fever.**
 - It begins as 1-3 cm in diameter, pink-to-red nonpruritic macules or papules located on the trunk and proximal limbs but never on the face.
 - The lesions spread outward to form a serpiginous ring with erythematous raised margins and central clearing. The rash may fade and reappear within hours and is exacerbated by heat.
- **Abdominal pain** usually occurs at the onset of acute rheumatic fever
- **NSAIDs may suppress the full manifestations of the disease.**

Tests and Investigations

Lab Studies:

- **Throat culture:** *USELESS as by the time you get heart symptoms it may have been decades since the first strep infection.*
- **Rapid antigen detection test:**
 - This test allows rapid detection of group A streptococcal antigen

- **Antistreptococcal antibodies:**

clinical features of RF begin at the time antistreptococcal antibody levels are at their peak.

antistreptococcal antibody testing is useful for confirming previous group A streptococcal infection. **THIS SATISFIES THE THIRD CRITERION**

COMMONEST ANTIBODIES TESTED:

- antistreptolysin O (ASO),
- anti-deoxyribonuclease (DNase) B,
- antihyaluronidase,
- antistreptokinase,
- antistreptococcal esterase,
- and anti-DNA.
- antistreptococcal polysaccharide,
- antiteichoic acid antibody,
- and anti-M protein antibody.

In general, the ratio of antibodies to extracellular streptococcal antigens rises during the first month after infection and then plateaus for 3-6 months before returning to normal levels after 6-12 months. When the ASO titer peaks (2-3 wk after the onset of rheumatic fever), the sensitivity of this test is 80-85%. The anti-DNase B has a slightly higher sensitivity (90%) for detecting rheumatic fever or acute glomerulonephritis. Antihyaluronidase results are frequently abnormal in rheumatic fever patients with a normal level of ASO titer and may rise earlier and persist longer than elevated ASO titers during rheumatic fever.

Acute phase reactants:

The C-reactive protein and erythrocyte sedimentation rate are elevated in rheumatic fever due to the inflammatory nature of the disease. Both tests have a high sensitivity but low specificity for rheumatic fever. They may be used to monitor the resolution of inflammation, detect relapse when weaning aspirin, or identify the recurrence of disease.

Heart reactive antibodies: Tropomyosin is elevated in acute rheumatic fever.

Rapid detection test for D8/17:

This immunofluorescence technique for identifying the B cell marker D8/17 is positive in 90% of patients with rheumatic fever. It may be useful for identifying patients who are at risk for developing rheumatic fever.

Imaging Studies:

Chest Xray:

- Cardiomegaly,
- pulmonary congestion,
- other findings consistent with heart failure may be seen on chest x-ray. When the patient has fever and respiratory distress, the chest x-ray helps differentiate heart failure from rheumatic pneumonia.

Doppler-echocardiogram: the KING of heart valve imaging

!! identifies and quantitates valve insufficiency and ventricular dysfunction!!

mild carditis= Doppler evidence of **mitral regurgitation** may be present during the acute phase... resolves in weeks to months.

moderate-to-severe carditis = persistent mitral and/or aortic regurgitation.

The most important echocardiographic features of mitral regurgitation from acute rheumatic valvulitis are
annular dilatation,
elongation of the chordae to the anterior leaflet,
and a posterolaterally directed mitral regurgitation jet.

The leaflets of affected valves become diffusely thickened, with fusion of the commissures and chordae tendineae. **Increased echodensity of the mitral valve may signify calcification.**

ECG

BUT MOST IMPORTANTLY: ATRIAL FIBRILLATION
as the result of atrial dilation, secondary to valve incompetence

Sinus tachycardia

First-degree atrioventricular (AV) block (prolongation of the PR interval)

Second-degree (intermittent) and third-degree (complete) AV block

→ with progression to ventricular standstill

Heart block in the setting of rheumatic fever typically resolves with the rest of the disease process.

Pericarditis? → ST segment elevation may be present and is marked most in lead II, III, aVF, and V₄-V₆.

Disease Definition

cross-reactivity resulting in loss of self tolerance, leading to autoimmune mitral valve scarring

secondary to inflammation, causing obstruction of ventricular inflow leading to:

increased pressure in pulmonary vasculature (pulmonary oedema);

increased pressure and dilatation of right heart + decreased venous return;

poor cardiac output leading to increased fluid in peripheral vasculature pooling in tissues (peripheral oedema).

Management

Digoxin for atrial fibrillation

ANTICOAGULANTS to prevent atrial thrombus

Valve replacement for valve dysfunction

Loop diuretics for CHF

Heparin for atrial thrombus

Rheumatic fever was the leading cause of death in people aged 5-20 years in the United States 100 years ago. At that time, the mortality rate was 8-30% from carditis and valvulitis but decreased to a 1-year mortality rate of 4% by the 1930s. Following the development of antibiotics, the mortality rate decreased to almost 0% by the 1960s in the developed countries (still 1-10% elsewhere)

Prognosis

Manifestations of acute rheumatic fever **resolve over a period of 12 weeks** in 80% of patients
may **extend as long as 15 weeks** in the 20% remaining patients.

The type of treatment and the promptness with which treatment is initiated does not affect the likelihood of disappearance of the murmur.

Incidence of residual rheumatic heart disease at 10 years is 34% in patients without recurrences but 60% in patients with recurrent rheumatic fever.

Disappearance of the murmur happens within 5 years in 50% of patients.

~The disease is more severe in females than in males~

Epidemiology

- **The mitral valve** is most commonly and severely affected (65-70% of patients),
- **the aortic valve** is second in frequency (25%).
- **The tricuspid valve** is deformed in only 10% of patients and almost always is associated with mitral and aortic lesions.
- **The pulmonary valve** is rarely affected.
- **Severe valve insufficiency** during the acute phase may result in congestive heart failure and even death (1% of patients).
- **Pericarditis**, when present, rarely affects cardiac function or results in constrictive pericarditis.

Frequency:

- Incidence has decreased in the past 80 years.
- Prevalence in the United States now is less than 0.05 per 1000 population,
- In the early 1900s, incidence was reportedly 5-10 cases per 1000 population.

Internationally:

- the incidence **has not decreased** in developing countries.
- Estimations worldwide are that 5-30 million children and young adults have chronic rheumatic heart disease,
- 90,000 patients die from this disease each year.

Race:

- Native Hawaiian and Maori (both of Polynesian descent) have a higher incidence of rheumatic fever, 13.4 per 100,000 hospitalized children per year, even with antibiotic prophylaxis of streptococcal pharyngitis.
- Otherwise, race has not been documented to influence disease incidence.

Sex:

- Rheumatic fever occurs in equal numbers in males and females
- **but the prognosis is worse for females than for males.**

MECHANISM OF RHEUMATIC HEART DISEASE

~ Initial infection and immune disposal thereof ~

Acute Infection with B-hemolytic Group A Streptococcus (GAS)
reservoir = humans, cattle;
risk group = 5-15 year old
+ developing countries

Incubation 1-3 days

**Sore throat,
fever,
fatigue**

**Specific
immune
response**

**HLA DR-2, 4
phenotype
predisposes**

Immune response wipes out the GAS, but at what cost!!
B-cell mediated response: thus
**IgG Antibodies
are produced**

~ 1-5 weeks later: Rheumatic Fever PANCARDITIS ~

symptoms recur each time
a strep infection is encountered
and IgG titres rise

M-proteins
→ cross-react with MYOSIN in
the myocardium

Hyalouronate
→ cross-reacts with the HYALIN
lining of the heart valves
(and many other places)

M-proteins in bacterial cell wall
Hyalouronate in capsule
DNase B
Streptokinase
Streptolysin O

**COMPLEMENT
MEDIATED
PANCARDITIS**

**Aschoff nodules
granulomatous inclusions)**
begin to appear in the heart muscle

**COMPLEMENT-MEDIATED
LYSIS OF VALVE LINING**

Cross-reactivity leads to
inflammation of JOINTS
(migratory polyarthritits)
+ **erythema marginatum**
(ag-Ab complexes deposited
subcutaneously)
+ **CHOREA** somehow (?)

~DECADES LATER:

RHEUMATIC HEART DISEASE ~

Interruption of conduction in
scarred fibrotic myocardium
→ **ARRHYTHMIA**

Vegetations make excellent
substrate for development of
bacterial endocarditis

**Destruction of hyaline exposes
COLLAGEN TO THE BLOOD**

Clotted VEGETATIONS grow on
the exposed valve surfaces

ORGANISATION
i.e collagen deposition by fibroblasts

Reduced valve TRANSPARENCY
Reduced valve ELASTICIT
Increased valve VASCULARITY
~CALCIFICATION~
...thus cusp fixation

**Thickening and
shortening of the
CHORDAE TENDINAE**

REGURGITATION

STENOSIS

Mitral Stenosis

Mitral Regurg

Aortic Stenosis

Aortic Regurg

Pressure and/or volume overload
causing **atrial enlargement**

Chronic ventricular volume/pressure
overload cause dilation and hypertrophy

Pulmonary hypertension
causing R heart failure

↓ Cardiac Output
compensated by ↑ HR

Peripheral oedema

• **Dyspnea**
• **Pulmonary oedema**
• **Pink frothy sputum**
• **Fatigue**
• **Arrhythmia**
• **crackles**

• **Angina** due to ↑ O₂ demand
and decreased coronary
blood supply
• **Syncope**
• **Dyspnea**
• **Fatigue**
• **Decreased exercise
tolerance**

A stretched atrium is an unhappy, fibrotic atrium.
THUS: fibrosis causes interruption of normal conduction
THEREFORE : → **ATRIAL FIBRILLATION**
→ this leads to **STASIS** in the ATRIAL AURICLE
and therefore the risk of a huge **THROMBUS**
→ just waiting to lodge in your brain.

Pregnancy exacerbates symptoms
• ↑ metabolic demand
• progesterone induced
vasodilation ↑ cardiac
demand

Microbiology: KNOW THINE ENEMY

Group A *Streptococcus*

- **gram-positive coccus**
- frequently colonizes the skin and oropharynx.
- Group A streptococci elaborate the **cytolytic toxins streptolysins S and O**.
 - streptolysin O induces persistently high antibody titers
 - **THUS** = useful marker of group A streptococcal infection

Why is it called group A? = has a group A carbohydrate antigen in the cell wall that is composed of a branched polymer of *L*-rhamnose and *N*-acetyl-D-glucosamine in a 2:1 ratio. = barely relevant or memorable ☹

- The presence of the M protein is the most important virulence factor for group A streptococcal infection in humans. This is because anti-M antibodies against the streptococcal infection may cross react with heart tissue.
- Streptococcal antigens that are structurally similar to those in the heart include
 - hyaluronate in the bacterial capsule,
 - cell wall polysaccharides (similar to glycoproteins in heart valves),
 - and membrane antigens that share epitopes with the sarcolemma and smooth muscle.

Pathology of OEDEMA

1) **Oedema PITS**, i.e a depression remains when a finger is jabbed into the oedematous limb.

Factors which influence the movement of fluid:

the **hydrostatic pressure within the capillary** vs. the **hydrostatic pressure within the interstitial space**
(~ 25 mm Hg) (~ zero)

colloid osmotic pressure in the capillary vs. **colloid osmotic pressure within the interstitial space**
(~ 20 mm Hg)

*The rate at which fluid crosses the capillary wall is then
the sum of these four pressures multiplied by the capillary permeability
PLUS: Lymphatics can also remove the interstitial fluid.*

THEREFORE:

Oedema results when any of these variables change.

Eg: increase in hydrostatic capillary pressure caused by water retention (eg. RAAS-compensated heart failure)

Eg: decrease in plasma colloid osmotic pressure

Eg: increase in capillary permeability, such as caused by anaphylaxis

Eg: blockage of lymphatic drainage

Atrial Fibrillation

5.03

= the most common of the cardiac arrhythmias.

prevalence increases with age, and 2-5% of those older than 60 have AF.

Paroxysmal episodes of AF often precede chronic (permanent) AF.

- **Aetiology**

AF associated with:

- mitral valve disease,
- hypertensive heart disease,
- ischaemic heart disease,
- thyrotoxicosis,
- cardiomyopathy
- idiopathic (lone fibrillation).
- open heart surgery, 20 to 30% of patients in 1st week.

Persistent untreated AF leads to heart failure and thrombus formation within the distended auricle, where there is stasis. And if that thrombus breaks off...

Mechanism of atrial fibrillation

caused by multiple wandering depolarisation waves; minimum of 6 is required.
Increased atrial pressure → stretching of atrial wall → damage to myocytes
Therefore → fibrosis and interruption of normal depolarisation pathway.

!! AV node transmits all or nothing !!

THUS: AF turns into an **irregularly irregular rhythm**

In untreated AF the ventricular rate is usually between 150 and 200 beats per minute.

!! DANGEROUS !!

Symptoms

most common = **rapid irregular palpitations**. + fatigue.

If heart failure develops

- dyspnoea,
- ankle swelling
- abdominal distension.

Signs

Pulse = rapid and irregularly irregular.

pulse rate may be significantly lower than the heart rate.

This is known as the "pulse deficit".

Diagnosis by ECG:

P waves are absent and instead a **finely undulating baseline** is present.
(frequency of 350-600)

QRS complexes occur irregularly with an average rate of 150 to 200 beats per minute

Treatment

TREAT THE CAUSE!!

Drug Treatment

EITHER control the ventricular rate by increasing the degree of block in the AV node.

Drugs which are used for rate control include **digoxin, verapamil and beta blockers**.

OR give drugs to revert the AF and thereafter to decrease the frequency of further episodes.

Drugs used for this purpose include **sotalol, amiodarone and flecainide**.

DC Cardioversion

DC shock to the praecordium designed to revert the arrhythmia.

Anticoagulation : ABSOLUTELY VITAL

In patients with rheumatic valve disease and AF, the incidence of stroke is increased between 15 and 20 times above that of the general population

... but patients with AF and no heart disease do not have an increased risk of stroke.

The risk of serious thromboembolism in patients with AF is about 5% per year. Warfarin decreases this risk to about 1% per year. The risk of serious haemorrhage whilst taking warfarin is < 1% per year. **Patients with lone AF are not given warfarin.**

Aspirin has also been used to decrease the risk of thromboembolism but is only about 25%-50% as effective as warfarin.

Curative Procedures

"open-heart" surgical procedure in which a number of incisions are placed in the atria to create lines of block so that the multiple reentrant circuits cannot develop.

Several catheter ablation techniques have also been developed but currently these are regarded as investigational since the safety and efficacy have not yet been determined.

DRUG Tx FAILED? Try AV Nodal Ablation and Implantation of Pacemaker

In some patients with AF the ventricular rate remains high despite drug therapy. In these patients the ventricular rate may be controlled by intentionally destroying the AV node using catheter ablation techniques. A pacemaker must be implanted to treat the resulting bradycardia. Since the atria continue to fibrillate, anticoagulation must be continued after this procedure.

- changes occur **early in pregnancy** and
 - **precede** the fetal demand
 - **exceed** fetal demand
- are **all completely reversed** after delivery

The changes that involve the cardiovascular system specifically are

- the formation of a **low resistance vascular network in the uterus** which **contains approximately 1 litre of blood at term**
- progesterone induced vasodilatation in the body causing a marked increase in regional blood flow
 - kidney flow increases by 60% to improve excretion
 - skin flow increases by 50% to improve heat loss
 - liver flow increases by 50% to improve hepatic function
 - increase in gut flow improves nutrient absorption
 - increase in blood flow to the breast is approximately 200% over non pregnant levels to ensure that the breasts are developed ready for feeding the infant.
 - uterine flow increases from 30mls/min in the non-pregnant woman to 600mls/min at term 7
- **the only organ not to have increased blood flow is the brain**

PROGESTERONE VASODILATES; thus → proneness to syncope

The maximum of vasodilatation occurs in the middle trimester.

- **Plasma volume increases by 40%.** → due to RAAS (aldosterone produced by renin secretion)
- = related to fetus size
- **Red cell mass increases by 18-20%.** This increase is smaller than that of the plasma volume and a physiological anaemia therefore results with the normal haemoglobin level being between a 105-140 grams/litre at term.

PROGESTERONE VASODILATION → FALL IN BLOOD PRESSURE is offset by the INCREASE IN BLOOD VOLUME And INCREASE IN CARDIAC OUTPUT But:

cardiac reserve **decreases** (the ability to increase cardiac output above the normal level).

This means that pregnant women are prone to congestive heart failure if they have an abnormal heart or if they are treated with drugs or fluids that speed up the heart rate, drop the blood pressure, or increase circulating volume.

- **The increase in the uterine size causes an upward pressure on the diaphragm.**

This upward pressure on the diaphragm causes a **right axis shift on the ECG**

JVP is chronically (unreliably) raised with pregnant women

Activation of the Heart 5.03 LT

* FASTEST PACEMAKER DOMINATES! *

SA Node = PRIMARY; Rate ≈ 60 - 100 (∴ = DOMINANT)

AV Node = Secondary; Rate ≈ 40

Purkinje Fibres = TERTIARY; RATE = 25 - 40

	SAN	AVN	Purkinje	Ventricular muscle
Rate	60 - 100	~ 40	25 - 40	N/A
Conduction V	Small cells 0.05 m/sec	Small cells 0.05 m/sec	LARGE DIAMETER ∴ 4 m/sec	1 m/sec
Approx. delay				

HEART FAILURE AND VALVE DISEASE: *the vicious cycle*

Organic valve disease = deformity of the valve, eg. Rheumatic Valve Vegetations.

FUNCTIONAL valve disease → the valve is structurally normal, but it still malfunctions
Eg. BECAUSE the super-dilated ventricle won't let it close
(the ring which forms the valve ring is stretched too far for the cusps to meet; → regurg)

THERE ARE 2 COMPONENTS TO THIS:

Backward Failure (eg. venous congestion therefore oedema, pulmonary congestion)

Forward failure (eg. reduced output, analogous to shock hypotension and thus responsible for activating the RAAS system)

REACTION TO LEFT VENTRICULAR STRAIN:

IMMEDIATE DILATATION: thus immediate increase in force of contraction
via the Frank-Starling sarcomeric stretch response

LONG TERM HYPERTROPHY: limited by perfusion distances, i.e. there is only
so far you can thicken the heart wall until the
myocardocytes inside won't be getting enough nutrients.
Therefore, hypertrophy → ischaemic disease

DELAYED DILATATION at this point will indicate **DECOMPENSATION**

LV FAILURE → Increased Left Atrial afterload

Which has a weak thin wall and can't possibly pump
against that sort of afterload

THEREFORE it fails! → BUT the right ventricle is still
pumping away, being healthy, **THUS:**

Pulmonary blood is not being cleared quickly enough

THUS → PULMONARY VENOUS CONGESTION

When the pressure increases enough, the blood pools
there and RBCs extravasate into the alveolar lumen

→ **PINK FROTHY SPUTUM**

→ **ORTHOPNOEA** (when lying down, the oedematous
fluid spreads all over)

LA FAILURE → PULMONARY CONGESTION → RV FAILURE!!

Rt ventricle can't handle the afterload either;

→ **COR PULMONALE**

→ Rt ventricle is $\frac{1}{3}^{\text{rd}}$ the thickness of the left;
thus it fails three times as quickly

→ **RHF: hepatic (portal) hypertension, hepatosplenic
venous congestion**

THIS LEADS TO NECROSIS AND FATTY CHANGE

LOW ALBUMIN (failing ischaemic liver) →

→ **MORE OEDEMA**

→ **RAAS activated by renal ischaemia (from
forward failure)**

→ **HYPERTENSION !!**

→ **AMPLIFIED OEDEMA!!**

→ **MORE LOAD ON THE POOR FAILING LEFT VENTRICLE!! →**

~ DECOMPENSATED END-STAGE HEART FAILURE ~