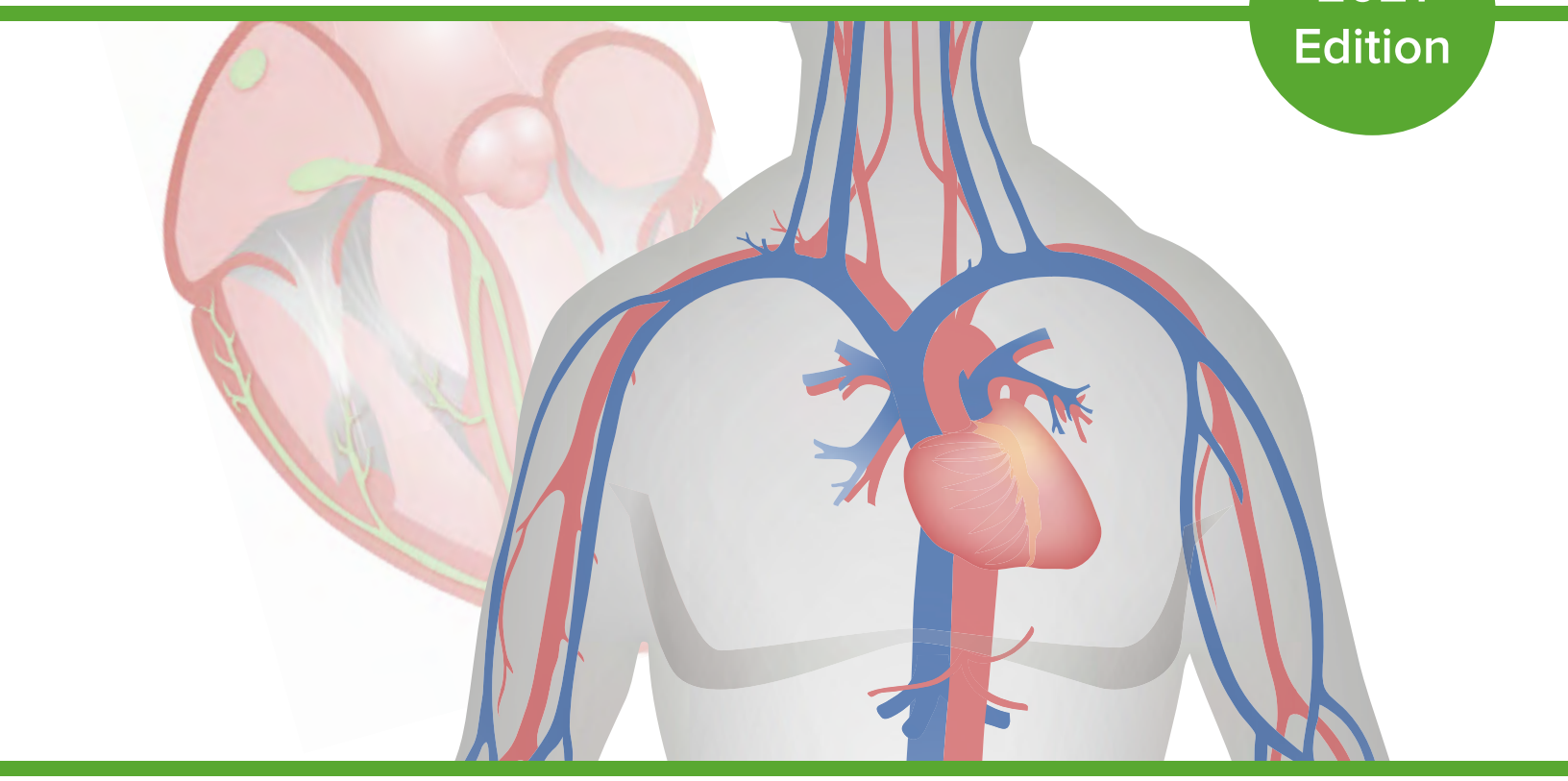
Cardiovascular Pathology

The Perfect Preparation for USMLE® Step 1

2021 Edition



> You cannot separate passion from pathology any more than you can separate a person‘s spirit from his body.
>
> *(Richard Selzer)*

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Cardiovascular Pathology eBook

> Live as if you were to die tomorrow.
> Learn as if you were to live forever.
> *(Mahatma Gandhi)*

Pathology is one of the most-tested subjects on the USMLE® Step 1 exam. At the heart of the pathology questions on the USMLE® exam is cardiovascular pathology. The challenge of cardiovascular pathology is that it requires students to be able to not only recall memorized facts about cardiovascular pathology, but also to thoroughly understand the intricate interplay between cardiovascular physiology and pathology. Understanding cardiovascular pathology will not only allow you to do well on the USMLE® Step 1 exam, but it will also serve as the foundation of your future patient care.

This eBook...

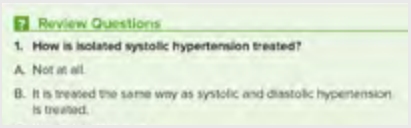
- ✓ ...will provide you with everything you need to know about cardiovascular pathology for your **USMLE® Step 1** exam.
- ✓ ...will equip you with knowledge about the most important diseases related to the cardiovascular system, as well as build bridges to the related medical sciences, thus providing you with the **deepest understanding** of all cardiovascular pathology topics.
- ✓ ...is specifically for students who already have a **strong foundation** in the basic sciences, such as anatomy, physiology, biochemistry, microbiology & immunology, and pharmacology.

Elements of this eBook

High-yield:
Murmurs of grade III and above are usually pathological. (...)

High-yield-information will help you to focus on the most important facts.

A number of **descriptive pictures, mnemonics, and overviews**, but also a reduction to the essentials, will help you to get the best out of your learning time.



Did you not only read the section but also understand it? Our **review questions** ensure your learning success.

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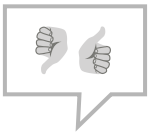

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Introduction

Cardiovascular diseases are conditions that affect different structures of the heart, ranging from vascular disorders such as coronary and peripheral arterial diseases, to cardiac disorders based on the affected anatomical structure of the heart. Ischemic heart disease (IHD) is the leading cause of death and disability worldwide and can be prevented by lifestyle changes such as quitting smoking, exercising, and following a healthy diet, and correcting its risk factors (such as diabetes, dyslipidemia, and obesity) in their early stages. IHD can range from asymptomatic coronary heart disease through to stable/unstable angina and myocardial infarction, with several consequences, such as chronic heart failure, arrhythmias, and even death. Valvular heart diseases are also common in practice, taking the forms of stenosis, insufficiency, or a combination of the two. These structural changes result from either underlying congenital conditions or acquired causes, including infections, ischemic heart disease, or degenerative processes. The type of valvular disease is determined by the levels of ongoing cardiac stress and the severity of presenting symptoms. In this eBook, we will describe the different cardiovascular disorders in detail, providing a high-quality review for your USMLE exam.

Chapter 1:
Heart Sounds

General Introduction

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Types, Origins and Timing of Heart Sounds

On auscultation, 2 heart sounds are heard from a normal heart, which are described as the **first and second heart sounds**. Additional heart sounds may be present, namely the third and fourth heart sounds. Further sounds such as **murmurs** may also be heard upon auscultation of the heart.

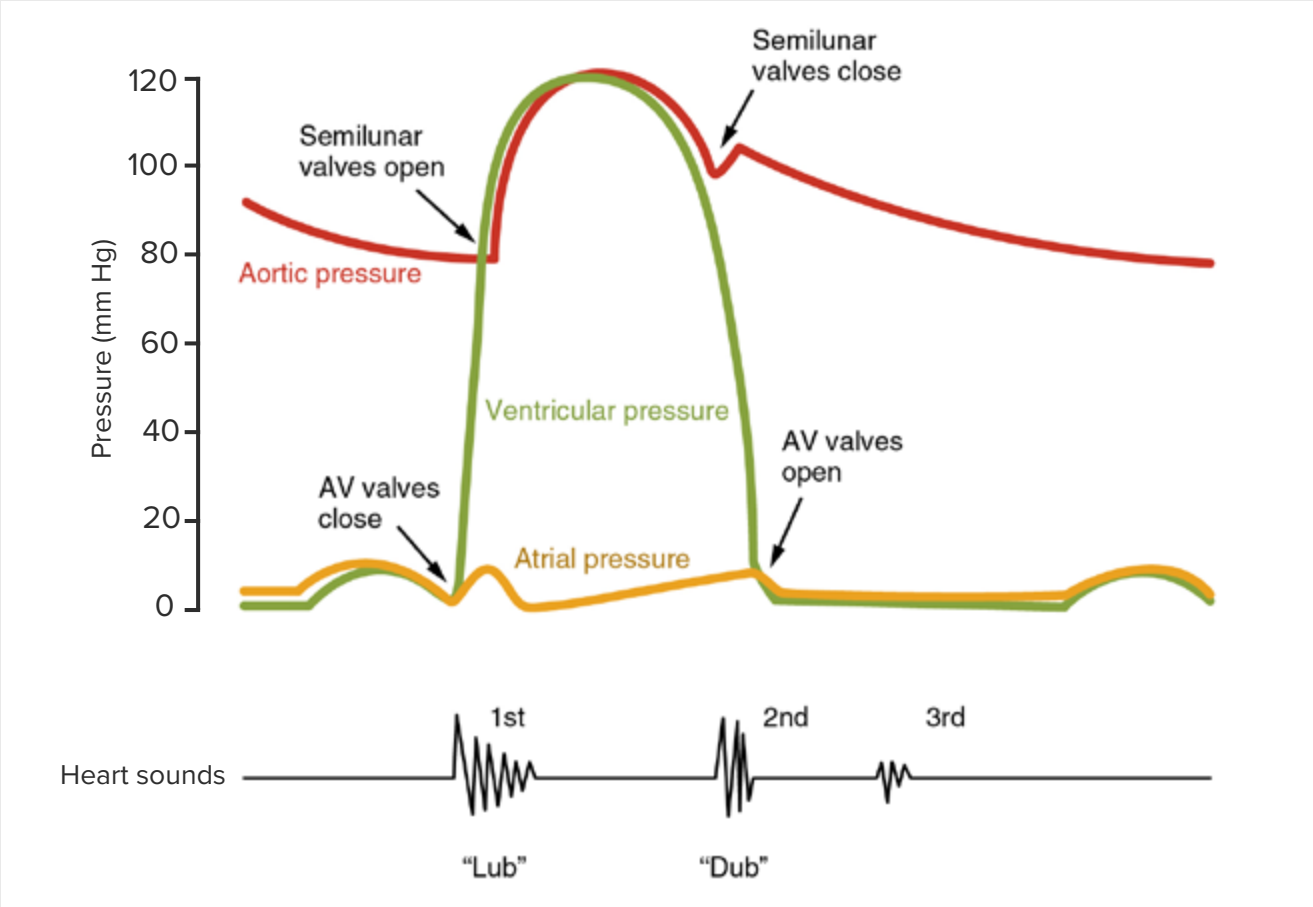


Fig. 1-01: Heart Sounds and the cardiac cycle

First and second heart sounds

The closure of the heart valves produces vibrations that are picked up as the 2 heart sounds.

The first heart sound, S1, corresponds with the **closure of the atrioventricular valves** – the tricuspid and mitral valves of the heart. S1 represents the **start of ventricular systole**. The closure of the mitral valves precedes the closure of the tricuspid valves; however, the time between them is minimal so that S1 is usually heard as a single sound. S1 is best heard at the apex of the heart.

The second heart sound, S2, corresponds with the **closure of the semilunar valves** – the aortic and pulmonary valves of the heart. S2 signifies the **end of ventricular systole** and the **beginning of diastole**. Compared to the first heart sound, S2 is shorter, softer, and slightly higher in pitch. A reduced or absent S2 indicates pathology due to an abnormal aortic or pulmonic valve.

Fig. 1-02: (A) Heart sound S1 (B) Heart sound S2

The aortic valves shut before the pulmonary valves. This is due to lower pressures in the pulmonary circulation which allows blood to continue flowing into the pulmonary artery after systole ends in the left ventricle. In 70 % of normal adults, this difference can be heard as the splitting of the second heart sound.

The pulmonary component of S2 is referred to as P2; the aortic component is called A2. Splitting is best heard in the pulmonary area (second left intercostal space) and at the left sternal edge.

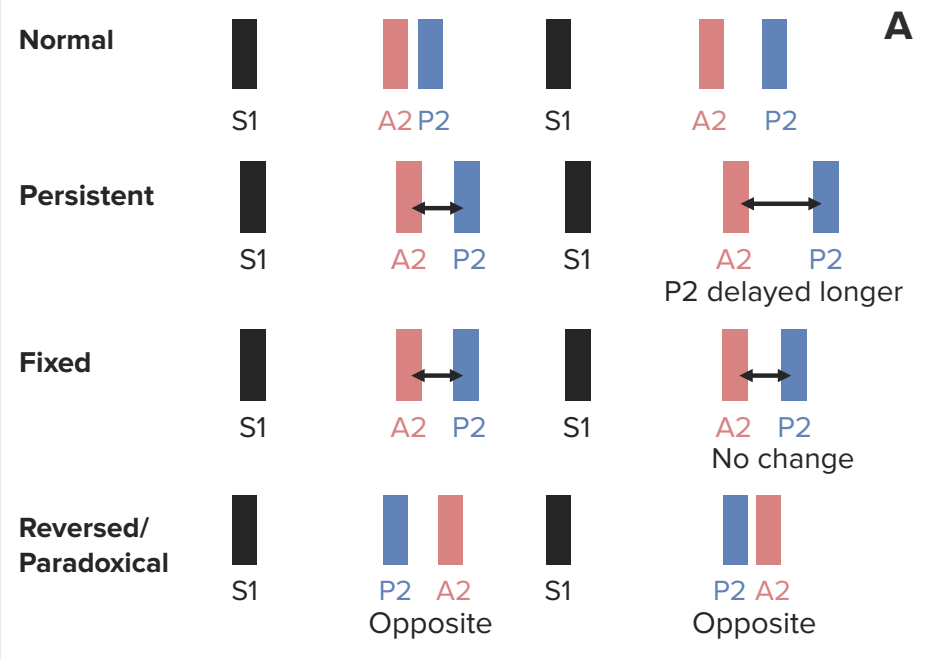
Splitting of the second heart sound

1) Physiological splitting of S2:

- Inspiration delays closure of the pulmonary valves by about 30—60 milliseconds due to increased venous return and decreased pulmonary vascular resistance. This is called **the physiological splitting of S2.**

2) Abnormal splitting of S2:

- Wide splitting of S2: An exaggerated (persistent) physiological split that is more pronounced during inspiration.
- Fixed splitting of S2: Fixed delay of P2 closure due to increased right-sided volume (ASD or advanced RV failure).
- Reversed or paradoxical splitting of S2: Aortic valve closure delayed due to obstruction (AS) or conduction disease (LBBB). Split narrows with inspiration as pulmonic valve closure is delayed moving P2 closer to a delayed A2 where the sound becomes single.



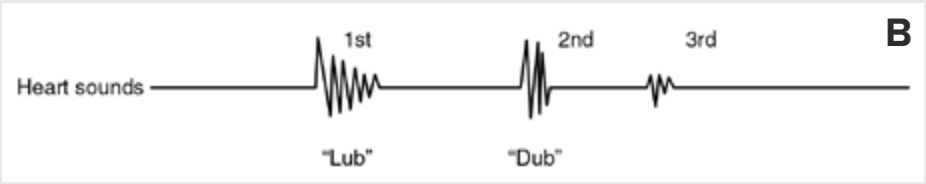


Fig. 1-03: *(A) Types of abnormal splitting of S2 are wide, fixed and paradoxical splitting (B) Heart sounds*

Extra Heart Sounds

Third heart sound (S3)

Extra heart sounds include the third and fourth heart sounds. The **third heart sound (S3) is a mid-diastolic, low-pitched sound**. With the presence of S3, heart sounds are described as having a **gallop rhythm**, simply because its addition alongside S1 and S2 make it sound like a horse galloping. S3 occurs after S2, during the rapid passive filling of the ventricle.

A physiological S3 is produced when there is rapid filling during diastole as can happen in conditions which increase cardiac output such as thyrotoxicosis and pregnancy; this might also be a pediatric finding. On the other hand, **a pathological S3** is produced when there is decreased compliance of the ventricle (dilatation or overload), causing a filling sound.

Causes of a pathological S3 include conditions that reduce left ventricular compliance, such as left ventricular failure, left ventricular dilation, aortic regurgitation, mitral regurgitation, patent ductus arteriosus, and a ventricular septal defect. Conditions with reduced right ventricular compliance can also cause a pathological S3. These include right ventricular failure and constrictive pericarditis.

High-yield:

Absent splitting of S2 can be seen in:

- *Severe aortic stenosis (in elderly patients)*
- *VSD with Eisenmenger syndrome (in pediatric patients)*

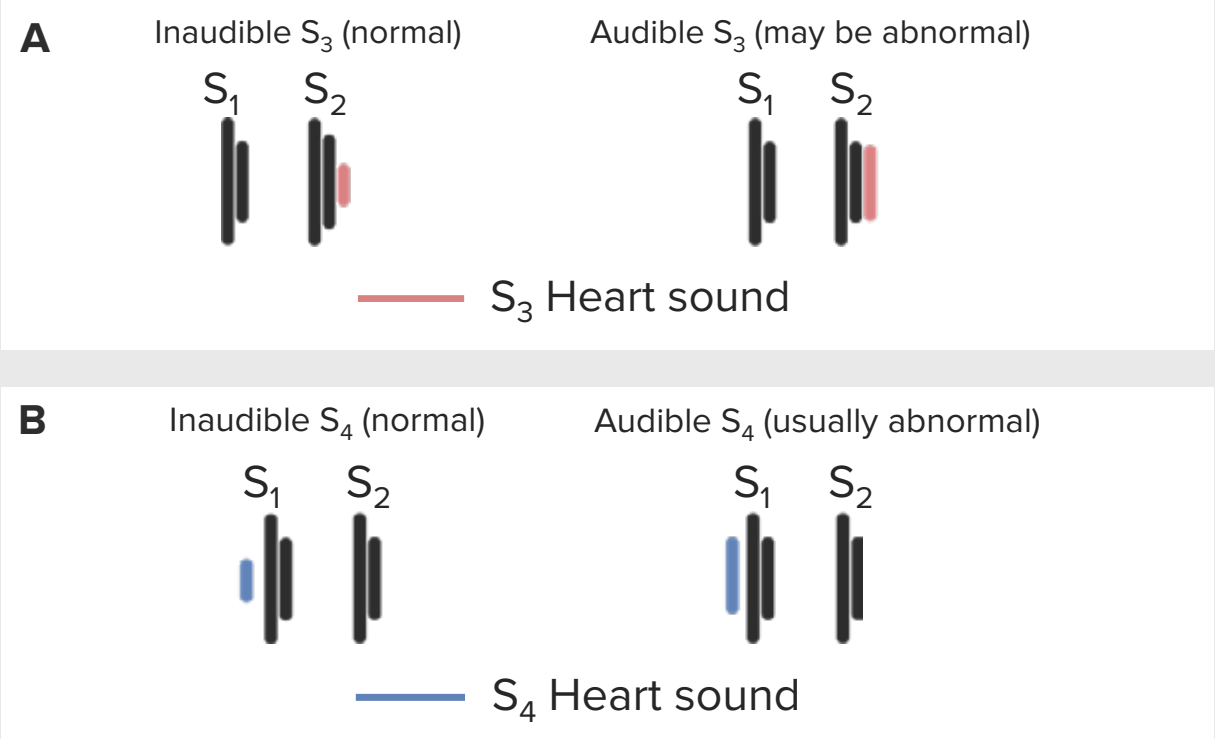


Fig. 1-04: *(A) Heart sound S3 (B) Heart sound S4*

Fourth heart sound (S4)

The fourth heart sound (S4) is a late diastolic sound. It is of a slightly higher pitch than S3. S4 also sounds similar to a **triple gallop rhythm**. S4 occurs slightly before S1 and is associated with atrial contraction and rapid active filling of the ventricle.

S4 is caused by decreased ventricular compliance. Reduced left ventricular compliance, as in aortic stenosis, mitral regurgitation, hypertension, angina, myocardial infarction, and old age, can produce an S4. Reduced right ventricular compliance, as in pulmonary hypertension and pulmonary stenosis, can similarly cause an S4.

It is possible for the third and fourth heart sounds to co-exist, in which case this is called a **quadruple rhythm**. This indicates significantly impaired ventricular function. If S3 and S4 are superimposed when tachycardia is present, a **summation gallop** is produced.

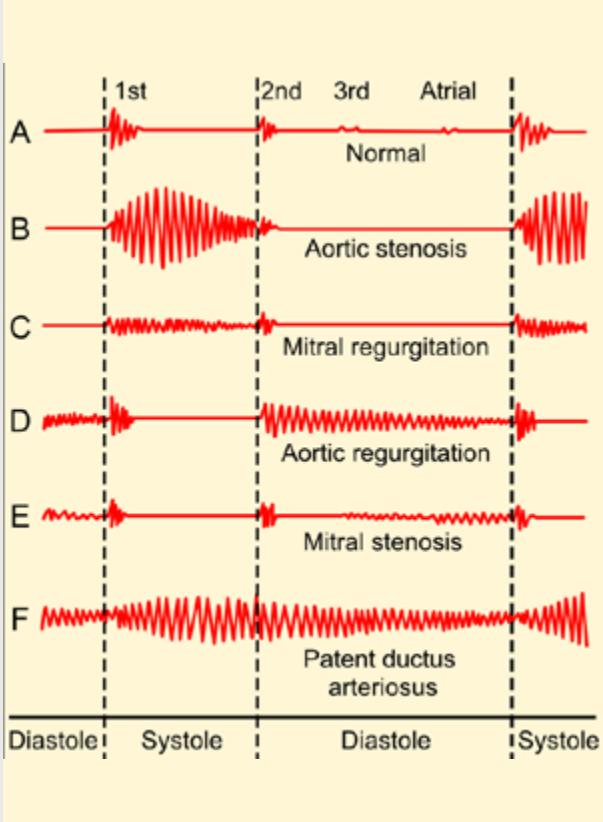


Fig. 1-05: Phonocardiograms from normal and abnormal heart sounds

Murmurs

A **murmur** is a sound produced by turbulent blood flow across a heart valve. Turbulent flow can occur due to 2 reasons: firstly, when the blood flows across an abnormal heart valve, and secondly when an increased amount of blood flows across a normal heart valve. Heart murmurs may be classified as physiological or innocent, with **pathologic murmurs being based upon the cause of the turbulence.**

A **physiological murmur** is heard when there is an **increased turbulence of blood flow across a normal valve**, as can happen in the conditions thyrotoxicosis and anemia, as well as during fever and exercise. Physiologic murmurs are always systolic murmurs, as increased blood flow occurs during ventricular systole. They are more likely to be found in young people. Innocent murmurs also have the qualities of being soft, short, early peaking, mostly confined to the base of the heart, having a normal second heart sound, and generally disappearing with a change in position. The rest of the cardiovascular exam is normal in cases of physiologic murmur.

Pathologic murmur occurs when there is turbulence of blood flow across an abnormal valve. This can be due to either stenosis or regurgitation.

Stenosis

Stenosis refers to the abnormal narrowing of a valve orifice. The narrowing of a valve prevents it from opening completely; as a result, stenosis murmurs can only occur when the valve is attempting to open.

Regurgitation

Regurgitation refers to the abnormal backward flow of blood from a high-pressure chamber to a low-pressure chamber, often due to an incompetent valve (i.e. a valve that cannot shut properly).

Systolic murmurs

Systolic murmurs are murmurs that are produced during systole (contraction) of the ventricles, which is the period between S1 and S2. These murmurs can be midsystolic (ejection), late systolic, and pansystolic murmurs. Systolic murmurs can be either normal or abnormal.

Midsystolic ejection murmurs

Midsystolic ejection murmurs have their highest intensity in the middle of systole. They are often described as having a crescendo-decrescendo quality. This can be a physiological murmur, caused by an increased flow through a normal valve; or, it can indicate pathologies, such as aortic stenosis or pulmonary stenosis. In cases of congenital aortic or pulmonary stenosis, an early high-pitched systolic ejection click may be heard, representing the sudden opening of these valves, which are still mobile.

Late systolic murmur

Late systolic murmur occurs when there is a gap between hearing S1 and the murmur. This can be caused by mitral regurgitation, as in the case of papillary muscle dysfunction or mitral valve prolapse.

Pansystolic murmur

Pansystolic murmur extends from S1 to S2. The pitch and loudness of this murmur stay the same during systole. The murmur is caused by leakage from a high-pressure chamber to a low-pressure chamber. Causes of pansystolic murmurs include mitral or tricuspid regurgitation and ventricular septal defect.

Diastolic murmurs

Diastolic murmurs, as their name implies, occur during diastole of the ventricles. They are always pathological. Compared to systolic murmurs, they are softer and more difficult to hear.

Early diastolic murmur

Early diastolic murmur starts with S2 and is a decrescendo murmur which is loudest at its commencement. It produces a high-pitched sound. Causes of an early diastolic murmur include aortic regurgitation or pulmonary regurgitation. The decrescendo quality mirrors the peak in aortic and pulmonary pressures at the start of diastole.

Mid-diastolic murmurs

Mid-diastolic murmurs occur in the later phases of diastole. Compared to early diastolic murmurs, they are lower in pitch. Mid-diastolic murmurs can be caused by mitral or tricuspid stenosis or an atrial myxoma (rare). In mitral stenosis, the diastolic murmur may be preceded by a high-pitched opening snap which represents the abrupt opening of the stenosed mitral valve.

Continuous murmurs

Continuous murmurs occur during both systole and diastole without a pause. The sound is created by unidirectional flow in the presence of communication between a high-pressure and a low-pressure source. The constant pressure gradient results in a continuous flow. Causes include patent ductus arteriosus, arteriovenous fistula, and venous hum.

Grading of murmurs

If a murmur is heard, various dynamic maneuver tests are required to characterize it further. These maneuvers alter circulatory hemodynamics and, in doing so, change the intensity of different murmurs.

- Grade 1: Murmur is very soft, and is initially not heard
- Grade 2: Murmur is soft, but can be readily heard by a skilled examiner
- Grade 3: Murmur is easy to hear
- Grade 4: Murmur is slightly loud and accompanied by a palpable thrill (these murmurs are always pathological)
- Grade 5: Murmur is very loud, and the accompanying thrill is easily palpable
- Grade 6: Murmur is so loud that it is audible even without direct placement of the stethoscope on the chest

Note:
A mid-systolic murmur in an asymptomatic individual is most likely physiological, in contrast to diastolic murmurs which are always pathological.

Note:
It is usually easy to auscultate systolic murmurs as they usually radiate, unlike diastolic murmurs which may require certain maneuvers to accentuate them.

Note:
The intensity of the murmur doesn't always correlate to the severity of the lesions, as a smaller VSD produces louder murmurs than a larger VSD.

High-yield:
Murmurs of grade III and above are usually pathological.

Thrills are palpable murmurs, and can only be felt in murmurs of grade IV and above.

Auscultation

There are **4 chest areas** over which a stethoscope can be placed in order to listen to heart sounds and identify any abnormal findings. Auscultation can be carried out in a clockwise manner, starting with the aortic then the pulmonic and mitral areas, followed by the tricuspid area.

To identify the difference between the 2 heart sounds on auscultation, palpation of the pulse (carotid or radial) while listening to the heart can be helpful. The pulse indicates systole, therefore corresponding to the first heart sound S1. Being aware of when systole and diastole occurs is useful in case an additional heart sound is heard so that it can be timed in the cardiac cycle and accurately described.

Fig. 1-06: *Stethoscope placement for auscultation*

The **aortic area** is located in the second intercostal space, at the right sternal edge. The diaphragm of the stethoscope can be placed at this site to listen for aortic stenosis.

The **pulmonic area** is at the left second intercostal space, opposite the aortic area. The diaphragm is placed here to listen for a loud P2 and pulmonary flow murmurs.

The **mitral area** is also referred to as the apex of the heart. It is located in the fifth intercostal space, at the midclavicular line. This area is listened to with both the bell and diaphragm of the stethoscope. Low-pitched sounds, such as the diastolic mitral stenosis murmur and third heart sound, can be better appreciated with the bell. The diaphragm can be used to detect high-pitched sounds, such as a fourth heart sound or mitral regurgitation.

The **tricuspid area** is also located in the fifth intercostal space but at the left sternal edge. The diaphragm is placed at this site to listen for tricuspid regurgitation.

Even when a murmur is heard more clearly at a certain part of the chest, this might not always be helpful in determining its origin. Because **murmurs can radiate**, they can be heard in other areas too. For example, a mitral regurgitation murmur is best heard in the mitral area but it may also be heard anywhere else on the chest. This murmur is also characterized by its radiation to the axillae. An ejection systolic murmur of aortic valve origin may characteristically radiate to the carotid arteries.

Dynamic auscultation

Altering heart sounds by changing circulatory hemodynamics. **This method can be used to distinguish the clinical cause of similar auscultatory findings and is a frequently tested topic on board exams**. If you understand the physiologic alterations caused by certain maneuvers, this is more simply understood.

Changing venous return is a change that is useful.

Increasing venous return	Decreasing venous return
• Increased volume of blood into the RA/RV then LA/LV (increased preload) • Preload is the volume of blood in the ventricle	• Decreased volume of blood into RA/RV the LA/LV, thus decreasing preload (increased afterload) • Afterload is the effective pressure seen by the LV in the ascending aorta

Dynamic maneuvers

If a murmur is heard, various dynamic maneuver tests can be used to characterize it further. These maneuvers alter circulatory hemodynamics and, in doing so, change the intensity of different murmurs. Respiration can be used to differentiate between right-sided and left-sided murmurs. **Inspiration** has the effect of increasing venous return and, as there is an increase in blood flow to the right side of the heart, right-sided murmurs are accentuated. On the other hand, **expiration** causes left-sided murmurs to become louder.

Another respiration maneuver is deep expiration. As the patient leans forward and expires for an extended period, the base of the heart is brought closer to the chest wall. In this maneuver, the murmur of aortic regurgitation be better appreciated.

1) The Valsalva maneuver

This is a well-known, often-used dynamic maneuver. It accentuates the murmurs of hypertrophic cardiomyopathy and mitral valve prolapse when listening over the left sternal edge. It involves getting the patient to expire fully against a closed glottis. There are 4 phases to the Valsalva maneuver:

- **Phase I:** This marks the start of the maneuver. Intrathoracic pressure increases, with a temporary rise in cardiac output and blood pressure.
- **Phase II:** This is the **straining phase** of the maneuver. **Venous return decreases**, and so does cardiac output and stroke volume. There is a fall in blood pressure and an increase in heart rate. Most murmurs become softer, but the **systolic murmur of hypertrophic cardiomyopathy increases** and the **mitral valve prolapse murmur can be heard**.
- **Phase III:** This phase occurs at the maneuver‘s release. Right-sided murmurs are louder for a short interval, followed by the left-sided murmurs.
- **Phase IV:** Blood pressure rises upon activation of the sympathetic nervous system.

2) Squatting

Squatting is another dynamic maneuver which causes an increase in venous return. In this test, the patient quickly moves from a standing position to a squat. This makes most murmurs louder, including those associated with aortic stenosis and mitral regurgitation murmurs, while the murmur of hypertrophic cardiomyopathy and mitral valve prolapse is softer or shorter. When the patient does the opposite, and stands up quickly from a squatting position, the opposite changes occur.

3) Isometric exercise

Isometric exercise can also be used for eliciting certain types of murmurs. For this exercise, the patient sustains a handgrip for half a minute. This exercise increases afterload (or peripheral resistance). The murmur of mitral regurgitation is accentuated. The murmur of aortic stenosis and hypertrophic cardiomyopathy becomes softer, while a mitral valve prolapse murmur becomes shorter.

Summary table

Heart sound	Causes
First heart sound (S1)	Closure of the mitral and tricuspid valves
Second heart sound (S2)	Closure of the aortic and pulmonary valves
Extra heart sounds	
Third heart sound (S3)	A physiological S3 is caused by rapid diastolic filling (e.g. pregnancy, thyrotoxicosis, and some pediatric cases). A pathological S3 is caused by reduced compliance of the left ventricle (e.g. left ventricular failure, aortic regurgitation, mitral regurgitation, patent ductus arteriosus, ventricular septal defect) or reduced compliance of the right ventricle (right ventricular failure, constrictive pericarditis)
Fourth heart sound (S4)	Decreased ventricular compliance of the left ventricle (aortic stenosis, mitral regurgitation, hypertension, angina, myocardial infarction, old age) or the right ventricle (pulmonary hypertension, pulmonary stenosis)
Murmurs Systolic murmurs	
Midsystolic murmur	Increased flow through a normal valve (physiologic or innocent murmur), aortic stenosis, pulmonary stenosis, hypertrophic cardiomyopathy, atrial septal defect
Late systolic murmur	Mitral regurgitation (MR), due to papillary muscle dysfunction, mitral valve prolapse or infective endocarditis
Diastolic murmurs	
Early diastolic murmur	Aortic regurgitation, pulmonary regurgitation
Mid-diastolic murmur	Mitral stenosis, tricuspid stenosis, atrial myxoma (rare), acute rheumatic fever (Carey Coombs murmur)
Other	
Presystolic murmur	Mitral stenosis, tricuspid stenosis, atrial myxoma
Continuous murmur	Patent ductus arteriosus, arteriovenous fistula, venous hum

Review Questions

Test your knowledge:
Heart Sounds

Question 1.1: What auscultation technique can be used to best appreciate the murmur of aortic regurgitation?

A. At the left lower sternal edge, with the patient in the left lateral decubitus position, after a short exercise.

B. At the aortic area and carotid arteries to assess for radiation.

C. At the base of the heart, with the patient sitting up, leaning forward, and holding the breath after expiration.

D. At the left sternal edge, during phase II of the Valsalva maneuver

Question 1.2: What distinguishes a grade 6 murmur from other grades in the Levine system?

A. It is a murmur that is soft and difficult to hear.

B. It is a murmur that can be heard without direct placement of the stethoscope.

C. It is a murmur with a palpable thrill accompanying it.

D. It is a murmur that can only be heard by someone experienced in auscultation

Question 1.3: What is the cause of the physiological splitting of the second heart sound?

A. Closure of the mitral and tricuspid valves just before ventricular systole.

B. Increase in venous return during inspiration, causing the aortic valves to remain open for longer.

C. Aortic regurgitation with retrograde leakage through the valve during ventricular diastole.

D. Delayed closure of the pulmonic valve due to lower pressures in the pulmonary circulation and increased venous return during inspiration.

Practical Guide to Cardiovascular Examination

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Vital Measurements

You will likely require the vital measurements of every patient you clinically examine. These will normally include **heart rate**, **respiratory rate**, and **blood pressure**. Vital signs can be measured with basic equipment (a watch, a sphygmomanometer, and a stethoscope) in most situations and constitute a part of any physician's basic skill set. It is very important that you learn to perform these examinations, as well as the basic rules associated with each measurement. Some establishments (such as hospitals) will readily provide this data. Some establishments also provide temperature and oxygen saturation measurements. Record this data and consider it carefully as you complete the clinical examination of the heart.

The patient should be resting comfortably in **supine position**. Access to the chest, arms, and legs is essential. Do not perform the exam through clothing, exposed skin is necessary. Having the patient dress in a hospital gown with a draping sheet available is recommended but not required.

Observation

With the anterior chest exposed, observe your patient's thorax and the rest of his or her body. Observe the following: thorax, eyes, upper and lower extremities, and signs of jugular venous distention.

Thorax

- Scars indicative of cardiac surgery. A vertical scar down the sternum is an indication of previous open heart surgery.
- Chest deformities including **pectus excavatum** (a sunken sternum and ribs, a symptom of several connective tissue diseases such as Marfan syndrome) and **pectus carinatum** ('pigeon chest', a protrusion of the sternum and ribs).

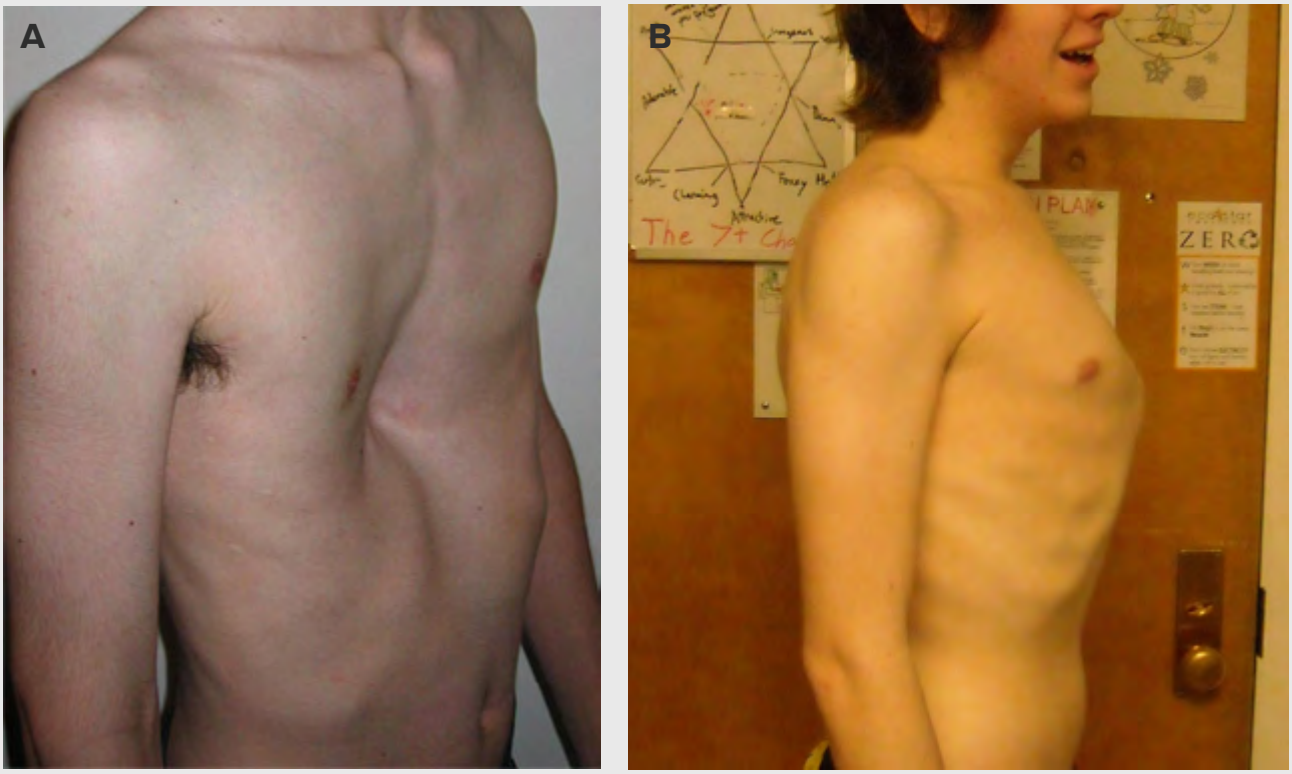

Fig. 1-07: *(A) Pectus excavatum deformity (B) Pectus carinatum*

Fig. 1-08: Xanthelasma palpebrarum

Eyes

- Yellow plaques around the eyes and eyelids, called xanthelasma, are a sign of hypercholesterolemia. These are a risk factor for cardiovascular disease.
- Roth's spots are observed on the retina with an ophthalmoscope. They appear as a red ring surrounding a white center and are indicative of infective endocarditis.

Upper and lower extremities

- **Clubbing of the fingers or toes**. The distal part of the digit flattens and widens. This is a sign of lung disease and a chronic hypoxemia.
- **Cyanosis**, blue discoloration of the digits implies poor perfusion. Cyanosis can be detected in the extremities or the lips.
- Infective endocarditis lesions on the hands and feet. Osler's nodes are raised, painful, red lesions on the hands and feet. They are caused by immune complex deposition. Janeway lesions are small, red, and painless. They are caused by microemboli. **Splinter hemorrhages** form vertically underneath the nails. They are also caused by small blood clots floating through the bloodstream.

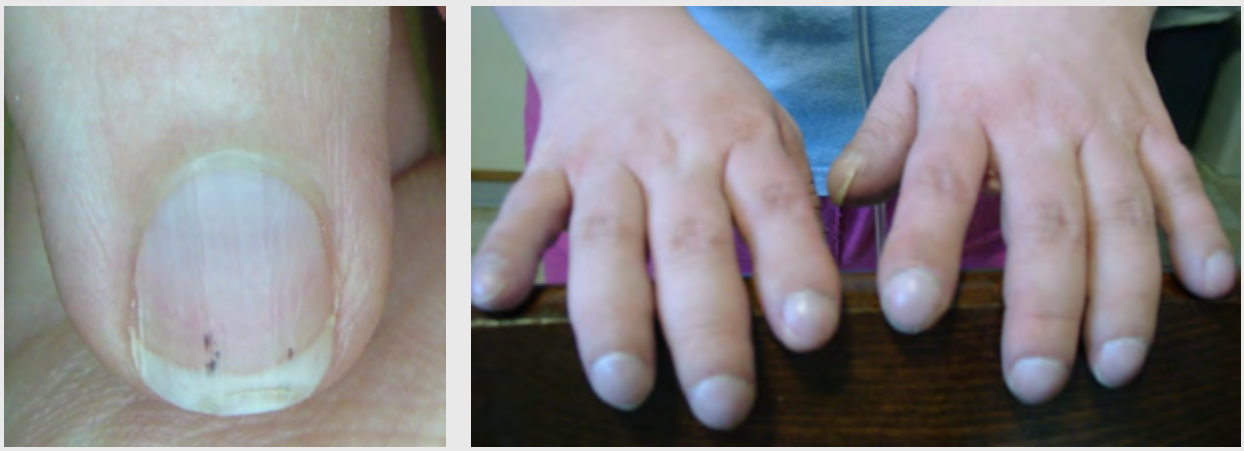

Fig. 1-09: (A) Splinter hemorrhages. (B) Example of clubbing, secondary to pulmonary hypertension, in a patient with Eisenmenger's syndrome.

Jugular venous distention

The observation part of the cardiovascular exam includes observing the right internal jugular vein (IJV). This test is very useful when evaluating right heart function and central venous pressure.

Procedure

1. Elevate the patient's head at an angle of between 15° and 30°.
2. Identify the right internal jugular vein. This may take some practice. It crosses deep to the sternocleidomastoid muscle and anteriorly to the right ear. Ask the patient to turn their head to the left or perform a Valsalva maneuver. Additionally, use hepatojugular reflux to find the internal jugular vein. Apply firm pressure to the liver (right upper quadrant of the liver) for a few seconds and the IJV will fill with blood. Finally, a penlight can be very useful when trying to find the IJV.
3. The IJV pulsates, but so does the carotid artery. If the pulse rate matches the rate of the radial pulse, you have located the carotid artery.
4. Measure the top of the IJV fluid level in cm above the Angle of Louis (sternal angle). A normal measurement is 3 cm above the sternal angle.

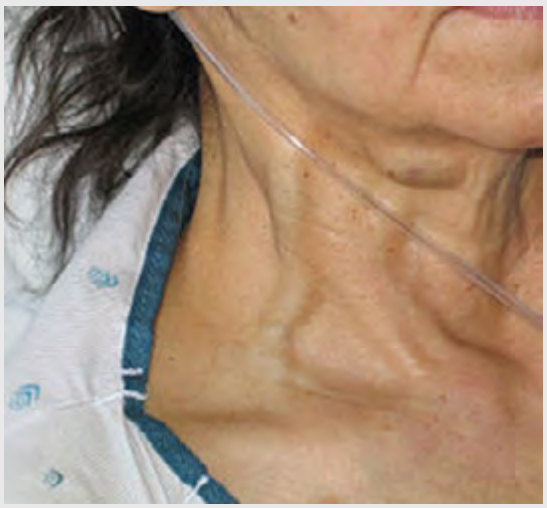

Fig. 1-10: *Obvious external jugular venous distention in a patient with severe tricuspid regurgitation. Note the rope-like, almost vertical vein in this near-upright sitting patient.*

Palpation

The palpation portion of the cardiovascular exam includes **evaluating the extremities and the carotid pulses, as well as determining the point of maximum impulse (PMI)** and evaluating it. A relatively strong vibration is created when the ventricles contract.

This vibration is transmitted down the apex of the heart and into the chest wall. In a healthy individual, the PMI is located at the 5th intercostal space along the left midclavicular line (just medial to and below the left nipple).

Evaluation of the extremities

Temperature

Evaluate the extremities for temperature. Gently touch the hands and feet to determine their temperature. A well-perfused extremity will be slightly warm or at body temperature. A **cold extremity indicates poor perfusion** or blood may be being shunted away from the skin. A too warm extremity indicates a reduction of vascular resistance and may be a sign of septic shock.

Peripheral pulses

There are a variety of pulse points you should be familiar with. Some are used regularly (radial pulse, carotid pulse) and some are used much less frequently (femoral pulse). A thorough cardiac exam requires an **evaluation of all peripheral pulses**. Always **compare the paired pulses** (if one pulse stronger than the other).

- Carotid artery
- Radial artery
- Femoral artery
- Popliteal artery
- Posterior tibial artery
- Dorsalis pedis artery
- Palpating the extremities is the preferred method when quantifying peripheral edema. The 2 types of edema are pitting and non-pitting edema.

Peripheral edema

Palpating the extremities is the preferred method when quantifying peripheral edema. The 2 types of edema are **pitting and non-pitting edema**. Pitting edema will form indentations when palpated, as you are effectively pushing fluid out of the tissue. Pitting edema is a sign of poor liver function or heart failure based on abnormal Starling's forces. An injured, malfunctioning liver produces less albumin; this lowers the oncotic pressure of blood inside the capillaries, allowing fluid to pass into the tissue. An injured, malfunctioning heart produces less hydrostatic pressure within the capillaries with the same result. Extreme fluid overload is another cause of pitting edema.

Non-pitting edema is a completely different process involving metabolic factors resulting in subcutaneous tissue swelling.

Procedure

1. Starting with the hands, press firmly into the flesh of the palm. Continue up the forearm and arm until indentations no longer form. Pitting is measured by the table below.

1+	Barely detectable impression when a finger is pressed into the skin
2+	Slight indentation, 15 seconds to rebound
3+	Deeper indentation, 30 seconds to rebound
4+	> 30 seconds to rebound

2. Report edema in numerical form at the highest point of detection (i.e. 2+ pitting edema at the height of the mid forearm).
3. Repeat for the lower extremity. Pitting edema usually occurs in the legs and feet well before the condition is sufficiently severe to result in edema of the hands and arms.

Point of Maximal Impulse (PMI)

Procedure

1. Place the center of your palm at the PMI. The heel of your palm should rest at the sternal border. Your fingers should wrap around the patient laterally.
2. Apply some pressure to the chest wall until you feel the heartbeat in your palm.
3. Identify the point of maximum impulse on the chest wall. It will be a small area, about 1 cm wide, with the strongest vibration.

Obesity will make this part of the exam difficult. Again, the **PMI of a healthy person with a normal and healthy heart will be located near the 5th intercostal space, along the midclavicular line**. The PMI of a dilated ventricle will be displaced laterally.

Thrill

A thrill may be detected if there is valvular disease present. This is a vibration associated with turbulent blood flow through a damaged or malformed valve. Thrills are located near the valve listening points.

Chapter 2:
Hypertension

Most Important Facts about Hypertension

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Definition of Hypertension

- JNC 8 definition: systolic blood pressure of ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg
- AHA/ACC definition (2017): systolic blood pressure of ≥ 130 mmHg and/or diastolic blood pressure ≥ 90 mmHg

Epidemiology of Hypertension

Approximately 75 % of the world's population suffers from arterial hypertension. Of this 75 %, about half are unaware of it. Moreover, up to 50 % of those who receive an antihypertensive do not achieve good control of their blood pressure. The prevalence of arterial hypertension increases with age and body weight.

Etiology of Hypertension

According to the etiology, arterial hypertension is divided into 2 types, primary hypertension (also known as essential hypertension) and secondary hypertension.

Primary hypertension

More than 90 % of hypertensive patients have primary hypertension. This type of hypertension is idiopathic or without any known cause. Diagnosis is made through the principle of exclusion.

The risk factors associated with primary hypertension are:

- Nutritional factors such as: excess weight, alcohol consumption, and a sodium-rich diet
- Stress
- Tobacco smoking
- Advanced age
- Low socioeconomic status

Secondary hypertension

There are several factors causing secondary hypertension:

- Neurogenic, psychogenic, and iatrogenic causes; the latter includes contraceptives, NSAR drugs, consumption of illicit drugs, and toxic substances such as licorice
- Medical conditions such as obstructive sleep apnea syndrome, coarctation of the aorta, and atherosclerosis

Renal (caused by fibromuscular dysplasia, renal parenchymal diseases-PKD, diabetic kidney diseases, atheromatous diseases; ACE inhibitors can precipitate renal failure) and **endocrine** (caused by primary or secondary hyperaldosteronism, pheochromocytoma, Cushing syndrome, thyrotoxicosis, hyperparathyroidism) **hypertension** are also considered to be secondary hypertension. The mechanism of renovascular hypertension is primarily due to renal ischemia. Renal artery stenosis results in increased levels of renin and angiotensin I and II, and are associated with increased vasoconstriction, hence hypertension and an increased sympathetic tone. Aldosterone production is also increased in these patients, resulting in higher levels of sodium retention. The increased retention of sodium is associated with increased water retention and can lead to extracellular blood volume. The interplay between these 2 mechanisms is the main cause of hypertension in this group of patients.

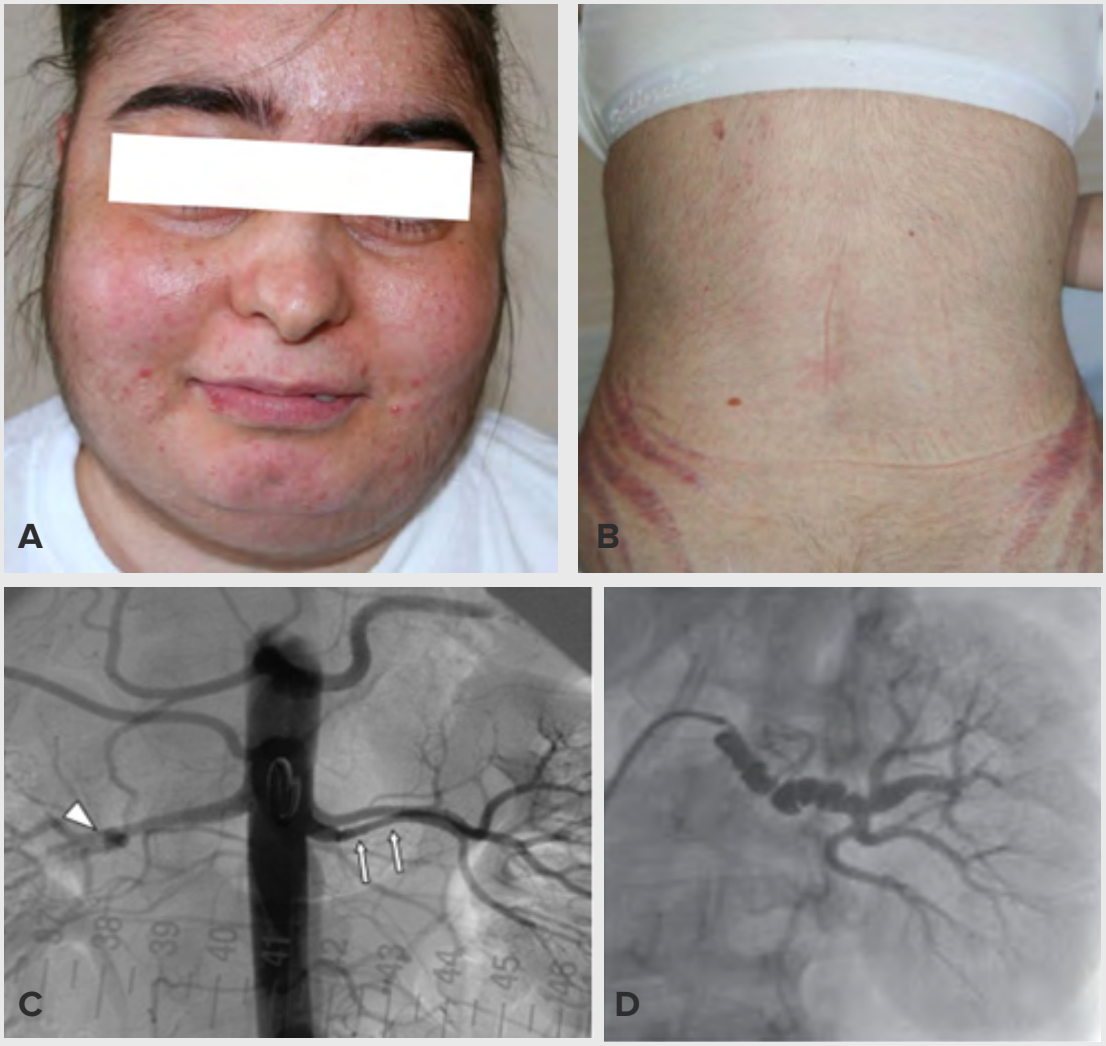

Fig. 2-01: *Cushing syndrome: Impaired fasting glucose, buffalo hump, (A) moon faces, (B) abdominal striae; 24 hour urinary cortisol or high dose dexamethasone suppression; (C) Angiography of renal artery stenosis; (D) 'String of beads' on angiography characteristic of fibromuscular dysplasia*

Secondary hypertension is characterized by sudden changes in BP and onset prior to the age of 30 or after the age of 55. Another type of arterial hypertension is **hypertensive disease of pregnancy**. Risk factors include increasing maternal age and multifetal pregnancies.

Hypertensive disorders of pregnancy are divided into:

- Gestational hypertension (hypertension not associated with proteinuria)
- Pre-eclampsia (hypertension associated with proteinuria)
- Eclampsia (pre-eclampsia with at least 1 episode of convulsion due to cerebral dysrhythmia)

Classification of Hypertension

Hypertension is divided into several stages. An increase in blood pressure as a result of physical exertion is not considered hypertension. Accordingly, the American College of Cardiology has updated its guidelines to define hypertension in 4 different stages as follows:

Term	Systolic BP (mmHg)	Diastolic BP (mmHg)	Notes
Normal	< 120	< 80	
Elevated	120–129	and < 80	
Stage 1	130–139	or 80–89	Treatment is needed
Stage 2	140–179	or 90 or more	Treatment is needed
Hypertensive crisis	> 180	or > 120	Patient also needs an immediate change to blood pressure control medication or should be hospitalized.

Hypertensive crises can be divided into 2 types: hypertensive urgency and hypertensive emergency. The former differs from the latter in that there is no organ damage in hypertensive urgency while hypertensive emergency always considers end organ damage such as encephalopathy, hemorrhagic/ischemic CVA, retinal hemorrhage/papilledema, CHF, ACS, aortic dissection, aneurysm of the abdominal aorta, ARF, hematuria, or MAHA.

There are different treatment approaches for these 2 types of hypertensive crises. In hypertensive urgency, BP should be reduced slowly, over hours or days. In cases of hypertensive emergency, BP should be decreased by 25 % in minutes to hours with IV agents: NTG, nitroprusside.

Pathophysiology of Hypertension

Arterial hypertension develops due to disturbances of the regulatory mechanism that usually keeps blood pressure stable. Disturbances include an increased peripheral vascular resistance, increase in cardiac output, or a combination of both.

During disease progression, several compensatory mechanisms take place to consistently keep the blood pressure at an elevated level. In order to maintain cardiac output, the cardiac muscle hypertrophies which helps to permanently withstand the increased pressure. The resisting blood vessels also undergo hypertrophy. Baroreceptors located in blood vessel walls detect high blood pressure, activating the so-called baroreceptor reflex, leading to higher BP values to be translated as ‘normal‘.

The kidneys are involved in this compensatory process, too. Even though renal blood flow and glomerular filtration rate are, on the whole, constant, increased sodium excretion (pressure natriuresis) accompanies the increase in blood pressure in order to counteract hypertension.

FIND MORE INFORMATION
Guidelines for prevention and management of High Blood Pressure

Clinical Features of Hypertension

Symptoms of arterial hypertension frequently manifest later on. Typical symptoms include:

- Early morning headaches
- Sleep disorders, dizziness
- Nose bleeds
- Ringing in the ears
- Non-specific cardiac symptoms
- Palpitations

In cases of secondary hypertension, symptoms of the individual's underlying disease will accompany those of hypertension.

Note:
Since hypertension is often asymptomatic, regular screening is necessary to prevent end-organ damage.

Subtypes and Variants of Hypertension

Special forms of arterial hypertension are isolated office hypertension and isolated ambulatory hypertension.

1. **White-coat hypertension (White-coat effect):**

- Known as isolated office hypertension and also referred to as 'white-coat hypertension', this variant is characterized by measurements of ≥ 140/90 mmHg in the physician's office, while measurements taken at home and during blood pressure monitoring are normal
- Diagnosed via 24-hour blood pressure monitoring

2. **Isolated systolic hypertension:**

- Defined as an increase in systolic blood pressure (> 140 mmHg) with diastolic blood pressure within normal limits (< 90 mmHg)
- Occurs in elderly populations due to decreased arterial elasticity and increased stiffness
- Patient usually has a high risk of cardiovascular events (MI, stroke, renal dysfunction)

3. **Isolated ambulatory hypertension:**

- Referred to as masked hypertension; in this case, blood pressure readings at the office are normal, however, readings at home or during blood pressure monitoring are elevated to more than 140/90 mmHg. This special form of hypertension may be linked to factors such as male gender and younger age, as well as smoking, alcohol consumption, and stress. Where the patient is already being treated for hypertension, this condition is referred to as masked uncontrolled hypertension (MUCH).

Diagnostics of Hypertension

Medical history and physical examination

Gathering a patient's medical history is essential because it helps to figure out possible symptoms and reveals previously measured blood pressure values as well as possible risk factors. It is very important to ask patients about their current medications, previous illnesses, and the patient's family history.

Aside from BP measurement, the patient's physical examination should include checking the radial and the femoral pulse, and performing an abdominal auscultation as this may be an indicator of renal artery stenosis. Furthermore, it is essential to look for signs of cardiac insufficiency and renal failure. The fundus of the eyes should be examined as well.

Measuring blood pressure

The focal point of diagnosing arterial hypertension is the non-invasive measurement of blood pressure according to Riva Rocci. Here, it is necessary to make sure that elevated blood pressure is established by taking at least 3 readings in 2 different days. It is also a fact that the first readings are frequently 10 % higher than subsequent readings.

In order to diagnose forms of white-coat hypertension (or to rule this form out) and to establish permanently elevated blood pressure, ambulatory blood pressure monitoring (ABPM) over a period of 24 hours is appropriate. The average daytime measurement should be below 135/85 mmHg and the average night-time measurement below 120/70 mmHg. The average 24-hour measurement should be below 130/80 mmHg.

Laboratory diagnostics

Hb and Hct are blood parameters that may indicate anemia due to underlying renal disease. Renal function may be tested by measuring creatinine and eGFR levels. Potassium levels will provide more information if Conn's syndrome is suspected. Furthermore, other parameters such as cholesterol, triglycerides, and glucose should be measured in order to determine the risk of atherosclerosis.

In order to evaluate the presence of endocrine hypertension, parameters such as T3, T4, TSH, aldosterone, and renin must be measured.

Urinalysis is another test of choice because microalbuminuria may be an early indicator of renal damage, especially in diabetic patients. Determining glucose levels is necessary to rule out potential diabetes mellitus. The presence of nitrites in the urine may reveal urinary tract infections. Increased levels of catecholamines in combination with severely high diastolic blood pressure (> 110 mmHg) indicates pheochromocytoma.

Instrument-based diagnostics

Instrument-based diagnostics are primarily used for diagnosing secondary hypertension. These include ECG screening to rule out left ventricular damage or coronary heart disease. Chest rradiograph may also be used to determine the presence of dilatation.

Echocardiography is used to determine ventricular circumference and to rule out the presence of heart pump function impairment. Carotid Doppler, renal or color duplex sonography of the renal arteries may also be an option in specific situations.

Treatment of Hypertension

Non-pharmacological treatment (lifestyle modifications)

- Weight reduction until a BMI of approximately 25 kg/m^2 has been achieved
- Diet low in sodium, with no more than 5–6 g NaCl per day
- Switching to a Mediterranean diet
- Adjusting lifestyle to reduce hypertension (smoking, alcohol and coffee intake should be reconsidered)

Medications that may cause hypertension should be discontinued. In addition, dynamic conditioning training including sports such as swimming, jogging, or bicycling should be pursued 3 to 4 times per week. Aside from these general measures, diseases that may cause secondary hypertension must be treated. According to the European Society of Hypertension (ESH), the target blood pressure values in individuals under the age of 60 years (**source**: JNC 8) are below 130/80 mmHg, in patients older than this, target values are below 150/90 mmHg.

Pharmacological treatment

It is recommended to start pharmacological therapy as a monotherapy. In the event of blood pressure values strongly deviating from normal values (> 130/80 mmHg) or in cases of comorbidities, primary combination therapy should be initiated.

First-line medications include:

- Thiazide diuretics
- ACE inhibitors
- ARBs
- Calcium channel blockers

While the above classes of medication are considered as primary antihypertensives, they can still be combined. Secondary antihypertensives are used when primary medications do not work or if there are special indications such as in hypertensive patients with ischemic heart disease.

Secondary antihypertensives include:

- Loop diuretics
- Potassium-sparing diuretics
- Beta-blockers
- Direct renin inhibitors
- Alpha-1 blockers
- Central alpha-2 blockers
- Direct vasodilators

Diuretics

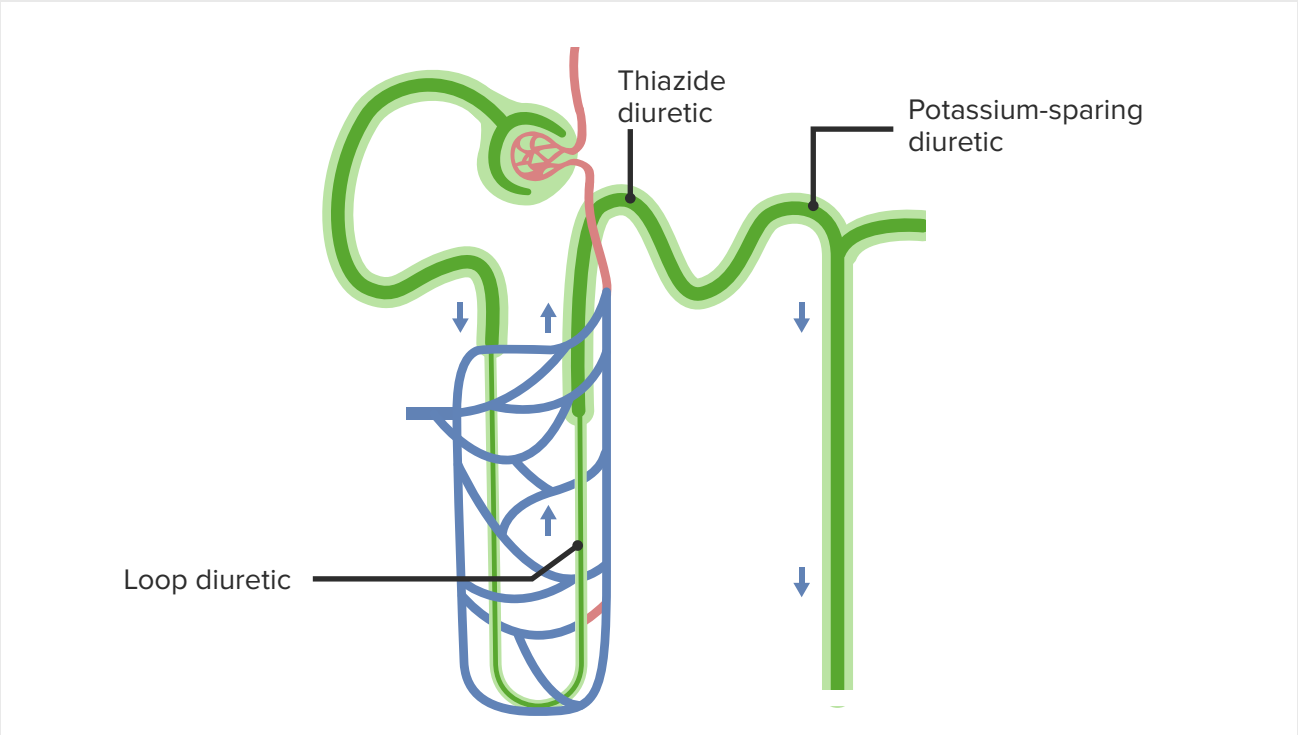

Fig. 2-02: Primary site of action of common diuretics used in the treatment of hypertension

Thiazide diuretics

- Excellent first-line therapy alone and in combination with other agents
- Generic and therefore inexpensive
- Shown to reduce cardiovascular event, such as stroke, in patients with hypertension
- Chlorothiazide, chlorthalidone, HCTZ, indapamide, metolazone

Adverse effects (AEs) of thiazide diuretics

- Hypokalemia – low blood potassium level – particularly a problem with chlorthalidone (dose-related, may affect clinical outcome)
- Glucose intolerance = diabetic tendency
- Gout
- Kidney damage

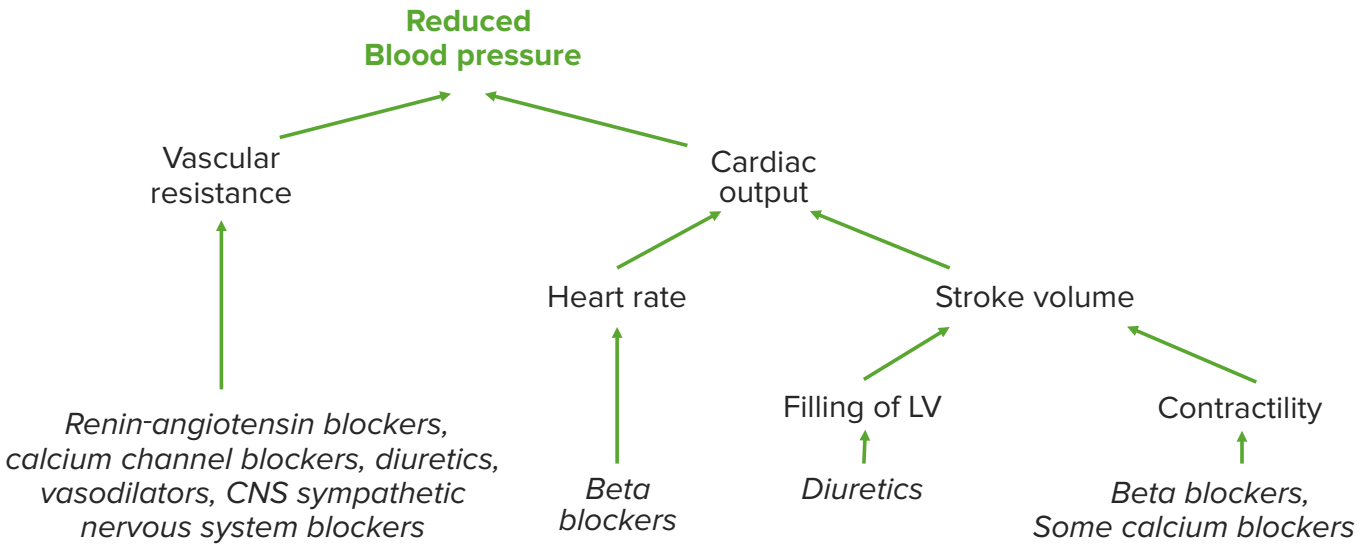

Fig. 2-03: Antihypertensive drugs: hemodynamic mechanism of BP reduction

Renin-angiotensin aldosterone system

The kidney is central to blood pressure control through the juxtaglomerular apparatus. Baroreceptors in the arterial system inform the central nervous system of blood pressure levels. Signals from baroreceptors lead to changes in autonomic nervous system activity. Renin initiates a biochemical sequence that eventually converts angiotensinogen, produced in the liver, into angiotensin, a strong vasoconstrictor. Angiotensin stimulates aldosterone release from the adrenal gland which causes the kidney to retain salt (NaCl) and water. Angiotensin stimulates the release of antidiuretic hormone from the pituitary gland which causes the kidney to retain water.

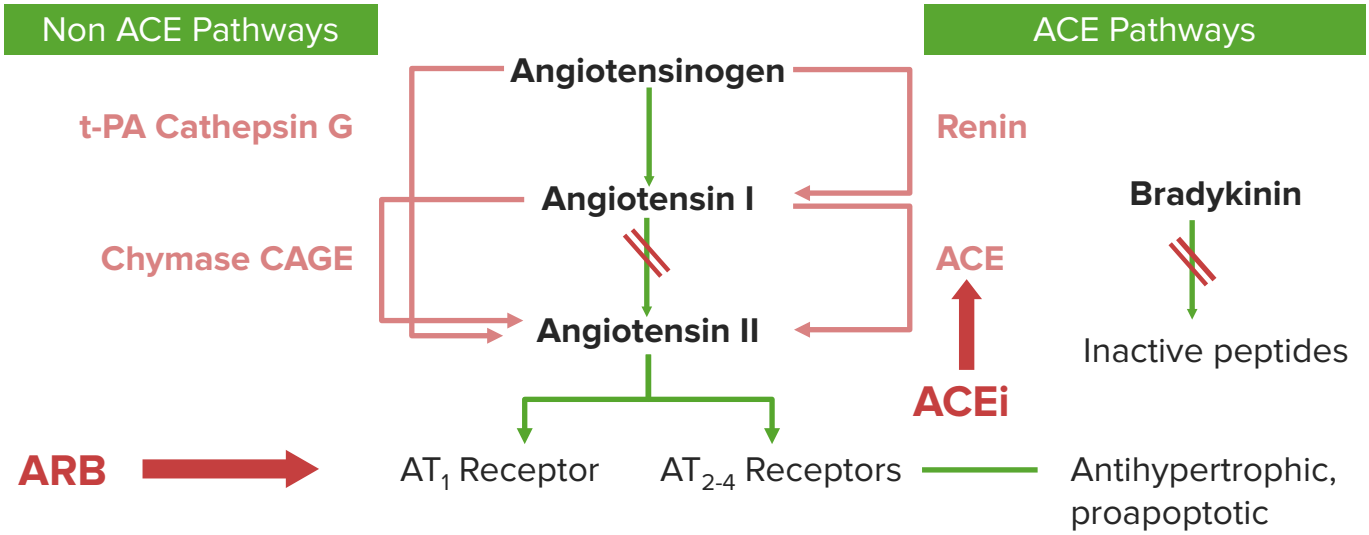

Fig. 2-04: Renin-angiotensin aldosterone system (RAAS) is considered a very important target of antihypertensives. ACEIs prevents Angiotensin I conversion into Angiotensin II by inhibition of Angiotensin Converting Enzyme (ACE), while ARBs act directly on the AT receptors preventing the action of the Angiotensin II.

This system is part of the body's defense against dehydration and/or blood loss. The idea is to restore blood volume to normal as quickly as possible.

Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB)

- Captopril – ACEI
- Enalapril – ACEI
- Lisinopril – ACEI
- Ramipril – ACEI
- Losartan – ARB
- Candesartan – ARB
- Valsartan – ARB

AEs with ACEI and ARB – 1st line Rx

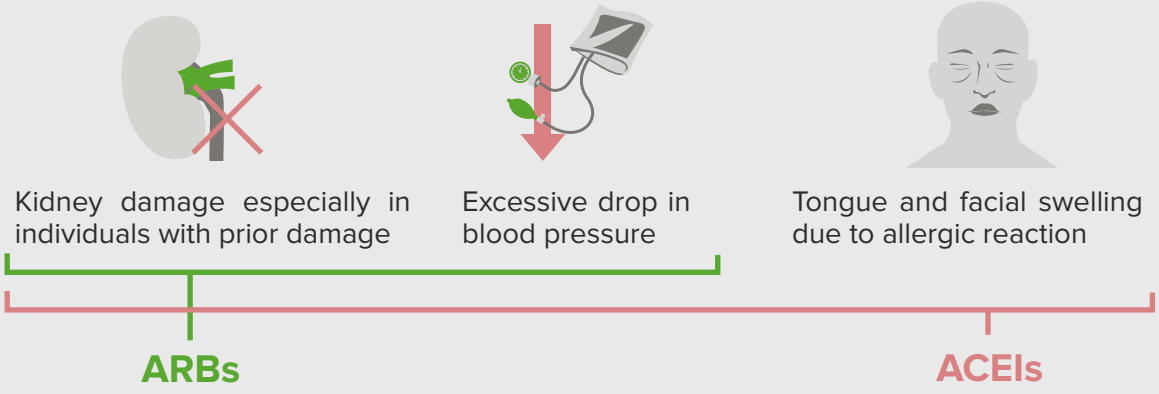

Fig. 2-05: Possible adverse effects of ACE inhibitors and ARBs

Aldosterone antagonists: mechanisms of action

- Block aldosterone binding at receptors in kidneys, heart blood vessels, and brain
- Blockade of aldosterone in renal tubule → increased Na^+Cl^- and water excretion and potassium retention

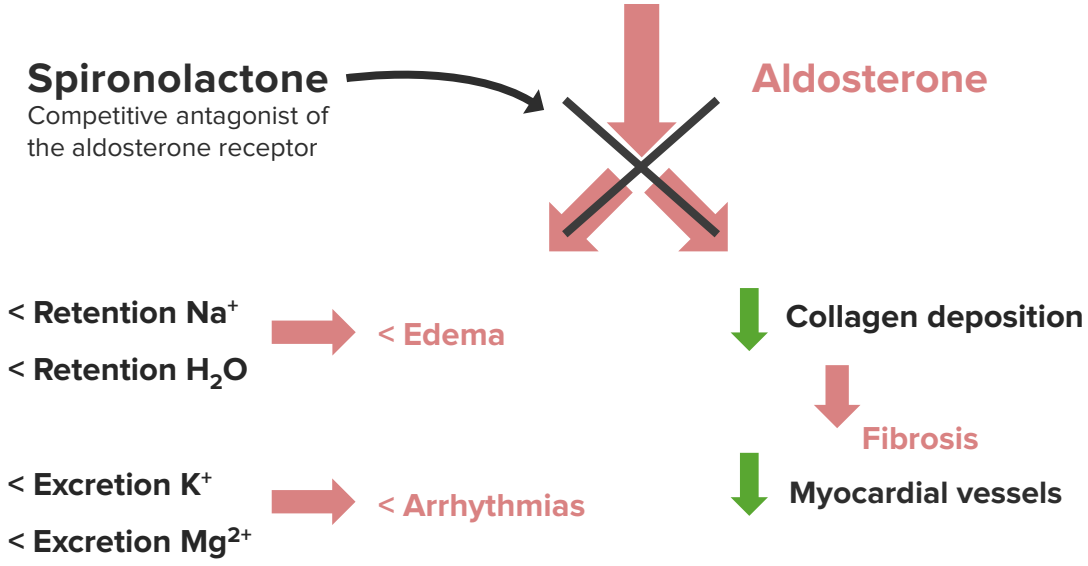

Fig. 2-06: Aldosterone inhibitors: spironolactone

Beta-blockers

Beta-blockers slow the heart rate and block the sympathetic nerve stimulation to the kidney (< renin release) and the peripheral nerves (< vascular resistance). They are considered to be second-line antihypertensive agents and include:

- Propranolol
- Metoprolol
- Atenolol
- Carvedilol
- Bisoprolol
- Labetalol

Adverse effects

Fluid retention worsened by heart failure is more likely to occur during initiation and the first several months of treatment; later, symptoms of heart failure improve. Hypotension is more likely with carvedilol. The risk of bradycardia and heart block is 5–10 % as the dose is increased. Fatigue and weakness may resolve with time or via dose reduction. Asthma will worsen or may develop.

Calcium channel blockers

Calcium channel blockers are first-line medications in patients with abnormal kidney function. They dilate the arterioles (resistance vessels) and thereby decrease vascular resistance. Calcium channel blockers include dihydropyridine and non-dihydropyridine.

Other forms of pharmacological therapy

Other drugs occasionally used in the treatment of hypertension:

- Minoxidil – very potent blood vessel dilator; also used for hair growth in androgenic alopecia
- Clonidine – blocks sympathetic activity in the brain and leads to decreased vascular resistance
- Peripheral sympathetic receptor blockers in vascular smooth muscle – alpha-blockers

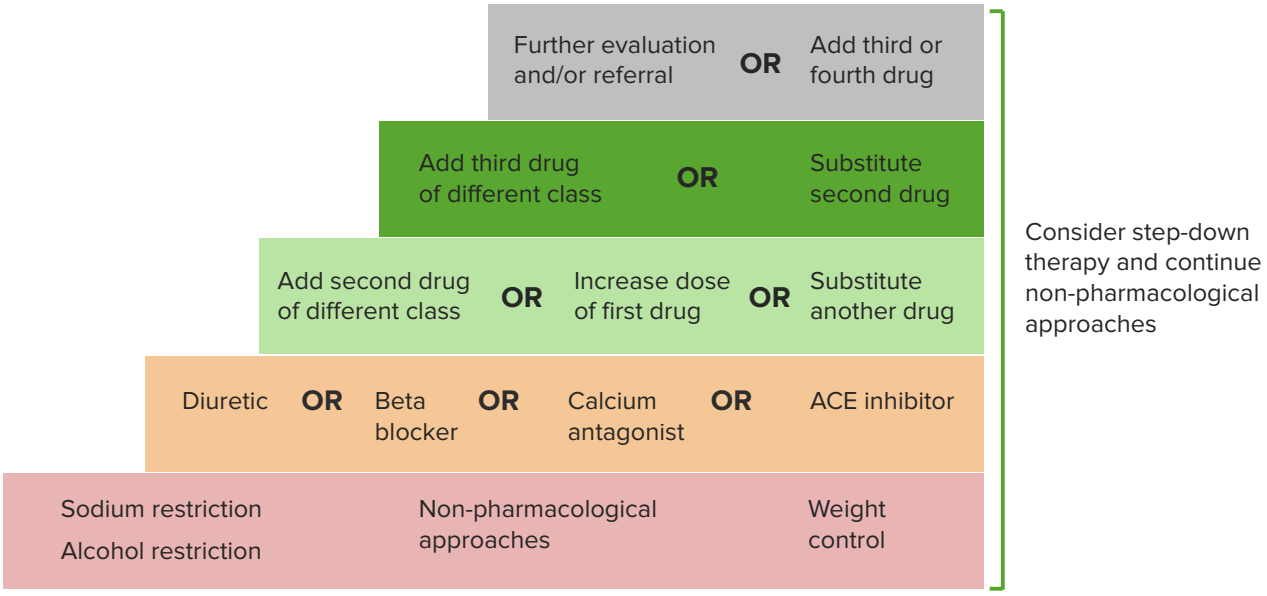

Fig. 2-07: *Step-by-step approach in management of hypertension.*

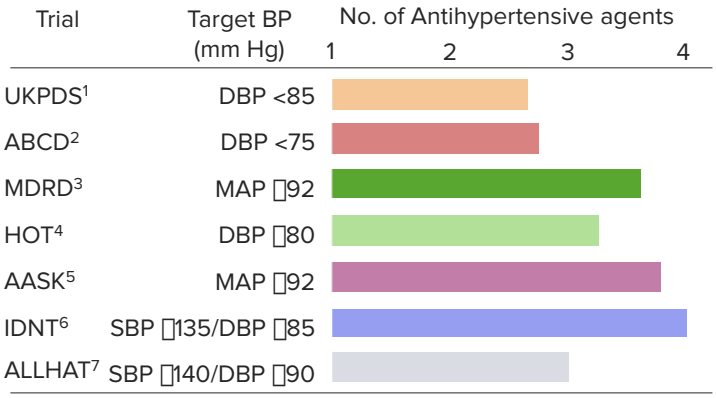

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Fig. 2-08: *Average number of antihypertensive agents used to achieve target blood pressure*

Complications of Hypertension

Double combination options consist of: administering a diuretic in combination with a beta-blocker, a long-acting calcium channel blocker, ACE inhibitors or AT1 receptor blockers. An alternative is the combination of a calcium channel blocker with a beta-blocker, ACE inhibitors or AT1 receptor blockers. Depending on the individual comorbidities, the respective medications may either gain or lose significance. A popular question in exams pertains to the following combinations: In cases of hypertension combined with heart failure, diuretics are an option. ACE inhibitors may be used in cases of heart failure or diabetic nephropathy. Beta-blockers are also used for the treatment of heart failure. When choosing individual medications, side effects, individual tolerability, and interaction with other medications must be considered. If 2 drug combination is not sufficiently effective, a 3 drug combination can be chosen for the treatment of hypertension. Isolated systolic hypertension should be treated in the same way as systolic and diastolic hypertension.

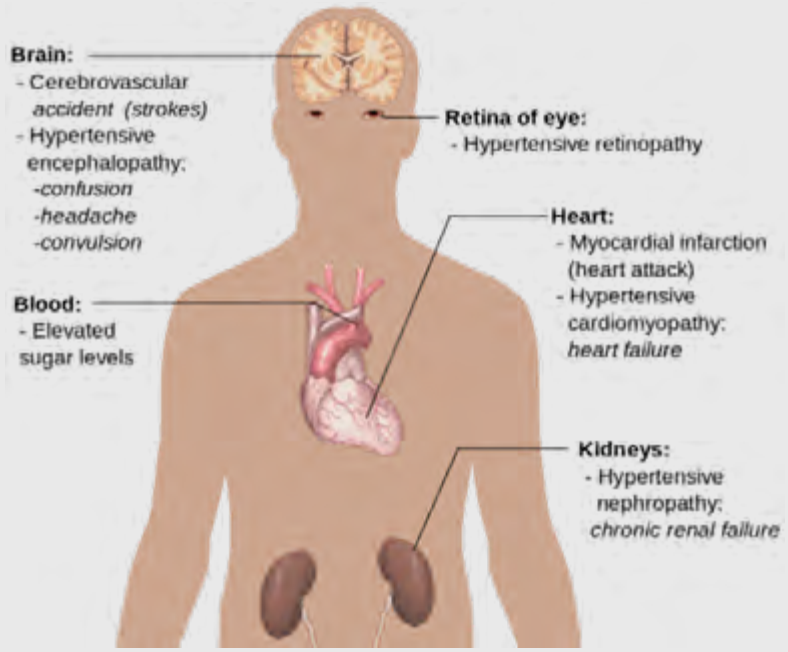

Fig. 2-09: *Main complications of persistent high blood pressure*

Note:
Calcium channel blockers of the non-dihydropyridine variety must not be administered in combination with beta-blockers as they may promote bradycardia or an atrioventricular block (AV block)!

High-yield:
Hypertension is considered the most common cause of ascending aortic aneurysm, while atherosclerosis is considered the most common cause of descending aortic aneurysm.

Prevention of Hypertension

Preventive approaches include the elimination of hypertension risk factors or their reduction.

Review Questions

Question 2.1: A 49-year-old male is diagnosed with hypertension. He has asthma. His creatinine and potassium are both slightly elevated. Which of the following antihypertensive drugs would be appropriate in his case?

A. Amlodipine

B. Propranolol

C. Enalapril

D. Hydrochlorothiazide (HCT)

E. Spironolactone

Question 2.2: A 60-year-old female comes to the urgent care clinic after she developed breathlessness 30 minutes ago. She also developed swelling of her tongue and lips. She has heart failure and was recently diagnosed with hypertension. She was started on a medication, the first dose of which she took this afternoon before her symptoms started. Her blood pressure is 167/88 mm Hg, respirations are 17/min, and pulse is 78/min. Physical examination reveals a skin rash on her back and anterior abdomen. There is a mild swelling of her lips and tongue. Chest auscultation does not reveal any abnormal breath sounds. Which of the following medications most likely led to her current symptoms?

A. Captopril

B. Amlodipine

C. Clonidine

D. Hydrochlorothiazide (HCTZ)

E. Propranolol

Chapter 3:
Atherosclerosis

Most Important Facts about Atherosclerosis

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Definition of Atherosclerosis

Atherosclerosis is the thickening of the arterial wall and a loss of elasticity due to variable pathogenesis. The term atherosclerosis is derived from the words 'atheroma' (focal plaques) and 'sclerosis' (overgrowth of fibrous tissue). The changes in atherosclerosis take place in the intima and media of blood vessel walls and lead to a stiffening of the vessel walls and narrowing of the vascular lumen. The term atherosclerosis includes atherosclerosis, medial sclerosis, and arteriolosclerosis.

Epidemiology of Atherosclerosis

Atherosclerosis is the leading cause of death in industrialized countries. Over 152,000 of the Americans who died by CVD each year are under the age of 65. In 2002, 32 % of deaths caused by CVD occurred prematurely (i.e., before age 75, which is close to the average life expectancy).

Etiology of Atherosclerosis

Atherosclerosis is a chronic inflammatory disorder that takes place in the walls of blood vessels. The inflammatory process involves the oxidation of LDL cholesterol. Lipids, calcium and other cellular debris are often stored within the intima of large and medium-sized arteries, thereby causing an inflammatory process which results in vessel wall thickening and plaque formation. The causes of atherosclerosis are dyslipidemia, hypercholesterolemia, and hypertriglyceridemia. Hypercholesterolemia can be caused by abetalipoproteinemia, lipoprotein lipase and apolipoprotein C-II deficiency, or familial dysbetalipoproteinemia.

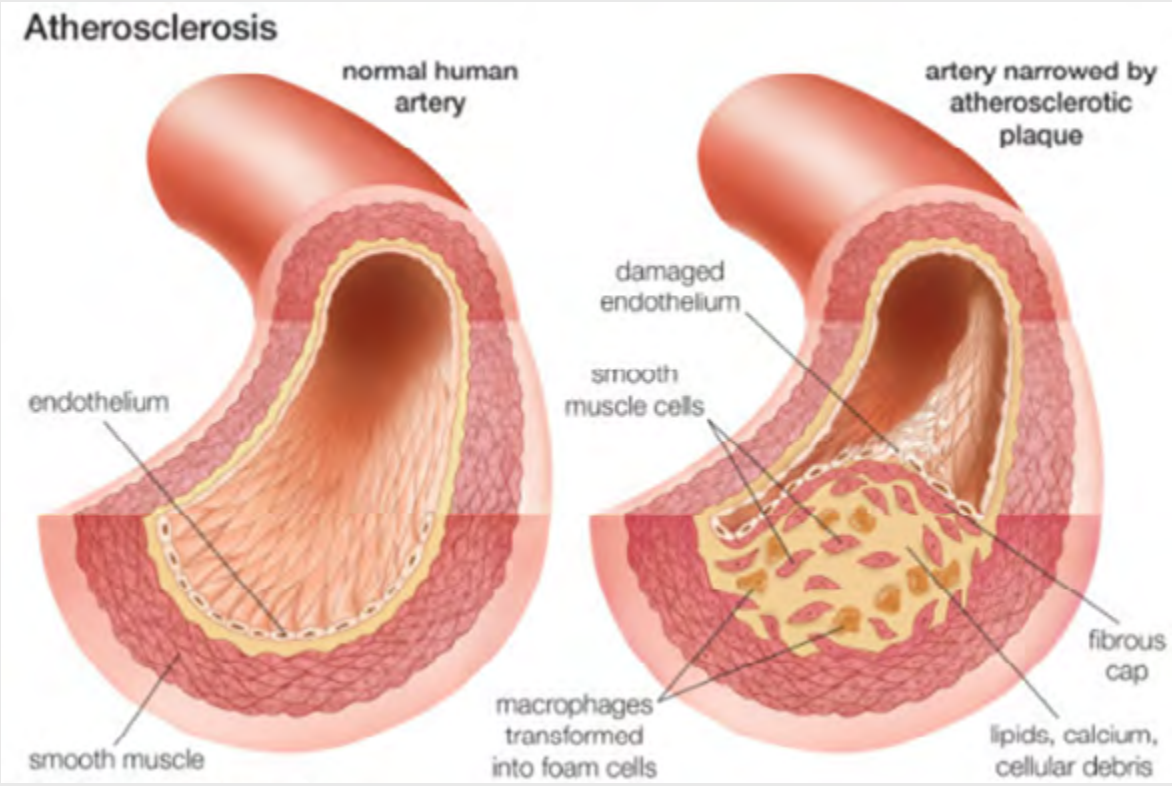


Fig. 3-01: *Coronary atherosclerosis*

The risk factors associated with the development of atherosclerosis are divided into modifiable and non-modifiable risk factors. Non-modifiable risk factors are male gender, age, and family history. As for the modifiable risk factors, they can be further divided into first order and second order risk factors.

First order modifiable risk factors

- **Nicotine abuse:** Smoking promotes the early development and rapid progression of atherosclerosis.
- **Arterial hypertension:** Due to the high-pressure load, endothelium damage occurs more rapidly.
- **Diabetes mellitus:** Increased blood glucose levels cause reactiveglycosylation, which in itself causes increased phagocytosis and endothelial damage.
- **Hyperlipoproteinemia:** Excessive LDL cholesterol increases the risk of atherosclerosis, especially if HDL cholesterol levels are concomitantly low.

Second order modifiable risk factors

- Lack of exercise
- Psychological or emotional stress
- Obesity
- Hyperuricemia
- Triglyceridemia
- Fibrinogenemia
- Homocysteinemia
- Glucose tolerance disorders
- Chronic renal failure
- Increased lipoprotein (a)

Classification of Atherosclerosis

Atherosclerosis is classified according to the affected vessels. We distinguish between macroangiopathies affecting the large and medium-sized arteries, and microangiopathy that occurs in the arterioles, capillaries or venules and is usually present in cases of diabetes mellitus. Another classification type is based upon severity.

Mild	Moderate	Severe
Endothelium becomes damaged	Damage causes an inflammatory response and white blood cells deposit cholesterol forming an atheroma	Plaque restricts blood flow
Factors: high blood pressure, cigarette smoke	Calcium salts and fibrous tissue form plaque	High blood pressure
	Artery loses elasticity and narrows	Increased blood pressure promotes the formation of more plaques

Clinical Features of Atherosclerosis

Atherosclerosis can be present for years or decades without any symptoms. Common manifestations include coronary artery disease, cerebrovascular disease, peripheral artery disease, and infrarenal aortic aneurysm.

Pathophysiology of Atherosclerosis

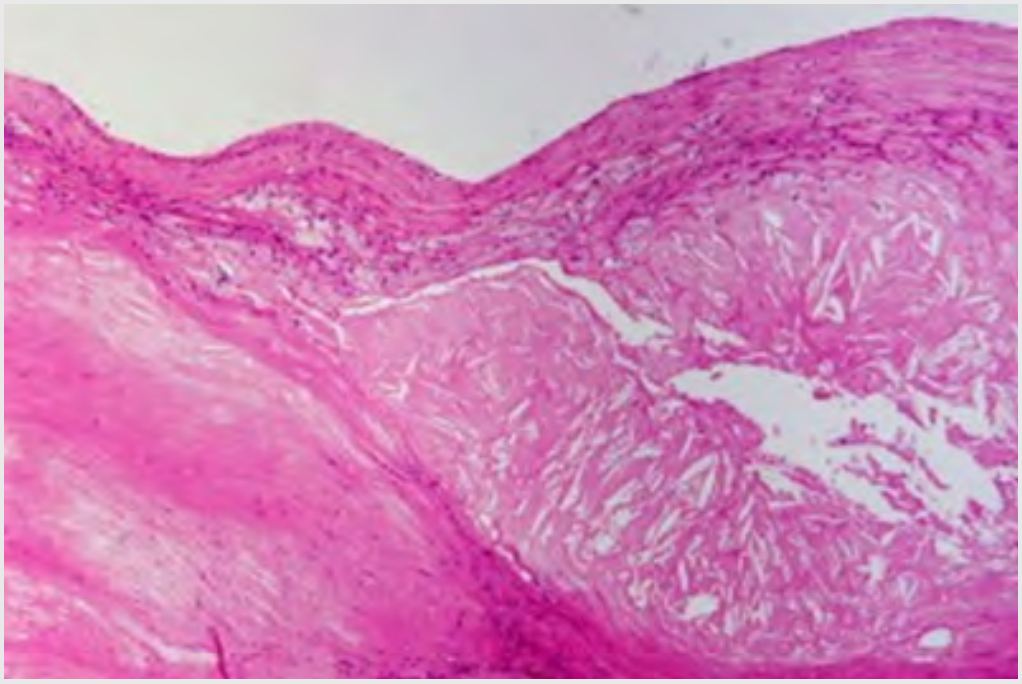


Fig. 3-02: *Atherosclerotic plaque with cholesterol crystal gaps, foam cells and fibrosis*

Initially, LDL cholesterol is deposited in the intima of the vessel wall. It is then oxidized and followed by a local inflammatory response, i.e. monocytes start to migrate to the tissue. If they phagocytize the LDL cholesterol, foam cells with embedded lipid droplets are formed. These early atherosclerotic lesions are referred to as fatty streaks and occur especially in areas with high mechanical stress (for example at the proximal left anterior descending artery (LAD) or at the carotid bifurcation).

Gradually, **lipids** and **cellular debris** accumulate within the intima. Different cells of the vessel walls release mediators, and muscle cells from the **tunica media** migrate into the **intima**.

The fatty core is surrounded by connective tissue which makes it hard and inaccessible; the stored LDL cholesterol cannot be degraded. These plaques may contain newly formed vessels originating from the **vasa vasorum** that can cause bleeding into the plaque.

Calcium starts to accumulate in the growing plaques. Activation of a coagulation cascade through tears in the endothelium causes thrombosis. The plaques initially develop extra-luminally. If more than 40 % of the lumen is obstructed, stenosis occurs. Due to the vascular wall damage, NO synthesis is disrupted and endothelial dysfunction occurs.

High-yield:

Metabolic syndrome refers to the presence of at least 3 of the following risk factors:

- *Abdominal obesity (waist circumference > 102 cm in men, > 88 cm in women)*
- *Elevated triglycerides (> 150 mg/dL)*
- *Low HDL (< 40 mg/dL in men, and < 50 mg/dL in women)*
- *Fasting glucose > 100 mg/dL*
- *Blood pressure > 130/85 mmHg*

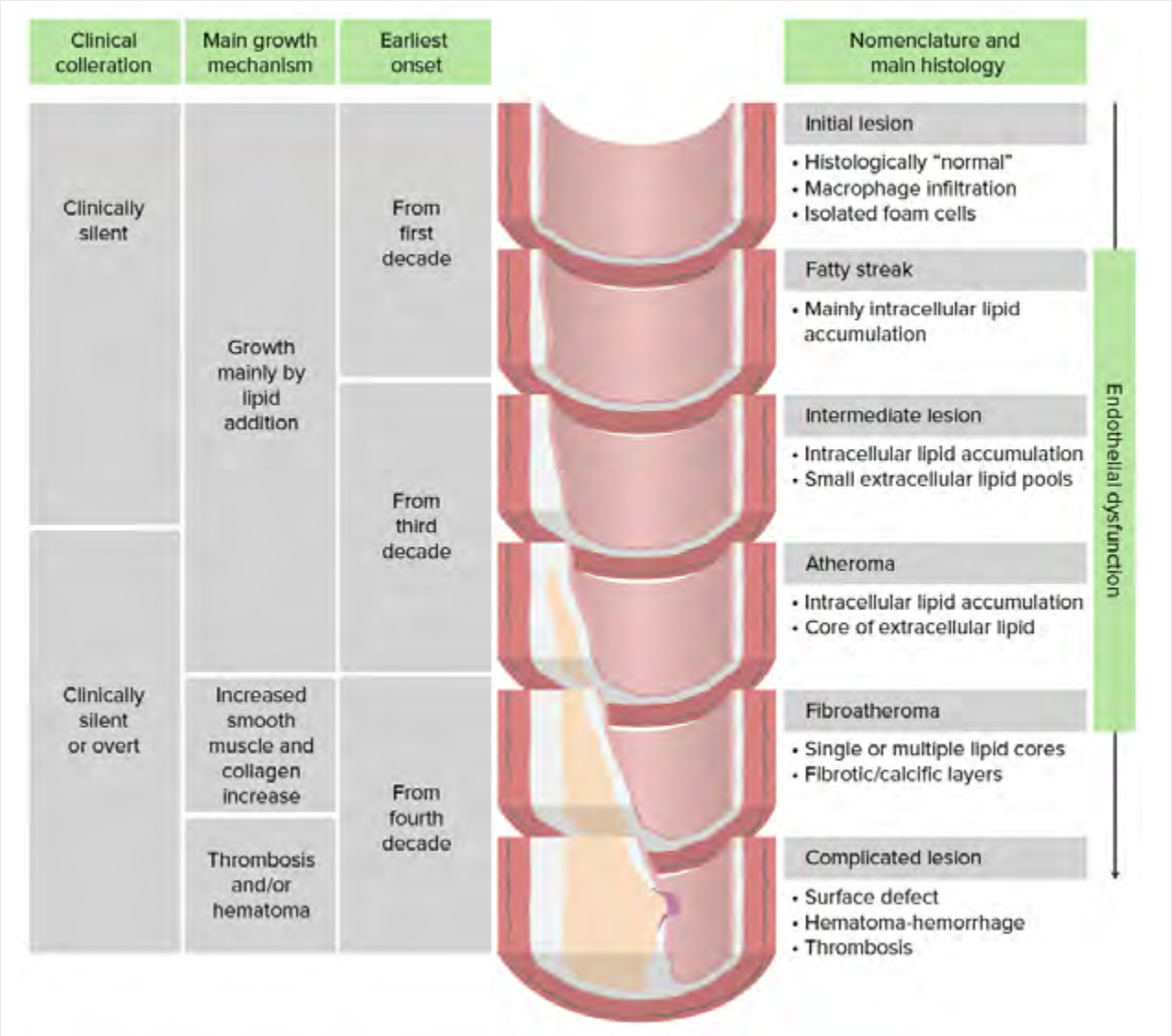


Fig. 3-03: Stages of endothelial dysfunction in atheroscerosis

Plaques that have a large fatty core and only a thin fibrous cap are at risk of rupture. The coagulation system is so strongly activated under certain circumstances that it can lead to a complete thrombotic occlusion of a vessel. Myocardial infarction happens when 90 % or more of the blood vessel diameter is occluded.

Plaque rupture can cause cholesterol embolisms to remote blood vessels (for example, to the renal arteries).

Another consequence of atherosclerosis is the formation of aneurysms due to changed **atherosclerotic vascular tissue**. Prolonged restructuring processes may cause the supply to the **tunica media** to be damaged, causing the tissue to atrophy, together with decreased vessel wall stability.

Whether the endothelial dysfunction ('Response-to-Injury Hypothesis') or the oxidation of LDL cholesterol ('lipoprotein-induced atherosclerosis hypothesis') is ultimately the starting point of plaque formation is still unclear and controversial.

As vascular lumen diameter is reduced due to the atherosclerotic plaque, coronary arteries aren't able to carry enough oxygen to the heart. This results in an imbalance between oxygen demand and supply, leading to the development of ischemic heart diseases.

Diagnostics and Differential Diagnoses of Atherosclerosis

History and physical examination of atherosclerosis

Patient history is taken to identify the risk factors, including family history. The patient should also be asked about comorbidities, medications, and walking distance tolerance.

Physical examination provides information about skin color, temperature, and ulcerations due to circulatory disorders if they are present. The heart should be auscultated. ECG or stress ECG can be helpful.

Laboratory tests

Lipid profile consisting of total cholesterol, LDL and HDL cholesterol, triglycerides, lipoprotein (a), and homocysteine should be carried out. If myocardial infarction is suspected, cardiac enzymes, such as troponins, CK and CK-MB, GOT, LDH, and myoglobin tests must be tested.

Inflammatory markers, such as CRP, and glucose metabolism markers, such as fasting blood glucose and HbA1c, should also be analyzed. Other tests include:

- Complete blood count
- Sodium and potassium
- Coagulation parameters
- TSH
- Creatinine
- Rheumatoid factors

Diagnostic imaging

Sonography

Doppler sonography offers a good, non-invasive way to take a better look at the vessels. It is used for both closure and perfusion measurement and the determination of the **ankle-brachial index**, as well as for the measurement of flow velocities.

Color duplex sonography combines 2 methods and allows the examination of **morphologically conspicuous** vessel sections and gives a color code depending on blood flow direction. Intravascular ultrasound (IVUS) can be used for **coronary artery** assessment.

An echocardiogram can be done to assess structural or functional abnormalities of the heart. Ejection fraction and heart contractility are 2 important functional parameters that can be assessed using an ECG.

Angiography

CT and MR angiography also offer the advantage of non-invasive diagnostics over conventional angiography. The presentation is detailed and enables 3D reconstruction for precise treatment planning. The CT angiography offers a rapid assessment especially in emergency diagnosis, whereas MR angiography has the advantage of low radiation exposure.

Conventional angiography, however, has the advantage of simultaneous intervention options (such as the stent angioplasty) and is still the gold standard in terms of vascular imaging accuracy.

Differential diagnoses

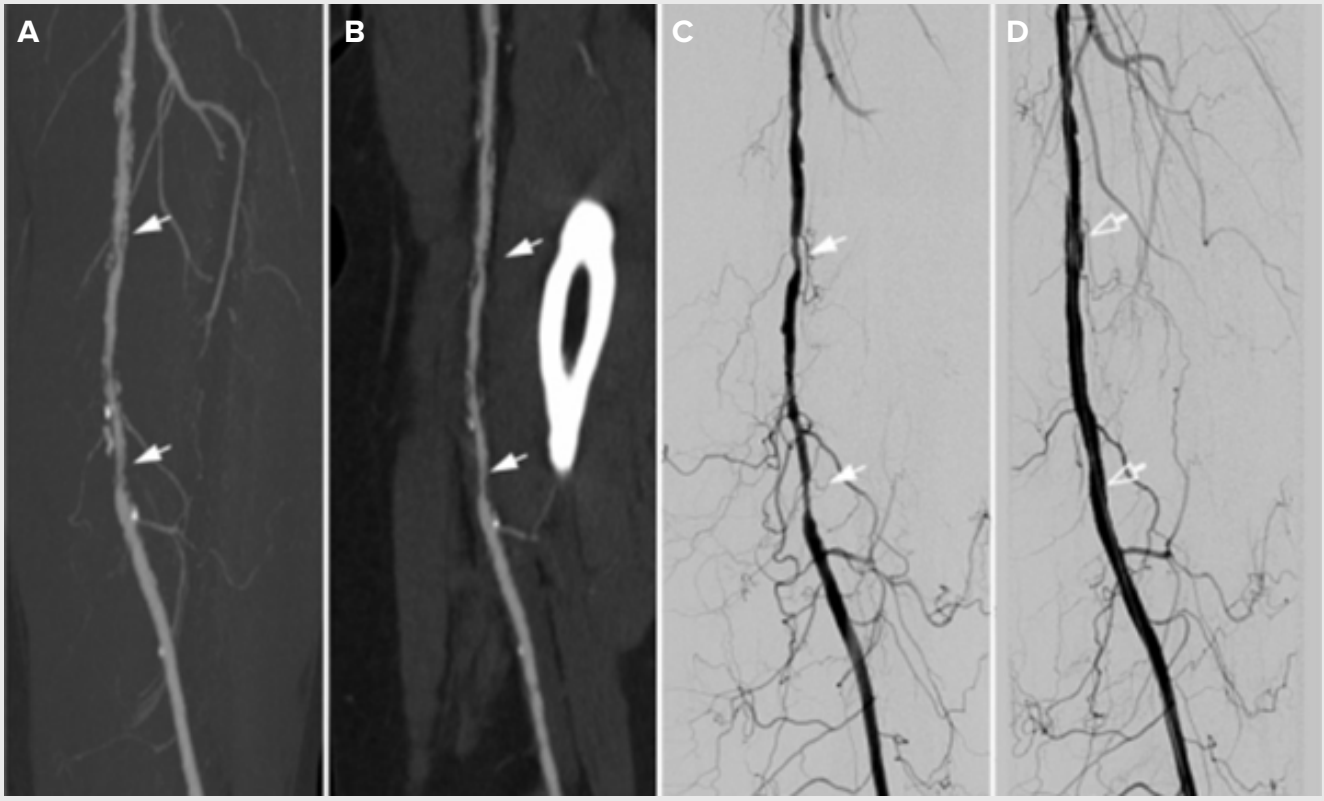


Fig. 3-04: *Example of a runoff CTA with sufficient diagnostic confidence and diagnostic image quality. 69 year-old female with intermittent claudication of the left lower leg (Fontaine stage IIB). Run-off CTA showed multiple stenoses (white arrows) of the left superficial femoral artery (TASC B) in the MIP images (A) and curved MPR (B). Stenoses were confirmed by DSA (C) and successfully treated by percutaneous transluminal angioplasty and stenting (D) (empty white arrow).*

Vascular diseases similar to atherosclerosis

In addition to atherosclerosis, other vascular diseases can cause structural wall changes and, lead to stenosis. Examples of these include inflammatory diseases that cause 5 % of stenotic vascular diseases. Inflammation may be caused by autoimmune or infectious processes, wherein the former clearly prevails. If there is an inflammation, the vascular wall thickens due to inflammatory infiltrates and secondary vessel wall edema. If the endothelium is damaged, thrombosis may be formed. Excluding stenosis, the inflammatory process can lead to vascular wall dilation or dissection.

Autoimmune diseases similar to atherosclerosis

Among autoimmune diseases, Buerger‘s disease (thromboangiitis obliterans), and giant cell arteritis or Takayasu arteritis can be possible causes of vessel wall inflammation. Bacteria such as E. coli, S. aureus, and herpes virus can also cause vessel wall inflammation.

Mechanical damage

Mechanical damage, such as arterial trauma, may also cause stenosis. Malignant tumors can cause infiltrative growth into the vascular wall. Even benign tumors can result in vasoconstriction.

Treatment of Atherosclerosis

Treatment of atherosclerosis includes lifestyle modifications, medications, and surgical intervention.

Non-pharmacological treatment (lifestyle modifications)

These include weight normalization in combination with sufficient aerobic physical activity such as jogging, swimming, or cycling, together with a healthy diet. Smoking cessation is also important, as well as avoiding stress.

Walking exercise strategy

Exercising, such as regularly walking for periods of at least 30 continuous minutes 3 times a week can improve symptoms by encouraging the formation of new, collateral blood vessels and improving muscle efficiency. Many patients experience a dramatic increase in the distance they are able to walk without pain.atients can also benefit from a vascular rehabilitation program, involving 45 minutes of supervised exercise every week.

Pharmacological treatment

Pharmacological treatment aims to control the modifiable risk factors of atherosclerosis. Antihypertensives, lipid-lowering, and anticoagulation medications are examples of what we might use in the treatment of atherosclerosis.

Complications of Atherosclerosis

Complications include coronary artery disease and angina pectoris, cerebrovascular insufficiency, PAD, and renal artery stenosis. Subclavian steal syndrome or mesenteric stenosis can also result from chronic stenosis.

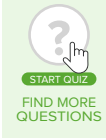
Acute vascular occlusions can also cause complications. Mesenteric infarct, renal or splenic infarction, as well as transient ischemic attack (TIA) and stroke, are examples of acute complications. Aneurysms at various vessel segments, such as an infrarenal or thoracic aortic aneurysm or thoracic aortic dissection, as well as iliac or popliteal aneurysms are consequences of atherosclerosis.

Prevention of Atherosclerosis

Reduction of modifiable risk factors is important. Prevention is aimed primarily at promoting a healthy diet, adequate physical activity in the form of aerobic exercise, and controlling underlying diseases such as diabetes mellitus and hypertension. Smoking cessation is the most important preventive measure against atherosclerosis and its complications.

Note:
Smoking cessation, healthy diet, adequate physical activity, and the control of underlying diseases such as diabetes mellitus and hypertension lower the risk of atherosclerosis.

Review Questions



Test your knowledge:
Atherosclerosis

Question 3.1: A 67-year-old man comes to the office due to pain in the lower part of his calves. The pain starts when he walks and is relieved by rest. He has a history of myocardial infarction, hypertension, hyperlipidemia, diabetes mellitus, and smoking. He has a pulse of 75/min, respiratory rate of 17/min, temperature of 37.6°C (99.6°F), and blood pressure of 145/90 mm Hg. Examination of the legs shows atrophic changes and diminished pedal pulses. Which of the following is the most appropriate initial treatment?

A. Clopidogrel

B. Metoprolol

C. Pedal pumping

D. Revascularization of the extremities

E. Smoking cessation, exercise, blood sugar, and hypertension control

Question 3.2: A 31-year-old man comes to the office because of chest pain with activity for the past 6 months. He is a businessman, and he says his job is stressful but has not been more stressful than usual. He has diabetes mellitus. Examination shows a BMI of 28.5 kg/m^2 and blood pressure of 142/85 mm Hg. Coronary angiogram shows > 75% narrowing of the left anterior descending coronary artery. Which of the following risk factors is most significant for this patient?

A. Diabetes mellitus

B. High carbohydrate intake

C. Lack of exercise

D. Obesity

E. Stress

Dyslipidemia / Hyperlipidemia

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Definition of Dyslipidemia

Dyslipidemia is a condition where serum concentrations of total cholesterol > 200 mg/dL, LDL > 130 mg/dL, HDL < 40 mg/dL, or triglycerides > 150 mg/dL. It is one of the main causes of the development of atherosclerosis.

Etiology of Dyslipidemia

Causes of dyslipidemia can be primary, as in familial hypercholesterolemia, or secondary to underlying diseases such as diabetes mellitus, hypothyroidism, nephrotic syndrome, and hepatic disease.

Clinical Features of Dyslipidemia

Dyslipidemia is usually asymptomatic. However, yellowish fatty growths (xanthomas) are sometimes present under the skin in areas surrounding the eyes and joints. Most often, dyslipidemia is diagnosed upon routine investigation or after a cardiovascular event e.g. myocardial infarction or stroke. Other clinical features of dyslipidemia include corneal arcus, Achilles tendon xanthomas, eruptive xanthomas, and hepatosplenomegaly.

Types of Dyslipidemia

Type	Serum elevation	Lipoprotein	Molecular
I	Cholesterol and triglycerides	Chylomicrons	↓CPL or ↓apo C-II
IIa	Cholesterol	LDL	↓LDL receptors (liver)
IIb	Cholesterol and triglycerides	LDL; VLDL	↓LDL receptors (liver)
III	Cholesterol and triglycerides	IDL	↓apo E
IV	Triglycerides	VLDL	Usually lifestyle
V	Cholesterol and triglycerides	VLDL, chylomicrons	↓CPL

Treatment of Dyslipidemia

Non-pharmacological treatment (lifestyle modification)

Lifestyle modifications remain the most important therapeutic option for the control of dyslipidemia as they lower the risk of cardiovascular disease. They include:

- Dietary changes: It is recommended to limit saturated fat and cholesterol intake
- Weight reduction
- Daily aerobic exercise or regular exercise

High-yield:
Regular exercise is proven to increase HDL and decrease LDL levels.

Pharmacological treatment

1. Statins

Initiation of **moderate-intensity or high-intensity statin therapy** is recommended in the following indications:

1. Clinical atherosclerotic cardiovascular disease (ASCVD): high-intensity statin therapy (age > 75 years: moderate-intensity statin therapy)
2. LDL ≥ 190: high-intensity statin therapy
3. Age 40–75 years + Diabetes (if LDL 70–189)
4. Age 40–75 years + 10 year ASCVD risk > 7.5 % (if LDL 70–189)

The decision to start pharmacological treatment for dyslipidemia that does not meet the indications listed above depends on the patient's 10-year risk of coronary heart disease (CHD). The following table summarizes the LDL cholesterol goal in each risk category and indicates situations when pharmacological therapy is needed for the treatment of dyslipidemia.

Risk category	LDL cholesterol target	Threshold to start pharmacological treatment
High-risk: • Coronary heart disease or risk equivalent (diabetes, peripheral arterial disease) • 10-year CHD risk > 20 %	< 100 mg/dL or < 70 mg/dL if the patient is considered very high-risk	When LDL cholesterol is > 100 mg/dL Consider even if LDL cholesterol is below 100 mg/dL
Moderately high-risk: • 2 risk factors or more (cigarette smoking, hypertension, low high-density lipoprotein (HDL) cholesterol, family history of premature CHD, male > 45 years, female > 55 years) • 10-year CHD risk 10–20 %	< 130 mg/dL Lower to achieve under 100 mg/dL	When LDL cholesterol is > 130 mg/dL Consider in patients with LDL cholesterol between 100 mg to 129 mg/dL
Moderate risk: • Same as a moderately high-risk but with a 10-year CHD risk below 10 %	< 130 mg/dL	Optional if LDL cholesterol is equal to or above 160 mg/dL
Low risk: • Presence of 1 or no risk factors of those mentioned for moderately high-risk	< 160 mg/dL	Optional if LDL cholesterol is equal to or above 190 mg/dL

Note:
Aim is to achieve a 50 % reduction of the baseline LDL value.

Note:
High-intensity statins include rosuvastatin 20 or 40 mg and atorvastatin 40 or 80 mg.

Moderate-intensity statins include rosuvastatin 5 or 10 mg and atorvastatin 10 or 20 mg.

Contraindications to statins

Statins are contraindicated in patients with active liver disease and in pregnancy. The main side effects of statins are:

- Myopathies (1 %)
- Rhabdomyolysis (0.2 %)
- Elevated liver function tests (2 %)

Other statin-associated side effects include confusion, forgetfulness, dementia, depression, and erectile dysfunction. Introduction of statins in the management of dyslipidemia has improved the prognosis of IHD.

Statins were also found to be effective in lowering the risk of recurrent stroke in patients with a previous history of cerebrovascular disease. Unfortunately, statins were not found to influence overall mortality in the above-mentioned patients.

Initiating statins to lower LDL cholesterol levels in the acute setting of a cerebrovascular accident has been proven effective in improving clinical outcome and reducing patient disability.

2. Non-statins therapy

In addition to statins, other lipid-lowering medications can be used to lower LDL cholesterol level. Fibrates are known to lower the risk of future coronary events but not overall mortality. The combination of a statin and a fibrate is known to help with achieving a desired LDL goal, but was not found to be associated with lower mortality.

Niacin monotherapy for the secondary prevention of CHD is not effective. On the other hand, adding niacin to a statin for the secondary prevention of CHD might be effective and beneficial to the patient. Bile-acid binding resins are not effective for the secondary prevention of CHD and mortality related to it.

Niacin as monotherapy or an add-on therapy for the primary prevention of CHD in patients with isolated low HDL-cholesterol levels is a good example of an effective non-statin treatment for dyslipidemia.

The dietary supplementation of omega-3 fatty acids was found to be ineffective or to have a very small effect on the primary and secondary prevention of CHD. Omega-3 fatty acids do not affect overall mortality in patients with previous history of myocardial infarction.

Chapter 4:
Ischemic Heart Diseases

Introduction to Ischemic Heart Diseases

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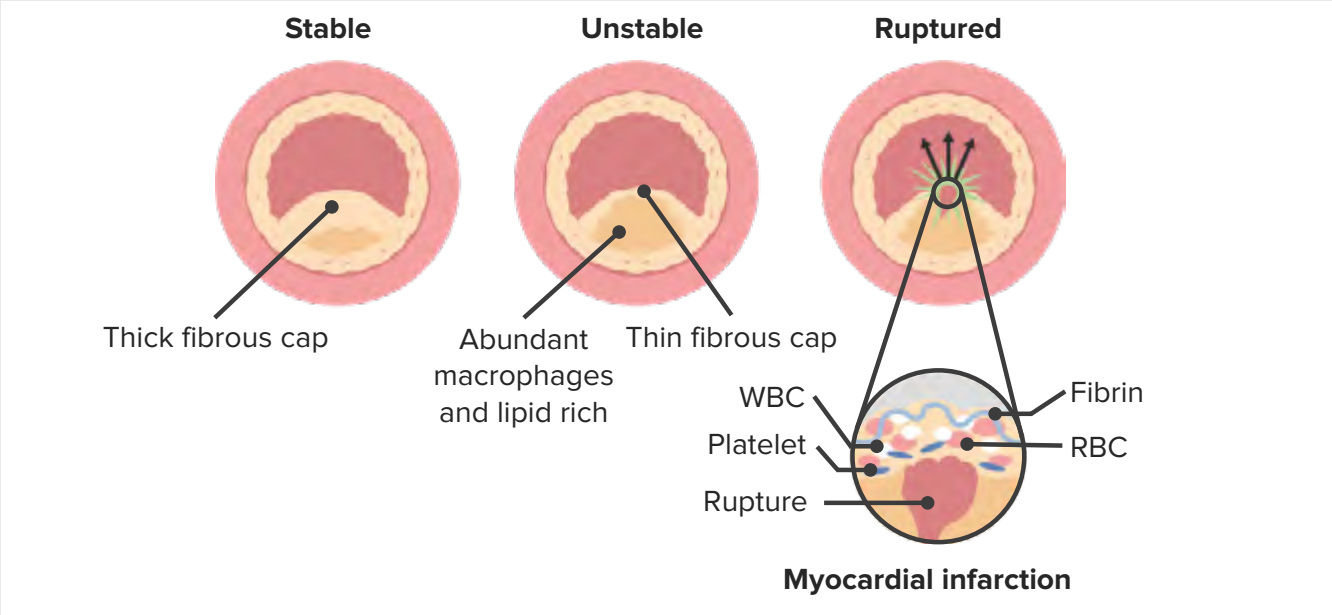

Fig. 4-01: Pathological progression of CAD with eventual development of myocardial infarction.

Definition of IHD

Ischemic Heart Disease (IHD), also termed Coronary Artery Disease (CAD), are terms used to describe a wide range of clinical conditions in which an imbalance in oxygen supply and myocardial demand results in partial ischemia of the myocardium. IHD can be classified into stable disease (stable angina) and unstable disease (acute coronary syndrome). The most important coronary vessels are the Right Coronary Artery (RCA) and the Left Coronary Artery (LCA), the Left Circumflex Anterior Artery (LCx) and the Left Anterior Descending (LAD) artery.

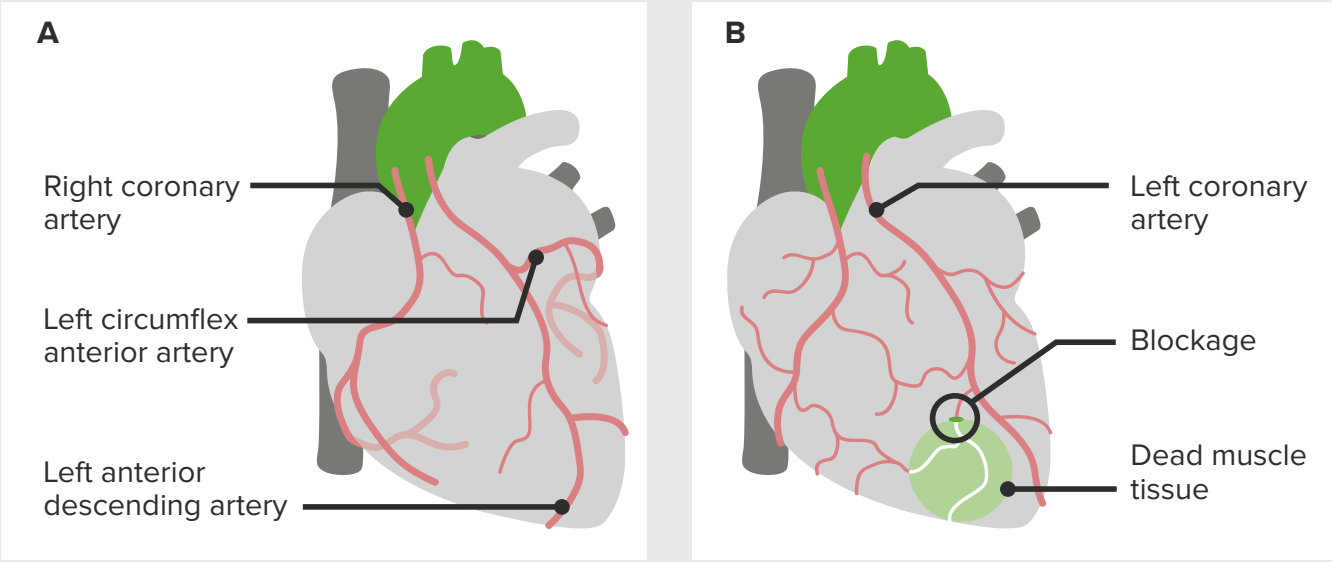

Fig. 4-02: This image illustrates the normal epicardial coronaries, and how myocardial infarction affects the muscle tissue. (A) Normal coronary circulation (B) Ischemic heart disease.

Epidemiology of IHD

Ischemic heart disease is one of the leading causes of death worldwide. It is considered the most common serious chronic illness in the United States, as more than 13 million patients currently suffer from ischemic heart disease in the country. More than 6 million have angina pectoris and more than 7 million have experienced myocardial infarction. Because of the large increase in the prevalence of IHD worldwide, it is likely to become the leading cause of death by 2020.

Lifetime risk of coronary heart disease:

- Age 40: 49 % in men and 32 % in women
- Age 75: 35 % in men and 24 % in women

Risk Factors of IHD

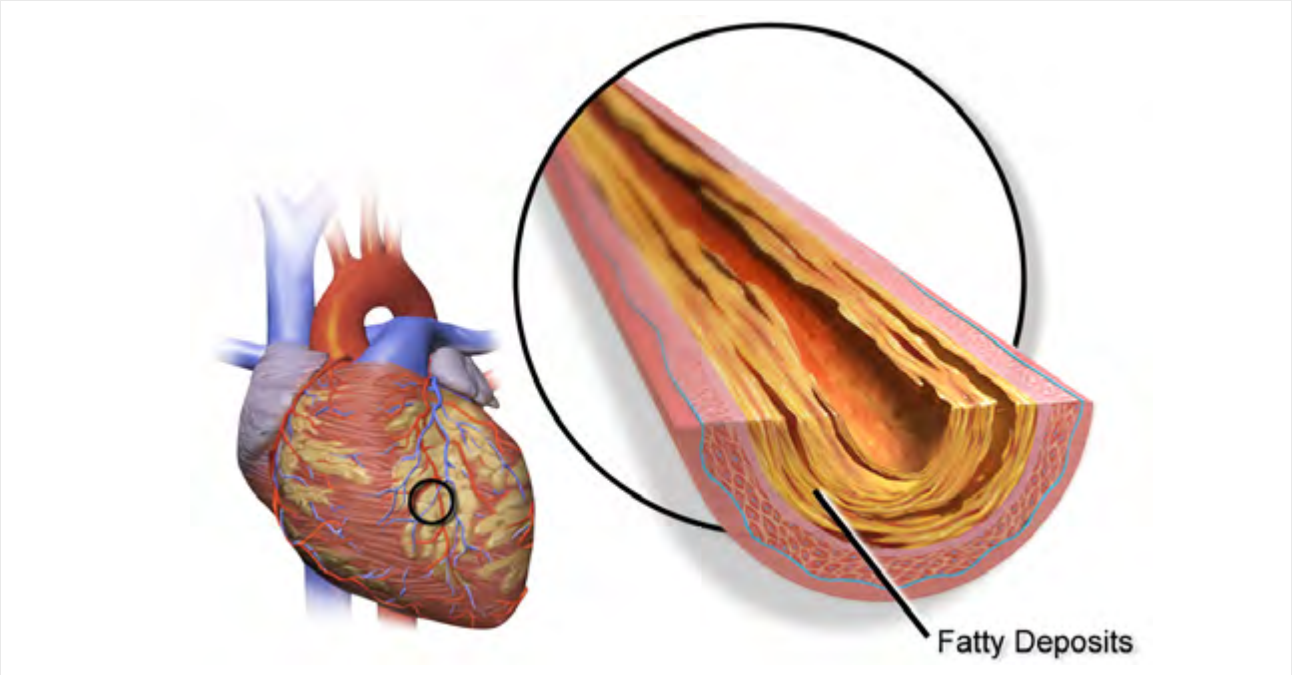

Fig. 4-03: *Atherosclerosis in a coronary artery*

The most common risk factor of coronary heart disease is atherosclerosis of the epicardial coronary arteries, resulting in partial or complete obstruction with subsequent inadequate perfusion of the area of the myocardium supplied by the involved coronary artery.

Many risk factors are involved in the pathophysiology of coronary heart disease. Listed among the main risk factors (in addition to increased LDL or low HDL cholesterol) are arterial hypertension, diabetes mellitus, smoking, a positive family history, and male gender.

In patients who suffer a heart attack at a younger age (< 30 years), other causes may play a role. These include familial lipid metabolism disorders as well as hypothyroidism and vasculitis. Coronary anomalies, antiphospholipid syndrome, and hyperviscosity syndrome should also be excluded. During history taking, possible drug abuse should be questioned.

Fixed risk factors	
Age	Risk increases with age and is rare during childhood, except in cases where the patient has familial dyslipidemia.
Male sex	Men have a higher incidence of ischemic heart disease than premenopausal women. The incidence of atherosclerosis in women increases after menopause due to deficiency of estrogen.
Family history	Positive family history is defined as development of coronary heart disease in a first-degree relative before the age of 50 years.
Modifiable risk factors	
Dyslipidemia	Indicative cholesterol levels, especially increased low-density lipoprotein (LDL) and decreased high-density lipoprotein (HDL), are associated with an increased risk of atherosclerosis.
Hypertension	Systolic and diastolic hypertension are associated with an increased risk of coronary heart disease.
Cigarette smoking	Number of cigarettes smoked is directly related to the risk of coronary heart disease. Cessation of smoking reduces risk by 25 %.
Diabetes mellitus	Abnormal glucose tolerance, or diabetes mellitus, increases the risk of ischemic heart disease and progresses the other risk factors, such as dyslipidemia, obesity, and hypertension.
Lack of exercise	It is recommended to exercise regularly for 30 minutes at moderate intensity 5 days/week.
Obesity	Reduction of body weight by exercise and healthy diet decreases the risk of coronary heart disease and controls both diabetes and insulin resistance.
Alcohol	Moderate intake of alcohol (1 or 2 drinks/day) is associated with a reduced risk of ischemic heart disease. At higher levels, the risk is increased.

Pathophysiology of IHD

Pathology of atherosclerosis

Chronic stress on the endothelium of the coronary arteries due to arterial hypertension causes endothelial dysfunction followed by:

- Inflammatory cell invasion through the disturbed endothelium (monocytes and lymphocytes)
- Platelet adhesion to the damaged endothelium
- Inflammation of the vessel wall causes smooth muscle cell (SMC) proliferation and invades the tunica intima

Macrophages and SMCs take up cholesterol from oxidized LDL and transform into so-called foam cells which accumulate to form fatty streaks, eventually forming a fibrous plaque.

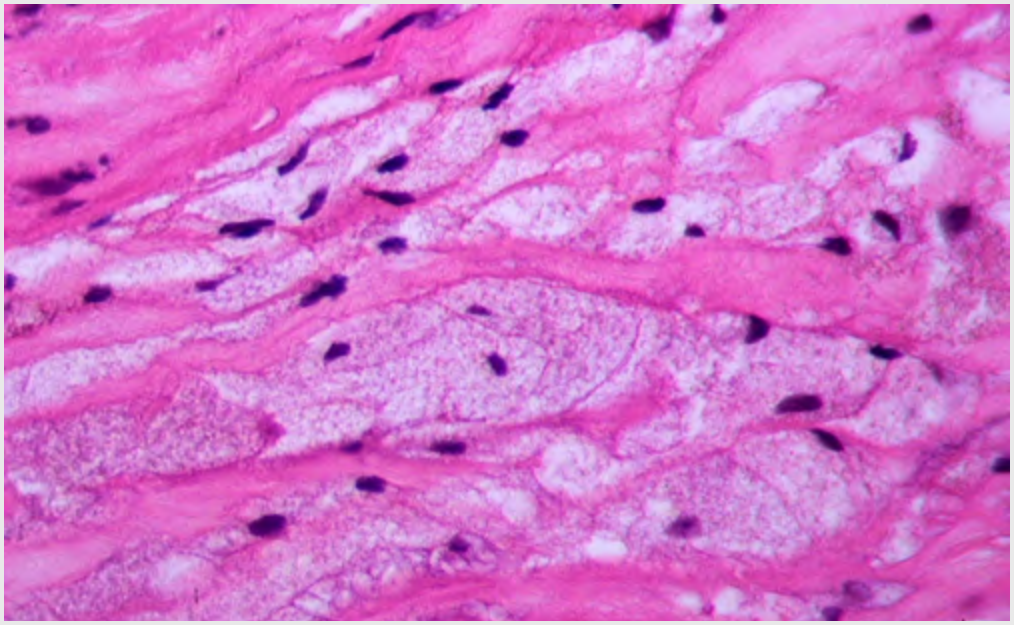

Fig. 4-04: *Foam cells in atherosclerotic plaque. Histology.*

Plaque rupture results in exposure of thrombogenic materials such as collagen, with subsequent thrombus formation and vascular occlusion.

Coronary artery stenosis

Stenosis of the coronary arteries can lead to an insufficient supply of oxygen to the heart upon exertion from a 50% narrowing, as oxygen demand in this situation increases by approximately 4. The so-called coronary reserve, i.e., the difference between the minimum blood flow and the up to 4 times increased maximum blood flow during exercise, is so severely limited in patients with coronary heart disease that often even an increase of blood flow to 2 times the resting blood flow is impossible.

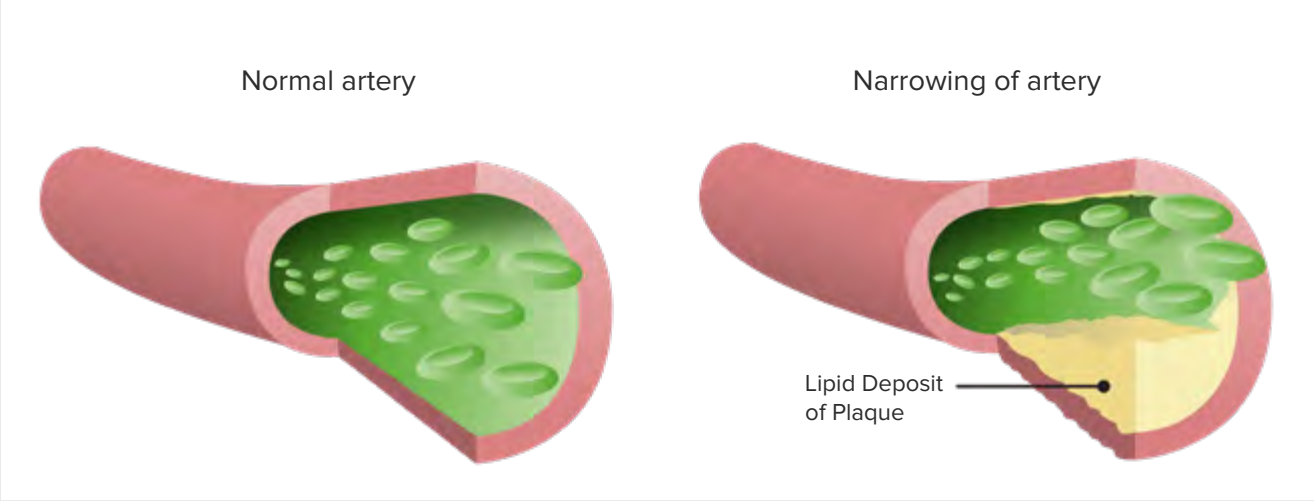

Fig. 4-05: *Ischemic heart disease*

Myocardial oxygen demand

4 major factors determine the oxygen demand of the myocardium:

1. Heart rate
2. Systolic blood pressure (afterload)
3. Tension on myocardial wall (preload)
4. Myocardial contractility

Any clinical condition which increases these factors will also increase myocardial oxygen demand and can result in ischemia. These conditions include extreme tachycardia, hypertension, and ventricular hypertrophy.

Myocardial oxygen supply

The capacity of the blood to carry oxygen to the myocardium is affected by different factors, such as the hemoglobin and oxygen tension, and the amount of hemoglobin-extracted oxygen which reaches the tissue, and is related to 2,3-diphosphoglycerate levels. Another factor is coronary artery blood flow, which is affected by the following factors:

- Coronary artery diameter: Coronary atherosclerosis is the most frequent cause of narrowing and obstructing the coronary artery.
- Coronary artery tone: Coronary vasospasm as in variant or Prinzmetal's angina, reduces the oxygen supply without significant underlying atherosclerotic changes.
- Perfusion pressure: Determined by the pressure gradient from the aorta to the coronary artery.
- Heart rate: Coronary artery flow occurs mainly during diastole, therefore extreme tachycardia will decrease the duration of diastole, and thus decreases the blood flow into the coronary arteries.

Any clinical condition affecting these factors will reduce myocardial oxygen supply and can result in ischemia.

Classification of IHD

Patients with coronary heart disease (IHD) can present with either:

1. Chronic artery disease (CAD), which most commonly presents as stable angina.
2. Acute coronary syndromes (ACSs), which is a term that encompasses:
    - Unstable Angina (UA)
    - Myocardial infarction, divided into:
        - ST-segment elevation myocardial infarction (STEMI)
        - Non-ST-segment elevation myocardial infarction (NSTEMI)

Note:
When appearing for the first time, angina pectoris is considered unstable!

Special Forms of IHD

Variant angina

- Variant angina is caused by a vasospasm which occurs at rest.

Silent myocardial ischemia

- Silent ischemia occurs when typical symptoms are absent. It occurs frequently in diabetics (due to neuropathy), patients with renal insufficiency, women, and elderly patients.
- The symptoms can be very non-specific. Dizziness and nausea, as well as shortness of breath and symptoms that radiate into the epigastrium, are often at the foreground.

Post-infarction angina

- Postinfarction angina may occur within the 2 weeks following a myocardial infarction.

Prognosis of IHD

Several prognostic indicators determine the outcome of coronary heart disease (IHD):

- **Function of the left ventricle**: Increased left ventricular end-diastolic pressure, increased ventricular volume and reduced ejection fraction are associated with poor prognosis.
- **Location and severity of coronary artery stenosis**: Stenosis of the main left anterior descending coronary artery is associated with greater risk and poor prognosis.
- **Number and severity of risk factors**: A large number of risk factors for atherosclerosis are associated with increased risk of myocardial infarction with a worse prognosis.

Stable Angina

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Definition of Stable Angina

Stable angina is defined as chest pain repeatedly triggered by specific events, such as physical exertion, psychological stress, and exposure to the cold. It usually subsides within < 20 minutes of rest or after administration of nitrates.

Note:
Stable anginal pain is always of the same intensity and quality.

Diagnostics of Stable Angina

History

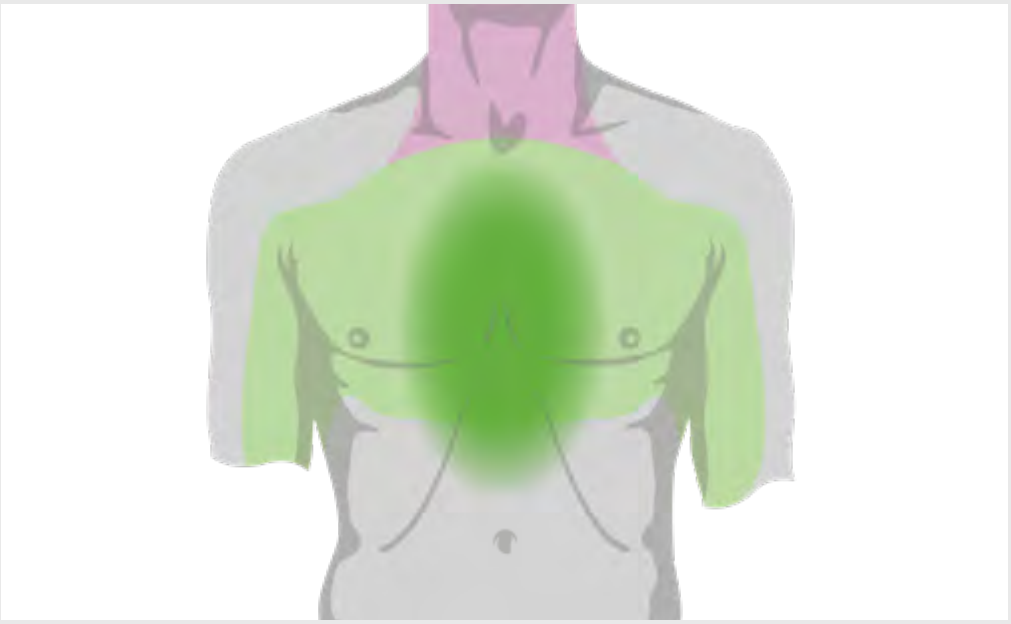

Fig. 4-06: *Diagram of discomfort caused by ischemic heart disease. Pressure, fullness, squeezing or pain in the center of the chest. Can also feel discomfort in the neck, jaw, shoulder, back or arm.*

The typical patient presents with **episodes of chest discomfort** described as a sense of pressure, choking, heaviness, or tightness in the chest.

Onset, course and duration

The pain starts gradually, with the **intensity increasing and decreasing** (crescendo-decrescendo in nature) within minutes and typically lasting for 2–5 minutes. It generally does not last for 20–30 minutes, unless the patient has acute coronary syndrome.

Site of pain

Coronary pain is usually described as **central substernal discomfort** in which patient can't localize the site of pain and typically places a hand or clenched fist over the **sternum**.

Radiation

The pain radiates to any dermatome **from C8 to T4**, most often to the left shoulder and left arm (especially the ulnar surface). It can also radiate to the interscapular region, back, epigastrium, and lower jaw.

Precipitating and relieving factors

Episodes of angina are provoked by **physical exertion and intense emotion** and relieved within minutes by rest and sublingual nitroglycerin.

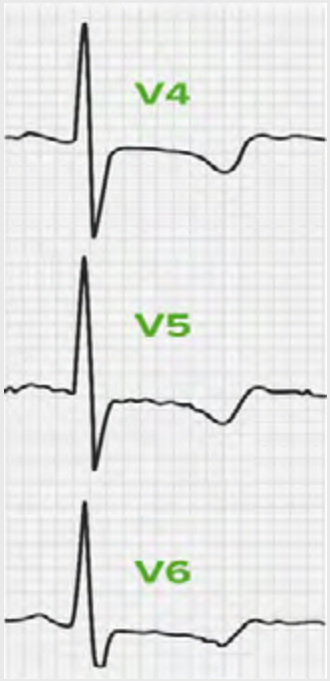

Fig. 4-07: ST segment depression with T wave inversion in setting of chest pain, which is suggestive of myocardial ischemia.

Associated symptoms

Angina is usually associated with shortness of breath, diaphoresis, dizziness, lightheadedness, and fatigue.

Examination

Physical examination is usually unremarkable in patients with stable angina when asymptomatic; however, clinicians should search for:

- Important risk factors such as hypertension and diabetes mellitus
- Evidence of atherosclerosis at other sites, such as carotid bruits and peripheral vascular disease
- Evidence of valvular disease and left ventricular dysfunction

Investigations

Resting ECG

It is normal between attacks and may show evidence of previous myocardial infarction. During the pain, reversible ST-segment depression (injury pattern) or elevation, with or without T wave inversion, is suggestive of myocardial ischemia.

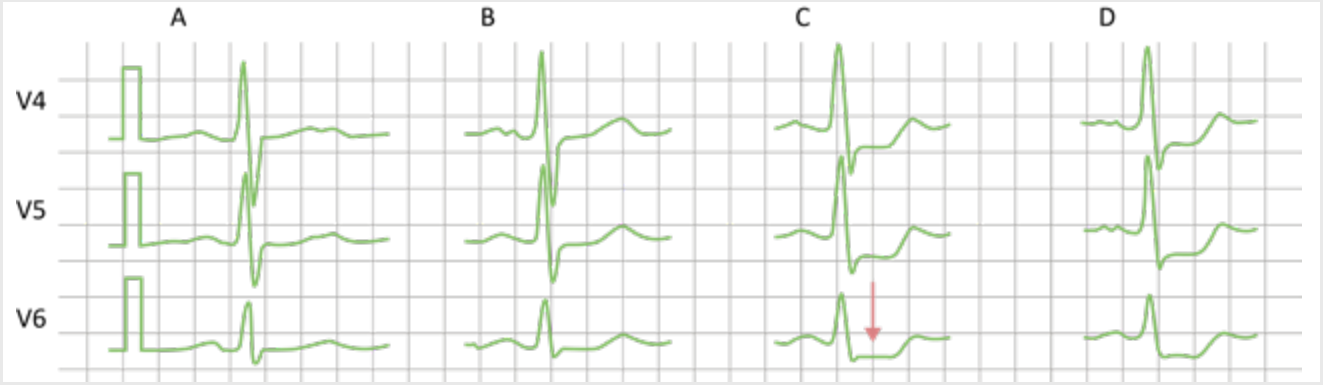

Fig. 4-08: Stress-ECG with ST-segment-depression (arrow) beginning at 100 W (C).

Exercise ECG

Ischemia that is not present at rest is detected by provoking chest pain using a treadmill. Planar or downsloping ST-segment depression of 1 mm or more is indicative of ischemia.

Isotope scanning

Thallium scan can show areas of diminished uptake of radioactive isotope by coronary myocardium at rest or during exercise.

Angiography

Visualizes the location, number, and severity of coronary artery stenosis, and is indicated when coronary revascularization is being considered.

Treatment of Stable Angina

General measures

1. Lifestyle modification and control of the previously mentioned risk factors.
2. Assessment of the extent and severity of atherosclerosis affecting various body organs.

Medical treatment

1. Antiplatelet therapy:

Low-dose aspirin or clopidogrel (if aspirin intolerant) should be prescribed for all patients.

2. Antianginal therapy:

Nitrates:

- Causes venous and arterial dilatation, thus lowering myocardial oxygen demand by reducing the preload and afterload on the heart
- Sublingual glyceryl trinitrate (GTN) should be taken during attack, relieves pain within 2–3 minutes
- Taken prophylactically before strenuous exercise

Beta-blockers:

- Lower myocardial oxygen demand by reducing heart rate and force of contraction
- Aim of therapy: relieve angina and ischemia, and reduce mortality and re-infarction rates after myocardial infarction

Calcium channel antagonists:

- Lower myocardial oxygen demand by reducing blood pressure and myocardial contractility

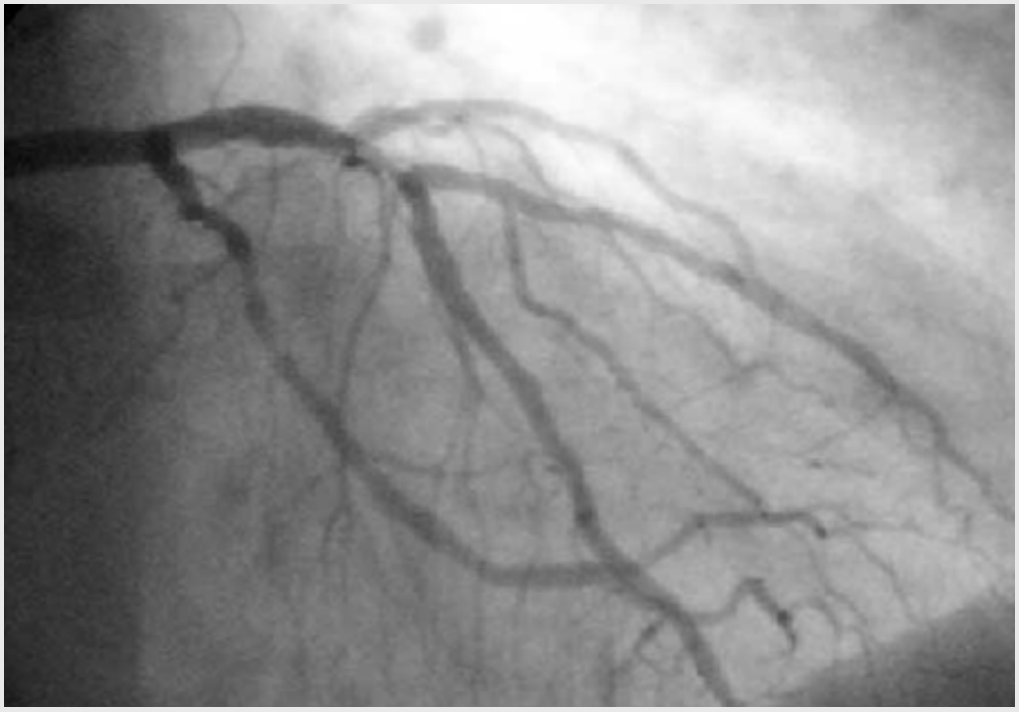

Fig. 4-09: Coronary angiogram, showing the circulation in the left main coronary artery and its branches.

Coronary revascularization

It is more appropriate to start treatment of stable angina with medical treatment. Coronary revascularization should be considered in:

- Low exercise capacity or ischemia at low workload
- Large affected area of coronary myocardium
- Impaired LV function with ejection fraction < 40 %

Percutaneous coronary intervention is mainly used in patients with single-vessel or 2-vessel disease with suitable anatomy, whereas **Coronary Artery Bypass Grafting (CABG)** is mainly used in patients with 3-vessel or left main stem disease.

Vasospastic Angina

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Definition of Vasospastic Angina

A sudden coronary artery spasm that leads to a reduction in coronary blood flow, thus causing severe chest pain (angina) at rest, is called vasospastic, Prinzmetal's, or variant angina. This type of angina occurs at rest, rather than on exertion, without any initiating factors. This chest pain can last less than 15–30 minutes.

Vasospastic angina is a variety of angina pectoris (chest pain) occurring at rest, rather than on exertion. In this angina type, myocardial ischemia is due to transient vasospasm with or without any underlying pathology.

Epidemiology of Vasospastic Angina

Vasospastic angina is an uncommon cause of myocardial ischemia, responsible for approximately 5 % of angina cases. Patients are generally **younger** than those with stable or unstable angina secondary to coronary artery atherosclerosis. Variant angina more commonly affects **women**.

This syndrome has a higher incidence in **Japan** compared to Western countries. The overall incidence has decreased significantly over the past thirty years. It is believed that this decline is due to increased use of calcium antagonists to treat hypertension.

Etiology of Vasospastic Angina

Causes of vasospastic angina

Coronary artery spasm can occur as a result of various risk factors such as **stress, smoking, cocaine use, insulin resistance**, and **medications** that have the effect of constricting blood vessels, such as triptans.

Rarely, coronary artery vasospasm may be triggered after coronary artery bypass surgery or close to a drug-eluting stent. The specific trigger is generally unknown. Many patients don't usually display the classical coronary risk factors, apart from heavy smoking.

Variant angina is associated with systemic vasomotor disorders such as migraine and Raynaud's phenomenon. This suggests the presence of a general vascular disorder.

Pathophysiology of Vasospastic Angina

The underlying mechanism causing vasospasm in vasospastic angina is debatable, and many theories have been put forward in recent years. Vasospasm occurs in response to local **vasoconstrictor stimuli** in the coronary segment. Impaired regulation of myofibril contraction in smooth muscle cells of coronary vessels causes smooth muscle hyperactivity, resulting in vasospasm.

Other abnormalities of the endothelium such as **defect in the enzyme** endothelial nitric oxide synthase can lead to reduced levels of nitric oxide. Nitric oxide is a natural vasodilator, and its decreased synthesis can lead to vasoconstriction. Current studies also show that coronary artery vasospasm can result from impairment of K+ ATP-dependent channels and hyperactivity of an intracellular enzyme, rho-kinase. **Sudden vasoconstriction** resulting from any of the aforementioned phenomena leads to decreased coronary blood flow which causes myocardial hypoxia which triggers angina.

In vasospastic angina, **focal coronary artery spasm** occurs and significantly reduces the diameter of the coronary artery lumen, causing temporary occlusion and leading to myocardial ischemia. This vasospasm can occur in normal-appearing arteries as well as arteries affected by atherosclerosis. The most common artery affected is the right coronary artery; the second most commonly affected is the left anterior descending artery.

The exact mechanisms that cause coronary artery spasm are not yet well understood. Some proposed theories relate to **endothelial dysfunction and increased contractility of vascular smooth muscle**. In endothelial dysfunction there is an imbalance between relaxing and contracting factors produced by the endothelium.

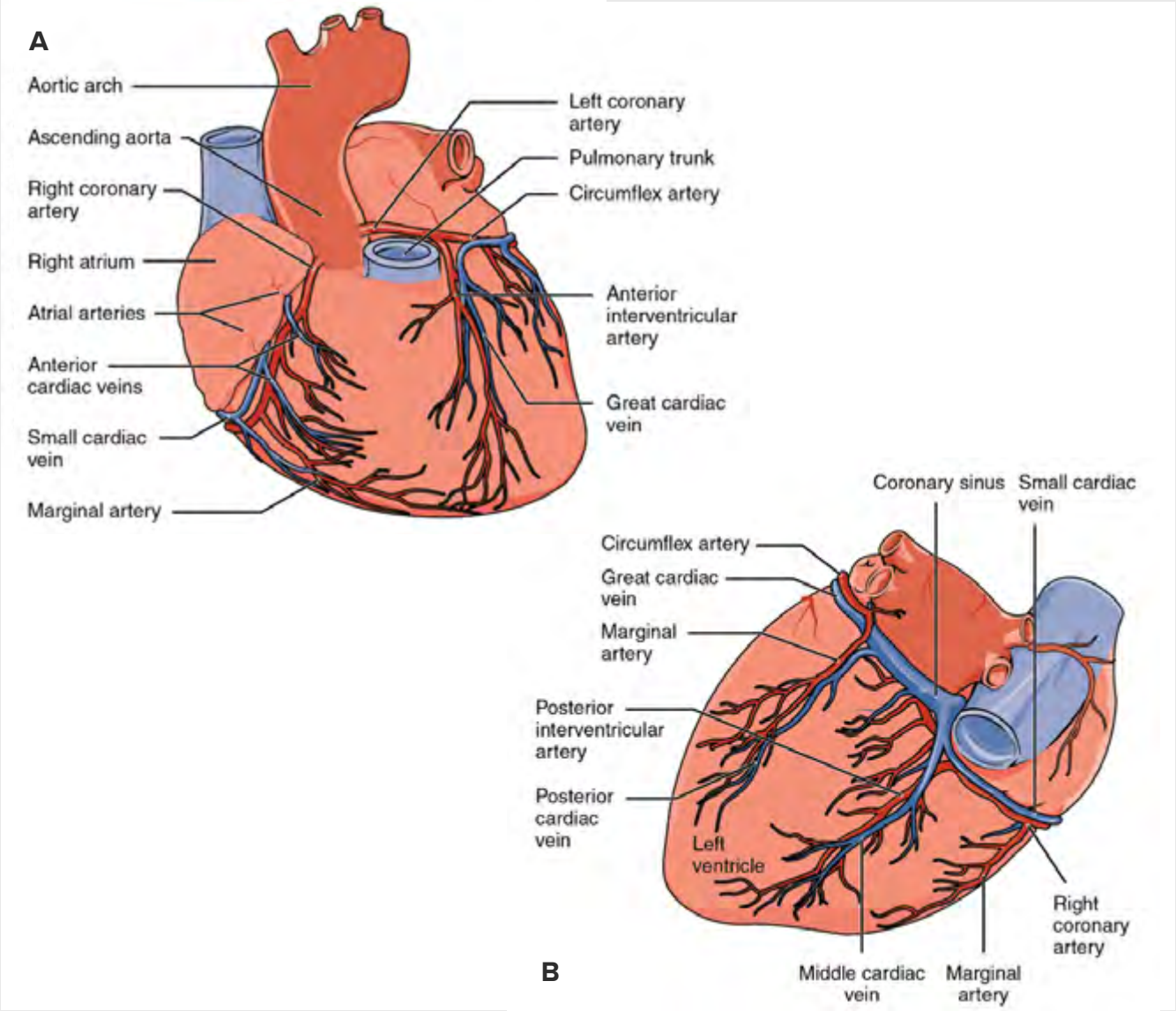

Fig. 4-10: Coronary circulation. (A) Anterior view (B) Posterior view

One important mechanism is related to **decreased nitric oxide (NO) production** by the dysfunctional endothelium, which is normally produced from L-arginine by endothelial NO synthase. As NO has potent smooth muscle relaxation and vasodilatory effects, reduced levels can contribute to vasoconstriction. **Increased activity of phospholipase C** (PLC) has also been reported, which is an enzyme that mobilizes intracellular calcium and may cause smooth muscle contraction.

Another theory is that repeated episodes of coronary vasospasm may cause neointimal hyperplasia, contributing to stenosis in the artery. Rho-kinase is also believed to play a role in the pathogenesis of this condition, involved in regulating vascular smooth muscle contractility.

Other factors that have been suggested as contributory to the pathogenesis of coronary artery spasm include **autonomic nervous system dysfunction, magnesium deficiency, chronic low-grade inflammation,** and **increased oxidative stress** (with smoking). **Genetic factors** may be involved, as there is a 3-fold greater incidence in the Japanese when compared to Caucasians. It is possible that certain genetic mutations predispose to coronary artery spasm, such as those affecting the endothelial NOS gene.

Clinical Features of Vasospastic Angina

Symptoms of vasospastic angina

Patients experience **very severe central chest pain**, which is the same type of pain as classic angina. These attacks tend to happen at **rest** or during normal activity. Some patients may also experience these attacks during or after exercise, including those who have co-existing fixed coronary artery stenosis. Other symptoms include shortness of breath and palpitations. Patients typically experience attacks of angina in **clusters, from midnight to early morning** (midnight – 8:00 am).

Patients with variant coronary syndrome may also experience **asymptomatic ischemic episodes**. If coronary artery spasm causes a prolonged disturbance in coronary blood flow, it can cause a myocardial infarction **Syncope** may also occur if there are disturbances to the heart rhythm such as asystole, atrioventricular block, or ventricular tachyarrhythmias. **Fatal arrhythmias** and **sudden cardiac death** may also occur.

Diagnostics of Vasospastic Angina

Laboratory

With vasospastic angina, blood tests are generally negative for cardiac enzymes, including troponins and CK-MB.

ECG

Electrocardiography is the **key to diagnosing vasospastic angina**. ECG changes demonstrate **transient ST-segment elevation** during periods of chest pain, which resolves when the pain settles. ST-segment elevation represents transmural myocardial ischemia and is accompanied by **reciprocal ST depressions**.

Other changes in the ECG that may be detected include a **taller T wave**, a **taller and wider R wave**, and **loss of the S wave**. On occasion, negative U waves may present in the same leads as the ST-segment elevation, after the ST elevation starts to resolve. In addition, arrhythmias may be detectable during an episode of variant angina, such as ventricular tachycardia, atrioventricular block, and bradyarrhythmia. If silent episodes of coronary spasm or arrhythmias are suspected, then **ambulatory 24 hours Holter ECG** monitoring should be utilized. This is also helpful for recording ECG changes during symptomatic episodes.

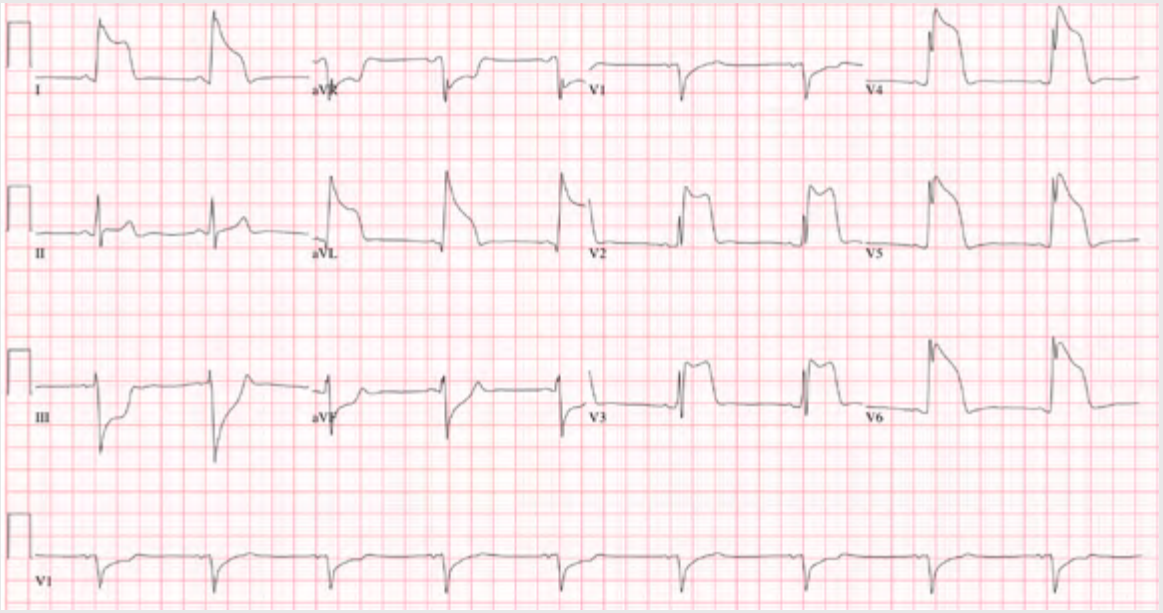

Fig. 4-11: ECG of a patient with Prinzmetal's angina

Exercise testing

Exercise testing with ECG monitoring has variable results. Changes that can be detected in response to exercise include **ST elevation, ST depression**, or no change. ECG changes may point to fixed artery stenosis, coronary artery spasm, or an absence of problems.

Coronary angiography

Coronary angiography is considered the gold standard in the diagnosis of variant angina. There is usually an absence of organically stenosed arteries detected on an angiography; however, there are some patients who do have coronary artery stenosis co-existing with coronary artery spasm.

Provocation testing can be used for the definitive diagnosis of coronary variant syndrome. Coronary vasospasm can be provoked during angiography by injecting acetylcholine and ergonovine into the coronary arteries. ST-segment elevation and induction of angina confirm vasospastic angina.

Complications of Vasospastic Angina

This variant angina may lead to complications in some patients, resulting in **severe ventricular tachyarrhythmias** or bradyarrhythmias, **sinus arrest**, or even an **AV block** caused by a severe ischemic episode following vasospasm. **Sudden cardiac arrest**, with or without syncope, can occur due to ischemia-induced ventricular fibrillation. **Atherosclerosis** can also occur later on at the site of vasospasm, leading to **local coronary thrombosis**.

Treatment of Vasospastic Angina

Lifestyle modification

Patient should:

- Eat a healthy balanced diet and exercise regularly
- Quit smoking and limit the use of alcohol
- Report any change in the pattern or severity of chest pains to his or her healthcare provider right away

Regular follow up investigations include:

- Blood tests
- ECG cardiac stress tests or an ECG of the heart's function during exercise.

Medical treatment

- A **nitrate** can be administered to relieve an attack of angina in an acute setting.
- The main drug used to treat variant coronary syndrome is a **calcium channel blocker**, such as diltiazem. Calcium channel blockers are very effective in the prevention of ischemia. They may be given alone or together with isosorbide mononitrate, a **long-acting nitrate**.

New drugs

- Nicorandil is a K^+-channel agonist that can be added in recurrent cases.
- Fasudil is a novel drug which inhibits rho-kinase, preventing acetylcholine-induced vasospasm.

Surgery

- Complete cardiac denervation with plexectomy, with or without coronary artery bypass surgery, is an option for resistant cases; however, procedural risks are high and results have been inconsistent.

Note:
Beta-blockers are contra-indicated as they reduce the dilatation of the smooth musculature through blocking the beta-2 receptors and increase the tone of the coronary vessels.

Prognosis of Vasospastic Angina

If the condition is controlled from an early stage, the prognosis can be favorable. Complications, such as acute myocardial infarction, coronary artery bypass grafting, and cardiac death typically occur early on after the onset of angina. Patients who have coronary spasm in multiple arteries are prone to fatal arrhythmias.

Survival rates for vasospastic angina are **over 90 % at 5 and 10 years**. Individuals who do not have co-existing coronary artery stenosis generally have a more benign prognosis and better survival than those who have both severely diseased arteries and coronary artery vasospasm.

Review Questions

Test your knowledge: Ischemic Heart Disease

Question 4.1: A 57-year-old man presents to his primary care provider because of chest pain for the past 3 weeks. His chest pain occurs after climbing more than 2 flight of stairs or walking for more than 10 minutes and resolves with rest. He is obese, has a history of type 2 diabetes and has smoked 15 to 20 cigarettes a day for the past 25 years. His father died from a myocardial infarction at the age of 52 years. Vital signs reveal a temperature of 36.7 °C (98.06 °F), blood pressure of 145/93 mm Hg, and a heart rate of 85/min. Physical examination is unremarkable. Which of the following best represent the most likely etiology of this patient condition?

A. Multivessel atherosclerotic disease with or without a nonocclusive thrombus

B. Intermittent coronary vasospasm with or without coronary atherosclerosis

C. Sudden disruption of an atheromatous plaque, with a resulting occlusive thrombus

D. Fixed, atherosclerotic coronary stenosis > 70 %

E. Hypertrophy of interventricular septum

Question 4.2: A 57-year-old man presents to his primary care provider because of chest pain for the past 3 weeks. His chest pain occurs after climbing more than 2 flights of stairs or walking for more than 10 minutes and resolves with rest. He is obese, has a history of type 2 diabetes and has smoked 15 to 20 cigarettes a day for the past 25 years. His father died from a myocardial infarction at the age of 52 years. Vital signs reveal a temperature of 36.7 °C (98.06 °F), blood pressure of 145/93 mm Hg with a heart rate of 85/min. Physical examination is unremarkable. Development of which of the following would categorize the patient's condition as unstable angina?

A. Dyspnea on exertion

B. ST segment depression on ECG

C. Symptoms after climbing a flight of stairs or walking 50 metres

D. Rales on auscultation

E. S3 on auscultation

Correct answers: 4.1D, 4.2C

Acute Coronary Syndrome (ACS)

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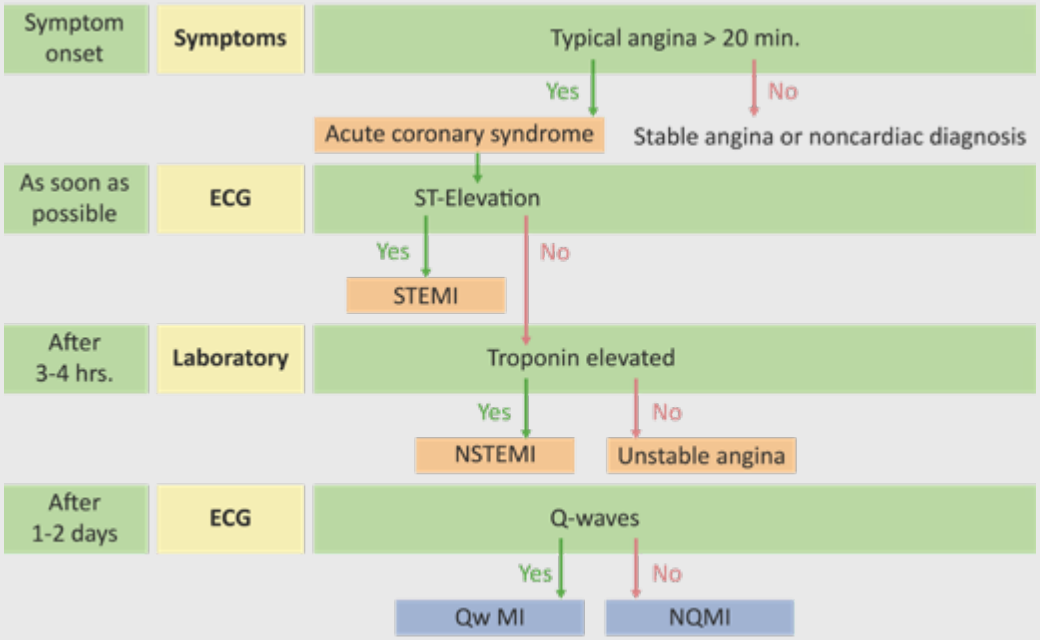


Fig. 4-12: Clinical presentation and classification of ACS

Definition of ACS

Acute coronary syndrome (ACS) is characterized by sudden onset severe chest pain due to partial or complete occlusion of a coronary artery resulting from unstable ruptured plaque in the setting of advanced ischemic heart disease.

ACS covers 3 clinical entities:

- Unstable angina pectoris
- Myocardial infarction, which includes:
  - Non-ST-segment elevation myocardial infarction (NSTEMI)
  - ST-segment elevation myocardial infarction (STEMI)

Note:
It is often difficult to distinguish between these 3 entities based on clinical symptoms alone.

Diagnosis	Clinical features	ECG findings	Laboratory findings
Unstable angina	Ischemic chest pain that occurs at rest or with previously tolerated levels of exertion	None, or ST-segment depressions	**None**
Non-ST-elevation Myocardial infarction (NSTEMI)	Ischemic chest pain in any setting	None or ST-segment depressions	**Elevated troponin**
ST-elevation Myocardial infarction (STEMI)	Ischemic chest pain in any setting	**ST-segment elevations**	Elevated troponin

Epidemiology of ACS

Acute coronary syndromes are the most frequent cause of death in industrialized countries. Every year, about 8 million people worldwide die of its consequences. The following figures summarize the epidemiology of ACS in the United States:

- **Incidence**: 780,000 cases/year
- **Mean age at onset**: 68 (IQR 56–79)
- **Male to female ratio**: 3:2

70 % of ACSs are non-ST elevation myocardial infarctions.

Etiology of ACS

In about 95 % of the cases, a ruptured plaque, formed inside the coronary arteries within the context of atherosclerosis, is responsible for the symptoms of acute coronary syndrome. Arthritides, endocarditis, the consumption of cocaine, emboli caused by heart valve prostheses, or other paradoxical embolisms are of less significance for etiology.

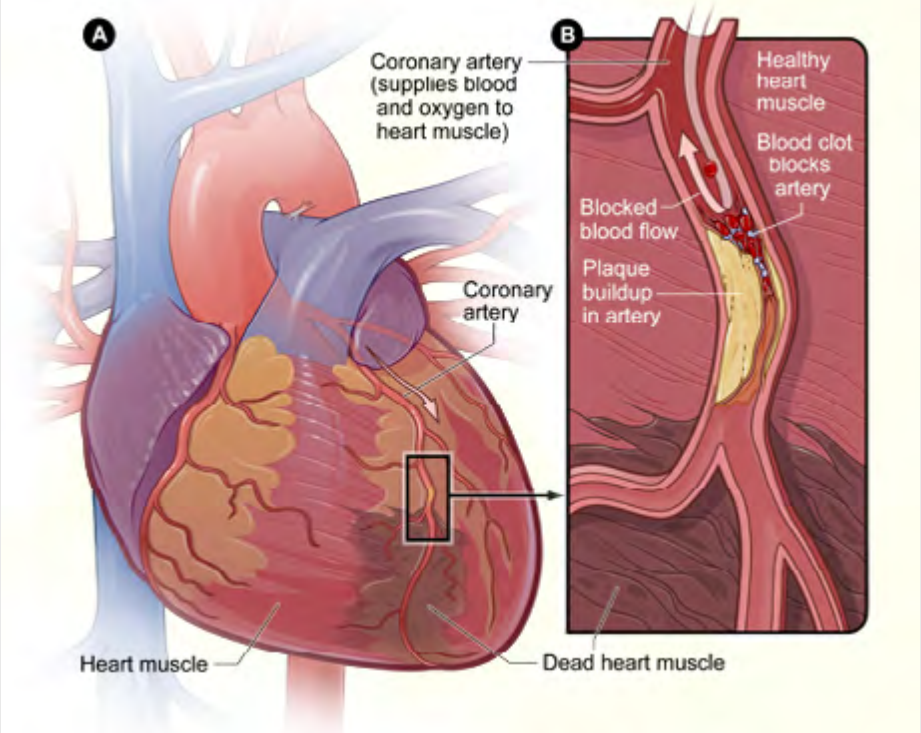


Fig. 4-13: (A) Overview of a heart and coronary artery showing damage (dead heart muscle) caused by a heart attack. (B) Cross-section of the coronary artery with plaque buildup and a blood clot resulting from plaque rupture.

Pathology of ACS

The pathology of ACS can be traced back to a lack of blood flow to the heart tissue. In perfusion of less than 25 % of the normal flow, the tissue is irreversibly damaged. After 6–12 hours, this damage can be seen by light microscope in the form of yellowish spots.

The damage results in a complete myocytolysis, beginning with fading of the nuclei and loss of cross-striation. After a few days, granulation tissue forms, containing a hemorrhagic edge and many marginal leukocytes. Only after 2 weeks is white scar tissue visible.

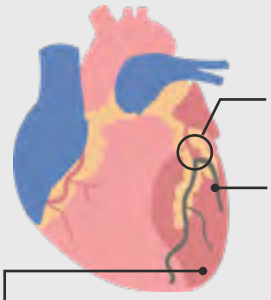
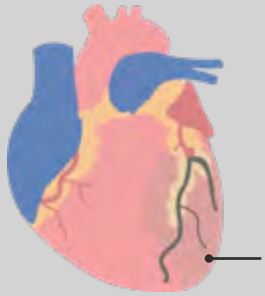
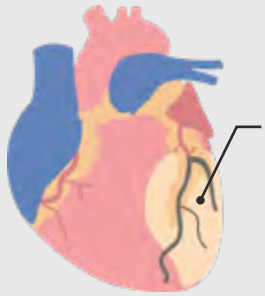
Tme	Gross	Light microscope
0–24 hours	 Occluded artery; Infarct; Dark mottling: pale with tetra-zolium stain	 Early coagulative necrosis, release of necrotic cell contents in blood; edema, hemorrhage, wavy fibers. Neutrophils appear. Reperfusion injury, associated with generation of free radicals, lead to hyperconcentration of myofibrils through ↑free calcium influx.
1–3 days	 Hyperemia	 Extensive coagulative necrosis. Tissue surrounding infarct shows acute inflammation with neutrophils.
3–14 days	 Hyperemic border: central yellow-brown softening – max. yellow and soft by 10 days	 Macrophages, then granulation tissue at margins.
2 weeks to 7 months	 Recanalized artery; Gray-white	 Contracted scar complete.

Fig. 4-14: *Temporal evolution of pathological changes.*

Location of infarct

Infarcts can be classified as transmural or non-transmural depending upon the extent of heart wall involvement. The different types and vessels involved are shown in the image below.

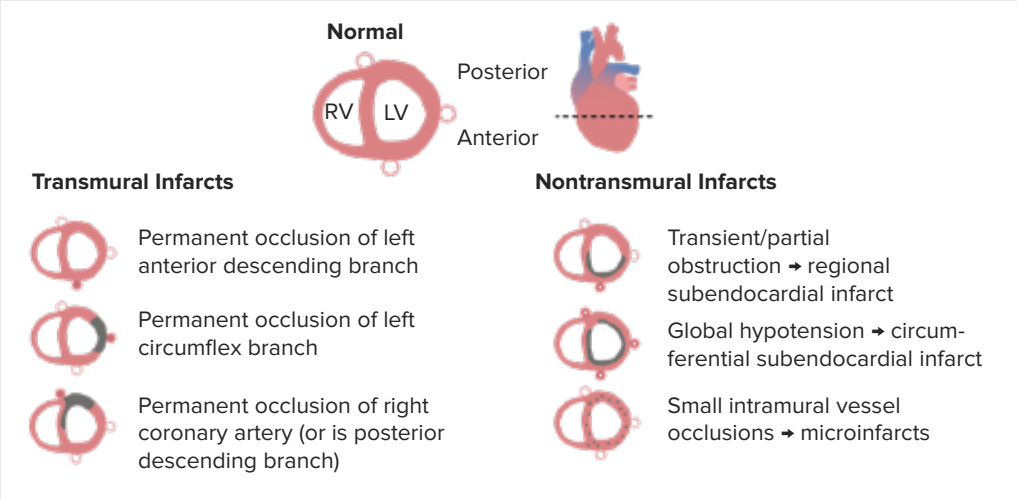


Fig. 4-15: *The difference between transmural and non-transmural infarcts.*

Clinical Features of ACS

There is often a **sudden, severe pain**, which typically radiates into the left shoulder and left arm. This often occurs **without previous exertion**, improves only slightly or not at all by administration of nitroglycerin or rest, and **lasts longer than 15 minutes**.

The pain can be described as an **unbearable, cramp-like tightness in the chest**. In addition, **dyspnea** and **fear of death**, as well as accompanying weakness, nausea, and sweating are typical. Radiation into the **upper abdomen**, spine, or neck can also occur. A drop in blood pressure and tachycardia, accompanied by cold sweating, can be signs of beginning cardiogenic shock. Infarcts often occur during **the early hours of the morning**.

Note:
Radiation to the right side of the body is also possible!

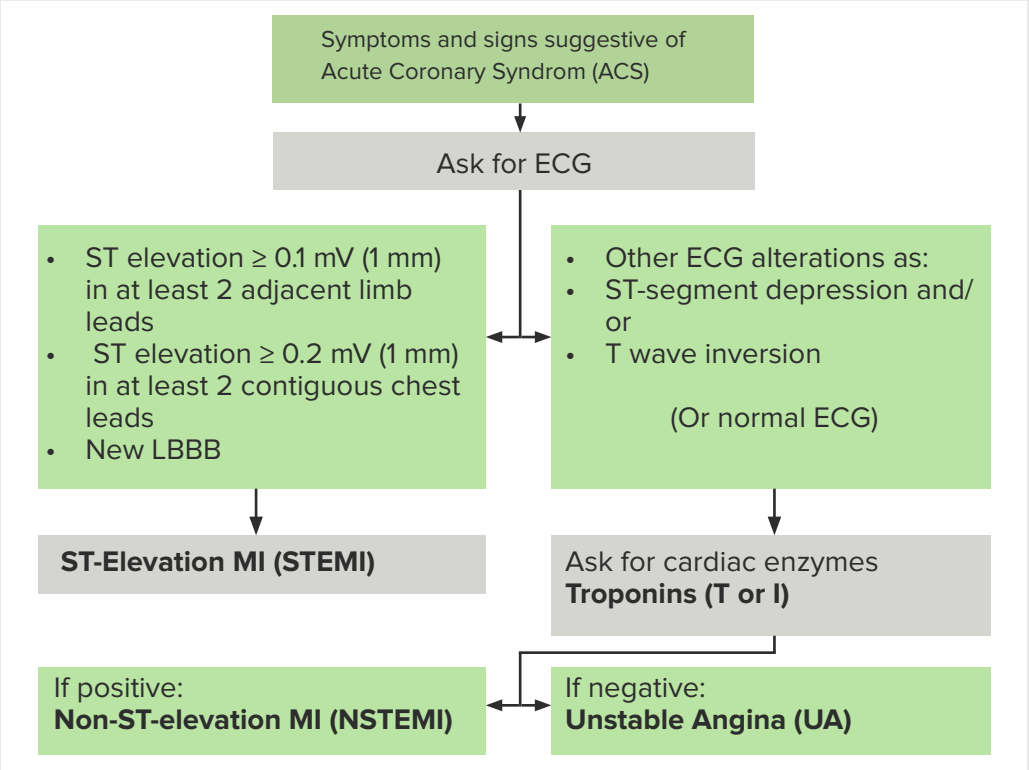


Fig. 4-16: Diagnostic algorithm for ACS

Diagnostics of ACS

In addition to the medical history and physical examination that hint to the typical pain characteristics (and, for example, can reveal blood pressure changes), a 12-lead ECG, and the determination of the cardiac enzymes CK, CK-MB (specific for myocardial infarction) and especially the troponins I and T are of crucial importance.

Laboratory tests

Assessment of cardiac enzymes (CK, CK-MB, and troponin) is important to differentiate between different entities of ACS.

- Unstable angina (UA) is characterized by a lack of increase in troponin levels.
- NSTEMI and STEMI are characterized by destruction of cardiac muscle tissue, which results in elevated cardiac enzymes in the blood.

The classification of cardiac enzymes provides information on the presence and extent of myocardial damage. Determination of troponin I or T is considered the gold standard. Troponin as a cardiac marker is specific to myocardial tissue.

Troponin increases shortly after an infarction. About 70 % of patients show an increase 3 hours after the incident and that number rises to 90 % 6 hours after the incident. This timeline stresses the necessity of measuring cardiac enzymes again at a later time, even when the initial result was negative.

Note:
Even if there is no direct increase in troponin, an infarct cannot immediately be excluded and testing must be repeated every 4–6 hours.

Post MI reinfarction cannot be diagnosed by TnT testing, as troponin concentrations only returns to normal after about 1–2 weeks. In contrast, myoglobin is unspecific and also increases when damage to skeletal muscles occurs, but returns to normal after a day at the latest. CK-MB is specific to the infarction, but only starts to rise 4 hours after ischemia. A CK-MB concentration of between 6–20 % of the total CK indicates myocardial damage.

LDH can serve as a long-term marker of myocardial damage. It starts to increase only after 6–12 hours, but reaches its maximum after 2–4 days and stays at an increased level for up to 2 weeks following an infarction. GOT, which is actually a marker for liver cells, also exists in the heart muscle and can also be used for diagnostic purposes.

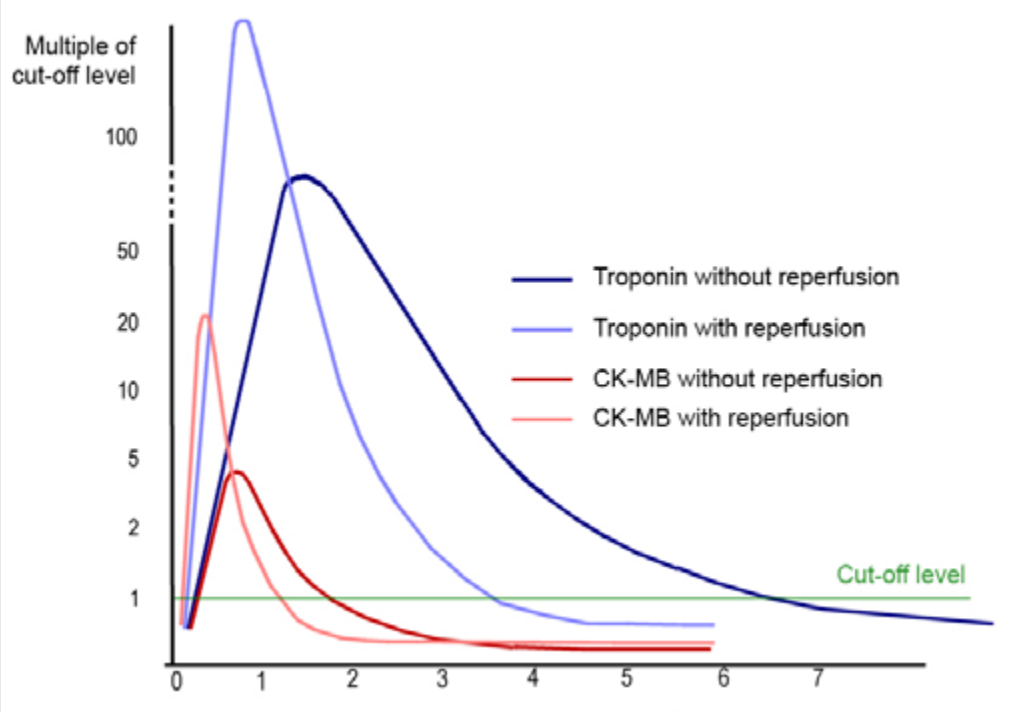


Fig. 4-17: *Typical changes in CK-MB and cardiac troponin in acute myocardial infarction.*

The following table provides an overview of the various parameters:

Parameter	Begin of increase	Maximum	Normal levels
Troponin	3–8 hours	12 hours	1–2 weeks
CK-MB	3–12 hours	24 hours	2–3 days
Myoglobin	1–4 hours	4 hours	1 day
LDH	6–12 hours	2–4 days	1–2 weeks
GOT	4 hours	48 hours	3–6 days

Note:
Troponin is not suitable for the diagnosis of re-infarction because levels remain elevated for about 2 weeks before returning to normal.

Note:
Cardiac markers can be influenced by other diseases, such as a pulmonary embolism, or even kidney insufficiency.

High-yield:
It's better to use the CK-MB marker rather than troponin to diagnose post-MI re-infarction.

ECG

In UA and NSTEMI

- ECG can be completely normal with no specific ECG changes
- ECG may show ST-segment depression or deep-negative T waves

In STEMI

ST-segment elevation myocardial infarction is characterized by a monophasic ST-segment elevation which directly passes into the T wave. Depending on the stage of the infarction, this alteration can vary:

Stage 0 (initial stage)	Up to 6 hours after infarction, typically marked by a peak increase of the T wave, labeled as suffocation-T
Stage 1 (acute infarct)	A few hours to days after infarction, characterized by the typical monophasic ST elevation
Stage 2 (intermediate stage)	The ST elevation, as well as the R-wave, deteriorate, the so-called R-loss and a magnification of the Q-wave occur, which, as Pardée-Q, signals the sinking of the myocardium; a peak negative modulation of the T wave is created
Stage 3 (final stage)	More than 6 months after infarction, the QRS-complex changes remain, the Pardée-Q typically even lasts for a lifetime, while the ST-segment and T wave normalize again

Echocardiography

Echocardiography is a valuable tool that can be used in the diagnostic workup of ACS. The following can be assessed by direct visualization of the heart:

1. Detect site/size of segmental wall motion abnormalities.
2. Assess LV systolic function.
3. Assessment of complications (aneurysm, valvular insufficiency, VSR, and pericardial effusion).

Coronary angiography

Considered the gold-standard in the diagnosis of ACS because it assesses the exact location and extent of coronary vessel stenosis before possible PCI/surgery.

Risk Assessment of ACS

This takes first priority in all patients with suspected ACS. There are many risk stratification tools available. Their goal is to predict major adverse cardiac events (MACE).

HEART score for chest pain patients

History	Highly suspicious	2
	Moderately suspicious	1
	Slightly suspicious	0
ECG	Significant ST depression	2
	Non-specific repolarization disturbance	1
	Normal	0
Age	≥ 65 years	2
	45–65 years	1
	≤ 45 years	0
Risk factors	≥ 3 risk factors or history of atherosclerotic disease	2
	1 or 2 risk factors	1
	No risk factors are known	0
Tropin	≥ 3x normal limit	2
	1–3x normal limit	1
	≤ normal limit	0

Risk factors

- Hypertension
- Diabetes
- Hypercholesterolemia
- Obesity (BMI > 30)
- Positive family history of ACS < 65 years of age
- Known cardiovascular disease (CAD, TIA/stroke, PAD)
- Smoking

HEART score	% patients	% MACE	Recommended management
0–3	32	1–2	Discharge
4–6	51	12–17	Observe, risk reduction, noninvasive testing
7–10	17	50–65	Admit, medical management, consider early invasive testing

Complications of ACS

Early complications

1. Sudden cardiac death.
2. AV block and ventricular tachyarrhythmias, which could be fatal.
3. Acute left heart failure (pulmonary edema) that results from acute pump failure of heart and acute mitral valve insufficiency secondary to papillary muscle dysfunction.
4. Cardiogenic shock is the most serious complication, with mortality rates exceeding 50 %.

Late complications

1. Pericarditis – further classified into:
   - Early infarct-associated pericarditis which occurs within the first week of MI
   - Dressler syndrome, a pericarditis that occurs 2–20 weeks post-MI without an infective cause secondary to circulating antibodies against cardiac muscle cells
2. Congestive heart failure.
3. Re-infarction due to an unstable plaque.
4. Atrial and ventricular aneurysms which may precipitate:
   - Thrombus formation and increased risk of thromboembolism
   - Cardiac arrhythmia
   - Rupture leading to pericardial effusion and cardiac tamponade

The following table shows complications of myocardial infarction:

Time	Complications
0–24 h	Ventricular arrhythmia, HF, cardiogenic shock
1–3 days	Postinfarction fibrinous pericarditis
3–14 days	Free wall rupture à Tamponade, Papillary muscle rupture à Mitral regurgitation, Interventricular septal rupture due to macrophage-mediated structural degradation, LV pseudoaneurysm (risk of rupture)
2 weeks to several months	Dressler syndrome, HF, arrhythmias, true ventricular aneurysm (risk of mural thrombus)

Prevention of ACS

95 % of acute coronary syndrome cases are manifestations of coronary heart disease, the goal is to avoid the latter. For the prevention of coronary heart disease, it is advised to eliminate the risk factors, especially the main risk factors like high cholesterol, arterial hypertension, diabetes mellitus, and smoking. Approaches are predominantly concerned with patient behavior, such as food and physical activity choices. These approaches can also be assisted by medication.

Unstable Angina

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Definition of Unstable Angina

Unstable angina refers to chest pain that persists **longer than 20 minutes**, is of **increasing intensity**, and **occurs even at rest**. Unstable angina (UA) is characterized by the absence of myocardial damage, in contrast to non-ST-elevation MI (NSTEMI) which presents with evidence of myocardial necrosis.

Diagnosis of Unstable Angina

The diagnosis of UA depends mainly on history, ECG abnormalities, and cardiac biomarkers.

History

Chest pain is similar in character to stable angina pectoris, but is characterized by at least 1 of the following 3 features:

1. It is severe and of new onset.
2. It occurs on minimal exertion or even at rest, and lasts longer.
3. It is more intense and worsens rapidly (crescendo angina), not fully relieved by rest or nitroglycerin.

Aside from the above, UA usually preceded by vigorous exercise or emotional stress which results in an imbalance between oxygen supply and myocardial demands.

ECG abnormalities

- Transient or persistent ST-segment depression and/or T wave inversion in 30–50 % of patients
- ECG can be normal

Cardiac biomarkers

Cardiac enzymes are used to differentiate between Unstable Angina (UA) and non-ST-elevation MI (NSTEMI).

- Unstable angina ➔ no myocardial damage ➔ thus, normal cardiac enzymes
- Non-ST-elevation MI (NSTEMI) ➔ evidence of myocardial damage ➔ elevated cardiac enzymes such as CK-MB and troponin I and T (more specific and sensitive marker)

Myocardial Infarction – NSTEMI vs. STEMI

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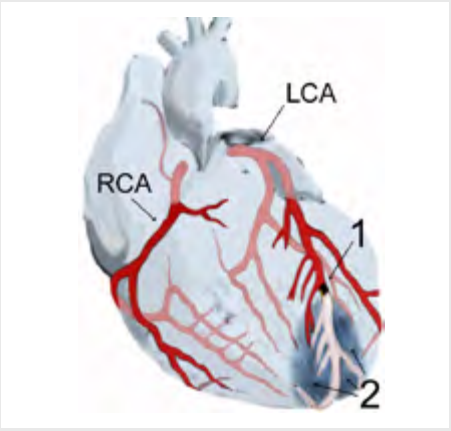

Fig. 4-18: Myocardial Infarction

Definition of Myocardial Infarction

The term myocardial infarction refers ischemia of the myocardial tissue due to a partial or complete obstruction of the **coronary artery**.

This acute event is usually accompanied by an increase in cardiac enzymes, typical ECG changes, and pain symptoms, or a thrombus or wall motion abnormality that is detected by means of medical imaging.

Classification of Myocardial Infarction

Non-ST-Segment Elevation Myocardial Infarction (NSTEMI)

- Typical symptoms of myocardial infarction persisting > 20 minutes
- Normal, or non-specific ECG changes: ST depression and T wave inversion
- Mildly increased cardiac enzymes

Note:
NSTEMI is distinguished from STEMI by ECG as cardiac enzymes are elevated in both.

ST-Segment Elevation Myocardial Infarction (STEMI)

- Typical symptoms of myocardial infarction persisting > 20 minutes
- ST-segment elevation, or new-onset LBBB
- Markedly increased cardiac enzymes

European Society of Cardiology (ESC) classification

ESC has proposed an MI classification based on etiology, which includes the following types:

- **Type 1:** The infarction is spontaneous and can be attributed to a primary coronary incident
- **Type 2:** The infarction is related to ischemia, the cause of the ischemia being e.g. coronary embolism or anemia
- **Type 3:** The symptoms preceding cardiac death or an autopsy point to myocardial ischemia
- **Type 4a:** The myocardial infarction occurs as part of a Percutaneous Coronary Intervention (PCI)
- **Type 4b:** The myocardial infarction is caused by a stent thrombosis
- **Type 5:** The myocardial infarction develops in connection to Coronary Artery Bypass Grafting (CABG)

Pathophysiology of Myocardial Infarction

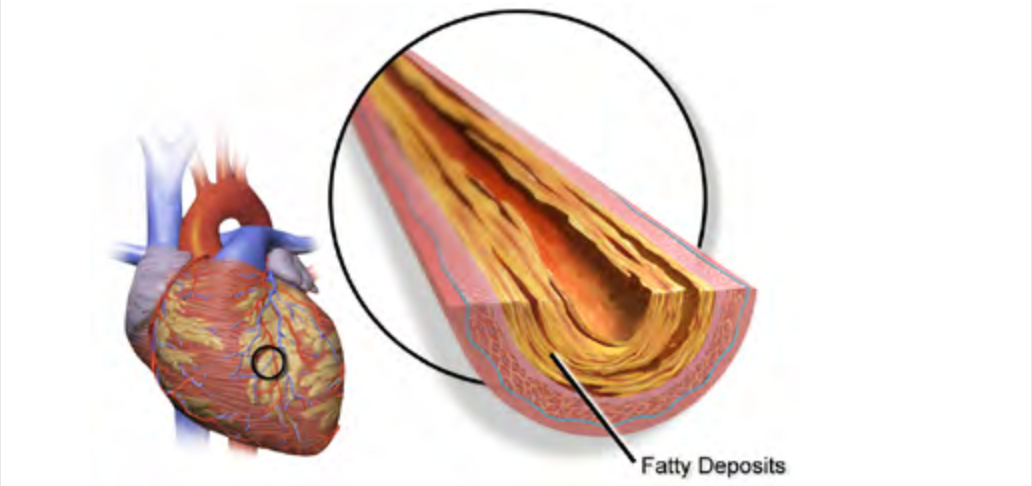

Fig. 4-19: Ischemic heart disease.

As a result of atherosclerosis, plaques start to form in the **coronary arteries** which are, at first, stable with a thick fibrous cap. Over the course of time, an unstable or vulnerable plaque forms, with abundant macrophages and lipids. The rupturing of this plaque leads to a thrombotic obstruction (with a complex formation of white blood cells, platelets, fibrin and red blood cells) of one of the **coronary arteries, hypoxia** of the tissue fed by the **coronary artery**, and ischemia, followed by necroses.

The rupture can be triggered by physical or psychological stress, drastic blood pressure fluctuations, or circadian rhythms typically accompanied by changes in coagulation activity (stronger coagulation early in the morning).

Clinical Features of Myocardial Infarction

The typical symptoms include severe retrosternal pain that radiates to the left or right arm, neck, and upper jaw and does not improve after nitroglycerin administration. These symptoms are observed in only about 40 % of patients.

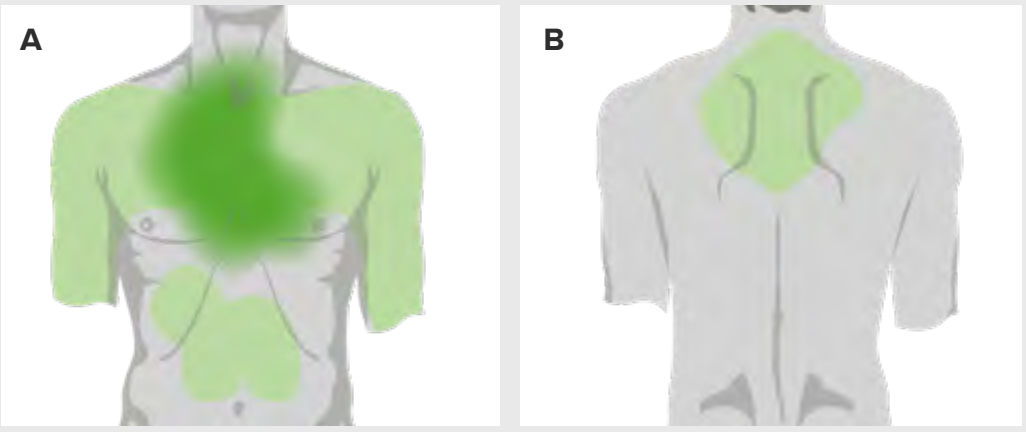

Fig. 4-20: (A) Pain in acute myocardial infarction (front). (B) Pain in acute myocardial infarction (rear).

Note:
When ischemia occurs, a phenomenon called coronary steal syndrome can occur. This event is an alteration of blood fluid patterns leads to a reduction in flow to the coronary arteries, which can exacerbate when a coronary vasodilator is administered, such as a calcium channel blocker.

Painless infarctions (or silent infarctions) often accompany diabetic neuropathy, but are also particular to women and the elderly. These painless infarctions are present in about 20 % of all cases.

Infarction pain can also be atypical, manifesting as upper abdominal pain, a feeling of faintness combined with vagal symptoms, such as fear and sweating, dyspnea, nausea, or vomiting.

Diagnostics of Myocardial Infarction

ECG diagnostics for myocardial infarction

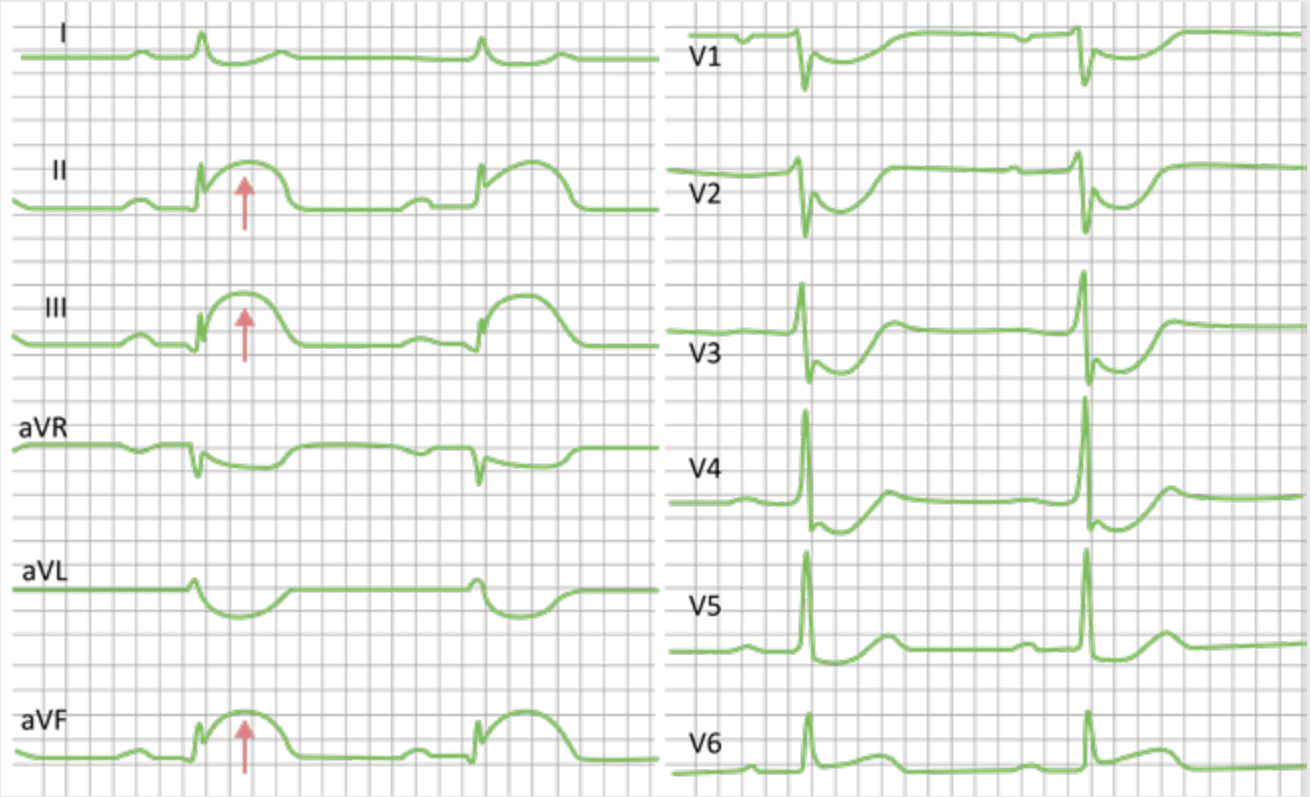

Fig. 4-21: *Diagram showing a representation of myocardial infarction on an ECG.*

In NSTEMI

In the case of NSTEMI, the ST-segment may be temporarily depressed and accompanied by a negative pre-terminal T wave.

The ECG changes of NSTEMI are often atypical, which means that an infarction can only be ruled out through repeated heart enzyme testing.

In STEMI

In case of a STEMI, the ECG shows typical changes, such as the monophasic ST-segment elevation, which transitions directly into the T wave, with pathologically enlarged Q-spikes.

Various other ECG changes are typical, depending on the stage of the infarction.

- **Initial stage:** Up to 6 hours after the infarction, typically characterized by pointed elevation of the T wave, which is called anoxic T wave.
- **Acute infarction:** Few hours up to days after the infarction, characterized by the typical monophasic ST-elevation.
- **Intermediate stage:** The ST-elevation and R-spike decrease, so-called poor R-wave progression occurs, as well as enlargement of the Q-spike which, as a Pardee-Q, signals the end of the myocardium, and a pointed negativity of the T wave develops.
- **Final stage:** More than 6 months after the infarction, the changes of the QRS complex remain, while the ST-segment and the T wave go back to normal.

Localization of infarction

Depending on the lead in which the ECG changes are detected, information can be acquired regarding which coronary artery is likely obstructed and where the infarction is located.

Localization of infarction	ECG changes
Extensive anterior MI	I, aVL, V1-6
Anterior MI	V1-6
Lateral MI	I, aVL, V5-6
Anteroseptal MI	V1-V4
Inferior MI	II, III, aVF
Posterior MI	V7-9, inverse in V1-V2

Imaging modalities

- **Echocardiography:** A diagnostic tool that helps to detect wall motion abnormalities, determines the remaining function, and exclude complications, such as **cardiac valvular defects**.
- **Cardiac catheterization:** Considered the gold standard and should be performed as quickly as possible in cases of STEMI.
- **MRI cardioangiography:** Serves as another means of detecting wall motion abnormalities and determining the size of infarction scars.

Treatment of Myocardial Infarction

Initial management of ACS

Symptomatic treatment

1. **Oxygen** (–8 L/min per nasal O_2 tube) can be administered from the initial treatment until the diagnosis is confirmed. Additionally, it is recommended to elevate the upper body for relief (30°) in the case of dyspnea or heart insufficiency.
2. Administering **nitroglycerin** (1 capsule or 2 puffs = 0.8 mg, 1–5 mg intravenously through a perfusor).
3. Morphine (3–5 mg intravenously every 5–10 minutes) can be administered for severe chest pain.
4. Consider loop diuretics (e.g. furosemide) in case of pulmonary edema.
5. Beta-blockers (IV or oral) that don't act as partial agonists on beta-receptors (e.g. metoprolol), unless there are contradictions as: hypotension, bradycardia, heart block, congestive heart failure, or cardiogenic shock.

Note:
Contraindicated in case of systolic blood pressure 90 mmHg and simultaneous administration of PDE-5 inhibitors.

Mnemonic:

MONA

- *Morphine*
- *Oxygen*
- *Nitroglycerin*
- *Aspirin*

Blood thinners

1. **Platelets aggregation inhibitors**

   a) Aspirin – all patients should receive **aspirin** (initial dose 150–300 mg) as soon as possible, PLUS:

   b) ADP receptor inhibitors (P2Y12 inhibitor), such as **clopidogrel** (initial dose 300 mg). Others are **ticagrelor** and **prasugrel**

   c) IIb/IIIa receptor inhibitors (e.g. tirofiban): may be considered in high-risk patients (based on TIMI score)

Platelet aggregation inhibition using aspirin has to be continued throughout life, whereas inhibition by means of P2Y12 inhibitors is only used for 12 months following infarction.

2. Anticoagulants

In addition to aspirin and clopidogrel, 4 anticoagulant options are available.

Note:
All patients should receive high-intensity statins, such as atorvastatin 40–80 mg.

   a) Unfractionated heparin (UFH)

   b) Low-molecular-weight heparin (LMWH) 'enoxaparin' is superior to UFH with less risk of hemorrhage. Fondaparinux is an indirect Factor Xa inhibitor, and is equal in efficacy to enoxaparin but has a lower risk of bleeding

   c) Bivalirudin is a direct thrombin inhibitor, and is equal in efficacy to UFH and LMWH

Specific treatment based on ECG changes

In UA and NSTEMI

Diagnostic cardiac catheterization is to be used in cases of UA and NSTEMI, which can be performed between 2–72 hours after the incident, depending on the risk factors of the respective patient.

Early invasive strategy

Only high-risk patients will benefit from coronary revascularization (PCI or coronary artery bypass grafting):

- Age > 65 years
- > 3 CAD risk factors
- ST deviation
- > 2 anginal events < 24h
- Elevated cardiac markers

The outcomes of conservative treatment are similar to invasive treatment in low-risk patients, therefore invasive treatment is not recommended in low-risk patients.

In STEMI

In the case of STEMI, the obstructed coronary vessel has to be revascularized as quickly as possible, because 'Time is Muscle'.

Primary Percutaneous Coronary Intervention (PCI)

Primary PCI is the therapy of choice if it can be performed in primary PCI-capable centers, and within 90–120 minutes.

Thrombolytic therapy

Thrombolytic therapy using substances such as streptokinase, alteplase, reteplase and tenecteplase. IV fibrinolysis is indicated, only in STEMI cases, if:

1. Primary PCI is not available, or
2. Delay to PCI would be > 1 hour longer than initiation of fibrinolysis

Contraindications of thrombolytic therapy should ruled out first, which are:

Absolute contraindications	Relative contraindications
Previous hemorrhagic stroke at any time	Severe uncontrolled hypertension > 180/110
Ischemic stroke within 3 months	History of ischemic stroke > 3 months
Known intracranial neoplasm	Prolonged CPR > 10 minutes
Closed head injury within 3 months	Major surgery < 3 weeks
Active bleeding, or bleeding diathesis	Recent (within 2–4 weeks) internal bleeding
Suspected aortic dissection	

In the case of non-ST segment elevation myocardial infarction (NSTEMI), anticoagulants, such as fondaparinux or enoxaparin should be administered instead as explained before.

Note:
No fibrinolytic treatment is given with non-ST segment elevation MI (NSTEMI).

Coronary angiography after fibrinolysis (rescue PCI)

Indicated in:

- Failure of reperfusion (as evidenced by < 50 % resolution of ST-segment elevation > 90 min after completion of fibrinolytic treatment).
- Spontaneous recurrent ischemia while in a hospital.
- High-risk features, e.g., extensive ST-segment elevation, signs of heart failure and hypotension (systolic blood pressure < 100 mmHg).

Review Questions

Question 4.3: A 73-year-old woman arrives at the emergency department due to an intense central chest pain for 30 minutes this morning. She says the pain was cramping in nature and radiated down her left arm. She has a history of atrial fibrillation and type 2 diabetes mellitus. Her pulse is 98/min, respiratory rate is 19/min, temperature is 36.8 °C (98.2 °F), and blood pressure is 160/91 mm Hg. Cardiovascular examination shows no abnormalities. ECG is shown below. Which of the following biochemical measures would most likely be elevated and remain elevated for a week after this acute event?

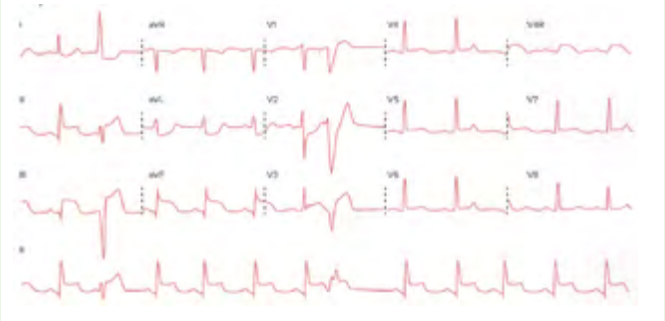

Fig. Q. 4.3

A. Alanine aminotransferase
B. Aspartate transaminase
C. Creatinine-kinase MB
D. Lactate dehydrogenase (LDH)
E. Troponin I

Question 4.4: **A 56-year-old male with known coronary artery disease presents to the emergency department complaining of chest discomfort and palpitations for 2 hours. His vitals on arrival were a blood pressure of 122/76 mm Hg, heart rate 180/min, respiratory rate of 22/min, temperature of 37 °C (98.6 °F), and SpO2 of 98% in room air. A 12-lead electrocardiogram demonstrated ST-segment elevation in anterolateral leads. Troponin level was 0.8 ng/mL (normal 0-0.4ng/mL). The patient refused primary percutaneous intervention and was treated with anti-fibrinolytics in the coronary care unit. After one hour of treatment, the patient becomes unconscious and his blood pressure falls to 60/40 mm Hg. Cardiac monitoring showed the following type of ECG pattern in lead II. What is the most likely cause of his condition?**

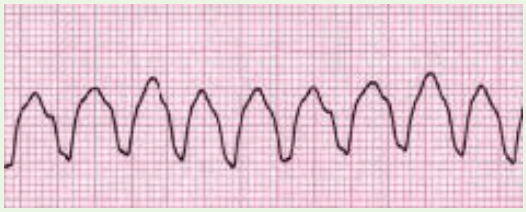

Fig. Q. 4.4

A. Premature ventricular contractions
D. Third degree heart block
B. Monomorphic ventricular tachycardia
E. Acute pericarditis
C. Mitral regurgitation

Correct answers: 4.3E, 4.4B

Chapter 5:

Valvular Heart Diseases

Mitral Valve Prolapse (Barlow Syndrome)

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Definition of Mitral Valve Prolapse

A mitral valve prolapse refers to the **bulging of parts of the mitral valve cusp during systole in the left atrium**. If symptoms occur, the disease is called mitral valve prolapse syndrome. The mitral valve prolapse can result in mitral regurgitation, and is considered the most common cause of isolated mitral regurgitation.

During late systole, the mitral valve leaflets bow back into the left atrium. The diagram shows the leaflets lying behind an imaginary line drawn between the posterior aortic root and the atrioventricular groove.

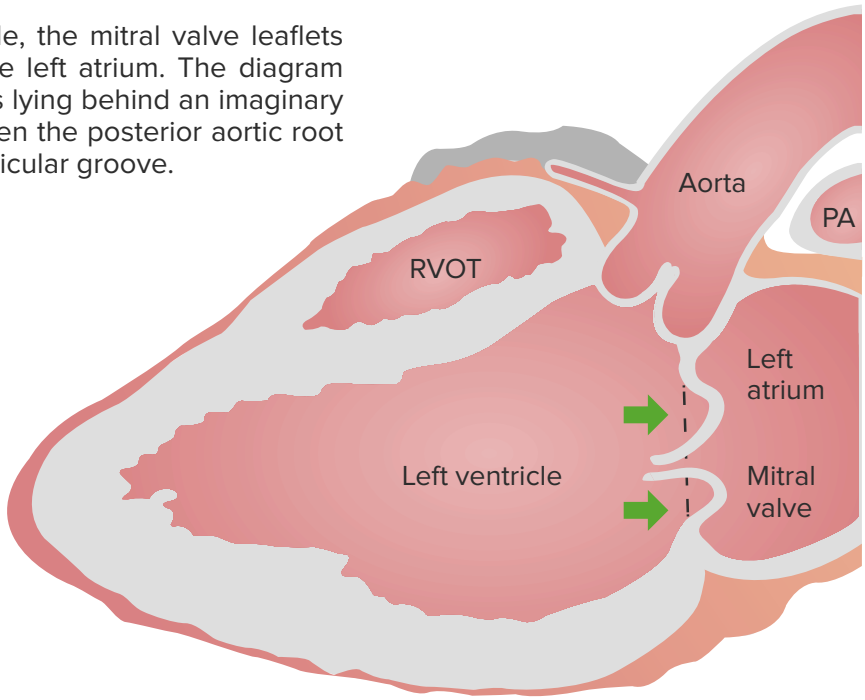


Fig. 5-01: *Heart mitral prolapse*

Epidemiology of Mitral Valve Prolapse

Mitral valve prolapse is common in industrialized countries. It is the most common cardiac valve anomaly in adulthood. 3–4 % of adults have this anomaly, for which an autosomal dominant inheritance is suspected. Women are affected more often than men.

Etiology of Mitral Valve Prolapse

The etiology of mitral valve prolapse may be **disproportion in the size of the valves, the left ventricle, and the valve-retaining apparatus**. A distinction is made between **primary idiopathic mitral valve prolapse** and **secondary mitral valve prolapse**.

Secondary mitral valve prolapse can be associated with:

1. Connective tissue disorders (Marfan syndrome, Ehler-Danlos syndrome, and osteogenesis imperfecta)
2. Acute rheumatic heart disease
3. Myocardial infarction
4. Infective endocarditis

Pathology of Mitral Valve Prolapse

The most common underlying pathological process is **myxomatous degeneration**. It involves increased deposition of glycosaminoglycans in the leaflets of the mitral valve, resulting in long, floppy leaflets with excessive valvular tissue.

Clinical Features of Mitral Valve Prolapse

Symptoms

Mitral valve prolapse is mostly benign and asymptomatic. Only about 10 % of affected individuals present with symptoms. These include arrhythmias and palpitations, syncope, presyncope, dyspnea, and diminished performance, as well as anxiety and atypical chest pain.

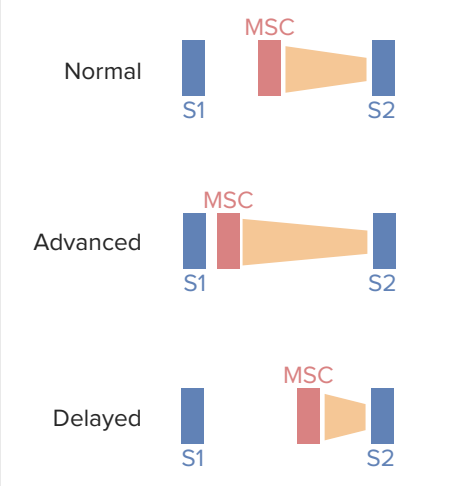


Fig. 5-02: *Mitral valve prolapse, physical exam.*

Signs

The exam often shows an **asthenic body type** with **decreased body weight** and **hypotension**.

Auscultation shows:

- Late systolic murmur with midsystolic click
- Regurgitation is not always present, and therefore lacks any associated MR murmur.
- Increased VR delays click and shortens murmur
- Decreased VR advances click and lengthens murmur

These sounds can be shifted toward the early systole when standing or during the Valsalva maneuver, and toward the late systole when squatting.

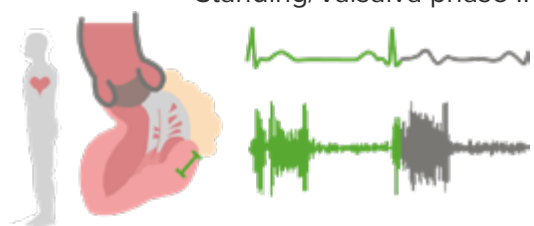
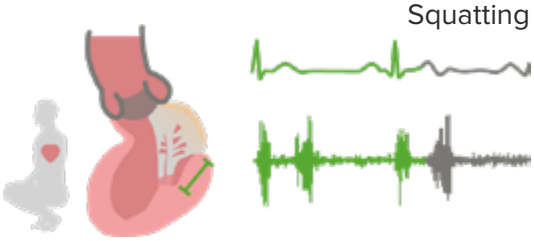
Maneuvers	S 1-click interval	Onset of late systolic murmur in relation to S1	Duration of late systolic murmur in relation to total duration of systole
Standing/Valsalva phase II 	Decreased	Early	Longer
Squatting 	Increased	Late	Shorter

Fig. 5-03: *Effect of dynamic auscultation in mitral valve prolapse (MVP)*

Diagnostics of Mitral Valve Prolapse

Echocardiography

- The MVP diagnostic test of choice.
- Defined echocardiographically as displacement of the mitral valve leaflets during systole by more than 2 mm above the mitral valve annulus in the long-parasternal axis view.
- Classified into 2 subtypes:
  1. Classical MVP (65 %): Leaflet thickness is > = 5 mm.
  2. Non-classic MVP (35 %): leaflet thickness is < 5 mm.

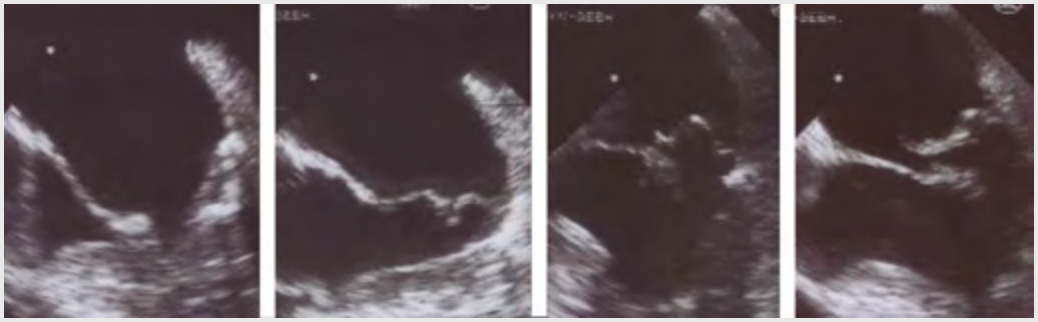


Fig. 5-04: *Transesophageal echocardiogram of mitral valve prolapse.*

Treatment of Mitral Valve Prolapse

If patients are asymptomatic and do not present with arrhythmia or mitral regurgitation, no treatment is necessary.

Patients with severe mitral regurgitation should:

1. Stop **nicotine**, **alcohol**, and **caffeine.**
2. **Avoid strenuous exercise** and **sports**.
3. Undergo mitral valve replacement if necessary.

Specific treatment of complications are needed if these develop. For example, oral anticoagulants for atrial fibrillation. Prophylaxis against infective endocarditis must be given. The administration of antiarrhythmic medication or an ICD implantation may also be indicated.

Note:
Re-checks should be performed at 5-year intervals.

Complications of Mitral Valve Prolapse

- Mitral valve prolapse can lead to **mitral regurgitation**, which in turn causes:
  1. Atrial fibrillation and increased risk of thromboembolic manifestations, such as transient ischemic attack (TIA) or stroke.
  2. Heart failure manifestations of the afterload increase, as in severe hypertension.
- **Infective endocarditis**
- **Sudden cardiac death** occurs at an incidence rate of approximately 1 %.

Mitral Stenosis
(Mitral Valve Stenosis)

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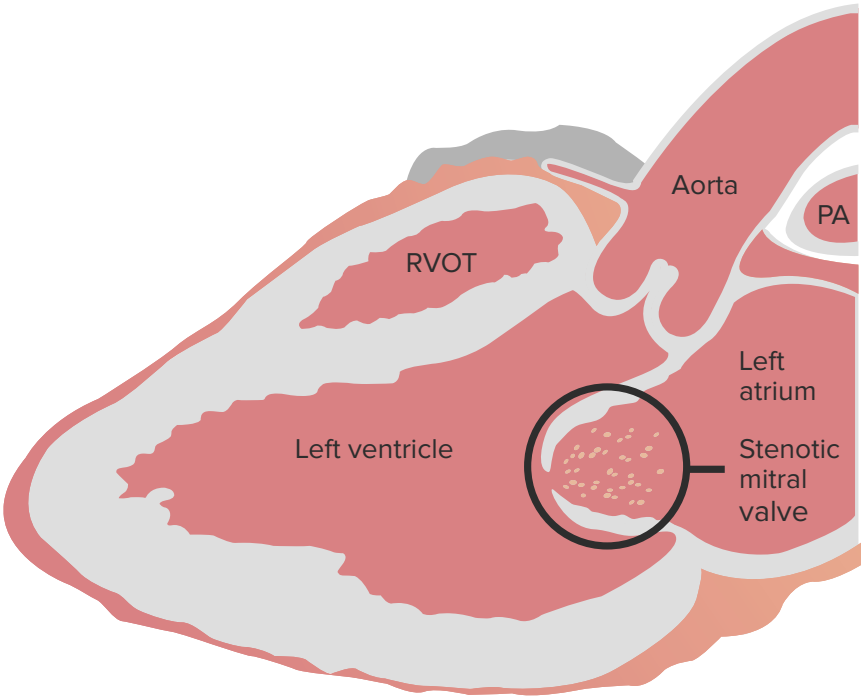


Fig. 5-05: *Mitral stenosis*

Definition of Mitral Stenosis

Mitral stenosis occurs as the mitral valve narrows and obstructs blood flow between LA and LV. Obstructed filling of the left ventricle.

Etiology of Mitral Stenosis

The major cause of mitral stenosis is rheumatic heart disease. Asking the patient about a possible history of frequent bacterial tonsillitis is important.

Other causes of mitral stenosis include:

1. Autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis
2. Congenital mitral stenosis
3. Degenerative mitral stenosis

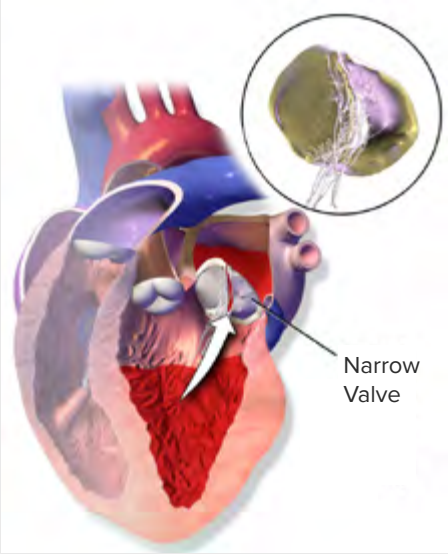


Fig. 5-06: Mitral valve stenosis

Classification of Mitral Stenosis

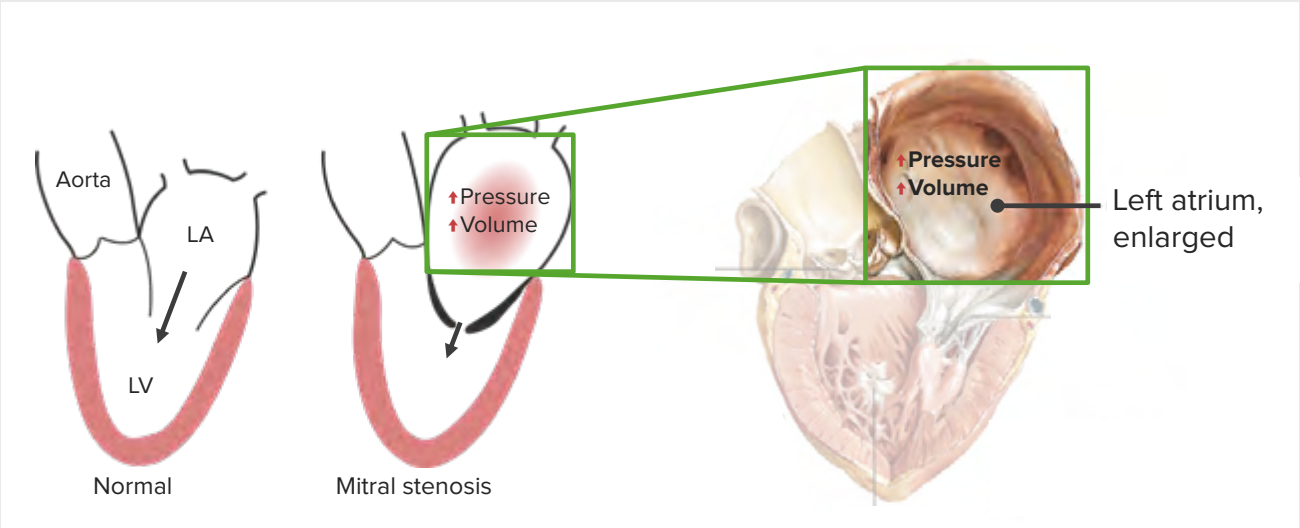
The 3 grades of mitral stenosis severity

Depending on the **remaining open area, mean pressure gradient**, and **mean pulmonary capillary pressure**, mitral valve stenosis can be divided into mild, moderate, and severe grades of severity.

	Mild	Moderate	Severe
Valve area (cm^2)	1.5–2	1–1.5	< 1
Mean gradient (mmHg)	> 5	5–10	> 10
Pulmonary artery mean pressure (mmHg)	> 30	30–50	> 50

Pathophysiology of Mitral Stenosis

What happens in mitral stenosis?



As the valve area decreases, the left atrium must work harder to pump blood into the left ventricle.

→

The LA is typically a low-pressure system and therefore will dilate under the increased workload.

→

The increased pressure is transmitted backward into the pulmonary vessels.

Fig. 5-07: Mitral stenosis increases the LA pressure significanly, resulting in LA dilatation.

Due to the stenosis of a mitral valve, blood cannot flow properly into the left ventricle. This causes blood **stasis in the left atrium, leaving the blood to flow back into the lungs to** the pulmonary veins, and ultimately to the right heart. Therefore, there is a risk of **right heart failure** and an increased risk of atrial fibrillation due to overstretching of the left atrium. Atrial fibrillation may increase the risk of embolization and may result in acute ischemia of the legs, stroke, or mesenteric ischemia

Clinical Features of Mitral Stenosis

Symptoms

The severity of the disease determines which symptoms occur.

- Main symptoms characteristic of mitral stenosis are progressive dyspnea on exertion and hemoptysis (from pulmonary vessels that rupture due to the high pressures).
- The expansion of the left atrium may lead to **atrial fibrillation and thrombi,** leading to **arterial embolisms.**
- Due to congestion of blood in the lungs, pulmonary hypertension develops, with symptoms such as **dyspnea** and **nocturnal cough**.
- Signs of **right heart failure** may also occur.

The reduced cardiac output leads to:

- Performance degradation
- Fatigue
- Peripheral cyanosis

Note:
In mitral stenosis, heart failure is a late finding and a poor prognostic factor. This means that the right ventricle can no longer keep up with the increased pressure transmitted backwards from the LA.

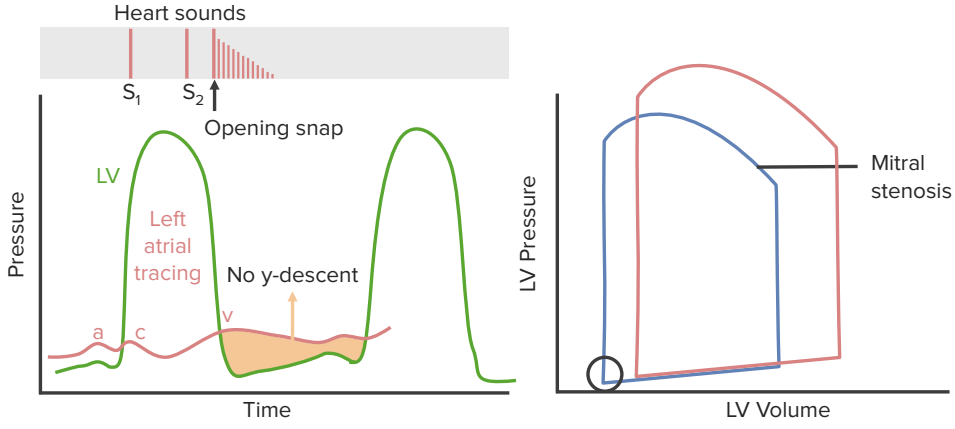


Fig. 5-08: *Mitral stenosis*

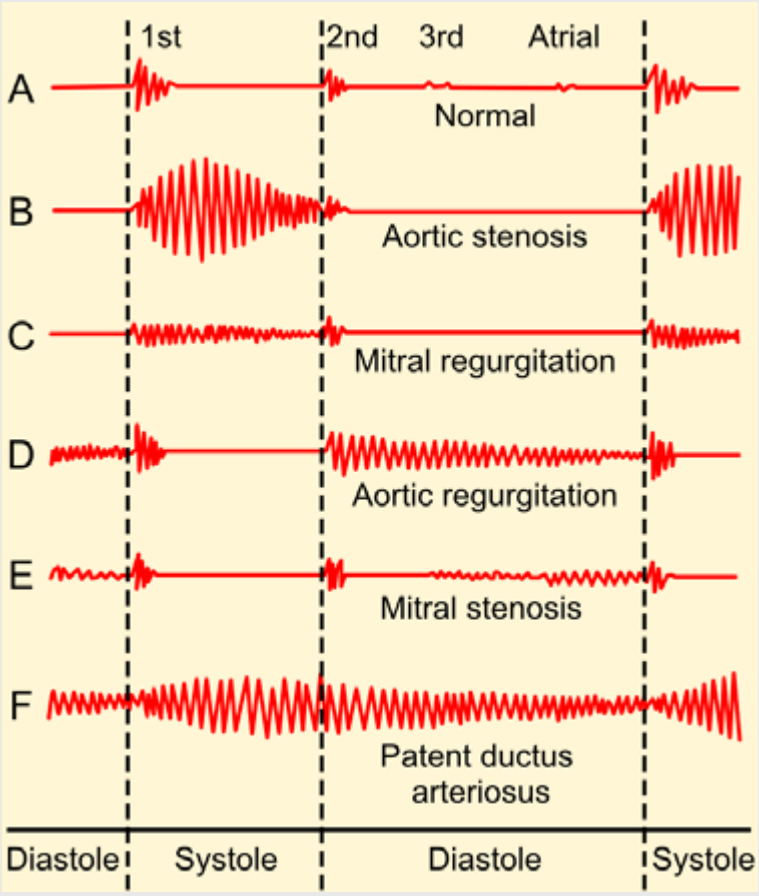


Fig. 5-09: Phonocardiograms from normal and abnormal heart sounds

Signs (cardiovascular examination)

- **Palpation:**
  - Apical slapping apex is characteristic of mitral stenosis.
  - Right ventricular heave can be felt if patient has pulmonary hypertension.
- **Auscultation:**
  - 1st heart sound is accentuated.
  - **Mid-diastolic rumbling murmur,** loudest at the 5th intercostal space at midclavicular line. It is best heard when the patient is lying on his left side.
  - Opening 'snap' can be heard as the calcific valve is forced open by the LA contraction.

Note:
Shorter interval between opening snap and S2 indicates more severe disease.

Diagnostics of Mitral Stenosis

ECG

- An ECG may show a P with double peaks, as well as a right ventricular hypertrophy mark, and a right axis deviation.
- Atrial fibrillation is common due to substantial MS.

Chest X-ray

A **radiograph** may also show:

- Right heart enlargement
- LA enlargement with prominent left auricle (straightening of the left cardiac border)
- Signs of pulmonary congestion

Echocardiography

During **echocardiography**, the valve can be readily assessed and a quantification of the grade of stenosis can be made. The following is assessed:

- Abnormal valve mobility
- Leaflet thickening
- Subvalvular thickening
- Calcification

Treatment of Mitral Stenosis

Conservative

1. Drug treatment of heart failure using diuretics, such as furosemide
2. Heart-controlling drugs such as beta-blockers, or CCB to control heart rate and increase diastolic filling time
3. Management of atrial fibrillation
4. Infective endocarditis prophylaxis

High-yield:
Rapid AF will decrease the diastolic filling time and may lead to frank pulmonary edema.

Interventional

Indicated in severe symptomatic mitral stenosis.

1. **Percutaneous Mitral Commissurotomy (PMC):**
   - Indicated as first-line treatment if valve anatomy is favourable, or if surgery is high-risk and contraindicated.
   - Contraindicated in:
     - Mitral valve area > 1.5 cm^2
     - Left atrial thrombus
     - More than mild MR
     - Severe bicommissural calcification
     - Concomitant IHD requiring bypass surgery
2. **Mitral valve surgery:**
   - Surgical repair or replacement of the mitral valve is considered if patient remains symptomatic despite medical treatment and PMC is contraindicated (see previous).

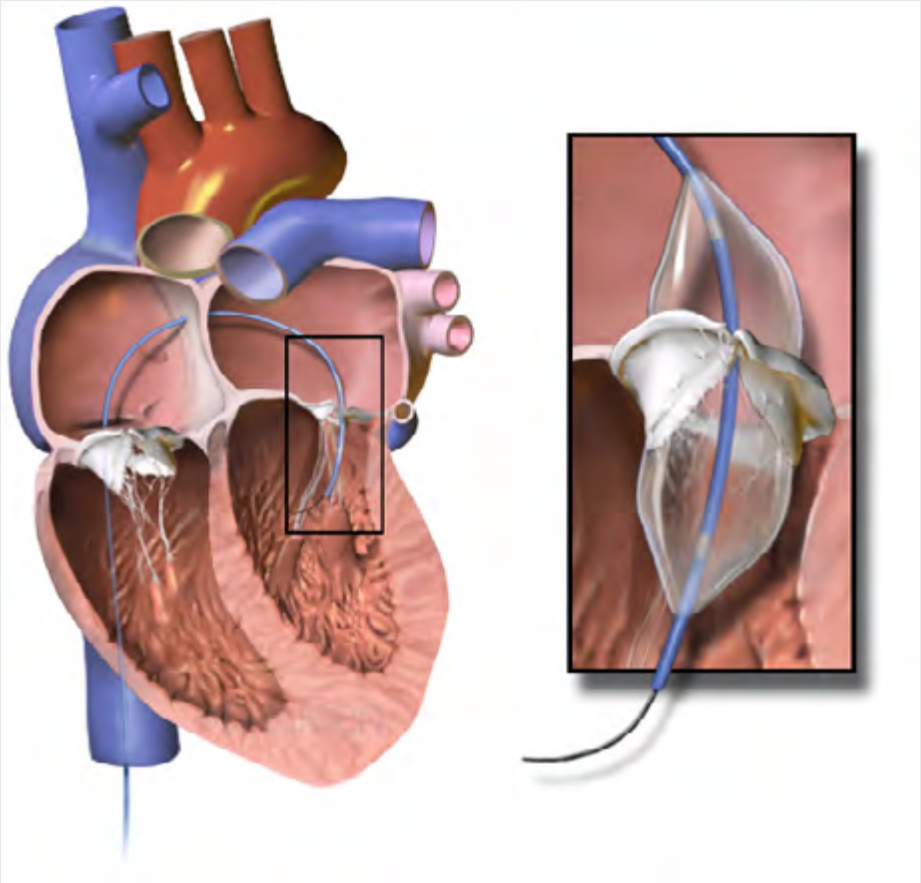


Fig. 5-10: Mitral valvuloplasty

Complications of Mitral Stenosis

- Atrial fibrillation with risk of thromboembolic events
- Congestive heart failure
- Pulmonary hypertension with right heart failure manifestations

Mitral Insufficiency (Mitral Regurgitation)

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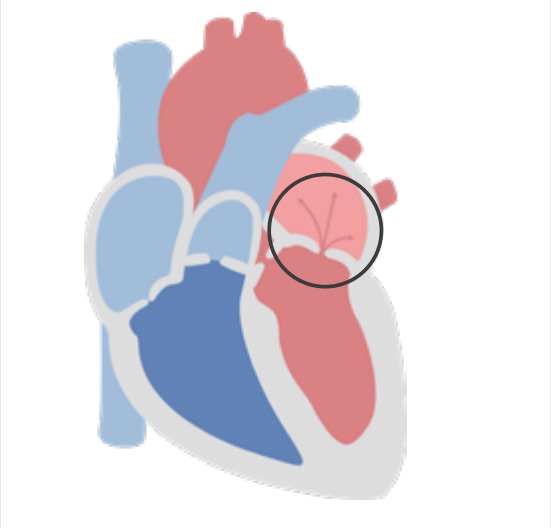


Fig. 5-11: Mitral regurgitation

Definition of Mitral Insufficiency

Mitral valve insufficiency or mitral regurgitation (MR) involves changes to the **mitral valve** so that it is **no longer able to close properly**, resulting in an abnormal flow of blood back into the LA from the LV across the incompetent valve.

These changes can affect both the annulus as well as the cusp, the chordae tendineae, and the papillary muscles.

Epidemiology of Mitral Insufficiency

Next to valvular aortic stenosis, mitral valve insufficiency is the **second most common disease of the heart valves** with an incidence rate of 2 % per year.

Etiology of Mitral Insufficiency

Causes of MR can be classified into:

1. **Primary MR**

   Involves conditions that affect the mitral valve apparatus and includes:

   1. Rheumatic heart disease (RHD). The most common cause of mitral regurgitation
   2. Degenerative mitral valve disease, as part of conditions such as Ehler-Danlos syndrome, Marfan syndrome, or mitral valve prolapse syndrome.
   3. Infective Endocarditis (IE), the destruction of the valve through infectious endocarditis can also cause mitral regurgitation.

2. **Secondary (functional) MR**

   Involves conditions that affect the left ventricle and lead to functional abnormalities of the mitral valve when the valve is unable to close due to annulus dilation. This can occur as part of a dilated cardiomyopathy.

Classification of Mitral Insufficiency

1. **Acute MR**

   - Acute disruption of mitral valve function occurs (as in acute flail leaflet or papillary muscle dysfunction in acute MI), resulting in a sudden increase of the LV end-diastolic volume, and subsequently rapid increase in left atrium pressure → pulmonary venous congestion (pulmonary edema).

2. **Chronic MR**

   - Chronic MR is further classified into **primary or secondary (functional) MR.**

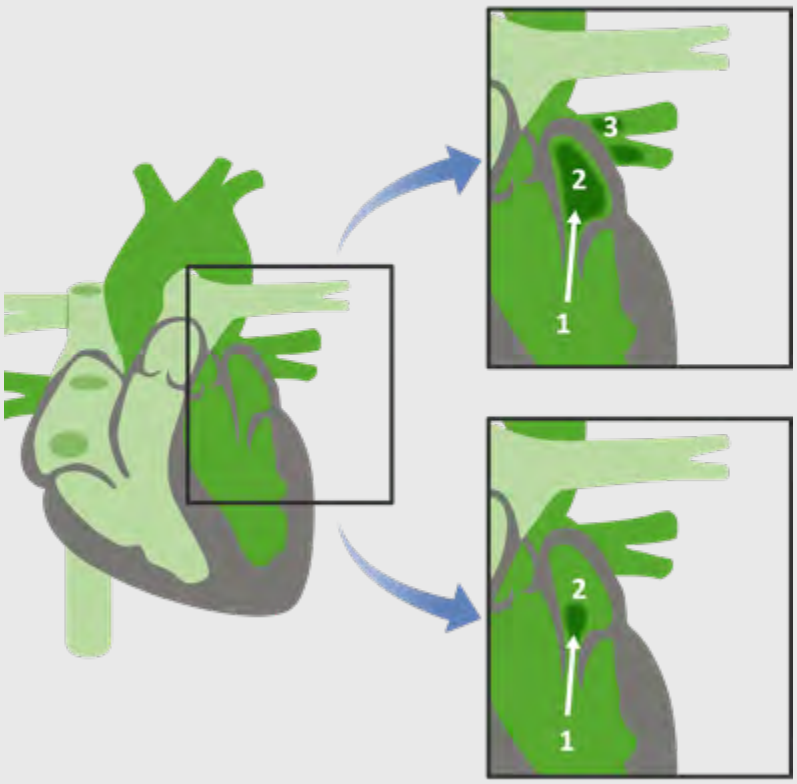


Fig. 5-12: Slight mitral insufficiency. The color cloud symbolizes the blood backflow, 1 Left ventricle – 2 Left atrium – 3 pulmonary vein

Stages of chronic MR

The American Heart Association (AHA) classification of chronic MR list 4 stages.

Stage A (At risk):

- No MR or small central jet area < 20 %
- Small vena contracta < 0.3 cm

Stage B (progressive MR):

- Central jet MR 20–40 % or late systolic eccentric jet MR
- Vena contracta < 0.7 cm
- Regurgitant fraction < 50 %
- Regurgitant volume < 60 mL

Stage C–D (severe MR):

- **Stage C:** Asymptomatic severe MR
- **Stage D:** Symptomatic severe MR
  - Central jet MR > 40 % or holosys tolic eccentric jet MR
  - Vena contracta > = 0.7 cm
  - Regurgitant fraction > = 50 %
  - Regurgitant volume > 60 mL

Pathophysiology of Mitral Insufficiency

If the mitral valve does not close properly, blood from the left ventricle is only partially directed into the systemic circulation. The rest is pumped back into the left atrium and, since the pulmonary veins have no valves, pumped back into the pulmonary circulation. This leads to an **accumulation of blood in the** lungs and thus to **pulmonary hypertension, right ventricular load**, and **right heart failure**.

Since the cardiac output would fall into the left atrium due to the return flow, the left ventricle must intensify its work in order to maintain it. This therefore also causes an **increased strain on the left ventricle**, **leading to left ventricular hypertrophy and dilation**.

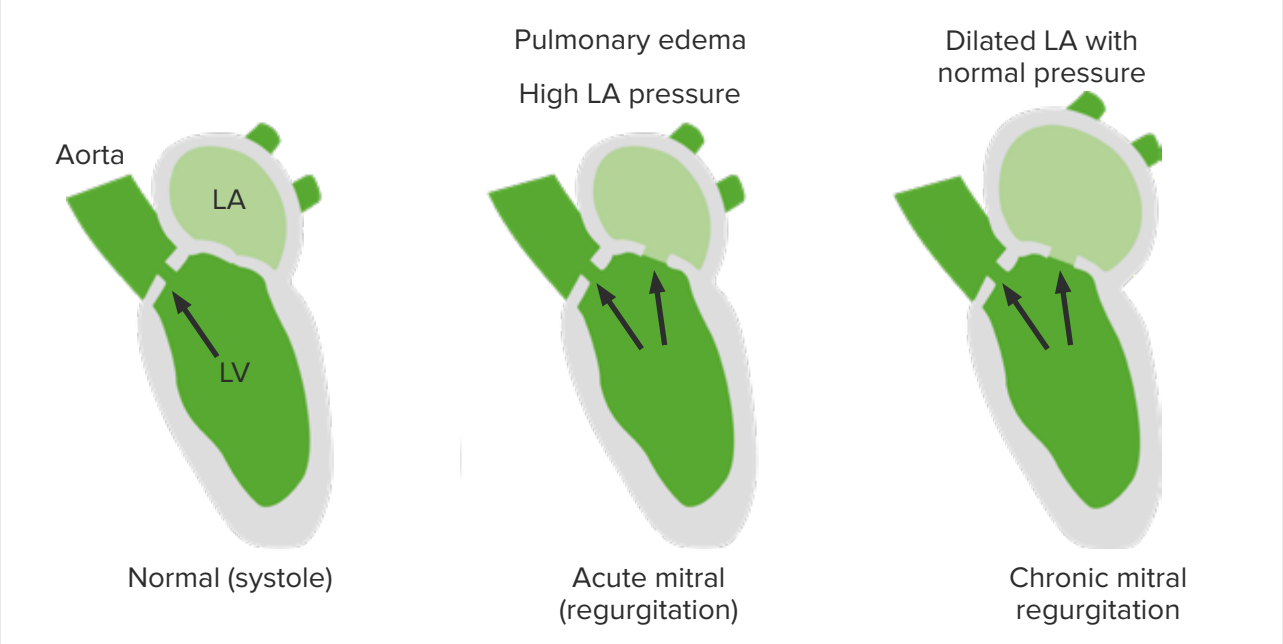


Fig. 5-13: LV dilates resulting in mitral annular dilation and worsening of MR.

Clinical Features of Mitral Insufficiency

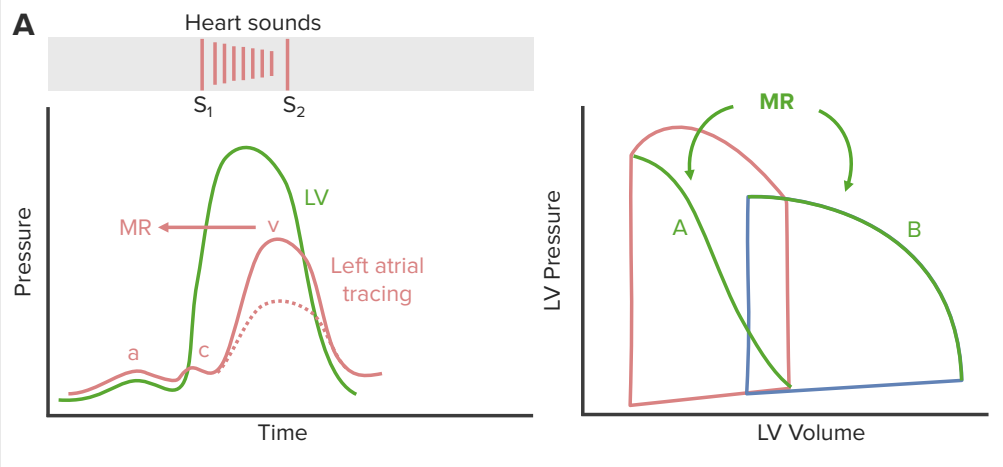
Symptoms in Acute MR

The acute form of mitral valve insufficiency quickly leads to **symptoms of heart failure with pulmonary edema**, even to **cardiogenic shock**, due to lack of time for decompensation.

Symptoms in chronic MR

The chronic form may be asymptomatic for a long time and is associated with a good prognosis, as the mechanisms of adaptation are very good.

The most common symptoms are progressive dyspnea, fatigue on exertion, orthopnea, paroxysmal nocturnal dyspnea, and palpitations.



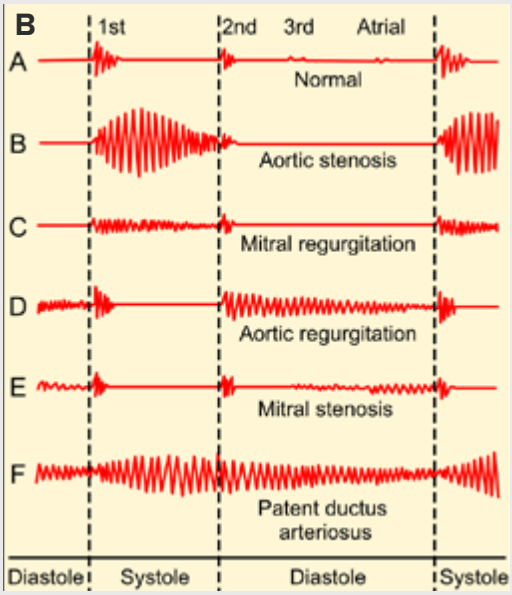


Fig. 5-14: (A) Mitral regurgitation (B) Phonocardiograms from normal and abnormal heart sounds.

Signs (cardiovascular examination)

- **Palpation**
  - Cardiac impulse is prominent.
  - Apical thrills can be felt in severe MR.
- **Auscultation**
  - 1st heart sound is muffled.
  - Holosystolic murmur, characterized as having a 'blowing' quality, heard loudest at the mitral area (apex) and radiates to axilla.
  - S3 gallop in advanced heart disease.

Note:
Sustained hand grip increases systemic vascular resistance and afterload. It is used to differentiate between aortic stenosis and mitral insufficiency. In MR, the murmur increases. In AS, it decreases.

Diagnostics of Mitral Insufficiency

ECG

- Signs of left ventricular hypertrophy and P-mitrale
- Later, if pulmonary hypertension has developed, signs of right heart strain with right axis deviation

Chest X-ray

- LV enlargement in the form of increased cardiac shadow
- LA enlargement in the form of straightening of the left cardiac border
- Signs of pulmonary congestion

Echocardiography

The gold standard to assess valvular apparatus and diagnose mitral regurgitation fraction and volume is echocardiography. The stages of MR based on echocardiography has been discussed earlier in the eBook.

Treatment of Mitral Insufficiency

Acute MR

1. Hemodynamic stabilization using...
    - ...IV diuretics to relieve pulmonary congestion.
    - ...Antihypertensive drugs to decrease the afterload.
    - ...IV nitrates to decrease the preload and relieve congestion.
    - ...Intra-aortic balloon pump or pharmacological management is insufficient.
2. Urgent mitral valve surgery

Chronic MR

Treatment of chronic MR depends primarily on whether the patient is symptomatic or not.

Asymptomatic

Asymptomatic patient with severe MR and:

- LV dysfunction (EF < 60 %): Surgical intervention is indicated.
- No LV dysfunction (EF > 60 %):
    - AND patient has new onset AF, or pulmonary artery pressure > 50 mmHg: Surgical intervention is indicated.
    - IF NOT: Conservative management and follow up.

Symptomatic

Symptomatic patient with severe MR and:

- LV dysfunction (EF > 30 %): Surgical intervention is indicated.
- Severe LV dysfunction (EF < 30 %):
  - Medical therapy is preferred.
  - Surgery is only indicated if patient is refractory to medical therapy.

Medical therapy

The goal of medical therapy should be to increase cardiac output through both a reduction in afterload and decreased pulmonary venous hypertension. Symptoms of CHF should also be treated.

- Decrease afterload through administration of ACEIs/ARBs, especially if mitral insufficiency is associated with systolic dysfunction.
- Decrease pulmonary congestion with diuretics and digitalis.

Follow up

- Asymptomatic patients with severe MR and preserved LV systolic function (EF > 60 %) should be followed clinically and undergo echocardiography every 6 months.
- Asymptomatic patients with moderate MR and preserved LV systolic function should be followed yearly, with echocardiography every 1–2 years.

Complications of Mitral Insufficiency

- Cardiac decompensation, which may cause pulmonary edema
- Atrial fibrillation and increased risk of thromboembolic events
- Increased risk of infective endocarditis

Aortic Stenosis (Aortic Valve Stenosis)

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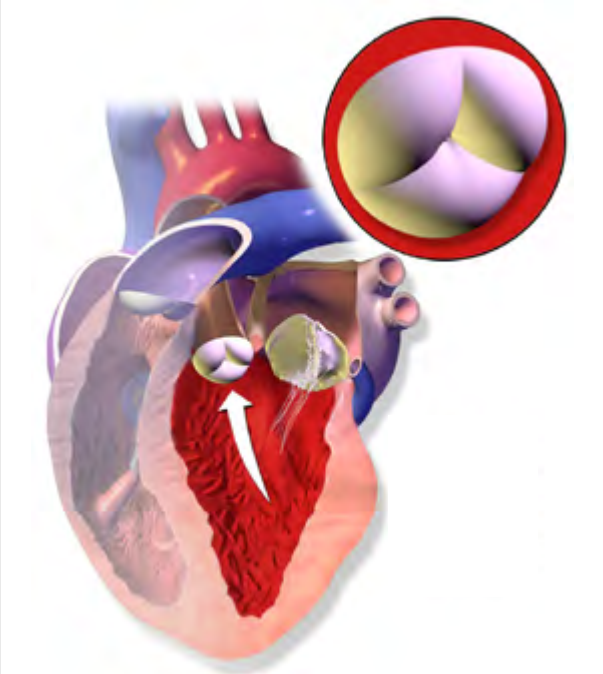


Fig. 5-15: Aortic stenosis

Definition of Aortic Stenosis

The term valvular aortic stenosis refers to a **narrowing of the aortic valve**, resulting in obstruction of the systolic outflow of blood from the LV into the aorta. This results in a markedly increased afterload on the leftventricle, and eventually its failure.

Epidemiology of Aortic Stenosis

Valvular aortic stenosis, as the **most common valvular heart disease**, is often a disease of **old age** and a **result of atherosclerotic changes**. Rheumatic forms have become rare in industrialized countries.

It remains asymptomatic for many years in 50 % of cases and is associated with a good prognosis. If the disease becomes symptomatic, the prognosis worsens to a 2-year survival rate of less than 50 %.

Etiology of Aortic Stenosis

There are 3 main causes of aortic stenosis:

1. Senile calcification:
   - The most common cause, especially among patients over 65 years of age. Incidence increases with advancing age.
2. Calcification of a congenitally bicuspid aortic valve:
   - Associated with Turner syndrome.
3. Rheumatic heart disease:
   - Frequently associated with rheumatic mitral valve disease.
   - It has become rare in industrialized countries due to early antibiotic treatment of the responsible streptococcal infections.

Classification of Aortic Stenosis

A distinction must be made according to localization:

1. Valvular
2. Supravalvular
3. Subvalvular

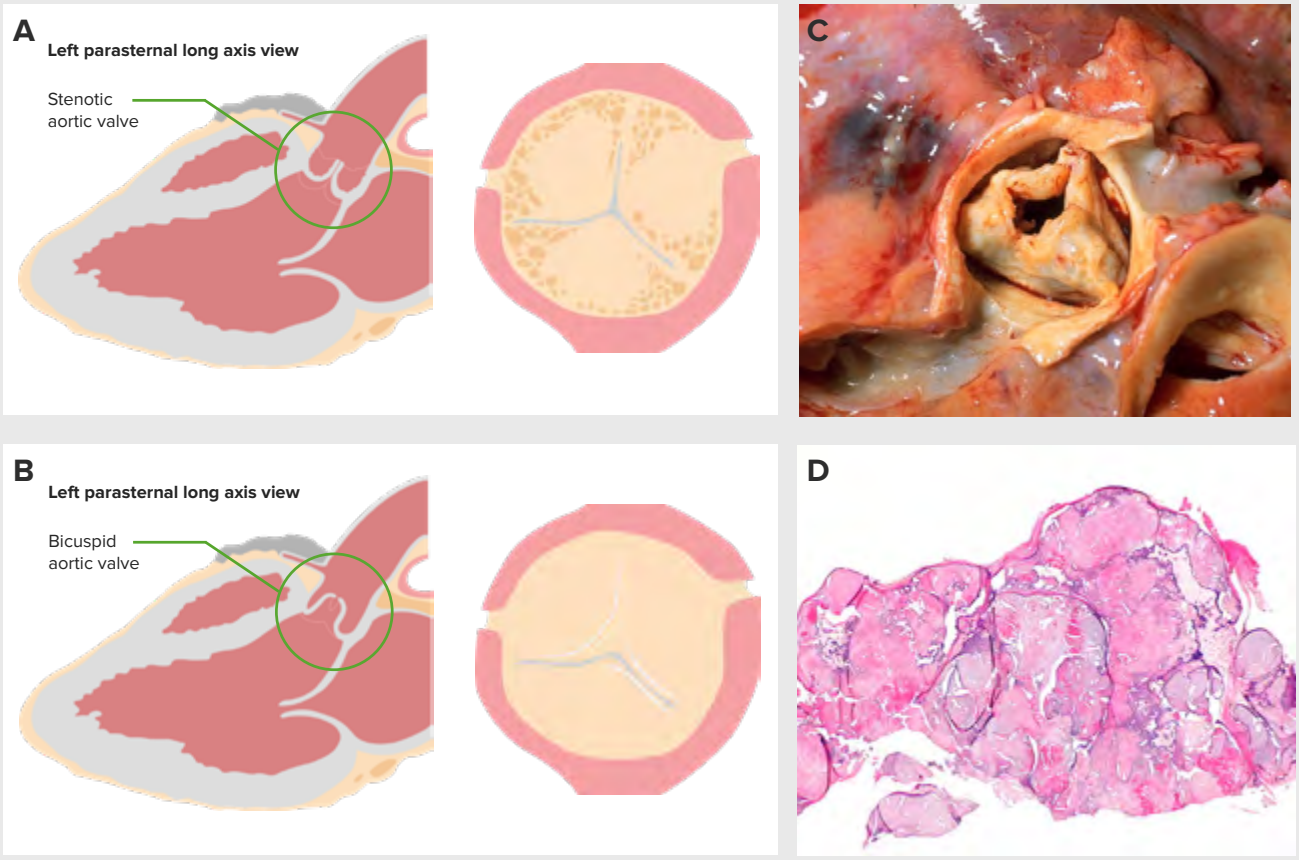


Fig. 5-16: (A) Aortic stenosis – senile type. (B) Aortic stenosis – congenital bicuspid aortic valve. (C) Gross pathology of rheumatic heart disease: aortic stenosis. (D) Calcific aortic stenosis.

Pathophysiology of Aortic Stenosis

As the valve area decreases, the left ventricle must work harder to pump blood throughout the body. → This increases the work of the LV and, in turn, increases LV myocardial oxygen demand. → In response to the increased workload, the myocardium of the left ventricle hypertrophies; (muscles get bigger when they work hard).

In valvular aortic stenosis, the left ventricle has to use more strength in order to maintain the cardiac output against the **pathologically increased pressure gradient of the valve**. This results in a **concentric hypertrophy of the left ventricle**. In the long run, **diastolic dysfunction** develops, resulting in **pulmonary congestion** and **signs of heart failure**.

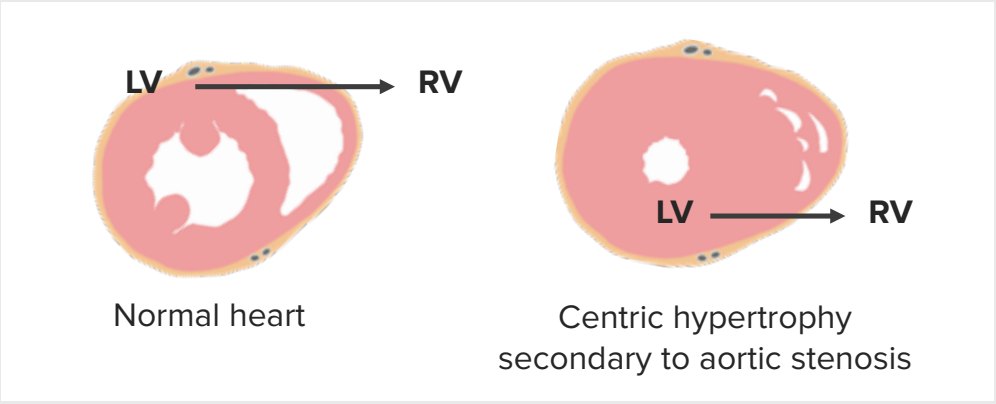


Fig. 5-17: Aortic stenosis increases the afterload and causes pressure overload on the heart, resulting in myocardial hypertrophy.

Clinical Features of Aortic Stenosis

Symptoms

1. Asymptomatic:
   - Patients with mild to moderate valvular aortic stenosis can remain asymptomatic for a long time.
2. Symptomatic
   - Symptoms develop late, when the aortic valve area < 1 cm^2, and the pressure gradient across the valve is 40–50 mmHg.
   - Symptoms are initially exertional only, unless severe AS develops.
   - Classic triad of aortic stenosis symptoms:
     A. Anginal chest pain: AS causes hypertrophy of the heart and a decrease in coronary perfusion. This may lead to angina pectoris.
     B. Exertional dyspnea: Cardiac output decreases as the disease progresses.
     C. Dizziness and syncope.

High-yield:
In asymptomatic patients, valvular aortic stenosis can lead to sudden cardiac death.

Mnemonic

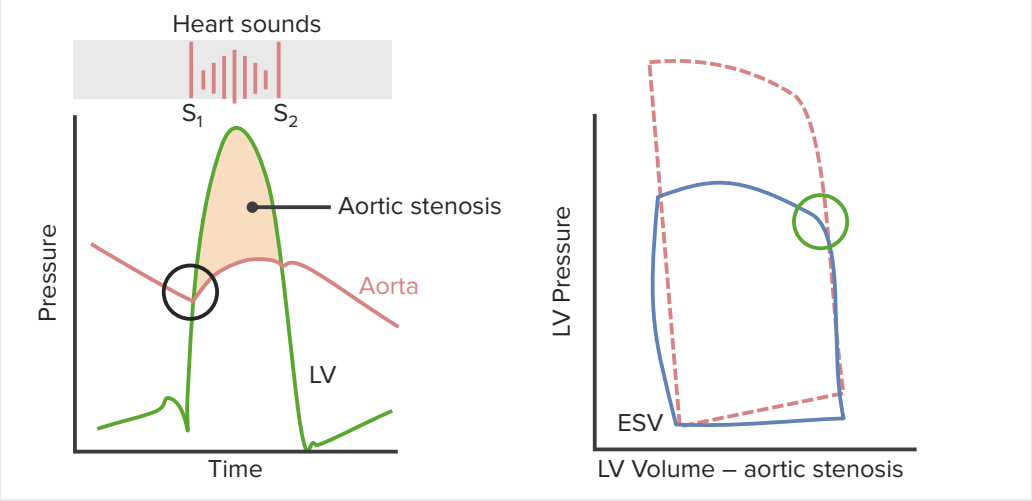
SAD triad

- ***S****yncope*
- ***A****ngina*
- ***D****yspnea*

Signs

General examination

- Pulsus parvus et tardus, or weak and delayed pulse.
- 'Slow and late' carotid pulse due to the delay in blood flow across the narrowed aortic valve
- Palpable systolic thrill over the bifurcation of the carotids and aorta.



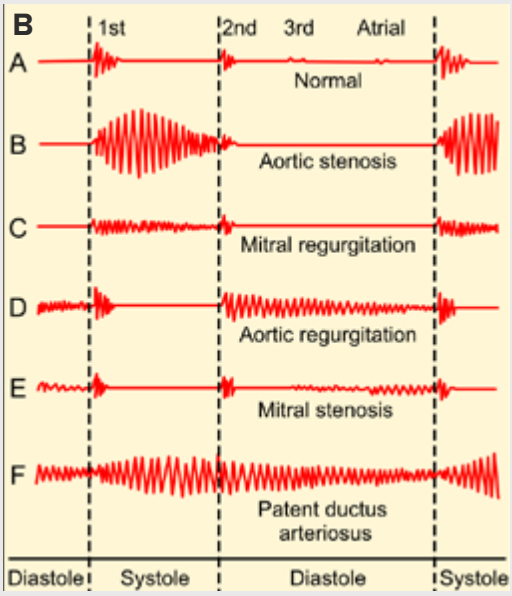


Fig. 5-18: *(A) Heart sounds aortic stenosis (B) Phonocardiograms from normal and abnormal heart sounds.*

Cardiovascular examination

Palpation

Left ventricular hypertrophy manifests as a visible and palpable heaving and widened apical impulse.

Auscultation

1. Paradoxical splitting of the 2nd heart sound.
2. Systolic crescendo-decrescendo murmur (diamond shape) is best heard at the right 2nd intercostal space (first aortic area) and radiates to the carotid artery.
3. Dynamic auscultation:
   - Valsalva and standing ➔ decreases venous return ➔ decrease ejection fraction ➔ decreases murmur.

Note:
Signs of heart failure can be clinically apparent. Heart failure is a late finding with a poor prognosis.

Diagnostics of Aortic Stenosis

ECG

- **Signs of left ventricular hypertrophy** (e.g., left axis deviation)

Chest X-ray

- **Calcification of the aortic valve,** representative of more advanced disease.
- Cardiomegaly can be seen secondary to left ventricular hypertrophy, especially in decompensated severe AS.

Echocardiography

- The gold standard, non-invasive method of assessing aortic stenosis etiology, severity and consequences.
- The following can be seen:
    - Concentric hypertrophy of left ventricles
    - Narrowing of the opening of the aortic valve annulus
    - Increased mean pressure gradient across the aortic valve using Doppler signals
- Using echocardiography, the stenosis can be classified as:

	Mild	Moderate	Severe
Aortic jet velocity (m/s)	2.6–3	3–4	> 4
Mean gradient (mmHg)	< 20	20–40	> 40
AVA (cm^2)	> 1.5	1–1.5	< 1

Treatment of Aortic Stenosis

Conservative

Medical treatment with 6 months follow up is recommended in the:

- Asymptomatic patient with mild to moderate AS
- Symptomatic patient, with severe AS who is physically inactive, with absence of the following risk factors:
    - Peak valve velocity by echocardiography > 5.5
    - Severe valve calcification with continuous yearly progression
    - Severe pulmonary hypertension > 60 mmHg

Medical treatments in AS mprove the symptoms, but they don't improve the outcome. Examples are:

- Heart rate controlling drugs
- Afterload reducing drugs

Surgery

Surgery is indicated for severe aortic stenosis in:

- Asymptomatic patients with LV dysfunction (EF < 50 %).
- Asymptomatic patients who are physically active where an exercise test has revealed classic AS symptoms or a fall in blood pressure below baseline.
- Symptomatic patients.

Surgery can be done using either:

- Aortic valve replacement (AVR) with mechanical prosthetic valves.
- Transcatheter aortic valve implantation (TAVI), recommended in patients unsuitable for surgical AVR.

Note:
Diuretics should be given with care to avoid reducing cardiac output.

Note:
If left untreated, 50 % patients with severe AS will die within 2 years of diagnosis.

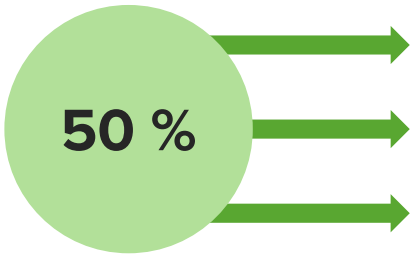
Complications of Aortic Stenosis

Complications of aortic stenosis are:

- Arrhythmias
- Sudden cardiac death
- Left ventricular failure

Prognosis of Aortic Stenosis

Rule of 5, 3, and 2



... of patients with **angina** will die in **5** years if aortic valve is not replaced.

... of patients with symptoms of **syncope** due to AS will die in **3** years if aortic valve not replaced.

... of patients with symptoms of **CHF** secondary to AS will die in **2** years if valve not replaced.

Aortic Insufficiency (Aortic Regurgitation)

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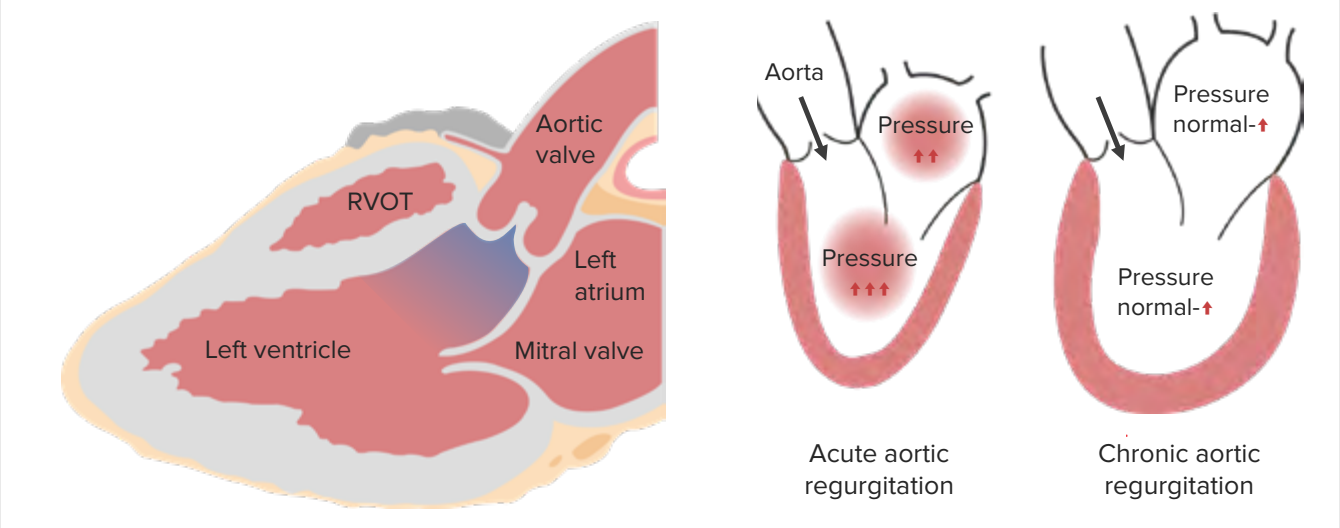


Fig. 5-19: Aortic regurgitation and chronic aortic regurgitation

Definition of Aortic Insufficiency

Aortic insufficiency, or aortic regurgitation (AR), is a valvular disorder characterized by incomplete aortic valve closure, resulting in regurgitation of blood from the aorta into the left ventricle during diastole. It can be either acute, which results in acute decompensation of the LV function as in an aortic dissection, or chronic, which may remain asymptomatic for a long time.

Epidemiology of Aortic Insufficiency

The incidence of AR increases with advanced age, typically peaking in the 4th to 6th decade of life. It is more common in men than women.

Etiology of Aortic Insufficiency

Aortic regurgitation results from valve leaflet abnormalities (Primary AR), dilation of aortic root or annulus (Secondary AR), or a combination of the two.

Primary AR

1. Rheumatic heart diseases (RHD):
   - The most common cause in developing countries.
2. Congenital bicuspid aortic valve:
   - Most common in young adults and developed countries.
3. Infective endocarditis:
   - Usually leads to acute AR.

Secondary AR

1. Aortic root dilatation:
   - Usually the result of proximal aortic aneurysm.
2. Aortic dissection, which usually leads to acute AR. Due to either:
   - Damage to the aortic annulus.
   - Flap prolapse into the aorta, but with intact aortic annulus and leaflets.

Classification of Aortic Insufficiency

AR can be classified as acute or chronic.

1. Acute AR

- Ascending aortic dissection
- Infective endocarditis
- Chest trauma

2. Chronic AR

- RHD
- Congenital bicuspid aortic valve
- Connective tissue disorders (Marfan syndrome, Ehlers-Danlos syndrome)
- Tertiary syphilis

Stages of AR

American Heart Association (AHA) has classified AR into 4 stages:

Stage A (at risk) – patient at risk of AR as a result of RHD or bicuspid aortic valve, but without significant AR.

Stage B (progressive AR) – patient has risk factors for AR, further classified into either:

1. Mild AR.
2. Moderate AR. Echocardiography shows:
   - Jet width < 25% of blood passing through left ventricular outflow tract (LVOT).
   - Vena contracta 0.3–0.6 cm
   - Regurgitant volume < 30 mL/beat
   - Regurgitant fraction < 30 %

Stage C–D (asymptomatic and symptomatic severe AR)

Patient has severe AR, which has the following echocardiographic features:

- Jet width > 65 % of blood passing through left ventricular outflow tract (LVOT)
- Vena contracta > 0.6 cm
- Regurgitant volume > 30 mL/beat
- Regurgitant fraction > 50%
- Holodiastolic flow reversal in the proximal abdominal aorta

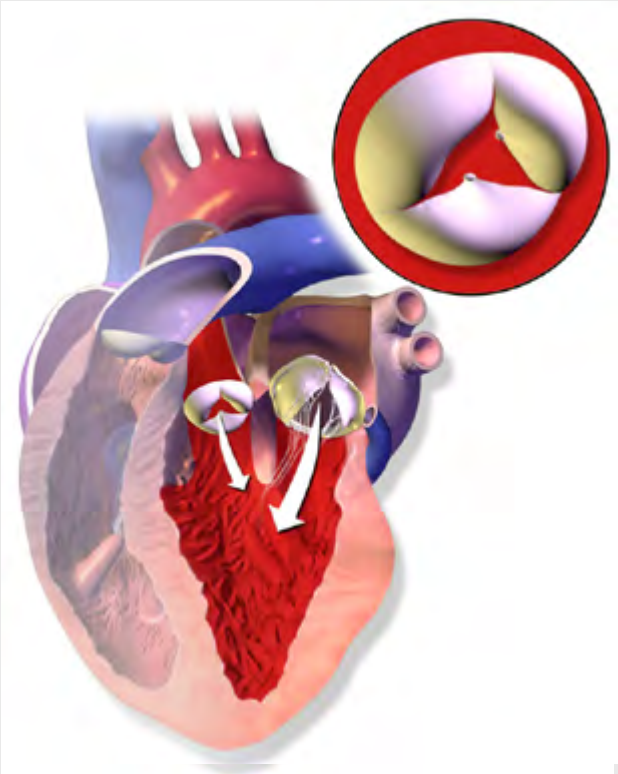


Fig. 5-20: Aortic regurgitation

Pathophysiology of Aortic Insufficiency

AR causes a constant backflow of blood into the left ventricle, with subsequent increase in the LV volume. Chronic aortic valve insufficiency therefore causes an **isolated left ventricular hypertrophy**.

Initially, cardiac output can be maintained and patients remain asymptomatic. With persistent insufficiency, however, **the compliance of the ventricle decreases**, so that the normal stroke volume can no longer be maintained.

Oxygenated perfusion to the left ventricle cannot be sufficiently secured, peripheral resistance increases, and the duration of the diastole is extended. This change can increase the magnitude of the insufficiency.

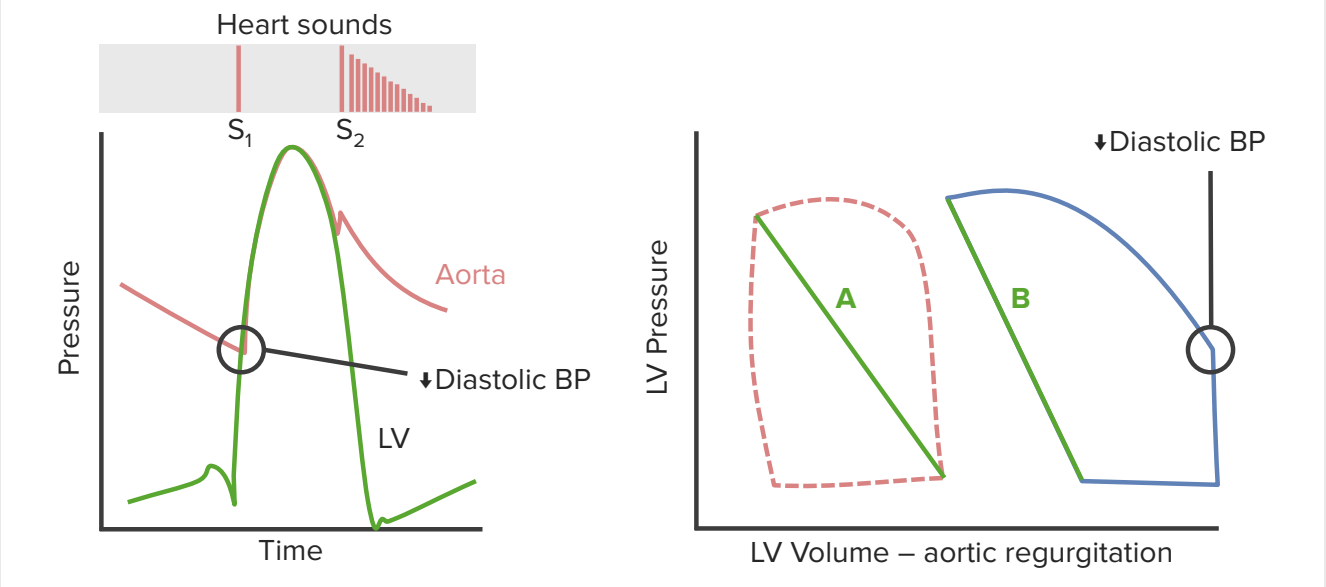
Clinical Features of Aortic Insufficiency

Symptoms in acute AR

- Sudden severe dyspnea
- Rapid left cardiac decompensation with pulmonary edema

Symptoms in chronic MR

- Chronic MR can be tolerated for decades and remain asymptomatic.
- First symptoms are usually palpitations.
- With the progression of the disease, reduced performance and symptoms of left ventricular failure become apparent:
  - Exertional dyspnea
  - Orthopnea
  - Arrhythmia and syncope
  - Anginal pain due to reduced coronary diastolic perfusion pressure
  - Easy fatigability



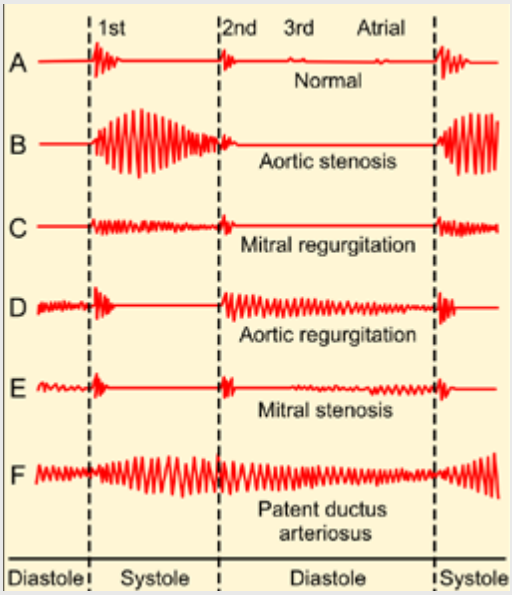


Fig. 5-21: *Aortic regurgitation causes diastolic decrescendo murmur over the 2nd aortic area. It also causes wide pulse pressure (hyperdynamic circultation) due to wide difference between systolic and diastolic blood pressure.*

Signs

General examination

1. Rapid and observable carotid pulse with sudden collapse can be seen.
2. Water hammer pulse (collapsing pulse/Corrigan's pulse): Forceful distension of arterial pulse with quick collapse.
3. De-Musset's sign: Head bobbing in synchrony with heart beats.
4. Quincke's sign: Capillary pulsations seen on light compression of nail bed.
5. Müller sign: Pulsation of the uvula that occurs during systole due to increased stroke volume.
6. Duroziez's sign: Bruits heard over femoral artery upon light compression by stethoscope.

Cardiovascular examination

Palpation

1. Apex is usually diffuse, displaced inferolaterally and characteristically hyperdynamic due to eccentric hypertrophy and increased stroke volume.

Auscultation

1. High-pitched, diastolic, blowing decrescendo murmur best heard at left third intercostal space (second aortic area) when sitting and leaning forward.
2. Dynamic auscultation: Squatting and hand grip → increased afterload → increased murmur.
3. S3 gallop may be heard due to volume overload.

Diagnostics of Aortic Insufficiency

ECG

Can be normal or shows nonspecific findings as left ventricular hypertrophy secondary to hypertension, which is the most common cause of ascending aortic dissection with subsequent acute AR.

Chest X-ray

- Prominent aortic root due to dilated ascending aorta.
- Enlarged cardiac shadow.

Echocardiography

Echocardiography is the gold standard for the assessment of underlying etiology, regurgitation fraction, and volume. The stages of MR based on echocardiography were covered earlier in this eBook.

Treatment of Aortic Insufficiency

Conservative

- Conservative medical treatment with follow up is recommended in the:
    1. Asymptomatic patient with mild–moderate AR.
    2. Asymptomatic patient with severe AR and normal LV function.
- Follow up:
    1. Patients with mild–moderate AR should be followed up yearly, with echocardiography performed every 2 years.
    2. Patients with severe AR and normal LV function should be followed up yearly, and if LV diameter and function show significant changes, follow up should then take place every 3–6 months.
    3. If ascending aorta is dilated (> 40 mm), CT is recommended.

Note:

Austin Flint murmur:

- *Occurs in severe AR.*
- *Low-pitched mid-diastolic or presystolic murmur that is best heard at apex, and might be mistaken as mitral stenosis.*
- *Occurs when the large amount of regurgitant blood strikes the anterior leaflet of the mitral valve, leading to premature closure of the mitral leaflets.*

- Medical treatment:
  1. Vasodilators to decrease afterload: ACEIs or ARBs.
  2. Symptomatic treatment of heart failure to relieve pulmonary congestion, such as diuretics.
  3. Beta-blockers can used in patients with connective tissue disorders, such as Marfan syndrome, to slow aortic root dilatation and reduce risk of aortic complications.

Surgery

Acute AR

1. Hemodynamic stabilization using:
   - IV diuretics to relieve pulmonary congestion.
   - Antihypertensive drugs to decrease the afterload.
   - Beta-blockers to control heart rate and reduce sharing force as in aortic dissection.
2. Urgent Aortic Valve Replacement (AVR)

Chronic AR

Indications for surgery in chronic AR depend mainly on whether the patient is symptomatic or not.

Surgery is indicated under the following conditions:

Asymptomatic

Asymptomatic patient with severe MR and:

1. LV dysfunction (EF < 50 %)
2. NO LV function (EF > 50 %) but with severe LV dilatation:
   - LV end-diastolic diameter (LVEDD) > 70 mm
   - LV end-systolic diameter (LVESD) > 50 mm

Symptomatic

Symptomatic patient with severe AR should undergo surgical aortic valve replacement (AVR).

Note:

Surgery is indicated in Marfan syndrome with aortic root diameter > =50 mm regardless of the symptoms and Echo findings.

Chapter 6:

Congestive Heart Failure

Heart Failure

Definition, Epidemiology, Etiology

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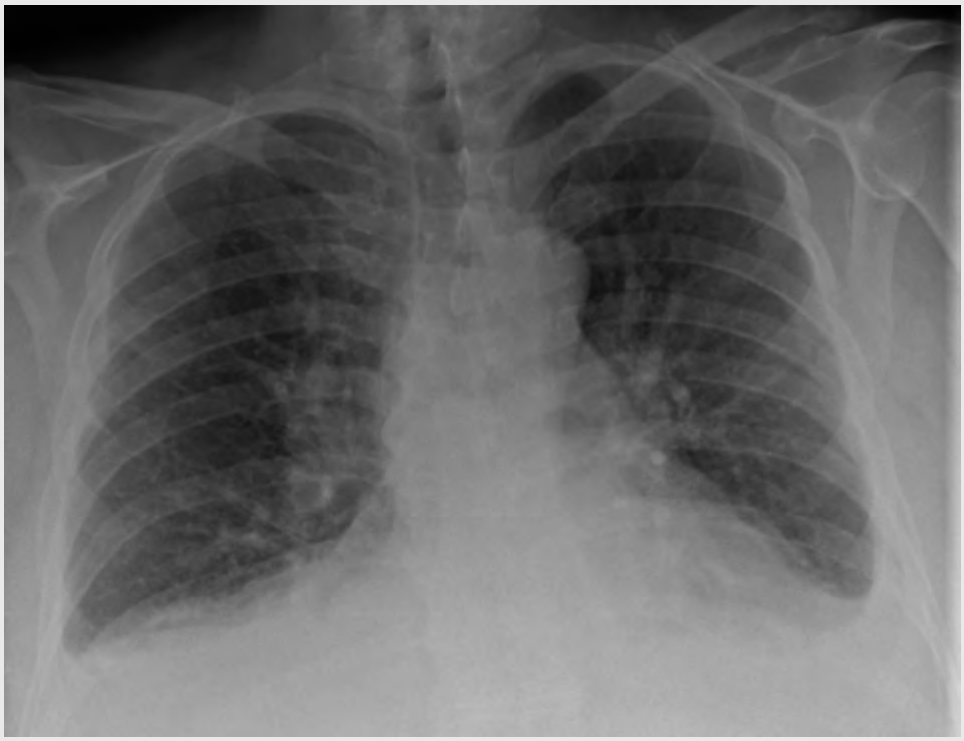

Fig. 6-01: *Chest radiography that shows enlarged heart, increased bronchovascular markings and small bilateral pleural effusion suggestive of congestive heart failure.*

Definition of Congestive Heart Failure

Cardiac insufficiency refers to the inability of the heart to supply the body with normal **cardiac minute volume** under normal end-diastolic pressure conditions.

- WHO defines cardiac insufficiency according to the degree of reduced physical capacity due to ventricular dysfunction.
- American Heart Association/American College of Cardiology (AHA/ACC) guidelines define heart failure as 'a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood'.

Epidemiology of Congestive Heart Failure

In cases of cardiac insufficiency, there is a clear prevalence with regard to old age. While CHF is measured at only 1 % in patients over 50, it increases to 10 % in patients over the age of 80. The male/female ratio is 1.5 : 1. HF is characterized by periodic exacerbations that require treatment intensification most often in a hospital setting, and is the single most frequent cause of hospitalization in persons 65-years and above. Approximately 30 % of patients with chronic heart failure are readmitted within 2 to 3 months.

CHF is associated with low survival and after the diagnosis of CHF, survival estimates are 50 % and 10 % at 5 and 10 years, respectively.

Note:
Systolic heart failure is the most common cause of heart failure.

Etiology of Congestive Heart Failure

The 3 major causes of systolic and diastolic heart failure are coronary artery disease, hypertension, and diabetes mellitus. Patients usually have multiple underlying risk factors contributing to the development of heart failure, such as:

- Obesity
- Smoking
- COPD
- Alcohol abuse

Specific causes of heart failure

Systolic dysfunction	Diastolic dysfunction
1. Cardiac arrhythmia (which causes tachymyopathy)	1. Constrictive pericarditis
2. Infectious causes such as Chagas disease	2. Restrictive cardiomyopathy
3. Viral myocarditis	3. Hypertrophic cardiomyopathy

Classifications of Heart Failure

Heart failure is categorized in a variety of ways:

1) Based on the pathomechanism of reduced cardiac output

Systolic ventricular dysfunction

- LV systolic dysfunction is considered the most common cause of HF.
- Results from damage and loss of myocytes (as in IHD), increased afterload (as in aortic stenosis), increased preload (as in aortic regurgitation) and high-output conditions.

Note:
Valvular heart diseases are considered a common cause of valvular cardiomyopathy.

Most common causes of valvular cardiomyopathy are:

- *Rheumatic heart disease*
- *Age-degenerative valvular cardiomyopathy (in old age)*

High-yield:
Causes of reversible cardiomyopathy are:

- *Viral myocarditis*
- *Metabolic acidosis (causes myocardial depression)*
- *Peripartum cardiomyopathy*
- *Tachycardia-induced cardiomyopathy*
- *Takotsubo cardiomyopathy (broken heart syndrome)*

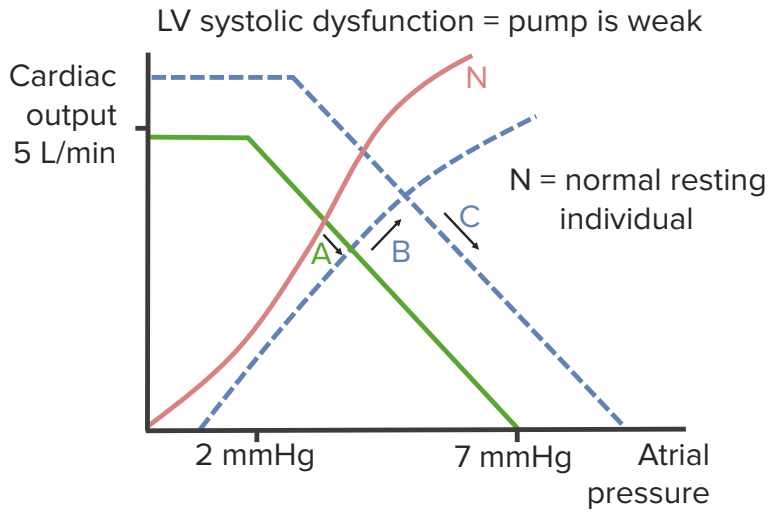

Fig. 6-02: Relationship between cardiac output and atrial pressure.

Diastolic ventricular dysfunction

- Results from decreased ventricular compliance and increased its stiffness, subsequently reduced diastolic ventricular filling, and cardiac output.
- This condition is most commonly caused by increased afterload, as in hypertension.

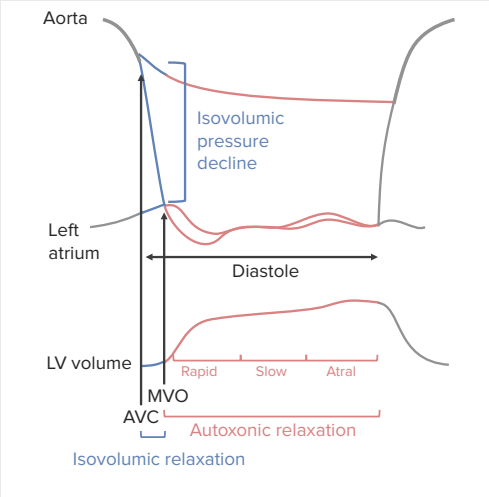

Fig. 6-03: Diastolic dysfunction

2) Based on the side of the heart

Depending on which chambers of the heart are affected, cardiac insufficiency may be referred to as left ventricular heart failure, right ventricular heart failure, or bilateral ventricular heart failure (congestive heart failure).

Left-sided heart failure

Results in reduced cardiac output leading to:

1. Poor organ perfusion, most commonly cardiorenal syndrome due to reduced renal filtration pressure.
2. Increased LV volume pressure, and backflow of blood into the lungs, resulting in pulmonary congestion.

Note:
It is difficult to clinically differentiate between systolic and diastolic dysfunction.

Note:
Diastolic dysfunction is only diagnosed through the observation of specific features using Echocardiography.

Right-sided heart failure

Results in systemic venous congestion manifested as ascites, hepatic congestion, and bilateral lower limb edema.

3) Based on the cardiac output

Low-output heart failure

Constitutes forward heart failure with insufficient cardiac output.

High-output heart failure

Occurs secondary to conditions associated with a high-output state, in which cardiac output is elevated to meet the demands of peripheral tissue oxygenation.

Examples of high-output state

- Anemia
- Hyperthyroidism
- Sepsis

Stages of Heart Failure

NYHA Classification

A well-known model is the NYHA classification (NYHA: **New York Heart Association**), which divides cardiac insufficiency into 4 classes according to their clinical severity, and it has prognostic value:

Class I	No symptoms and normal physical capacity.
Class II	Symptoms appear only during increased physical activity.
Class III	Symptoms already appear during light physical activity.
Class IV	Symptoms already appear at rest.

AHA Classification

According to the American Heart Association (AHA), cardiac insufficiency can also be categorized into 4 stages:

Stage I	The patient is symptom-free and does not show any signs of structural heart disease, but there are risk factors for the development of cardiac insufficiency.
Stage II	The patient does not display any symptoms of cardiac insufficiency, but has structural heart disease.
Stage III	Structural heart disease, in combination with cardiac insufficiency symptoms, is present.
Stage IV	Terminal cardiac insufficiency.

Pathophysiology of Congestive Heart Failure

A particular problem with cardiac insufficiency is the fact that insufficient cardiac output, along with insufficient blood supply to the organs, may lead to a number of **compensatory mechanisms.** Among these compensatory mechanisms are the activation of the sympathetic nervous system, the release of catecholamines, activation of the the activation of Renin-Angiotensin-Aldosterone-System (RAAS), and increased ADH production. The release of natriuretic peptides, as well as cardiac remodeling and cardiac hypertrophy are further compensatory mechanisms.

The problem with these compensatory mechanisms is that, while helpful at first, they will lead to a **significant deterioration** of cardiac insufficiency if **chronically activated.** The critical heart weight is, for instance, 500 grams. If it weighs more than this, the oxygen supply of the heart becomes critical. Furthermore, cardiac insufficiency frequently leads to a loss of contractility, despite pathological myocyte growth.

Clinical Features of Congestive Heart Failure

The symptoms of cardiac insufficiency are variable, depending on the severity of the insufficiency and the affected side of the heart.

Left-sided heart failure	Right-sided heart failure
Symptoms	
Dominant pulmonary symptoms	**Dominant venous congestion symptoms**
Dyspnea	Lower limb swelling
Orthopnea	Abdominal distension
Paroxysmal nocturnal dyspnea	Abdominal pain
Pulmonary edema in acute severe cases	Jaundice
	Nausea and loss of appetite (congestive gastropathy)
Signs	
1. Bilateral basilar rales	1. Peripheral pitting edema
2. Cardiac asthma	2. Signs of increased central venous pressure: Raised JVP and positive hepatojugular reflux
3. Pulsus alternans	3. Hepatomegaly
4. S3/S4 gallop	4. Ascitis
5. Laterally displaced apical heartbeat	
6. Diminished air entry in chest due to pleural effusion	
7. Cold extremities	

Symptoms include **dyspnea** on exertion or even at rest at more advanced stages, asthma (cardiac asthma) and orthopnea, paroxysmal nocturnal dyspnea, and **symmetric edema**, especially on the ankles, the tibia, and on top of the foot. There is also **nocturia** due to nocturnal voiding of edema.

Dyspnea and pulmonary edema are more likely caused by acute left ventricular heart failure, whereas right ventricular heart failure manifests as bilateral lower limb edema, ascites, and gastrointestinal disorders such as tender hepatomegaly secondary to systemic venous congestion.

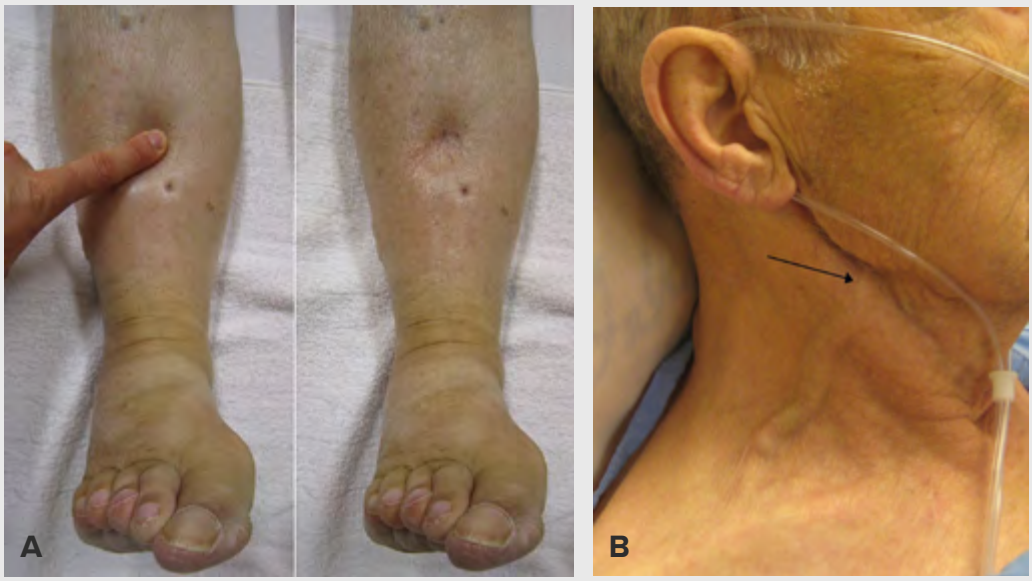

Fig. 6-04: *(A) Pitting edema during and after the application of pressure to the skin. (B) A person with congestive heart failure who presented with an exceedingly elevated JVP, the arrow is pointing to the external jugular vein*

High-yield:
Biventricular heart failure with features of left and right heart failure is more likely than isolated failure of one ventricle.

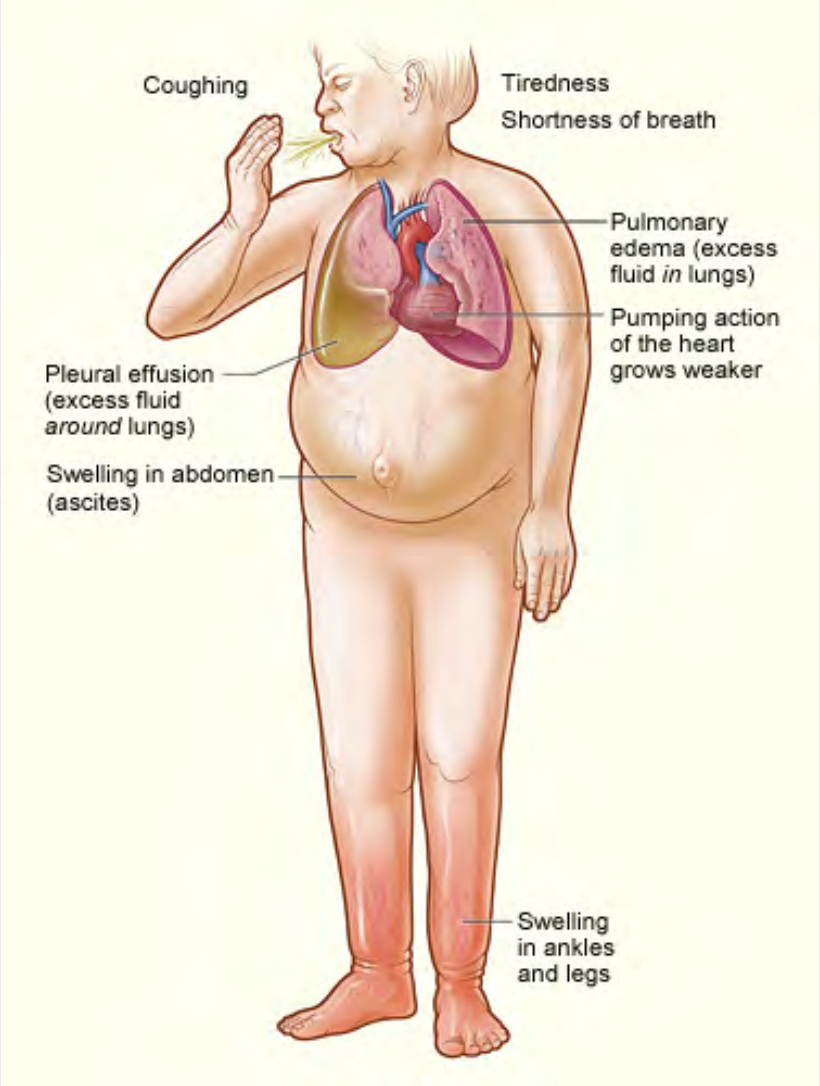

Fig. 6-05: *Major signs and symptoms of heart failure.*

Diagnostics of Congestive Heart Failure

Heart failure is mainly a clinical diagnosis. Laboratory investigations and different imaging modalities are used, mainly to assess the severity and cause of the condition.

BNP and NT-proBNP

Diagnostic markers of cardiac insufficiency are BNP and NT-proBNP in particular, both of which are released by cardiomyocytes during physical exertion. High levels of BNP in the presence of classical symptoms of heart failure confirms the diagnosis.

	HF is unlikely	HF likely
BNP (pg/mL)	< 100	> 400
NT-pro BNP (pg/ml)	< 300	> 450

Other laboratory tests

Other lab tests are non-specific, and usually carried out in order to determine comorbidities, possible causes, or to rule out differential diagnoses. Other laboratory tests include blood glucose, electrolytes, cardiac markers for myocardial damage, such as CK, CK-MB and troponin, liver and kidney function tests (GOT, GPT, g-GT, bilirubin, urea), cholesterol, triglycerides, and thyroid function tests (TSH, FT4).

Electrocardiogram (ECG)

ECG changes are usually seen in patients with HF, but they are neither specific nor diagnostic. They will usually give you clues regarding the underlying etiology:

1. Evidence of previous or acute MI: Pathological Q waves and poor R progression
2. Arrhythmias: Atrial fibrillation and ventricular tachycardia
3. Signs of LV hypertrophy: Left axis deviation with positive Sokolow-Lyon index
4. Signs of pericardial effusion: Low voltage ECG

Chest radiograph

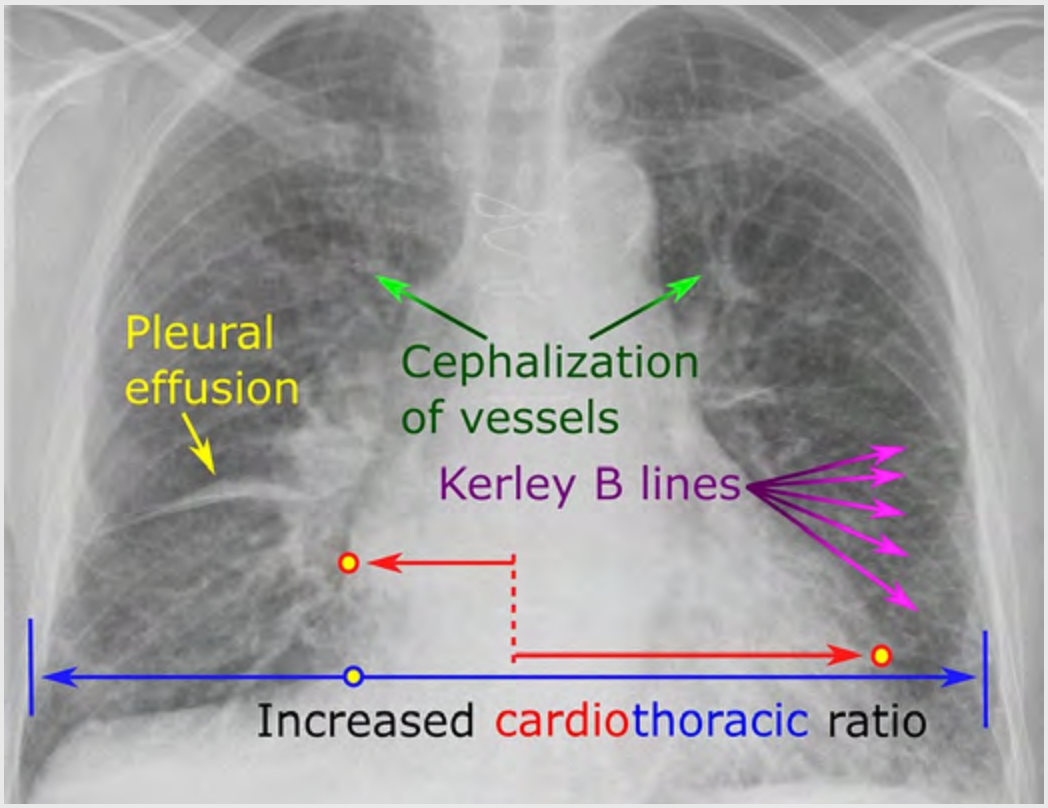

Fig. 6-06: *Chest x-ray features of congestive heart failure*

A simple, cheap, and rapid method to evaluate patients with dyspnea, and differentiate HF from other pulmonary causes.

1. **Signs of cardiomegaly:**
   - Increased cardiac-to-thoracic ratio > 0.5
   - Boot-shaped heart or PA view
2. **Assess pulmonary congestion:**
   - Evidence of vascular redistribution (cephalization)
   - Kerley B lines
   - Pleural effusion

Echocardiography

Echocardiography is mainly used for diagnosing the etiology and assessment of ventricular function and hemodynamics.

High-yield:
Echocardiography is the gold standard for evaluation of patients with HF.

Investigate etiology

Can reveal:

- Valvular heart disease
- Segmental wall motion abnormality which indicates prior MI
- Hypertensive heart disease which manifests as concentric LV hypertrophy with diastolic dysfunction

Assessment of ventricular function and hemodynamics

1. Atrial and ventricular size
2. Left ventricular ejection fraction
   - Normal EF > 55 %
   - Reduced EF < 50 %
   - Extremely reduced EF < 30 %
3. Diastolic function of the heart using Doppler signals

Treatment of Congestive Heart Failure

Several general measures in chronic heart failure management:

- Correct modifiable risk factors of heart failure, such as cessation of smoking and alcohol consumption.
- Treat underlying conditions and other comorbidities.
- Weight loss and exercise to improve functional capacity.
- Immunization with pneumococcal and influenza vaccine as pulmonary infection exacerbates HF symptoms.
- Salt restriction (< 3 g per day).
- Fluid restriction if HF patient develops edema and hyponatremia.
- Avoid hypokalemia and hyponatremia.

Note:
The goals of treatment are to correct underlying cause, improve quality of life, prevent hospitalization, and prolong life by neurohormonal blockade.

Pharmacological treatment

Several drugs are used in the treatment of heart failure.

Diuretics (Loop and thiazide diuretics)	• Loop diuretics (such as furosemide) should be used to treat volume overload • Thiazide diuretics may be added • Patient should be carefully monitored for hypokalemia
Digitalis compounds (e.g. digoxin)	• Positive inotropic agent • Work by poisoning Na-K-ATPase which results in increased intracellular Ca ions • Increased intracellular Ca ions lead to increased myocardial contractility • Controls heart rate in atrial fibrillation • Contraindicated in severe AV block
ACE inhibitors	• Reduce systemic vascular resistance (SVR) • Antagonize renin-angiotensin-aldosterone-system • Reduce left ventricular remodeling • Firstline therapy for CHF • Do not start if patient has acute renal failure • Side effects: cough, hyperkalemia, renal failure, angioedema
Angiotensin receptor blockers	• Block angiotensin receptor which is a potent vasoconstrictor, to decrease SVR • Best used in patients who are intolerant of ACEI • Side effects: hypotension, angioedema
Beta-blockers	• Metoprolol, carvedilol • Reduce SVR, antagonize sympathetic discharges to myocardium and slow the heart rate • Should not be used in patients with acute CHF since these may blunt the tachycardia that patient relies on to generate forward flow • Side effects: bradycardia, heart block, hypotension, bronchospasm
Nitrates	• Nitroglycerin, Isosorbide dinitrate/mononitrate • Decrease SVR by causing vasodilation • Useful when CHF is due to ischemic heart disease as they will maximize myocardial blood flow • Side effects: hypotension, headache, tolerance
Spironolactone	• Antagonizes RAAS and may prevent fibrosis • Indicated in class III and IV CHF • Side effects: hyperkalemia, gynecomastia
Ivabradine	• Used in combination with beta-blockers if the highest tolerable dose is reached and patient is still symptomatic. • Used in combination, used if the patient has sinus rhythm, EF < 35 % and a resting heart rate of > 70/min. • Not used in patients with atrial fibrillation.

High-yield:
Drugs that decrease mortality:

- *Beta-blockers*
- *ACE inhibitors*
- *Aldosterone antagonists*

High-yield:

Drugs that improve symptoms with no adverse effect on mortality:

- *Diuretics*
- *Digoxin*

Invasive procedures

Implantable Cardioverter Defibrillator (ICD)

- Patients with advanced CHF are at risk of sudden cardiac death from an arrhythmia.
- ICD can detect arrhythmia and shock the heart back into normal rhythm.
- Ischemic cardiomyopathy (> 40 days post MI) or non-ischemic cardiomyopathy with EF < 35 %, NYHA Class II-III on optimal medical therapy with survival > 1 year
- Side effects: expense, complications, not all benefit, inappropriate shocks

Cardiac Resynchronization Therapy (CRT)

- It is used in patients EF < 35 % and Left Bundle Branch Block (LBBB)
- It an be combined with ICD.

Cardiac transplantation

The last remaining option in patients with stage D heart failure (NYHA class IV) with severely depressed systolic function with no other available treatment options.

Complications of Congestive Heart Failure

Several serious complications may occur in patients with heart failure:

- Acute decompensated heart failure (pulmonary edema)
- Cardiorenal syndrome
- Cardiac arrhythmias
- Central sleep apnea syndrome
- Cardiogenic shock
- Stroke due to increased risk of arterial thromboembolisms (especially with concurrent atrial fibrillation)
- Chronic kidney disease
- Cardiac cirrhosis (congestive hepatopathy)

Prognosis of Congestive Heart Failure

Prognosis varies depending on patient's other comorbidities, type and severity of heart disease, and compliance with medical treatment. 1-year survival according to NYHA stage are:

Stage I	~95 %
Stage II	~85 %
Stage III	~85 %
Stage IV	~35 %

Cardiogenic Pulmonary Edema

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Definition of Pulmonary Edema

Acute pulmonary edema constitutes sudden accumulation of fluid in the lung tissue and alveoli due to either fluid redistribution as in hypertensive pulmonary edema, or fluid accumulation as in cardiogenic shock, due to pump failure.

Etiology of Pulmonary Edema

Risk factors which may contribute to worsening heart failure

Patients are prone to acute pulmonary edema if they have the following etiologies:

Mmnemonic:

CHAMP

1. Acute **C**oronary Syndrome
2. **H**ypertension Emergency
3. **A**rrhythmia (such as AF or VT)
4. Acute **M**echanical cause (as ventricular septal rupture)
5. **P**ulmonary embolism.

(**Source:** European Society of Cardiology Guidelines)

Classification of Cardiogenic Pulmonary Edema

Cardiogenic pulmonary edema can be either classified into:

1. **'Vascular-type fluid redistribution'** in which the hypertension predominates.
2. **'Cardiac-type fluid accumulation'** due to pump failure in which the congestion predominates.

Pathophysiology of Pulmonary Edema

The pathophysiology of pulmonary edema is based on an imbalance of fluid reabsorption and filtration. **Increased pulmonary capillary pressure** quickly leads to fluid build-up in the lungs and **massively impairs gas exchange**, which explains the respiratory failure. Lung compliance and vital capacity decrease, airway resistance, and range in path length to gas exchange increase. The pathophysiology of high-altitude pulmonary edema may be explained by a combination of a decrease in pulmonary oxygen content, pulmonary vasoconstriction, and decreased alveolar pressure.

Clinical Features of Pulmonary Edema

Depending on the stage of pulmonary edema, symptoms may include **dyspnea**, **cough**, thick **mucus discharge**, **tachycardia**, **signs of cyanosis**, as well as **restlessness**. While interstitial pulmonary edema is more characterized by tachypnea, dyspnea, orthopnea, and sharp breathing noises (cardiac asthma, 'asthma cardiale'), in cases of alveolar pulmonary edema, fear, cyanosis, paleness, and extreme dyspnea, and discharge, may occur, accompanied by **moist rattling sounds** that are audible with a stethoscope.

Special Forms of Pulmonary Edema

The progression of pulmonary edema can be divided into 4 stages:

Stage I	Connective tissue edema, meaning interstitial pulmonary edema
Stage II	Progression into alveolar pulmonary edema
Stage III	Increased fluid accumulation and formation of foam
Stage IV	Asphyxia

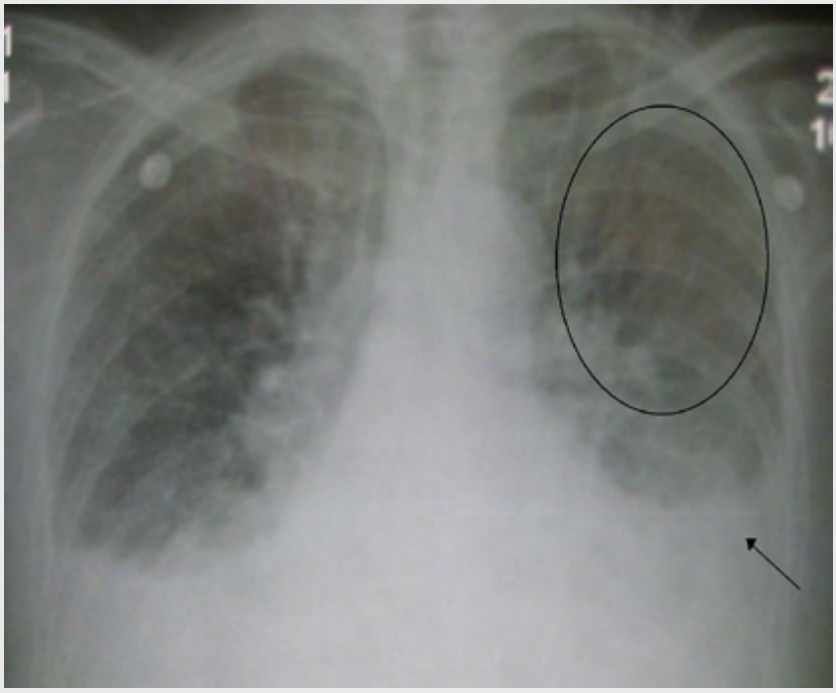

Fig. 6-07: *Acute pulmonary edema. Note enlarged heart size, apical vascular redistribution (circle), and small bilateral pleural effusions (arrow).*

Diagnostics of Pulmonary Edema

Aside from the medical history and clinical picture, moist rattling sounds are noticeable in cases of alveolar pulmonary edema which are, in part, already audible without the need for a stethoscope. Furthermore, **chest radiographs** and **echocardiography** may be helpful.

Differential Diagnosis of Pulmonary Edema

Cardiogenic vs. non-cardiogenic pulmonary edema

In cases of pulmonary edema, distinction has to be made between cardiogenic and non-cardiogenic pulmonary edema, whereby the first type does not involve lung disease, but occurs much more frequently in the clinical routine.

Cardiogenic pulmonary edema

Also called hydrostatic pulmonary edema, this is frequently caused by acute left ventricular heart failure when the heart is no longer capable of adequately pumping blood from the pulmonary circulation into the systemic circulation.

Non-cardiogenic pulmonary edema

The main pathology is a direct or indirect insult to the pulmonary capillary membrane, secondary to inflammatory mediators which results in an increased permeability of the endothelial cell layer.

The most common causes of non-cardiogenic pulmonary edema are:

- Severe infection (sepsis)
- Aspiration injury
- Allergic reactions
- Inhalation injury

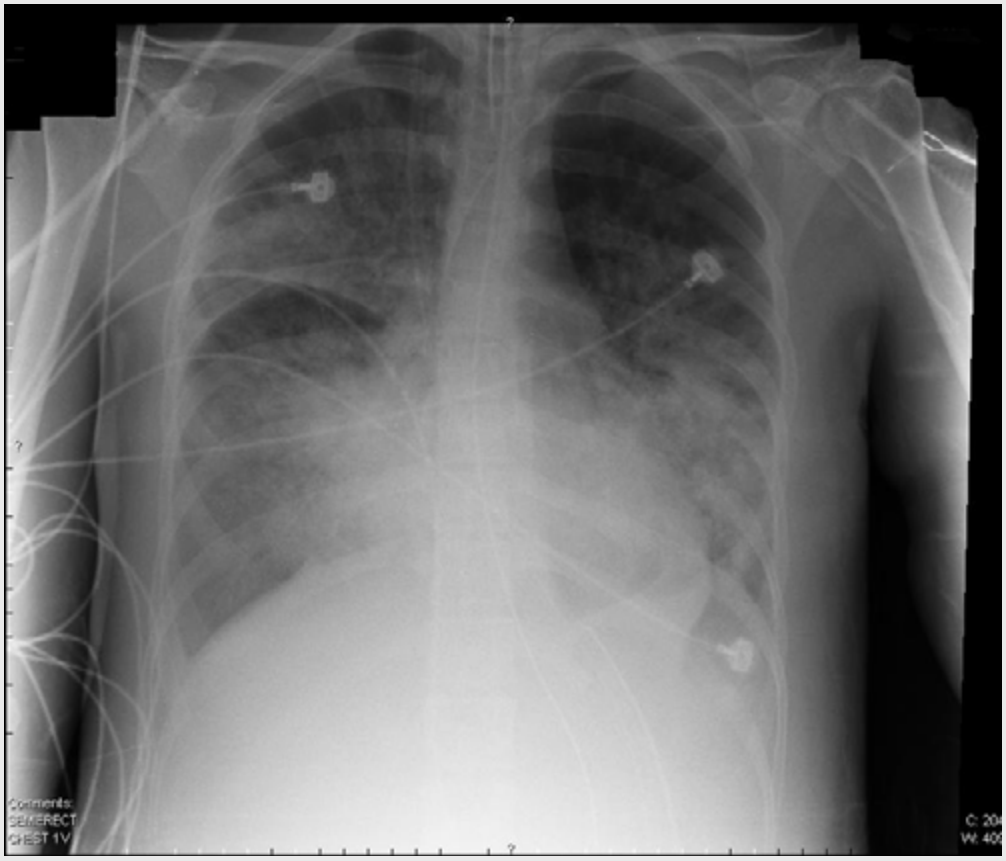

Fig. 6-08: *Pulmonary edema*

Treatment of Cardiogenic Pulmonary Edema

Immediate general measures

Immediate measures include, a **sitting position** with the legs dangling in order to improve pulmonary vascular pressure, **sedation, administration of oxygen**, and as **diuretics**, the immediate measures as well.

If the initial evaluation of a patient presenting with pulmonary edema reveals cardiogenic shock or respiratory failure, immediate CCU admission is necessary. If the patient presents with respiratory failure, ventilatory support using either non-invasive CPAP or intubation should be immediately implemented.

Specific treatment

- **'Vascular-type fluid redistribution'** requires vasodilators (as nitrates) initially, then diuretics.
- **'Cardiac-type fluid accumulation'** requires diuretics first, then nitrates and ultrafiltration if no response to diuretics, as in patients with impaired kidney function.

Patients in shock (cardiogenic shock) should be hypoperfused, also termed ‚wet-cold' hypoperfusion. In this scenario, the patient also requires vasopressors or inotropes. (**Source:** European Society of Cardiology Guidelines)

LMNOP mnemonic:

- **L***asix (furosemide)*
- **M***orphine*
- **N***itrates*
- **O***xygen*
- *(upright)* **P***osition*

Review Questions

Question 6.1: A 9-year-old girl comes to the emergency department with complaints of dyspnea, palpitations, and an unmeasured fever for a week. She also gives a history of bilateral knee pain for 5 days which has now shifted to both ankles over the past week. She developed bilateral leg swelling since yesterday. 10 days prior to admission, she had developed a severe sore throat accompanied by fever, chills, rigors, and diffuse myalgia. Today her respiratory rate is 22/min, temperature is 37.7 °C (100 °F), blood pressure 90/60 mm Hg, heart rate of 90/min, and SpO_2 of 88% in room air. On general examination, patient is ill-looking with pallor and bilateral pitting edema of legs. On physical examination, her apex beat is in the 5th intercostal space in the mid-axillary line with a prominent apex beat, and bilateral basal crepitations are heard in chest examination. A loud pansystolic murmur, 3/6, was heard at apex radiating towards axilla. S3 and S4 sounds are heard at the left sternal border and at the cardiac apex. What is the most likely condition is she suffering from?

A. Acute rheumatic fever
B. Mitral stenosis
C. Aortic regurgitation
D. Tricuspid regurgitation
E. Aortic stenosis

Question 6.2: A 79-year-old man presents to his primary care physician complaining of progressive shortness of breath on exertion for the past 2 months. He first recognizes having to catch his breath while gardening and is now unable to walk up the stairs in his house without stopping. He has type 2 diabetes mellitus for 30 years, for which he takes metformin and sitagliptin. His blood pressure is 110/50 mm Hg, his temperature is 37.1 °C (98.8°F), and his radial pulse is 80/minute and regular. On physical examination, there is a loud systolic murmur at the right upper sternal border radiating to the carotid vessels. Which of the following can increase the intensity of this patient murmur?

A. Squatting
B. Standing up from sitting position
C. Diuretics
D. Valsalva maneuver
E. Volume depletion

Test your knowledge:
Congestive Heart Failure

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Chapter 7:
Pericardial Disease

Pericardial Disease

Acute Pericarditis

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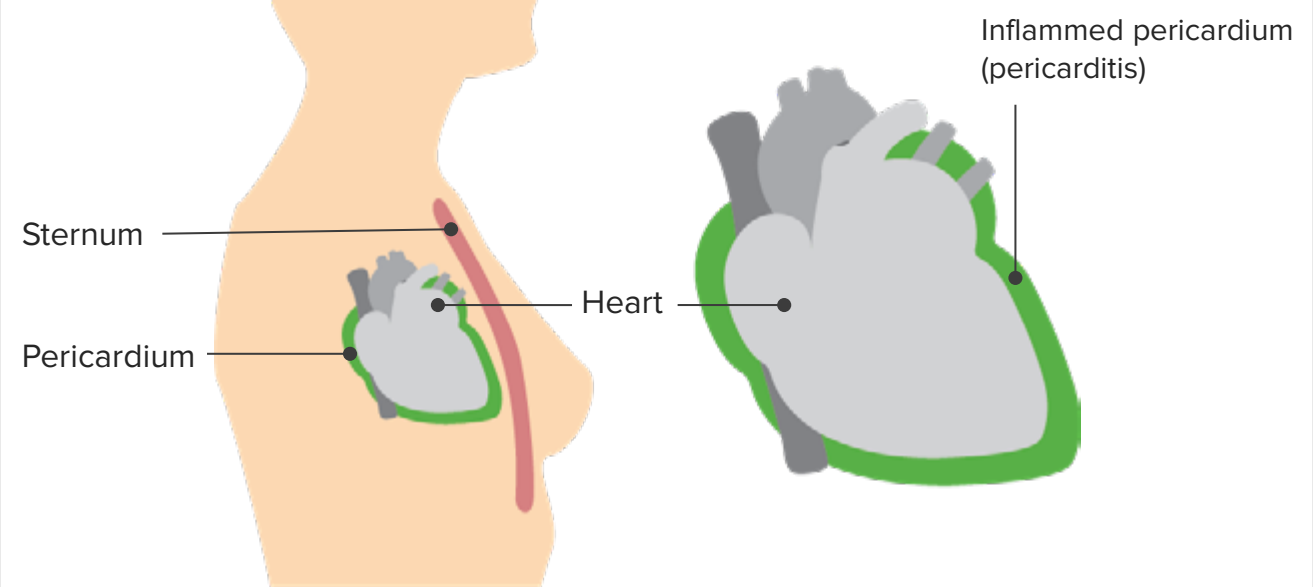

Fig. 7-01: *Pericardium is the outlying sac covering the heart.*

Definition of Acute Pericarditis

Pericarditis is an inflammation of the pericardium resulting from infection, autoimmune disease, radiation, surgery, or myocardial infarction, or is a post-surgical complication. It is manifested as fever, pleuritic chest pain that increases in the supine position, and an audible pericardial rub by auscultation.

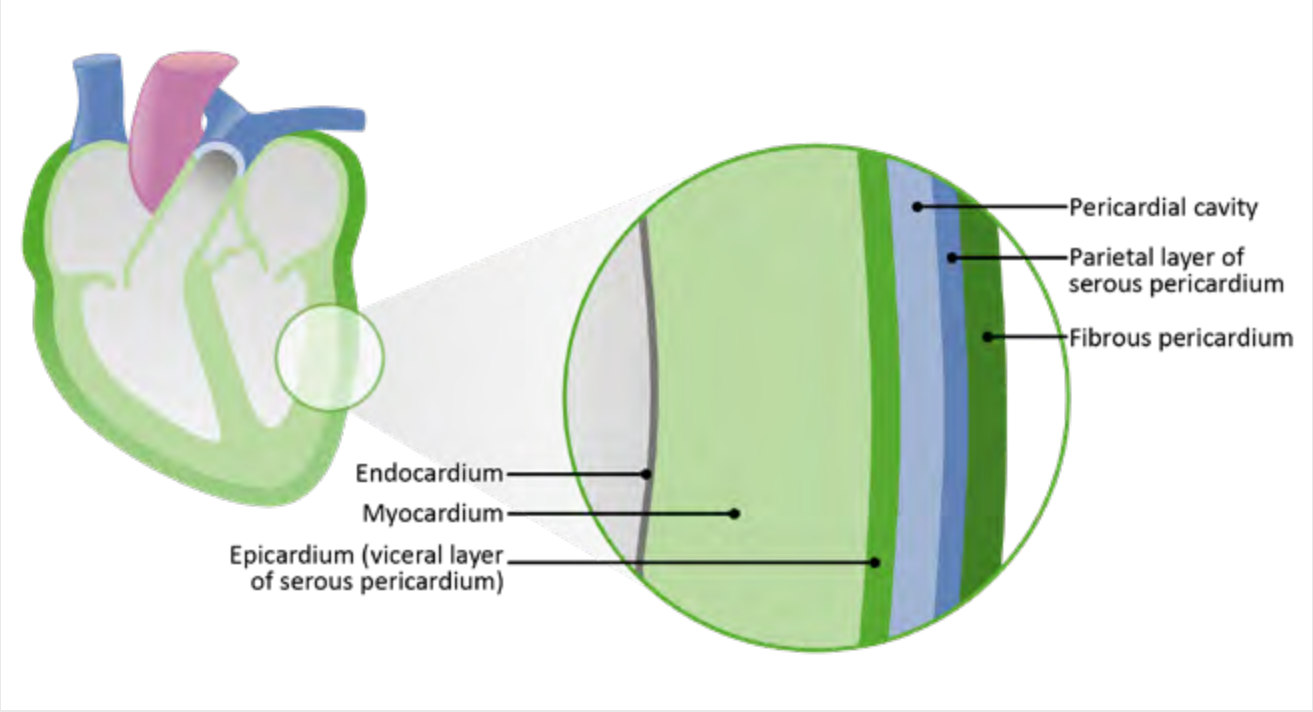

Fig. 7-02: *Pericardial membranes and layers of the heart wall.*

Anatomy

The pericardium pericardium is a double-walled sac consisting of two layers, with two sub-layers. The **fibrous pericardium** is the outer layer, composed of connective tissue. The **serous pericardium** is itself composed of 2 layers: the **visceral pericardium** attached to the outermost layer of the heart, or epicardium, and the **parietal pericardium** which lines the inside of the pericardial sac. The parietal pericardium is fused to the fibrous pericardium. The pericardial cavity between the visceral and the pericardial layers is filled with serous fluid.

Epidemiology of Acute Pericarditis

Acute pericarditis is diagnosed in about **1 in 1,000 hospital admissions**. It is more common in adults than children. Uremic pericarditis is seen in patients with chronic renal failure. **Purulent pericarditis** (pericarditis with pus in the pericardial space, as the result of bacterial infection) has become rare in the developed world due to the regular use of antibiotics, but is still common in the developing world.

Etiology of Acute Pericarditis

Causes of acute pericarditis

There are many causes of acute pericardial inflammation:

Viral infection	• Coxsackievirus B* • Influenza* • HIV • Echovirus
Bacterial infection	• Tuberculosis* • Streptococcus species • Pseudomonas • Staphylococcus species
Fungal Infection	• Histoplasma • Blastomyces • Coccidioides • Aspergillus
Autoimmune disease	• Rheumatoid arthritis • Systemic lupus erythematosus* • Sarcoidosis
Renal failure	• Uremia
Cardiovascular	• Myocardial infarction* • Aortic dissection • Takotsubo cardiomyopathy
Cancer	• Lung cancer • Breast cancer • Leukemia • Lymphoma

Medication	• Penicillin • Cromolyn sodium
Open heart surgery and trauma	–
Irradiation	• Iatrogenic to cancer treatment of the chest
Idiopathic*	–
*the most common causes of acute pericarditis	

Pathophysiology of Acute Pericarditis

The pericardium has 4 functions: it restricts the heart and so prevents excess dilation, it produces a negatively pressurized chamber that aids in atrial filling, it provides a frictionless environment, and it isolates the heart from the rest of the body.

An inflamed pericardium shows a **polymorphonuclear infiltrate on microscopy and vascularization**. Inflammatory signaling may stimulate the release of fluid that could result in effusion, or fibrinous reactants that could result in a constrictive complication. Tuberculosis, sarcoidosis, or fungal infections will show a granulomatous reaction with multinucleated giant cells and epithelioid cells on microscopy. The accumulation of urea, a metabolic toxin, within the pericardial space results in inflammation of the parietal and visceral layers.

Clinical Features of Acute Pericarditis

Symptoms

- Patient usually suffers from low grade intermittent fever, tachypnea, tachycardia, and diaphoresis.
- Persistent substernal chest pain (sharp or stabbing) that radiates to the trapezius or to the neck, and improves with leaning forward, or is made worse in supine position, with coughing, or during inspiration.
- Symptoms of the underlying disease.

Signs

- Pericardial friction rub: a high-pitched scratching sound best heard over the left sternal border during expiration while the patient is sitting up and leaning forward.
- Signs of pericardial effusion, seen in approximately half of these patients.

Diagnostics of Acute Pericarditis

Diagnosis of acute pericarditis is suspected in patient with pleuritic chest pain with audible friction rub and **abnormal findings on ECG**.

Laboratory tests

1. CBC could show leukocytosis
2. Positive blood culture implies an infectious etiology
3. Increased ESR and CRP
4. Abnormal renal function if the underlying cause is uremic pericarditis

ECG

Stage I	Diffuse ST-segment elevation, but ST depression in aVR and V1
Stage II	ST-segment is normalized in 1 week
Stage III	Inverted T waves can be seen
Stage IV	ECG returns into normal baseline after weeks to months

High-yield fact:
Uremic pericarditis doesn't have the characteristic ECG changes you would expect in other types of acute pericarditis.

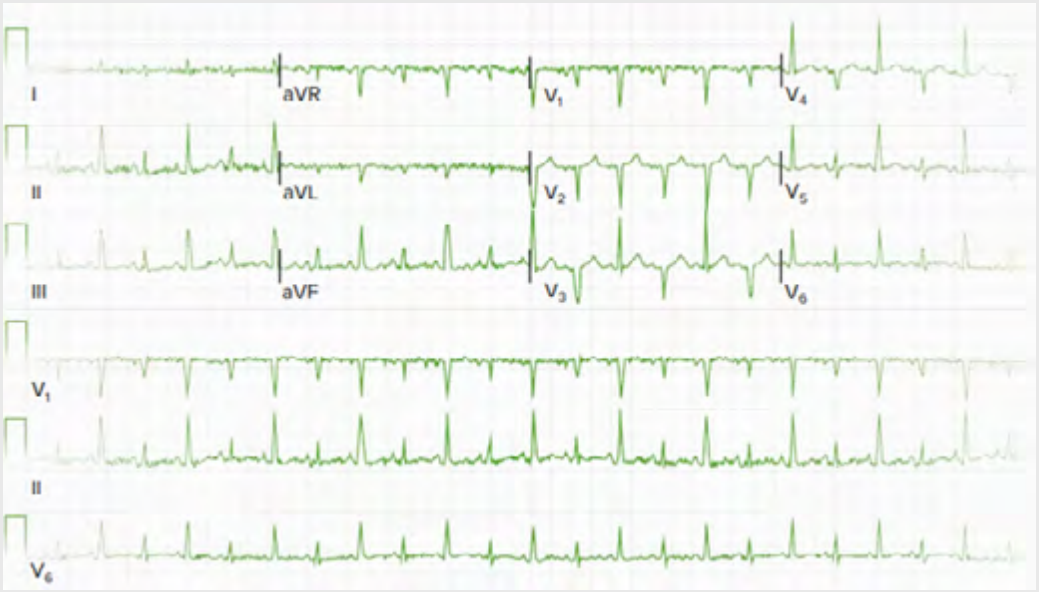

Fig. 7-03: *Electrocardiogram of acute pericarditis*

Note:
It is not necessary to notice all ECG changes, as these vary between patients.

Imaging tests

Chest Radiograph: Can be taken to rule out pericardial effusion.

Echocardiography: Often normal. It may shows signs of pericardial effusion.

Differential Diagnosis of Acute Pericarditis

Acute pericarditis should be differentiated from all other causes of chest pain.

- Acute coronary syndrome
- Esophageal spasm
- Gastroesophageal reflux disease
- Pulmonary embolism

Treatment of Acute Pericarditis

In general, **providing oxygen, ECG monitoring**, and recording **serial blood pressure evaluations**. Rule out myocardial infarction with ECG and cardiac enzymes (troponin, CK-MB, LDH). Treat pain with morphine. Otherwise, treatment depends on etiology.

- Treat with NSAIDs such as aspirin or indomethacin.
- Adjuvant therapy consists of colchicine. Colchicine can also be first-line or added to treatment regimen in cases of recurrent pericarditis.
- Steroids are not part of the treatment of acute or recurrent pericarditis and should be avoided as they can potentially lead to recurrent pericarditis.

Treat the underlying condition

- Antibiotics to treat tuberculosis or other bacterial etiology.
- Treat uremia with dialysis.

Prognosis of Acute Pericarditis

- Hospitalization for hemodynamically stable patients with normal laboratory results is rarely necessary.
- Viral and idiopathic pericarditis is often uncomplicated and self-limiting.
- Post-myocardial infarct pericarditis is usually a sign of a large infarct and increased mortality.
- Purulent pericarditis is associated with 40 % mortality, while tuberculous pericarditis is closer to 50 % mortality. Uremic pericarditis has a much lower mortality rate.

Review Questions

Question 7.1: A woman presents with fever and a sudden onset of a sharp, pleuritic retrosternal chest pain worsening while breathing and coughing. She has been recently diagnosed with systemic lupus erythematosus (SLE). A friction rub is present upon physical exam. Which of the following is most likely consistent with this clinical picture?

A. Serous pericarditis

B. Pericardial tamponade

C. Septic shock

D. Acute myocardial infarction

E. Constrictive pericarditis

Question 7.2: A 42-year-old female arrives at the emergency room with complaints of sharp pain in her chest upon coughing and inhalation. She had a butterfly rash on her face, joint pains, fatigue, and increased photosensitivity for a few weeks now. Which of the following is most likely to be observed in this patient?

A. Mid-systolic click

B. Pain improves with inspiration

C. Displaced apical impulse

D. High-pitched diastolic murmur

E. Breakthrough pain (BTP) improves with leaning forward

Test your knowledge: Pericardial Disease

Correct answers: 7.1A, 7.2E

Pericardial Disease

Constrictive Pericarditis

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Definition of Constrictive Pericarditis

Constrictive pericarditis is characterized by a thickened and scarred pericardial sac that lays around the heart and prevents proper diastolic filling. It occurs secondary to acute pericarditis.

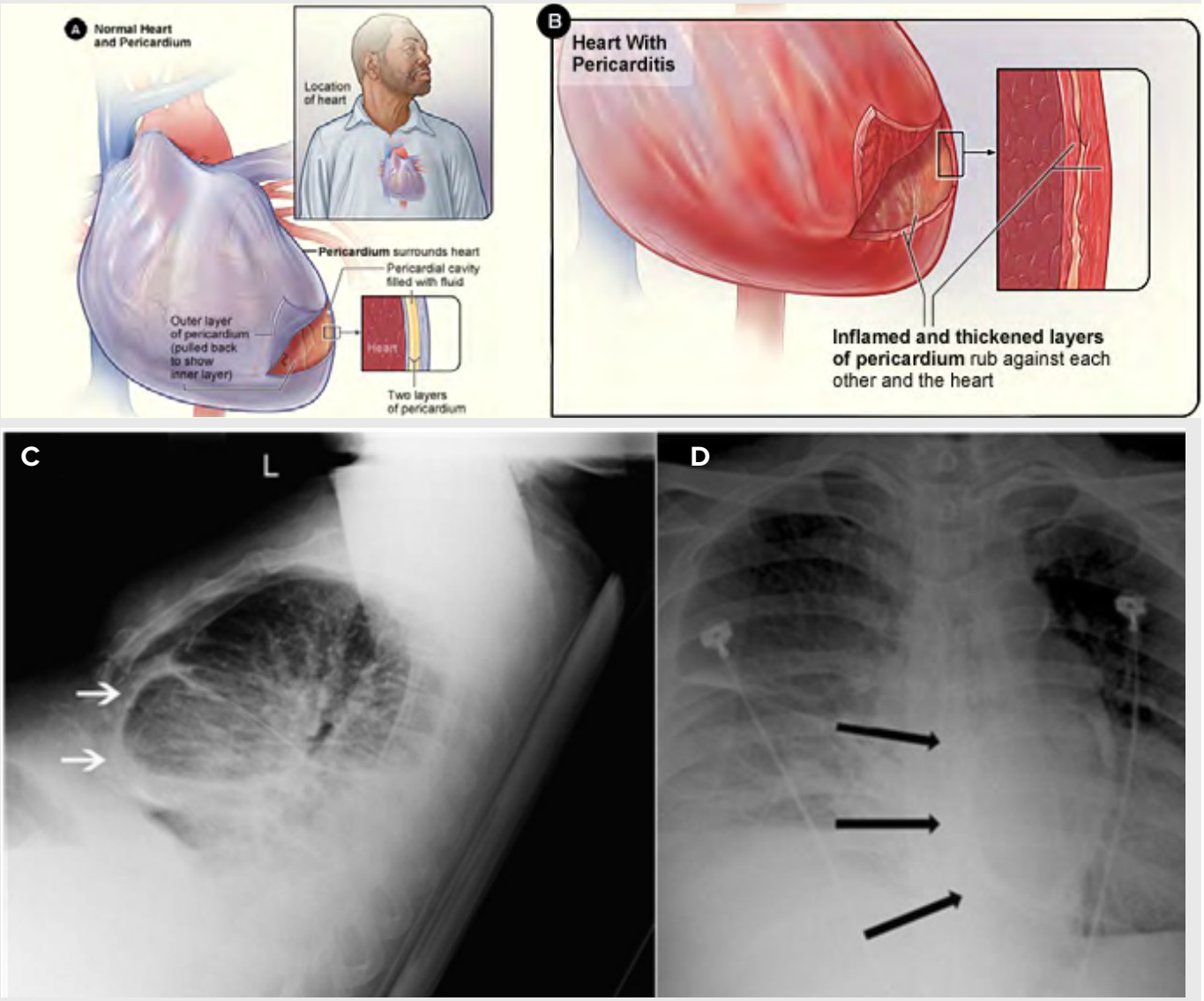


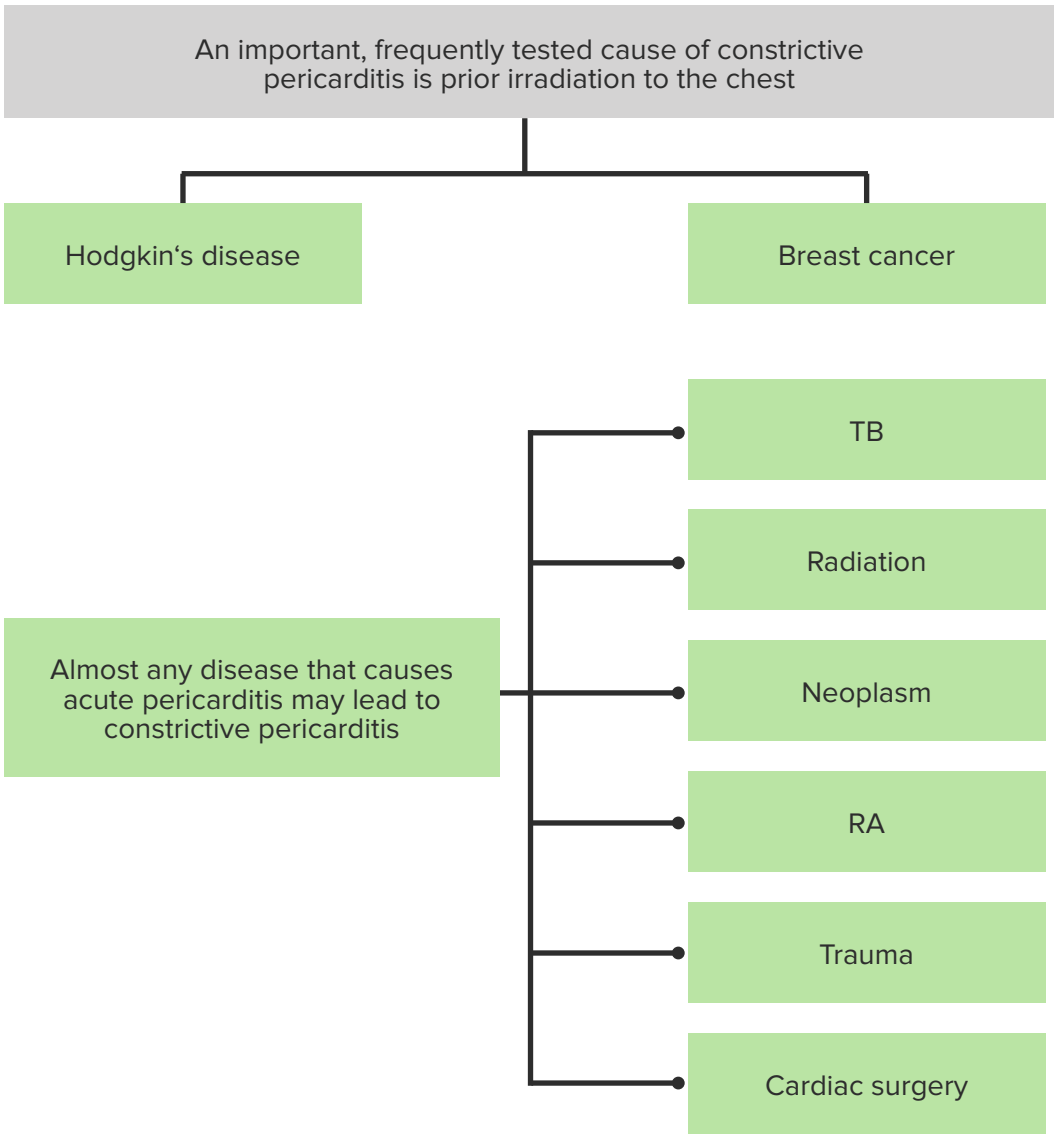
Fig. 7-04: *(A) Normal heart and pericardium (the sac surrounding the heart); The inset image is an enlarged cross-section of the pericardium that shows its 2 layers of tissue and the fluid between the layers. (B) The heart with pericarditis. The inset image is an enlarged cross-section that shows the inflamed and thickened layers of the pericardium. (C) and (D) Lateral and postero-anterior Chest X-rays showing pericardial calcifications.*

Epidemiology of Constrictive Pericarditis

Constrictive pericarditis is much less common compared to acute pericarditis. **Approximately 10 % of acute pericarditis cases progress to constrictive pericarditis**. Middle-aged males are the predominant group.

Etiology of Constrictive Pericarditis

In the past, constrictive pericarditis was associated with bacterial pericarditis and purulent pericarditis. In the developed world, this has become a rare finding. Constrictive pericarditis is often **iatrogenic** following open heart surgery or radiation therapy for the treatment of mastocarcinoma and other cancers. Radiation-induced constrictive pericarditis usually presents 10-years post therapy.



High-yield:
Tuberculosis is considered the most common cause of constrictive pericarditis In the developing world.

Pathophysiology of Constrictive Pericarditis

Inflammation of the pericardial sac results in the **release of fibrin** and the **formation of effusion**. If this results in active organization, the parietal and visceral linings will become thickened and fuse. This sclerotic pericardium cannot expand and will prevent the heart from filling during diastole, resulting in **right-sided heart failure**.

Note:
Pulsus paradoxus is a more than 10 mmHg drop in systolic blood pressure during inspiration.

Clinical Features of Constrictive Pericarditis

Symptoms

Constrictive pericarditis results in right-sided heart failure. Symptoms include:

- **Dyspnea**
- **Swollen abdomen:** Hepatomegaly, ascites
- **Hepatic congestion:** Right upper quadrant pain of the abdomen
- Other symptoms include: Fatigue, chest pain, palpitations

Note:
Pericardial knock is heard at the left sternal border and is due to sudden cessation of ventricular filling during early diastole.

Signs

- Jugular venous distension
- Kussmaul sign
- Edema of the extremities
- Ascitis
- Pericardial knock
- Pulsus paradoxus

Note:
Kussmaul sign is a paradoxical rising of jugular venous pressure during inspiration due to restricted late ventricular filling.

High-yield:
Kussmaul sign is also seen in restrictive cardiomyopathy.

Kussmaul sign is NOT seen in cardiac tamponade..

Diagnostics of Constrictive Pericarditis

Chest radiograph

Considered to be the best initial test which may show pericardial thickening and calcifications with normal cardiac shadow.

Echocardiography

Echocardiography can typically show:

1. Pericardial thickening (3–5 mm)
2. Abnormal ventricular filling
3. Bilateral atrial enlargement

It also excludes other causes, such as cardiomyopathy.

Cardiac MRI

Shows pericardial thickening and cardiac calcifications.

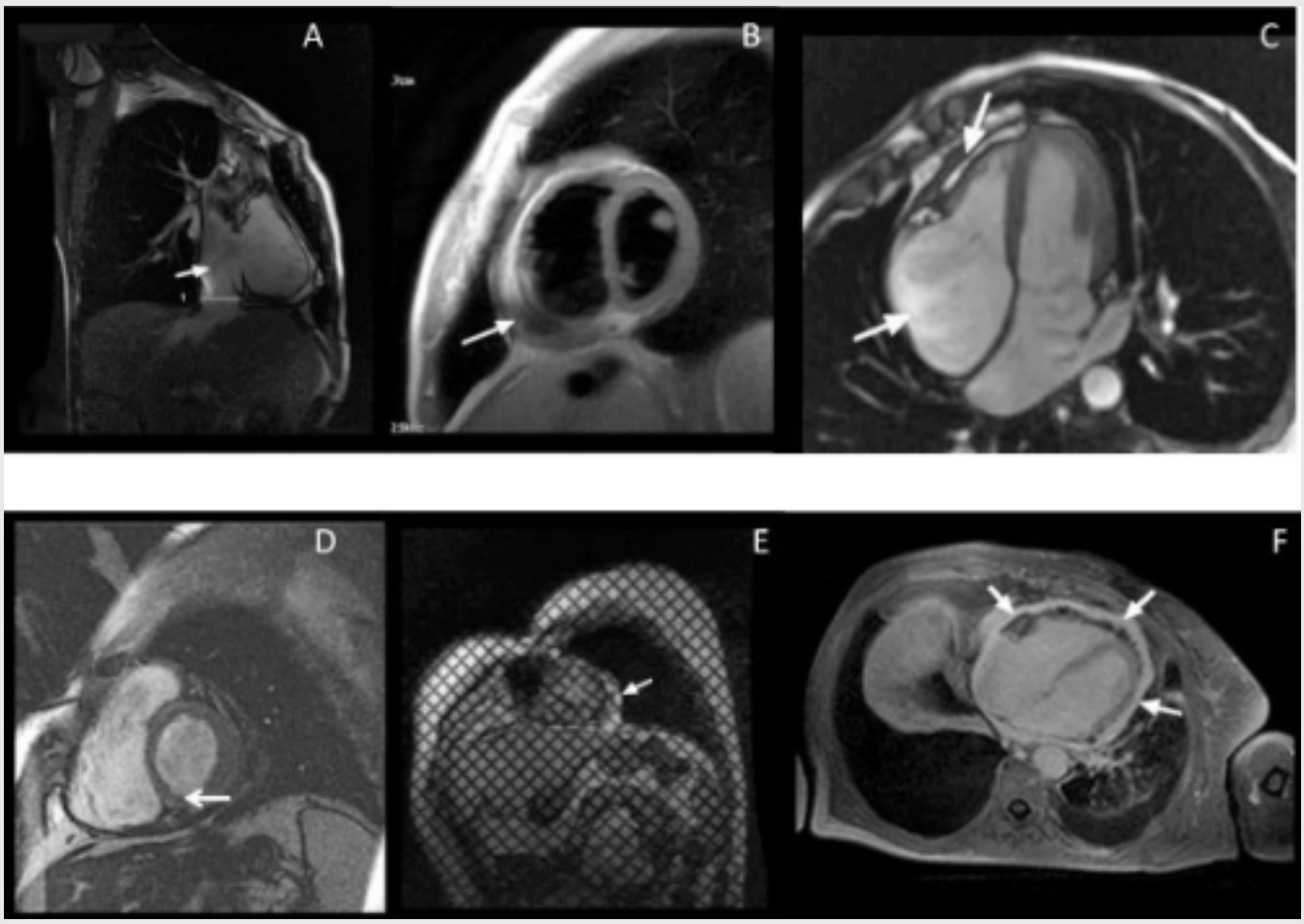


***Fig. 7-05**: MR appearances of constrictive pericarditis. (A) Right ventricular vertical long-axis image showing circumferential pericardial thickening, enlarged inferior vena cava; (B) short axis image showing circumferential pericardial thickening, encysted pericardial effusion. (C) four chamber image showing focal pericardial thickening in front of the right ventricle lateral wall, encysted pericardial effusion, enlarged right atrium; (D) short axis image showing focal pericardial thickening in front of the left ventricular inferior and lateral wall. (E) short axis tagging image showing focal pericardial thickening and adherence in front of the left ventricular lateral wall. (F) 4 chamber late gadolinium enhancement image showing enhancing pericardium.*

Cardiac catheterization

Can identify abnormal cardiac filling pressure, another sign of constrictive pericarditis. This is an invasive, and not first-line, diagnostic procedure. Classically, the diastolic waveform has the shape of a square root sign.

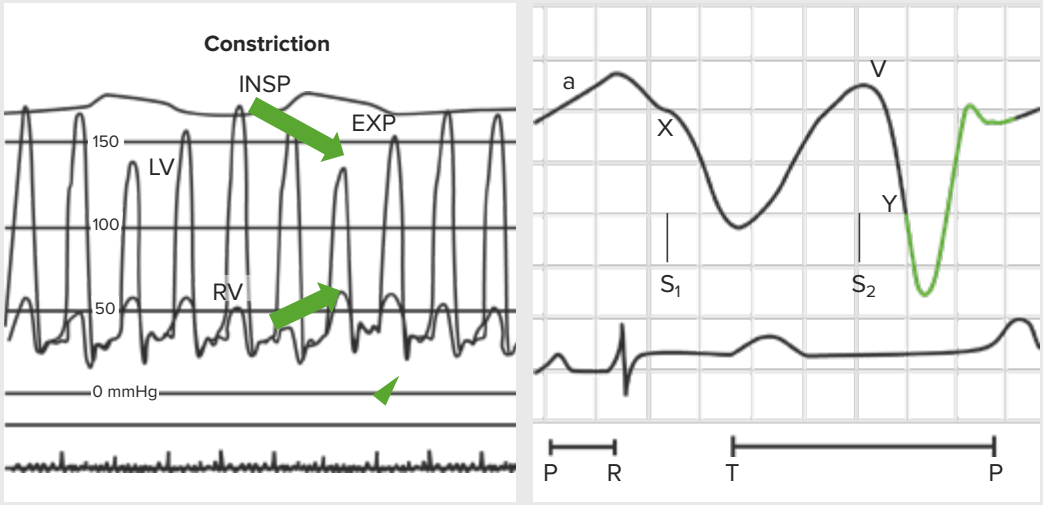


Fig. 7-06: Square root sign

Differential Diagnosis of Constrictive Pericarditis

- Cardiac tamponade
- Dilated cardiomyopathy
- Pericardial effusion
- Restrictive cardiomyopathy

Treatment of Constrictive Pericarditis

1. Treatment of underlying condition.
2. Symptomatic treatment, such as management of fluid overload with diuretics.
3. Definitive treatment is **pericardiectomy** or pericardial stripping. In pericardiectomy, some or most of the pericardium is surgically removed (only 50 % effective).

Prognosis of Constrictive Pericarditis

The best strategy in treating constrictive pericarditis is to both recognize it and **start treatment as early as possible**. Constrictive pericarditis responds poorly to medical intervention, while **surgical treatment is definitive but risky**. Long-term prognosis depends on etiology. Idiopathic constrictive pericarditis has the best prognosis, followed by post-surgical constriction. Post-radiation constriction has the worst prognosis.

Note:
ECG findings are non-specific: low voltage QRS and T wave inversion in all leads.

Review Questions

Question 7.3: A 27-year-old female comes to the clinic with her boyfriend because of a productive cough with a rust-colored sputum and breathlessness for a week. She does not speak English well so her boyfriend speaks on her behalf saying that she has no known medical conditions and that she has always been healthy except for a common cold which she had a week ago. Her weekly routine did not change despite feelings 'weak'. At the time she was consulted by the doctor, she still attended college. Her blood pressure is 120/80 mm Hg, pulse rate is 68/min, respiratory rate is 12/min, and temperature is 36.6 °C (97.9 °F). On examination, crackles are heard during inspiration. A chest X-ray is shown in the picture. What medication is known to be associated with the same condition that she is suffering from?

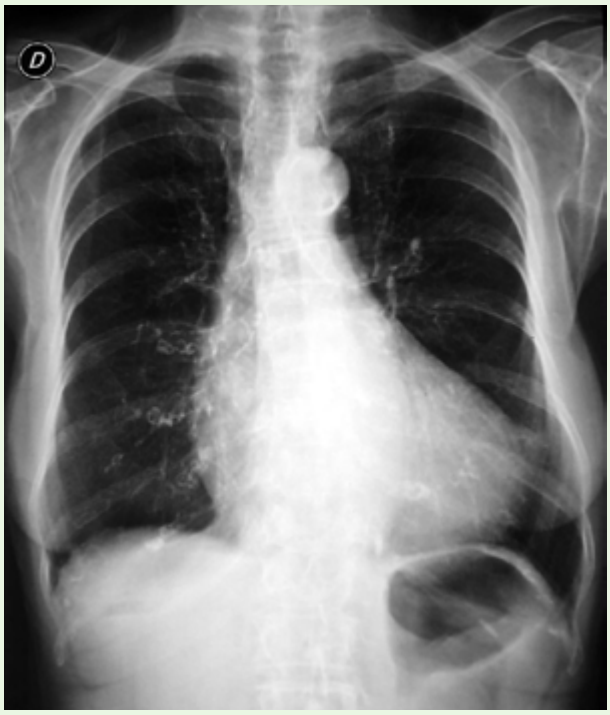


Fig. Q. 7.3

A. Quinidine

B. Anthracyclines

C. Metoprolol

D. Vincristine

E. Cisplatin

START QUIZ
FIND MORE QUESTIONS
Test your knowledge: Pericardial Disease

Pericardial Disease

Pericardial Effusion and Cardiac Tamponade

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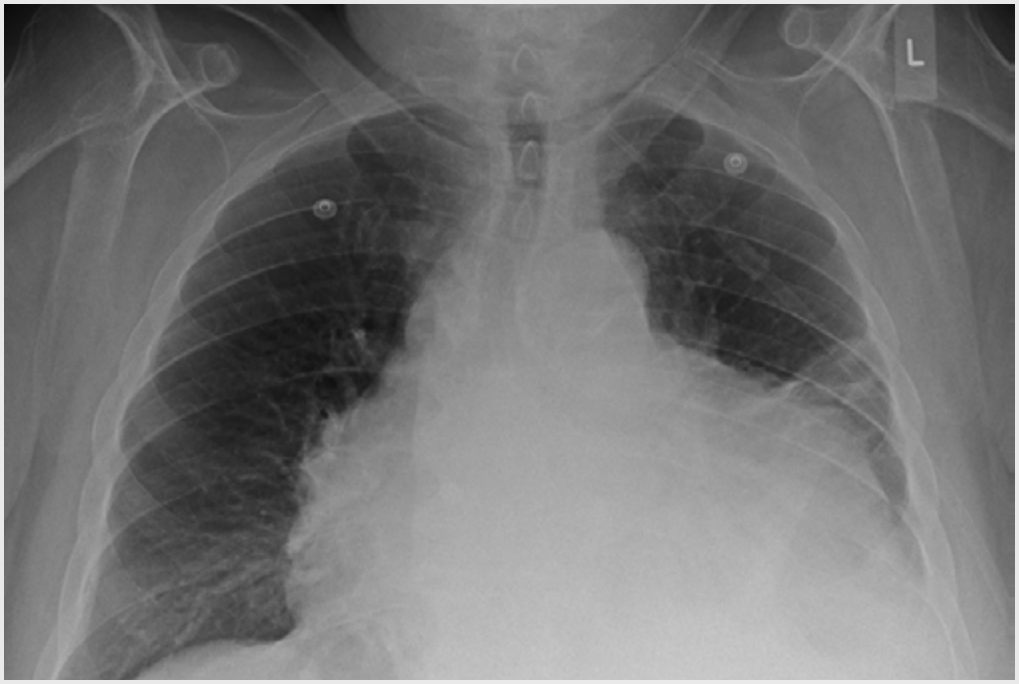

Fig. 7-07: *Pericardial effusion, showing the characteristic flask-shaped heart.*

Definition of Pericardial Effusion and Cardiac Tamponade

Pericardial effusion is defined as acute or chronic accumulation of fluid in the pericardial sac of the heart due to a variety of underlying disorders. The pericardium is stiff and does not expand. If enough fluid accumulates, cardiac filling becomes restricted and leads to a life-threatening reduction in cardiac output; this is called called **cardiac tamponade**.

High-yield facts:
Pericardial effusion and tamponade are primarily caused by pericarditis and malignancy.

Epidemiology of Pericardial Effusion and Cardiac Tamponade

Asymptomatic pericardial effusion presents in approximately **3 % of patients** at autopsy. The groups at greatest risk of developing pericardial effusion include patients with cancer, ESRD, and patients with HIV and AIDS.

Etiology of Pericardial Effusion and Cardiac Tamponade

Causes of pericardial effusion can be classified into:

Hemopericardium

- Cardiac wall rupture (e.g., complication of myocardial infarction)
- Chest trauma
- Aortic dissection
- Cardiac surgery (e.g., heart valve surgery, coronary bypass surgery)

Serous pericardial effusion

- Idiopathic
- Acute pericarditis (especially viral, but also fungal, tuberculous or bacterial)
- Malignancy
- Poststernotomy syndrome
- Uremic
- Autoimmune disorders
- Hypothyroidism

Pathophysiology of Pericardial Effusion and Cardiac Tamponade

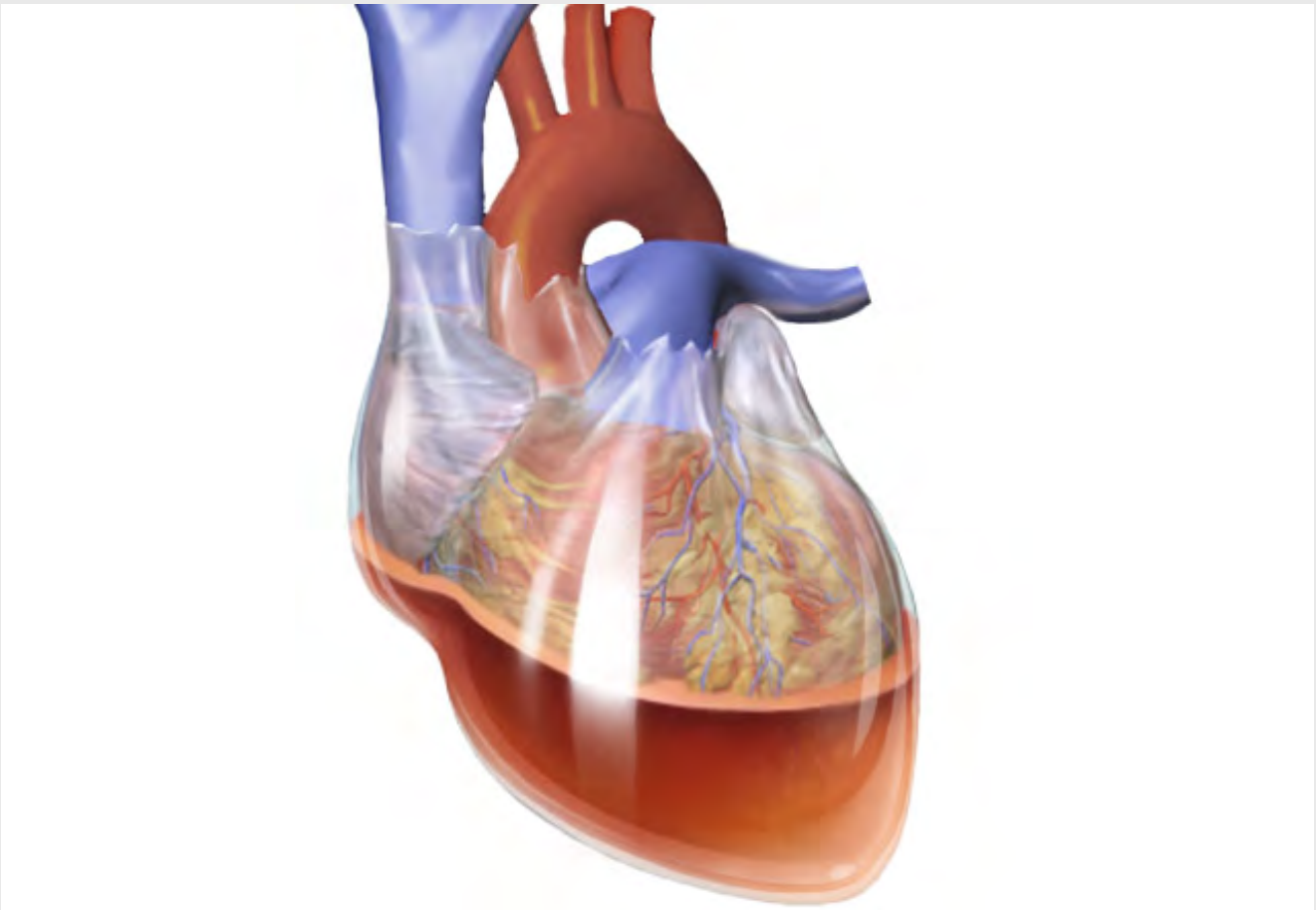

Fig. 7-08: *Cardiac tamponade*

The pericardial space normally contains a small volume of serous fluid. Under normal circaumstances, this cushions the heart and allows for a low-friction environment so the heart can move easily. If fluid were to fill the pericardial space rapidly, as in a penetrating chest trauma, as little as 150 ml could lead to tamponade. If fluid were to slowly accumulate (e.g in malignancy), then the pericardial sac could stretch to accommodate about 2 l of fluid without symptoms.

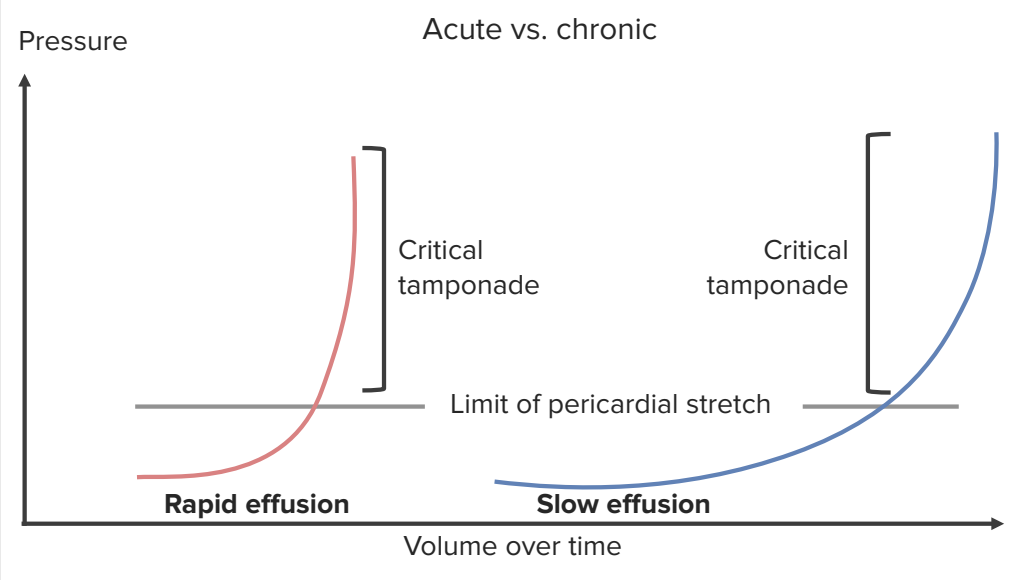

Fig. 7-09: Difference between acute and chronic accumulation of pericardial fluid (Volume over rapid or extended time) and how severely they affect intrapericardial pressure.

Pericardial effusions can be serous, hemorrhagic or serosanguinous (a pink mixture of serous and hemorrhagic). As the pericardial effusion continues to grow, **diastolic filling** will be affected. The physiologic response is to **increase the heart rate** in order to maintain cardiac output. Venous return is also hampered by the gathering fluid, resulting in intravascular buildup in the superior and inferior vena cava and collapse of the right atrium and ventricle, before collapse of the left ventricle with subsequent drop in cardiac output. Insufficient cardiac output eventually leads to shock.

Clinical Features of Pericardial Effusion and Cardiac Tamponade

Symptoms

Pericardial effusion is usually initially asymptomatic. As the effusion develops into a tamponade, the patient will suffer from:

- Dyspnea and orthopnea
- Hypoperfusion, leading to cold/clammy extremities
- Intolerance to minimal activity

Signs

- Tachycardia
- Pulsus paradoxus
- Beck's triad

Note:
Beck's triad:

- *Hypotension*
- *Distended neck veins*
- *Muffled heart sounds*

Diagnostics of Pericardial Effusion and Cardiac Tamponade

Small effusions found by accident are usually worked up to determine their etiology.

ECG

ECG shows low voltage and electrical alternans.

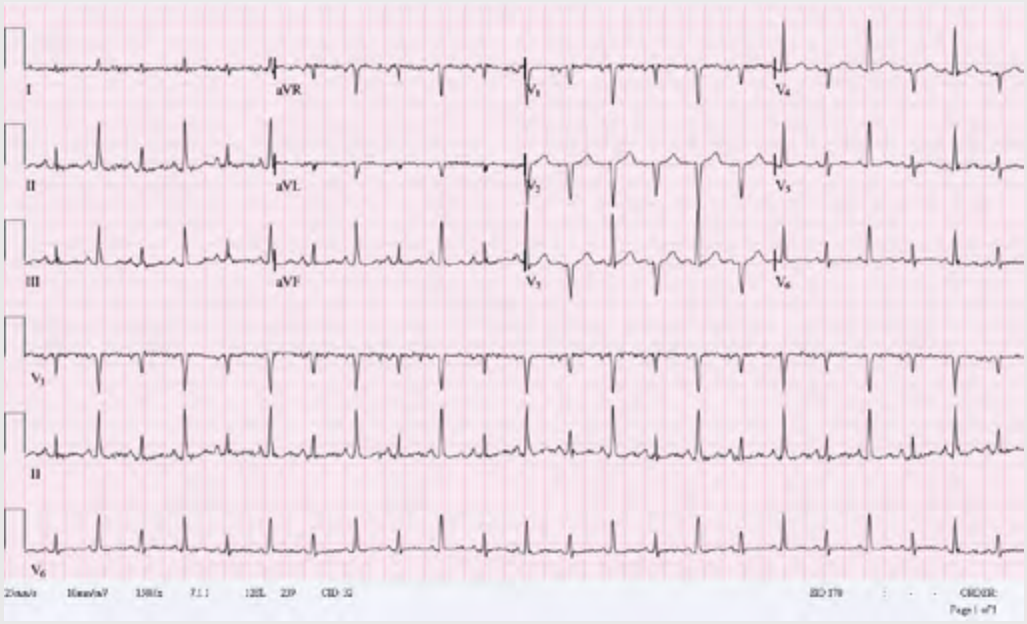

Fig. 7-10: *The ECG shows electrical alternans. This is a consecutive alternating of the height of QRS complexes.*

Note:

1. *Pulsus paradoxus is an abnormally large drop in systolic blood pressure (normal drop is < 10 mmHg).*
2. *Pericardial effusion doesn't cause Kussmaul's sign.*

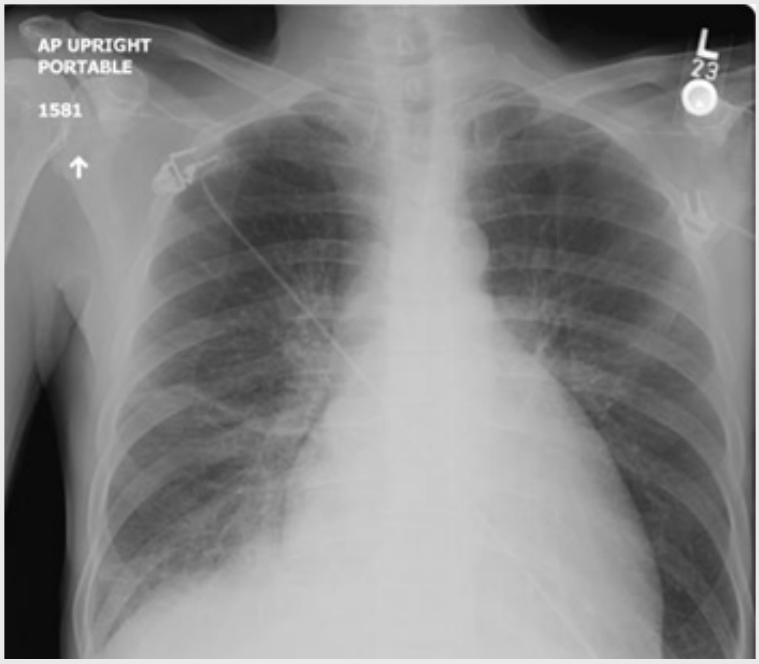

Fig. 7-11: Water bottle sign.

Imaging tests

Chest radiograph

On radiograph, the **pericardial silhouette is enlarged** and takes on a 'water-bottle' shape.

Echocardiography

Echocardiography is considered the gold-standard in the diagnosis of pericardial effusion and cardiac tamponade.

Pericardial effusion

It presents as an anechoic space between the pericardium and epicardium.

A large effusion may cause the pericardium to 'swing' on echo, as the motion of the heart is transmitted through the fluid to the pericardium.

Cardiac tamponade

Echocardiographic findings of cardiac tamponade are:

- Right atrial collapse
- Diastolic right ventricular collapse
- Trans-mitral and tricuspid respiratory variations under Doppler
- Dilation of the inferior vena cava

Note:
Remember bone appears white and fluid appears black on ultrasound and echocardiogram.

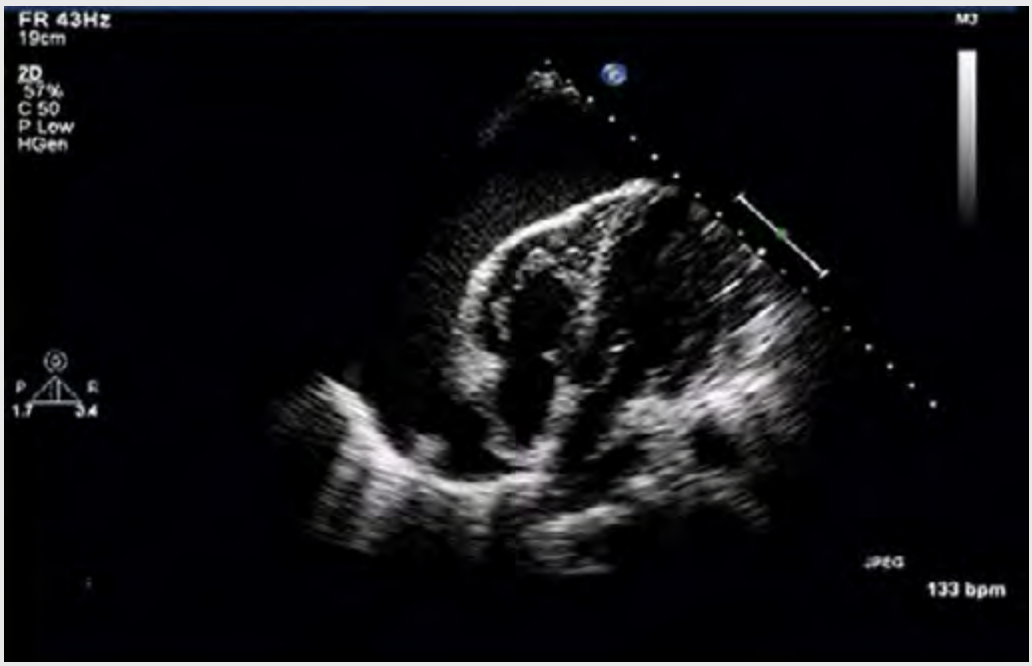

Fig. 7-12: *Pericardial effusion with tamponade (You can see a gif-video here.)*

CT chest

CT chest can be sometimes used to diagnose pericardial effusion and detect the underlying cause.

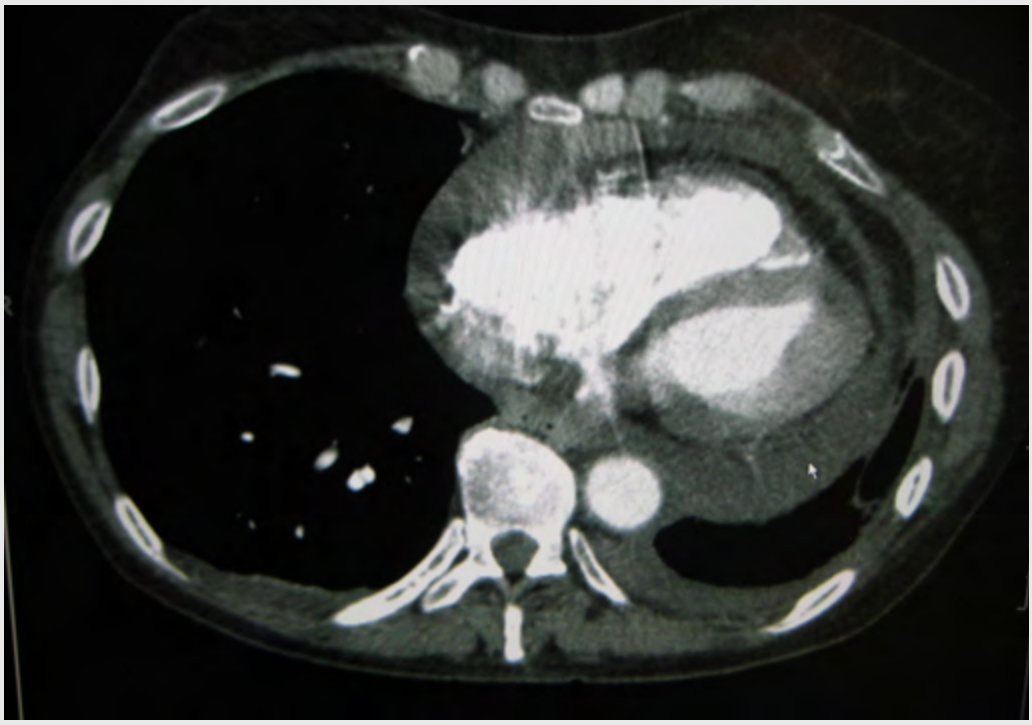

Fig. 7-13: *Pericardial effusion with tamponade*

Treatment of Pericardial Effusion and Cardiac Tamponade

Small effusions are only monitored by echocardiography. **Larger effusions** should be drained, either through ultrasound-guided **pericardiocentesis** or surgical drainage (pericardial window) if recurrent.

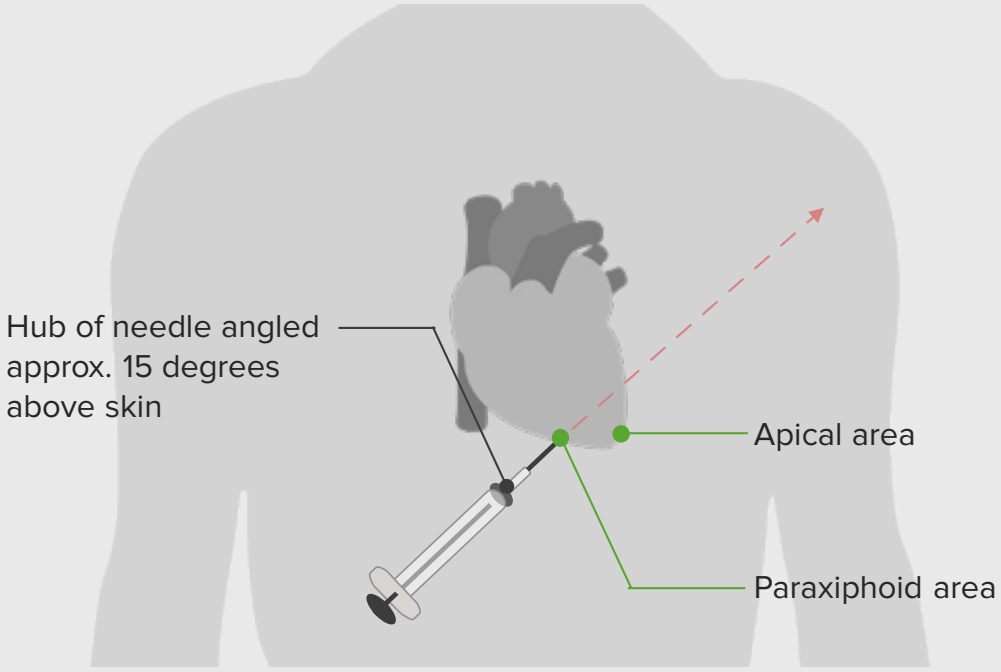

Fig. 7-14: *Treatment of Pericardial effusion*

Prognosis of Pericardial Effusion and Cardiac Tamponade

Prognosis of pericardial effusion **depends on the etiology.** Treating the underlying cause may be curative. Small effusions are simply monitored. However, untreated cardiac tamponade can rapidly cause death. Long term survival depends on etiology. Tamponade induced by malignancy has the worst long-term prognosis.

Note:
Acute pericardial effusion with pericardial tamponade is a life-threatening condition which requires immediate pericardial decompression.

Review Questions

Question 7.4: An 80-year-old man comes to the emergency department because of gnawing substernal chest pain that started an hour ago and radiates to his neck and left jaw. A 12-lead ECG is obtained and shows ST-segment elevation with newly developing Q-waves. He is admitted for treatment. 4 days after hospitalization he suddenly develops altered mental status, and his blood pressure falls from 115/75 mm Hg to 80/40 mm Hg. Physical examination shows jugular venous distention, pulsus paradoxus, and distant heart sounds. What is the most likely cause of this patient's condition?

A. Acute pulmonary edema causing right heart failure

B. Arrhythmia caused by ventricular fibrillation

C. Compression of heart chambers by blood in the pericardial space

D. Pericardial inflammation

E. Rupture of papillary muscle

Correct answer: 7.4C

Chapter 8:
Arrhythmia

Anatomy of the Electrical System of the Heart

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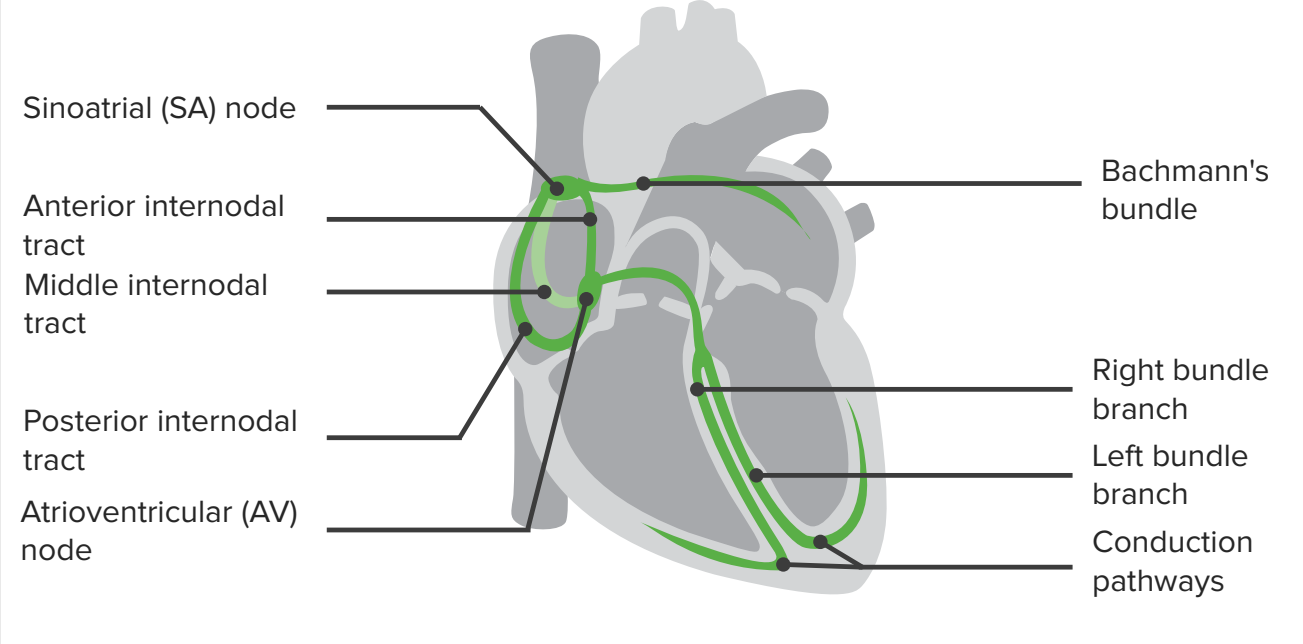

Fig. 8-01: Anatomy of the normal conduction system of the heart

Anatomy of the electrical system of the heart

Myocardial cells are striated muscle cells similar to skeletal muscle. They differ from other cells in that they have a single nucleus and many more mitochondria. These cells make up the walls of the atria and ventricles of the heart. They are electrochemically **connected to adjacent cells by gap junctions and intercalated disks.** Channels allow electrolytes such as sodium, potassium, and calcium to flow between cardiac cells and allow the heart to work synchronously. In contrast, skeletal muscle cells lack intercalated discs and act individually.

Pacemaker cells are modified cardiomyocytes. There are many groups of pacemaker cells throughout the heart. They have the ability to spontaneously develop a cardiac action potential, called automaticity.

The electrical impulse is generated in the sinoatrial (SA) node, the heart's natural pacemaker. The impulse then travels to the right and left atria through myocardial cells and Bachmann's bundle and to the right and left ventricle through AV node and His-Purkinje fibers. This electrical impulse stimulates the myocardial cells to contract.

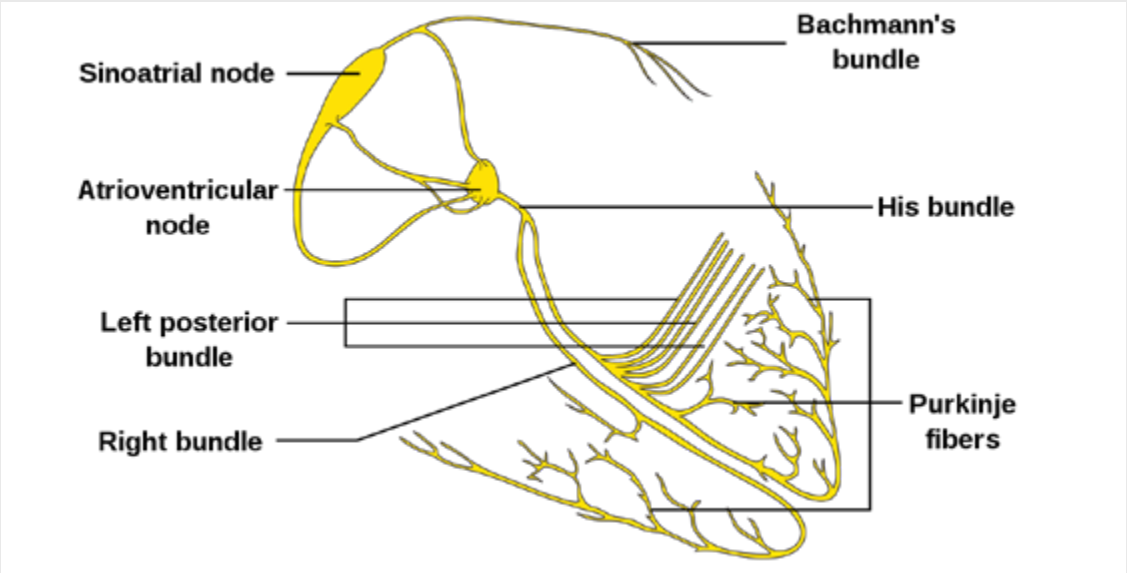

Fig. 8-02: A graphical representation of the electrical conduction system of the heart showing the sinoatrial node, atrioventricular node, bundle of His, Purkinje fibers, and Bachmann's bundle

Pacemakers of the Heart

Sinoatrial (SA) node

The SA node is located in the wall of the right atria and consists of electrically active cells. The blood supply for the SA node comes from the right coronary artery in approximately 60 % of the population and the left coronary artery in about 40 % of the population. Coronary artery occlusion may cause damage to the SA node. The SA node depolarizes spontaneously, approximately, 100 times per minute. Autonomic nervous system fibers are connected to the SA node. Sympathetic stimulation (epinephrine, norepinephrine) increases depolarization rate while parasympathetic inhibition (acetylcholine) decreases it. The parasympathetic inhibition is stronger, resulting in an average heart rate of between 60–100 bpm.

Atrioventricular (AV) node

The AV node is located in the interatrial septum. The **impulse** coming from the SA node **pauses for** a while **due to a slower conduction velocity.** This gives the ventricles time to fill before contraction. The right coronary artery supplies the AV node in 80 % of the population. The autonomic nervous system regulates conduction velocity through the AV node. It spontaneously depolarizes 40–60 times per minute, but this impulse is usually overwhelmed by the electrical impulse coming from the SA node. If the primary pacemaker (the SA node) is defective or damaged, the AV node becomes the pacemaker. The impulse from the AV node travels to the Bundle of His-Purkinje fibers.

Conduction System

Bundle of His and Purkinje fibers

The atria and ventricles are isolated from each other by the annulus fibrosus. **The Bundle of His** is the only **electrically conductive tract** that connects the upper and lower sections of the heart. The Bundles of His travel down into the interventricular septum. It separates into left and right bundle branches located in the walls of the left and right vertricles respectively. Its blood supply comes from the left anterior descending artery. The impulse then travels to the terminal branch of the conduction system, the Purkinje fibers. The left branch depolarizes first, resulting in left ventricle contraction, followed by right ventricle contraction. The Bundle of His spontaneously depolarizes at a rate of 30–40 times per minute, but the normal electrical impulse from the SA node usually overwhelms this signal.

Most Important Facts about Arrhythmia

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Definition of Arrhythmia

Arrhythmia is a group of impulse generation or conduction disorders located within the myocardium, resulting in irregular heart beats, bradyarrhythmia, or tachyarrhythmia.

Pathophysiology of Arrhythmia

In a healthy heart, pacemaker cell automaticity is influenced by the autonomic nervous system, electrolyte imbalance, and medications (beta-blockers, calcium channel blockers, etc).

- **Parasympathetic nervous system:** Slows the heart rate by releasing acetylcholine at the SA node.
- **Sympathetic nervous system:** Increases the heart rate by releasing catecholamines (epinephrine and norepinephrine) at the SA node.

The heart contains many pacemaker cells which are able to produce an electrical impulse. Under normal circumstances, the SA node is the primary pacemaker and controls the rate of electrical impulse production. Occasionally, other foci other than the SA node take over the function of impulse production, causing disorganization in the carefully regulated contraction process of the heart, resulting in arrhythmia. Cardiac tachyarrhythmias are primarily produced by 1 of 3 main mechanisms: **enhanced automaticity, triggered activity, or reentry circuits**.

Reentry

These arrhythmias sustain themselves by continuously following a pathway of 2 limbs; one takes the impulse away from the origin site, and the other carries the impulse back to it. For a reentry to occur, there must be an area with slow conduction and the 2 limbs must have different refractory periods.

Enhanced automaticity

This refers to spontaneous, repetitive, and forceful firing from a single focus which may originate from the sinus node or subsidiary pacemakers in the atrium, including the Eustachian ridge, Bachmann bundle, coronary sinus and AV valves, the AV node, His-Purkinje system, and the ventricles.

Triggered activity

Triggered activity depends mainly on the oscillations of the myocardium membrane potential (after-depolarizations). With absence of a new external electrical stimulus, after-depolarizations cause the development of new action potentials. There arrhythmias are produced by either:

1. **Early after-depolarizations:**
    - Membrane repolarization is incomplete, allowing a subthreshold stimulus to initiate action potential.
2. **Delayed after-depolarization:**
    - Membrane repolarization is complete, but the arrhythmia occurs because an abnormal intra-cellular calcium load causes spontaneous depolarization.

Disorders of impulse conduction

A slow heart rate of fewer than 60 beats/minute (bradycardia), is the result of a primary pacemaker dysfunction or a conduction block in the AV node or His bundles. In cases of SA node damage, the AV node, bundle of His, myocytes, or other non-pacemaker cells can generate electrical impulses that stimulate the heart to contract, but at a slower rate:

- 40–60 bpm if AV rhythm
- Less than 40 bpm if ventricular rhythm

Classification of Arrhythmias

Bradyarrhythmias	Tachyarrhythmias	
1) Atrioventricular blocks: • 1st degree • 2nd degree • 3rd degree (complete heart block) **2) Sinoatrial arrest**	**Supraventricular** • Atrial fibrillation • Atrial flutter • Multifocal atrial tachycardia • WPW	**Ventricular** • Torsades de pointes • Ventricular fibrillation • Ventricular tachycardia

Premature beats

These arrhythmias are relatively common and usually benign and asymptomatic. Premature beats are further divided into:

1. Premature atrial contractions (PACs) originating above the AV node from the atria.
2. Premature ventricular contractions (PVCs) originating below the AV node.

Supraventricular arrhythmia

These arrhythmias originate in the atria or AV node. Supraventricular arrhythmias include atrial flutter, atrial fibrillation, multifocal atrial tachycardia, Wolff-Parkinson-White syndrome, and paroxysmal supraventricular tachycardia.

Ventricular arrhythmia

These arrhythmias are very dangerous and require immediate medical intervention. They include Torsades de pointes, ventricular fibrillation, and ventricular tachycardia.

Bradyarrhythmias

A slow heartbeat is known as bradyarrhythmia. This can occur in healthy individuals such as professional athletes. They include AV block and sinoatrial arrest.

Symptoms of Arrhythmia

Many arrhythmias are asymptomatic. However, the most common symptom is palpitations. Arrhythmias can be sensed as a flutter or pressure in the chest. If the arrhythmia results in heartfailure, the patient may experience dyspnea or syncope. Some arrhythmias are lethal within minutes, such asventricular fibrillation.

Diagnosis of Arrhythmia

Most arrhythmias can be diagnosed based on:

12-Lead Electrocardiogram (ECG)

- A 12-lead ECG study is a non-invasive test but requires experience to interpret the results. It briefly measures the electrical signals the heart emits during depolarization of the cardiac muscle.

Holter ECG (portable 12-lead ECG)

- This is used to detect infrequent or occasional arrhythmias. It is carried by the patient for about 24 or even several days, and constantly monitors the electrical activity of the heart.

Stress ECG

- Some arrhythmias only occur when the patient is under stress. A **treadmill (or chemical)** stress test is required to provoke the arrhythmia which is then recorded on an ECG.

Electrophysiology

- A number of arrhythmias (such as WPW) require an **electrophysiological study** that is much more invasive and involves sedation and catheterization of the heart, usually through the arteries of the groin.

Echocardiography

- Echocardiography is a useful tool when diagnosing the underlying etiology of the arrhythmia as:
    - LV dilatation increases risk of ventricular arrhythmias such as ventricular tachycardia.
    - Dilated left atrium increases risk of atrial fibrillation.
    - Valvular heart disease, such as mitral stenosis, is commonly associated with supraventricular arrhythmias.

Review Questions

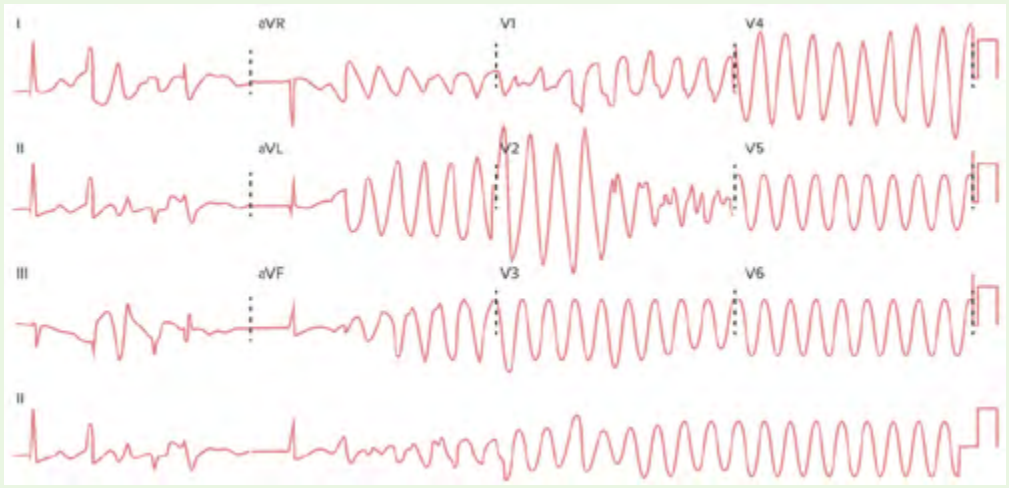

Fig. Q. 8.1

Question 8.1: A 28-year-old woman is brought to the emergency department by a friend after fainting at work and hitting her head. She is conscious, alert, and in pain, as she sustained a deep laceration above her right orbit. When asked about prior fainting episodes, she says that she has had them since childhood, but she felt it was "nothing serious." She also says she has frequent palpitations, shortness of breath, nausea, and, at times, chest pain and attributes this to "working too hard." Her pulse is 110/min, respirations are 20/min, temperature is 37.4°C (99.3°F), and blood pressure is 110/78 mm Hg. Physical examination shows tachycardia and mild hypotension. The patient's electrocardiogram is obtained and is shown below. Which of the following drugs is the preferable choice for first line treatment of this patient's condition?

A. Calcium gluconate

B. Epinephrine

C. Flecainide

D. Magnesium sulfate

E. Procainamide

Correct answer: 8.1D

Atrial Fibrillation (AFib)

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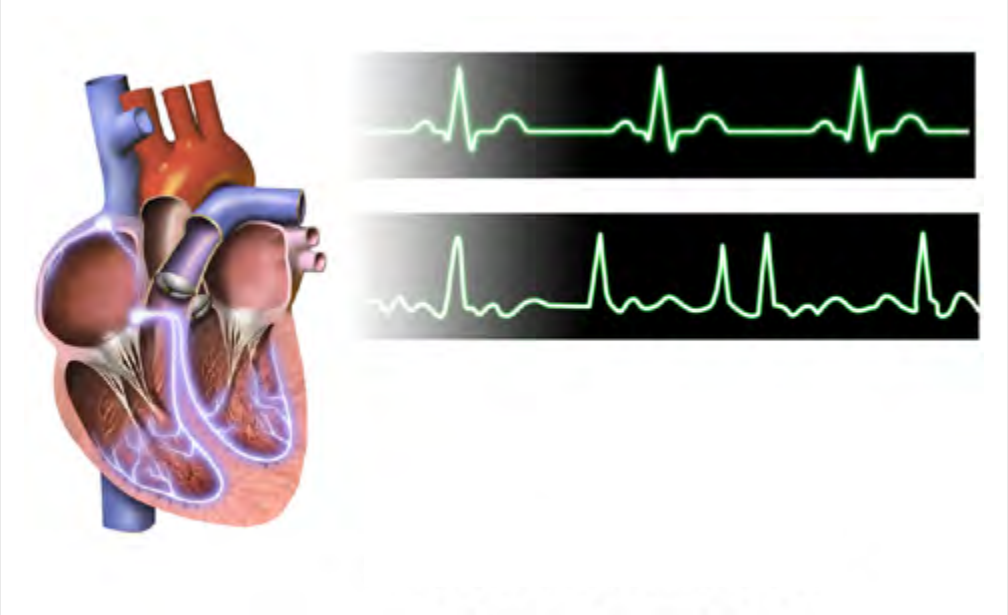

Fig. 8-03: Atrial Fibrillation

Definition of AFib

Atrial fibrillation (AF) is an exceedingly common rhythm disturbance often seen as chronic supraventricular tachyarrhythmia in elderly patients. It is characterized by irregular QRS complexes and a loss of synchronous atrial contraction.

Epidemiology of AFib

About 1–2 % of the general population will experience an episode of atrial fibrillation, which makes it the most common type of cardiac arrhythmia. AF incidence increases with age, with up to 10 % of the population over the age of 70 experiencing it. Men are more often affected than women.

Etiology of AFib

AF is caused by underlying risk factors that can be classified into cardiac and noncardiac causes.

Note:
Idiopathic AF (lone AF) occurs without risk factors and accounts for about 15 % of AF cases.

Cardiac causes

The most frequent cardiac cause of AF is a mitral valve defect. Other possible cardiac causes include hypertension, advanced congestive heart failure, ischemic heart disease, and cardiomyopathy.

Non-cardiac causes

Most common non-cardiac causes of AF are pulmonary diseases as pulmonary embolism and COPD, hyperthyroidism, electrolyte disturbances such as hypokalemia, or toxic substances such as alcohol, thyroxine, triptans, theophylline, or sildenafil.

Note:
AF that occurs after excessive alcohol ingestion, so-called binge drinking, is also known as holiday heart syndrome.

Pathophysiology of AFib

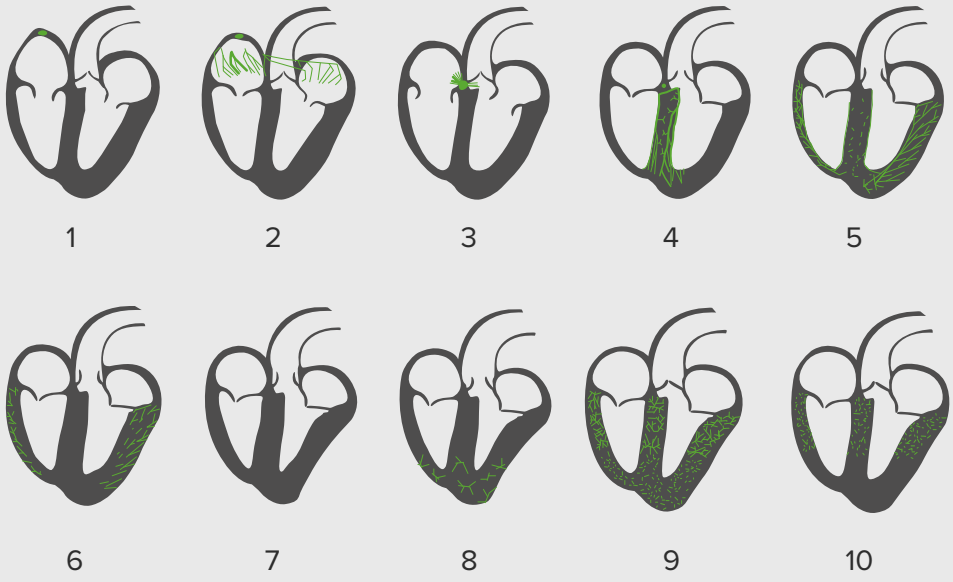

Fig. 8-04: Conduction of excitation in the heart in atrial fibrillation

The arrhythmia of atrial fibrillation is caused by a **reentrant tachycardia** of the atria, usually in the area close to the pulmonary veins. This means that the electrical impulses do not propagate in the normal physiological manner, i.e. starting at the sinus node, moving through the atria, and on into the ventricles; rather, they repetitively move in a **circular path** within the atria, which continuously depolarizes the atrial myocardium. This results in an **atrial frequency of 350–600 beats per minute.**

As the myocardium now contracts in an asynchronous manner, the atria can no longer effectively fulfill their pumping function. This leads to a **reduced cardiac output of 15 %** in healthy individuals, and even more in patients with pre-existing cardiac insufficiency. Because the AV node acts as a kind of blocker, not every excitation formed in the atria is conducted to the ventricles. The transmitted, often irregular, ventricular frequency usually ranges between 100-160 bpm.

Classification of AFib

With regard to the onset and duration of the disease, the following forms of AF can be distinguished:

- **First-time manifestation of AF**: First time witnessed AF.
- **Paroxysmal AF**: AF that terminates within 7 days either following treatment or spontaneously.
- **Persistent AF**: Continuous AF for more than 7 days.
- **Long-standing persistent AF**: Continuous AF for more than 1 year.
- **Permanent AF**: AF that is not treated following a joint decision by the patient and the physician.

Note:
Rapid AF → AF with ventricular rate > 100 bpm.

Slow AF → AF with ventricular rate < 60 bpm.

Another classification of AF based on the underlying etiology distinguishes:

Valvular AF:

- The most common cause is mitral stenosis. This type should be treated with an oral anticoagulant regardless the risk of thromboembolic events (CHADVASC score).

Non-valvular AF:

- AF in patients without valvular involvement.

Clinical Features of AFib

- AF often remains **asymptomatic** for long periods of time unless symptoms or complications developed.
- Symptoms that patients may experience are palpitations, irregular heart rate, anginal chest pain, dyspnea, lightheadedness, dizziness, and **syncope**.
- Sometime AF is only discovered following major complications:
  - Acute heart failure (pulmonary edema).
  - Thromboembolic events: stroke/TIA, renal infarct, splenic infarct, and acute limb ischemia.

Stroke risk stratification

Another crucial complication associated with atrial fibrillation is the **risk of thromboembolic events**. As the atria fail to have a coordinated electrical discharge, it leads to an ineffective contraction; they 'quiver' or fibrillate, leading to stasis of blood within the atria and an increased risk of clot formation. This risk can be assessed using the **CHA2DS2-VASc** score; the higher the result, the higher the risk of thrombus formation.

C	Congestive heart failure	1
H	Hypertension	1
A	Age (≥ 75 years)	2
D	Diabetes mellitus	1
S	Stroke or TIA	2
V	Vascular disease history	1
A	Age 65–74 years	1
Sc	Sex category (female sex)	1

Score	Annual stroke risk %
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8

Diagnostics of AFib

History and clinical examination

In the diagnostic process, initial suspicion usually arises from a **history** of repeated palpitations or episodes of tachycardia. In this case, it is especially important to inquire about duration, frequency, and triggering factors of the AF. Furthermore, underlying diseases like hyperthyroidism may indicate the presence of secondary atrial fibrillation. **Clinical examination** may be notable for an irregular heartbeat, a variable intensity of the **first heart sound**, and a difference between auscultated heart rate and palpable peripheral pulse **(pulse deficit)**. However, unremarkable findings do not rule out the presence of AF.

Investigations – ECG

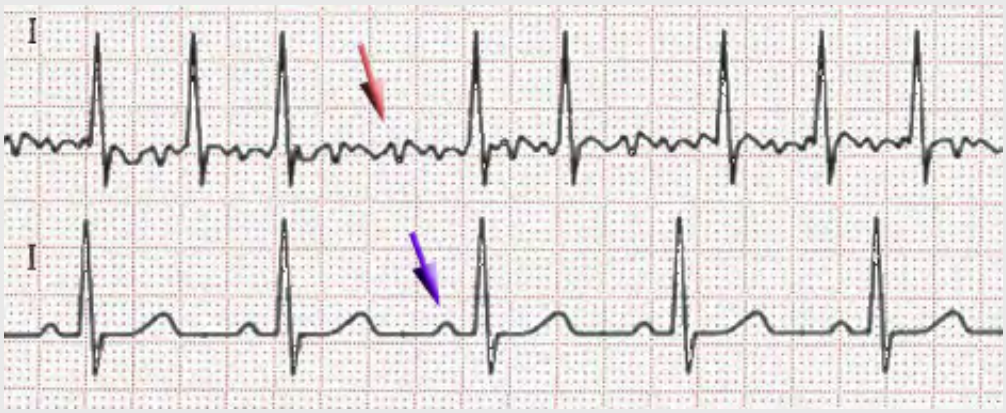

Fig. 8-05: Schematic representation of atrial fibrillation (red arrow) and sinus rhythm (blue).

The most important diagnostic measure for confirming a suspected AF is an electrocardiogram (ECG), characterized by the absence of P waves (atrial discharges) and 'irregularly irregular' conduction to the ventricles with irregular RR intervals.

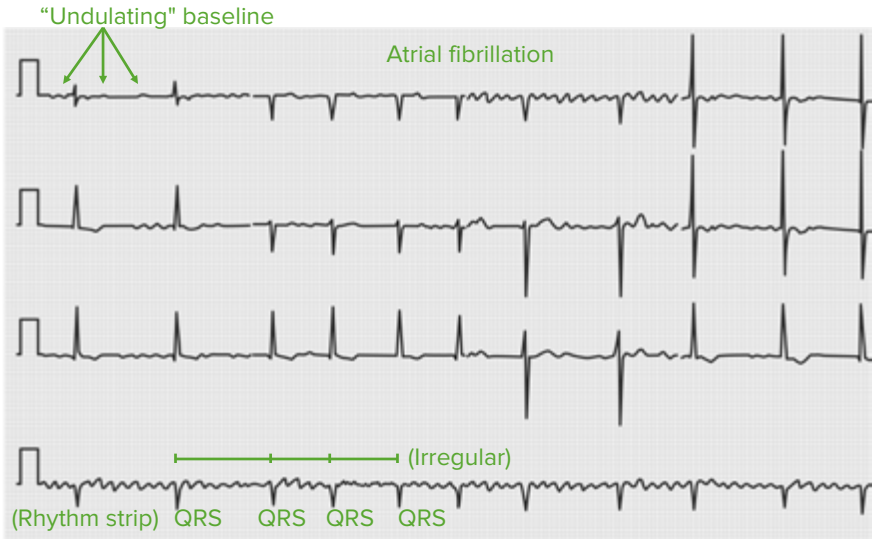

Fig. 8-06: Atrial fibrillation

AF can also be a coincidental finding on an ECG ordered for another reason. Based on the ventricular frequency, a further distinction between **tachycardia** (more than 100 bpm) and **bradycardia** (less than 60 bpm) can be made. Beside these phenomena, fibrillatory waves may be visible in lead V1, which is also caused by asynchronous excitation. QRS complexes are typically narrow in patients with AF.

Note:
ECG showing AF is sufficient to confirm the diagnosis.

24-hour holter ECG

Paroxysmal AF can be detected using Holter ECG monitoring for 24 hours or more. This is useful if patient complains of irregular palpitations and AF is suspected.

Echocardiography

Transthoracic Echocardiography (TTE): Indicated in all patients newly diagnosed with AF to assess cardiac function and determine the underlying etiology.

Transesophageal Echocardiography (TEE): Indicated in all patients with AF > 48 hours or of unknown duration for whom cardioversion is planned. TEE is used to exclude the presence of left atrial appendage thrombus before attempting cardioversion.

Note:
The most common atrial thrombus is the left atrial appendage thrombus.

Differential Diagnoses of AFib

Differential diagnosis of AF includes other irregular supraventricular tachyarrhythmias (with narrow QRS complex), such as:

1. Atrial flutter
2. Multifocal Atrial Tachycardia (MAT)

Distinguishing atrial fibrillation from atrial flutter

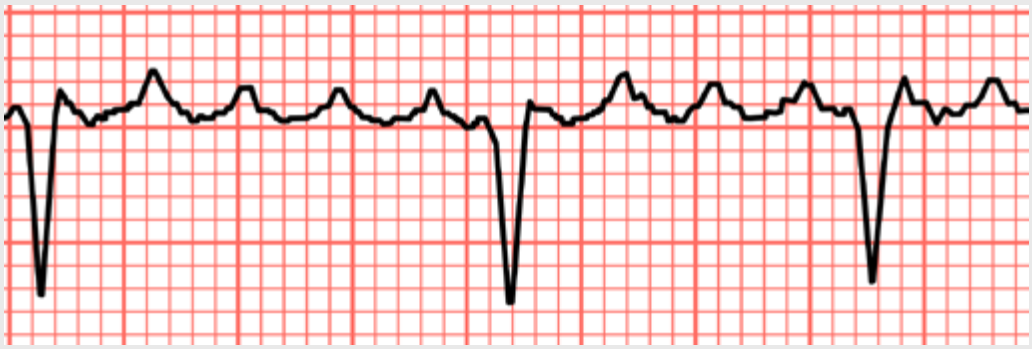

Fig. 8-07: *Atrial flutter, with characterstic saw-tooth appearance*

The most important differential diagnosis of atrial fibrillation is atrial flutter; both types of arrhythmia show very similar symptoms. A typical sign in the ECG of atrial flutter is **flutter waves**, caused by a **macro-reentrant circuit** in the atria. This sign takes the form of a **saw-tooth pattern.**

Type I atrial flutter (also known as typical or common atrial flutter) is characterized by negative flutter waves in the ECG and a frequency of 250–350 bpm; the less common **type II atrial flutter** (reverse typical atrial flutter) shows positive flutter waves with a frequency of 250–450 bpm. Treatment is causal, consisting either of trying to convert the arrhythmia or with radiofrequency ablation.

Treatment of AFib

The main principles of treating atrial fibrillation:

1. **Correcting any reversible risk factors**, such as electrolyte imbalance and hyperthyroidism.
2. **Rhythm control** for restoring the sinus rhythm and rate control for reducing the heart rate.
3. **Prophylaxis** of **thromboembolism** with anticoagulation.

Rhythm control

High-yield:
Signs of instability (3 H): Hypotension, Heart failure, Heart infarction (chest pain)

The goal of rhythm control is to reestablish sinus rhythm. Patients with atrial fibrillation are classified based on hemodynamics:

1. **Unstable patients:**

   Unstable patients should be treated with emergent synchronized electrical cardioversion (DC).

2. **Stable patients:**

   Management of hemodynamically stable patients depends mainly on the time onset of AF:

   - AF (< 48 hours):
     - AF should cease upon restoring sinus rhythm, either with medical or electrical cardioversion.
   - AF (> 48 hours or of unknown duration):
     - If the AF has lasted more than 48 hours the risk of left atrial thrombus formation increases significantly.
     - Treatment involves warfarinin combination with bridging therapy for 3 weeks before cardioversion, and up to 4 weeks after cardioversion has taken place.
     - TEE is recommended to rule out the left atrial appendage thrombi if anticoagulation therapy has not been administered for at least 3 weeks before the cardioversion.

Rhythm control methods

1. **Electrical cardioversion**
   - Carried out with a synchronized DC shock.
   - In this procedure, 120–150 J for biphasic devices and 200 J for monophasic devices are administered to the sedated patient, the timing of which is controlled by an integrated ECG to assure the optimal moment in the cardiac cycle (synchronization).
   - If unsuccessful, the amount of energy must be gradually increased.
2. **Pharmacological cardioversion**
   - **Antiarrhythmic medications** used for patients without any cardiac disorders; most are **class Ic drugs**, for example, **flecainide** and **propafenone**.
   - If the patient has any known pre-existing cardiac conditions, the more effective **amiodarone** can be administered; however, this drug carries a greater risk of side-effects.

Note:
Invasive option, especially for younger patients, is catheter-based radiofrequency ablation which aims at destroying the area of cardiac tissue responsible for the reentry mechanism.

Rate control

Rate control aims to slow the ventricular rate and thus avoid tachycardia-induced cardiomyopathy, and relieve the feeling of palpitations.

Rate control can be achieved using:

1. **Beta-blockers:**
   - Commonly used as 1st line treatment in absence of contraindications, especially if AF is secondary to hyperthyroidism.
   - Examples: Esmolol, propranolol, metoprolol
2. **Non-dihydropyridine Calcium Channels Blockers (CCB):**
   - Can be used if beta-blockers are contraindicated, as in COPD patients.
   - Contraindicated in patients with LV dysfunction, as they have strong negative inotropic effect.
   - Examples: Diltiazem and verapamil
3. **Digitalis (digoxin):**
   - Can be used in patients with heart failure in addition to atrial fibrillation. It can be used alone or with beta-blockers.

Note:
Amiodarone can be used as a last-resort option for heart rate control in patients with AF and rapid ventricular response, especially if the previous drugs are ineffective or contraindicated.

Note:
Invasive procedure is AV nodal ablation with implantation of a permanent pacemaker.

Long term anticoagulation

The **prevention of thromboembolism** in patients with atrial fibrillation is of the utmost importance because of their increased risk of embolic events, especially stroke.

In valvular AF

Long-term anticoagulation is required regardless the **CHA2DS2-VASc score.**

In non-valvular AF

This risk is assessed using the **CHA2DS2-VASc score** of the European Society of Cardiology (ESC):

- **Score 0:** Indicates a low risk and does not necessarily require anticoagulation.
- **Score 1:** Moderate risk (CHA2DS2-VASc of 1 or more), permanent anticoagulation will have to be considered – except when the risk factor is only based on the female gender.
- **Score of 2 or more:** Anticoagulation is imperative.

Types of anticoagulant drugs

1. Warfarin

- In the U.S., most patients are treated with the anticoagulant **warfarin** (brand name **Coumadin**), which requires regular checks and monitoring of the target INR level of 2–3.

2- Novel oral anticoagulants (NOAC)

- There are **newer oral anticoagulants** available which have proven to be effective. They don't require INR monitoring.
- These drugs include:
  - Dabigatran: direct thrombin inhibitor
  - Rivaroxaban: factor Xa inhibitor
  - Apixaban: factor Xa inhibitor

Prognosis of AFib

The prognosis for atrial fibrillation strongly depends on the underlying diseases and cardiac function. Patients with AF and mitral stenosis have 4 times the risk of thromboembolic manifestations than patients with non-valvular AF. Furthermore, it is particularly the risk for thromboembolic events that determine the course and mortality of the disease.

The different treatment approaches, rhythm control or rate control, do not influence the prognosis, except for patients with cardiac insufficiency, who benefit more from ongoing rhythm control therapy. Stroke risk can be reduced by about 60 % through the proper dosage of anticoagulation.

Review Questions

Question 8.2: An 81-year-old woman comes to the emergency department due to a left-sided paralysis for the past 2 hours. Her husband says her symptoms began suddenly, and she is also unable to speak. Her pulse is 90/min, respirations are 18/min, temperature is 36.8 °C (98.2 °F), and blood pressure is 150/98 mm Hg. An ECG is obtained and is shown below. Which of the following is the most probable cause of the patient's paralysis?

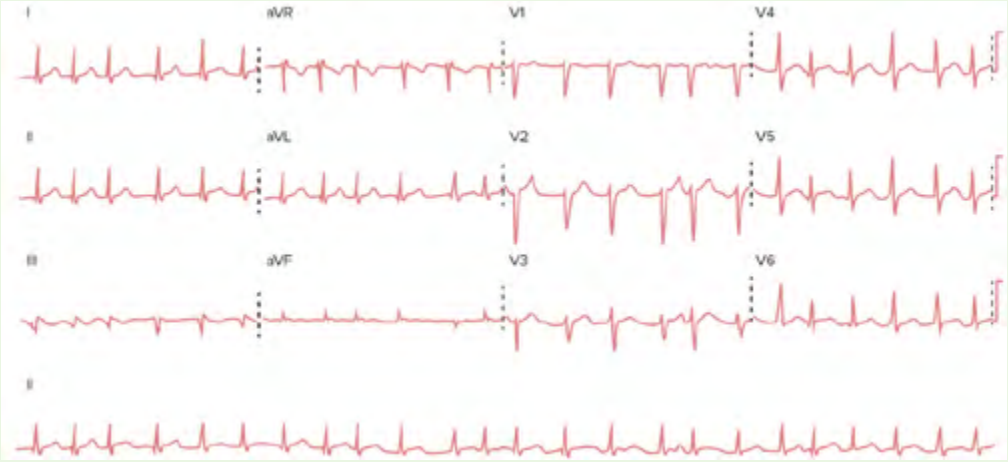

Fig. Q. 8.2

A. Cardioembolic stroke

B. Cocaine toxicity

C. Conversion disorder

D. Hemorrhagic disorder

E. Rupture of berry aneurysm

Bradyarrhythmias

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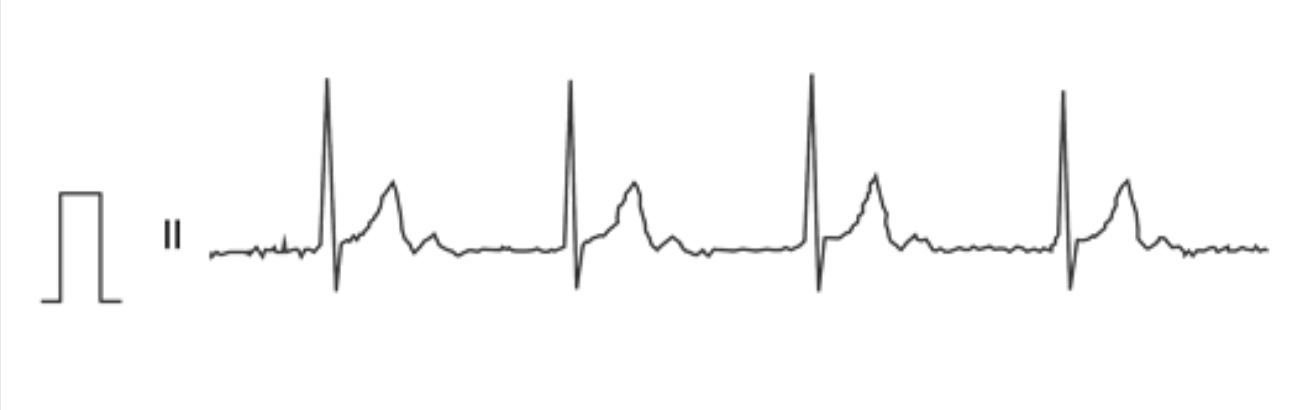


Fig. 8-08: *First-degree AV block, Type 1: PR interval > 200 ms. This ECG strip shows a heart rate of 65 bpm and a PR interval of 560 ms, a severe first-degree AV block.*

Definition of Bradyarrhythmias

Bradyarrhythmias are characterized by resting heart rate < 60 bpm. They are classified into two main categories: **Sinus node dysfunction and atrioventricular block**.

SA Node Bradycardias

SA node bradycardias involve an abnormality of the SA node or the atrial conduction system.

Sinus bradycardia

Sinus bradycardia is defined as a sinus rhythm with a heart rate slower than 60 bpm. Sinus rhythm is defined as a P wave followed by a QRS complex less than 100 milliseconds wide, and a constant PR interval. A sinus rhythm implies that the SA node is sending out electrical impulses at regular intervals. Sinus bradycardia is a relatively common condition in professional athletes (marathon runners) and the elderly.

Etiology

- Medications (beta-blockers, calcium channel blockers), hypothyroidism, hyperkalemia, and SA node dysfunction.
- Sinus bradycardia rarely causes hemodynamic instability in healthy individuals.

Diagnosis

- It is important to be able to **distinguish sinus bradycardia from a bradyarrhythmia**. A bradyarrhythmia will have a slow heart rate and will lack a sinus rhythm. Diagnosis is via 12-lead echocardiogram.

Treatment

- **Asymptomatic patient**: Treatment involves regular monitoring and correcting any underlying condition.
- If sinus bradycardia is symptomatic due to low perfusion (syncope, dyspnea, edema in the extremities, etc.), it can be treated by the implantation of a permanent pacemaker to restore proper heart rate.

Sick Sinus Syndrome (SSS)

SSS is the classification for a group of conditions caused by damage to the SA node or the atrial conduction system. SSS is more common in the elderly and is a sequelae of cardiac surgery in pediatric populations.

Etiology

- This condition is seen in degenerative syndromes and conditions that lead to scar formation in the heart such as amyloidosis, sarcoidosis, hemochromatosis, and cardiomyopathies.

Diagnosis

- SSS may result in sinus bradycardia, bradyarrhythmia, tachycardia, or even bradycardia-tachycardia syndrome. Diagnosis is difficult for this reason. Holter ECG monitoring can be used to diagnose SSS.

Symptoms

- Symptoms include palpitations, dyspnea, fatigue and dizziness.

Treatment

- Treatment may consist of a pacemaker to treat bradycardia, medication to treat tachycardia, or both to treat bradycardia-tachycardia syndrome.

Sinoatrial pause or arrest

Sinus pause is a failure of the SA node to depolarize. Usually the AV node acts as a pacemaker and generates an electrical impulse 40–60 times per minute called an escape rhythm. However, this will be an abnormal rhythm since it did not originate at the SA node.

Diagnosis

- ECG will show prolonged absence of sinus node propagating activity (absent P waves) > 3 seconds in sinus node arrest and < 3 seconds in sinus node pause

Symptoms

- A sinus pause of less than 3 seconds is occasionally found in healthy adults.
- A pause longer than 3 seconds may require intervention and cardiac life support.

Atrioventricular Block

An AV block describes a slowing down of signal conduction or a complete drop in electrical impulse energy as it passes from the atria to the ventricles through the AV node.

First-degree AV block

This describes a prolonged PR interval of greater than 200 ms on ECG. The SA node produces a regular electrical impulse that travels through the atria and into the AV node where it stalls. A first-degree AV block is usually asymptomatic, and caused by increased vagal tone, or medications such as beta-blockers or CCB.

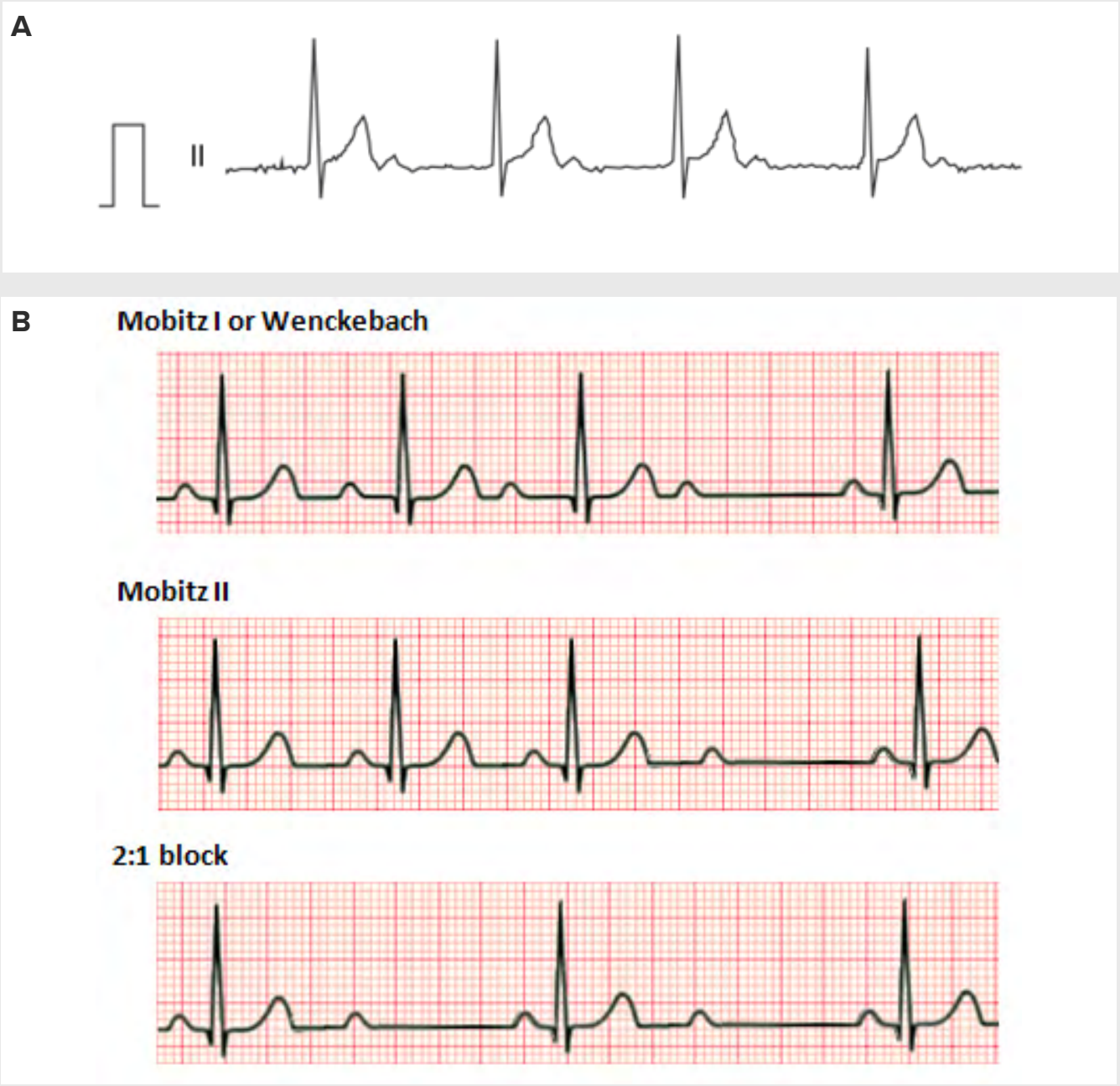


Fig. 8-09: *(A) First-Degree AV Block, Type 1: PR interval > 200 ms. This ECG strip shows a heart rate of 65 bpm and a PR interval of 560 ms, a severe first-degree AV block. (B) Different types of second degree heart block*

Second-degree AV block

There are 2 classes of second-degree AV block:

1. **Mobitz type 1 (Wenckebach)**

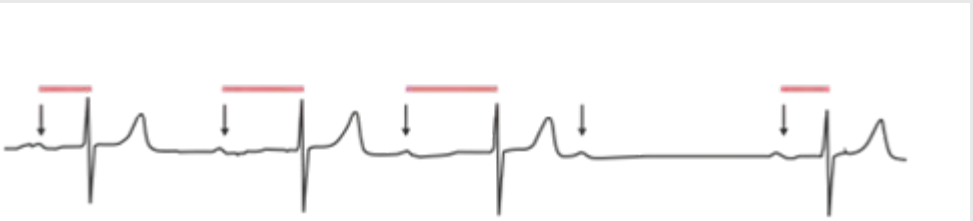


Fig. 8-10: *Second-degree AV block, Mobitz 1, Wenckebach: The PR interval progressively lengthens in an irregular rhythm until a QRS complex is dropped. Arrows indicated P waves, red lines indicate progressively prolonging PR interval.*

Mobitz type 1 second-degree AV block is of an irregular rhythm because the PR interval on the ECG increases with each beat until a 'beat is dropped' (meaning that there is a P wave without a corresponding QRS complex). The defect is at the AV node and is usually the result of excess parasympathetic tone on the AV node. It is often asymptomatic, does not progress, and does not require periodic monitoring.

Note:
Increased vagal tone via the parasympathetic nervous system will result in first-degree AV block and second-degree AV block, Mobitz type 1.

2. **Mobitz type 2**

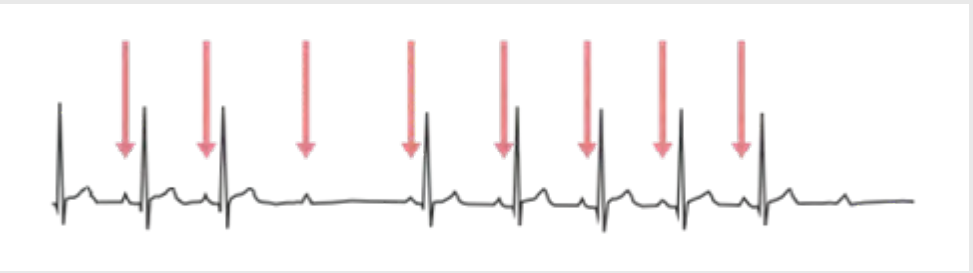


Fig. 8-11: *Second-Degree AV Block, Mobitz 2: A regular rate and rhythm but the impulse from the SA node is periodically dropped, resulting in a normal P wave followed by a drop of the QRS complex and T wave. In this ECG the red arrows indicated P waves.*

Mobitz type 2 second-degree AV block is characterized by intermittent 'dropped beats' (P waves without subsequent QRS complexes and T waves) without any changes in the PR interval. The rhythm on either side of the drop is normal.

Sometimes this drops form a pattern, for example: 3:1 block describes a rhythm where only every third P wave is followed by a QRS complex and T wave. Mobitz 2 second-degree AV block can progress into a third-degree block and requires careful monitoring and usually a pacemaker implantation.

Third-degree AV block

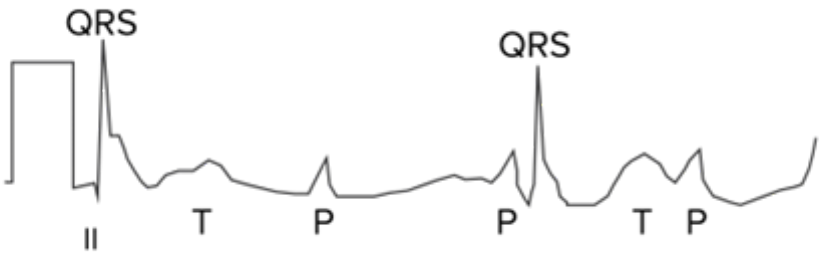


Fig. 8-12: *AV Block Type 3: The atrium and ventricles are out of sync and follow their own pacemakers. In this ECG strip there is compete asynchronicity between P waves and QRS complexes.*

This is also called 'complete heart block', and is characterized by **complete AV dissociation**. It means no relationship between the P waves and QRS complex. Third-degree blocks are very dangerous. Since the intrinsic ventricular rate is about 30 bpm, these patients are symptomatic. Symptoms include syncopal attacks. Cardiogenic shock might occur, requiring immediate emergency treatment. Treatment is the placement of a permanent pacemaker.

Treatment of AV Blocks

Treatment involves periodic monitoring, treating the underlying condition, and stopping medication that may be slowing the heart (acetylcholinesterase inhibitors, beta-blockers, etc.) When determining treatment, it is important to differentiate reversible conditions from irreversible conditions. Reversible conditions do not require a permanent pacemaker. They include:

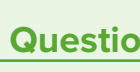
- Increased vagal tone
- Infections (myocarditis, endocarditis)
- Electrolyte imbalance (hyperkalemia, hypermagnesemia)
- Medications (beta-blockers, calcium channel blockers)
- Mild ischemic events

A mild inferior myocardial infarction (MI) may affect the right coronary artery and blood flow to the AV node. Damage to the right coronary artery may result in complete heart block (third-degree AV block), but this is often transient following a mild MI.

Pacemakers

- A temporary pacemaker may be implanted until the heart heals or the underlying condition is resolved.
- Permanent causes of AV block require a permanent pacemaker. These include degenerative changes, fibrotic changes (sarcoidosis and hemochromatosis), and surgery (ablations or valve repair).

Review Questions



FIND MORE QUESTIONS

Test your knowledge:
Arrhythmia

Question 8.3: A 69-year-old male comes to his primary care physician after 2 episodes of dizziness while watching television. On further questioning, he admits to progressive fatigue and shortness of breath on exertion for the past few weeks. His medical history is significant for hypertension for the past 25 years and congestive heart failure for the past 2 years for which he is on multiple medication. His blood pressure is 100/50 mm Hg, heart rate is 50/min and temperature is 36.6 °C (97.8 °F). Physical examination is within normal limits. A 12-lead ECG is obtained and the result shown.
Which of the following is the best initial step for management of this patient?

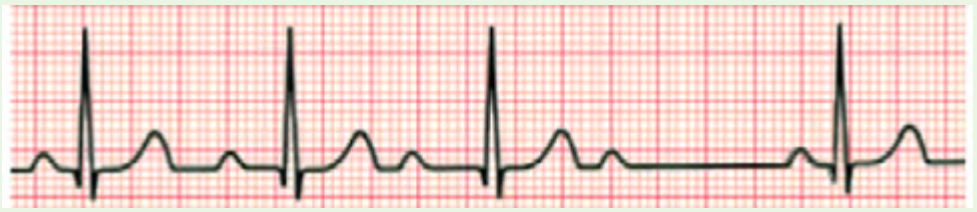


Fig. Q. 8.3

A. Observation and repeating ECG if symptoms recur

B. Temporary cardiac pacing

C. External defibrillation

D. Check the patient medication profile

E. Glucagon

Correct answer: 8.3D

Atrial Flutter

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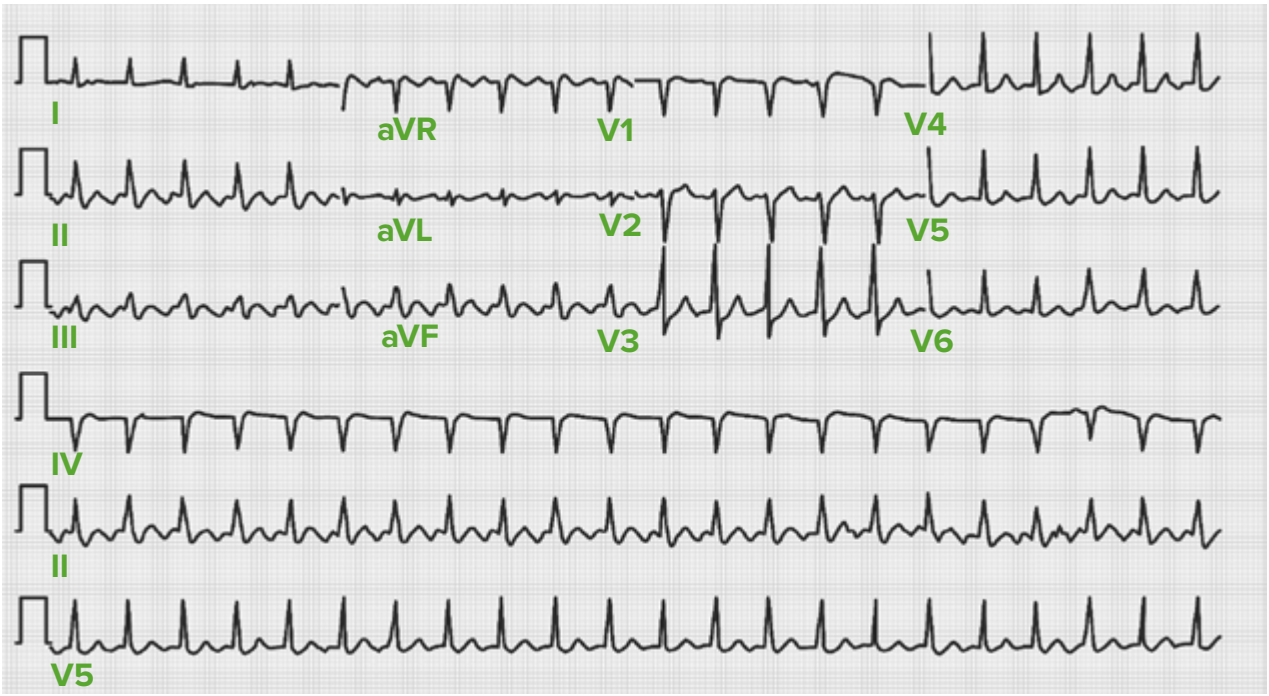


Fig. 8-13: ECG pattern of atrial flutter showing 2:1 ratio

Definition of Atrial Flutter

Atrial flutter is defined as a supraventricular tachycardia with an atrial origin that meets 2 requirements:

- Atrial heart rate between 240–400 bpm
- AV node conduction block

AF is also described by a **saw-tooth pattern** on ECG in leads II, III, and aVF. The QRS complexes will be narrow because the ectopic signal originates in the atrium. The ventricular heart rate will be constant, elevated above 100 bpm, and is considered a regularly irregular rhythm.

It is important to note that the atrial heart rate seen in atrial flutter is different from the ventricular heart rate. 1 of every 2 or 3 depolarization signals may pass through the AV node. A 2:1 or 3:1 ratio of P waves to QRS complexes are commonly seen on ECG. A patient may have an atrial heartbeat of 300 bpm but a ventricular heart rate of only 150 bpm. In this situation, the heart rate would be reported as 'Atrial flutter with a heart rate of 150 bpm'. Patients can be asymptomatic or they can present with some very dangerous symptoms, such as congestive heart failure.

Types of atrial flutter

There are 2 types of atrial flutter:

- **Type 1** – common or 'typical' atrial flutter has an atrial rate of 240–340 bpm and produces a characteristic saw-tooth pattern in leads II, III, and aVF on ECG.
- **Type 2** – atypical flutter is characterized by a much higher atrial rate of 340–440 bpm.

Epidemiology of Atrial Flutter

Atrial flutter is less common than atrial fibrillation. Atrial flutter is 2.5 times **more common in men** compared to women and is more often seen in the elderly with an **average age of onset of 64 years.**

Etiology of Atrial Flutter

A variety of cardiac and pulmonary diseases may result in atrial flutter. Any heart disease that results in inflammation or alteration to the structure of the heart may cause atrial flutter, including cardiomyopathy, congenital heart defects, rheumatic disease, and pericarditis. About 1/3 of patients with atrial flutter may not suffer from other cardiovascular diseases at all; however, about 1/3 of atrial flutter patients have coronary artery disease (angina and myocardial infarction), and another 1/3 suffer from hypertension.

Other common underlying conditions include:

- COPD
- Pulmonary embolism
- Electrolyte imbalance
- Digitalis toxicity
- Hyperthyroidism
- Post-bypass surgery
- Valvular heart disease
- Congestive heart failure

Post surgical structural heart defects (scar formation, ablation) and inflammation may result in atrial flutter. Pulmonary vein isolation to correct atrial fibrillation is also a risk factor. Atrial flutter is considered an unstable rhythm that may progress to atrial fibrillation or revert to sinus rhythm. Other etiologies should be considered in cases of chronic atrial flutter, such as Wolff-Parkinson-White syndrome.

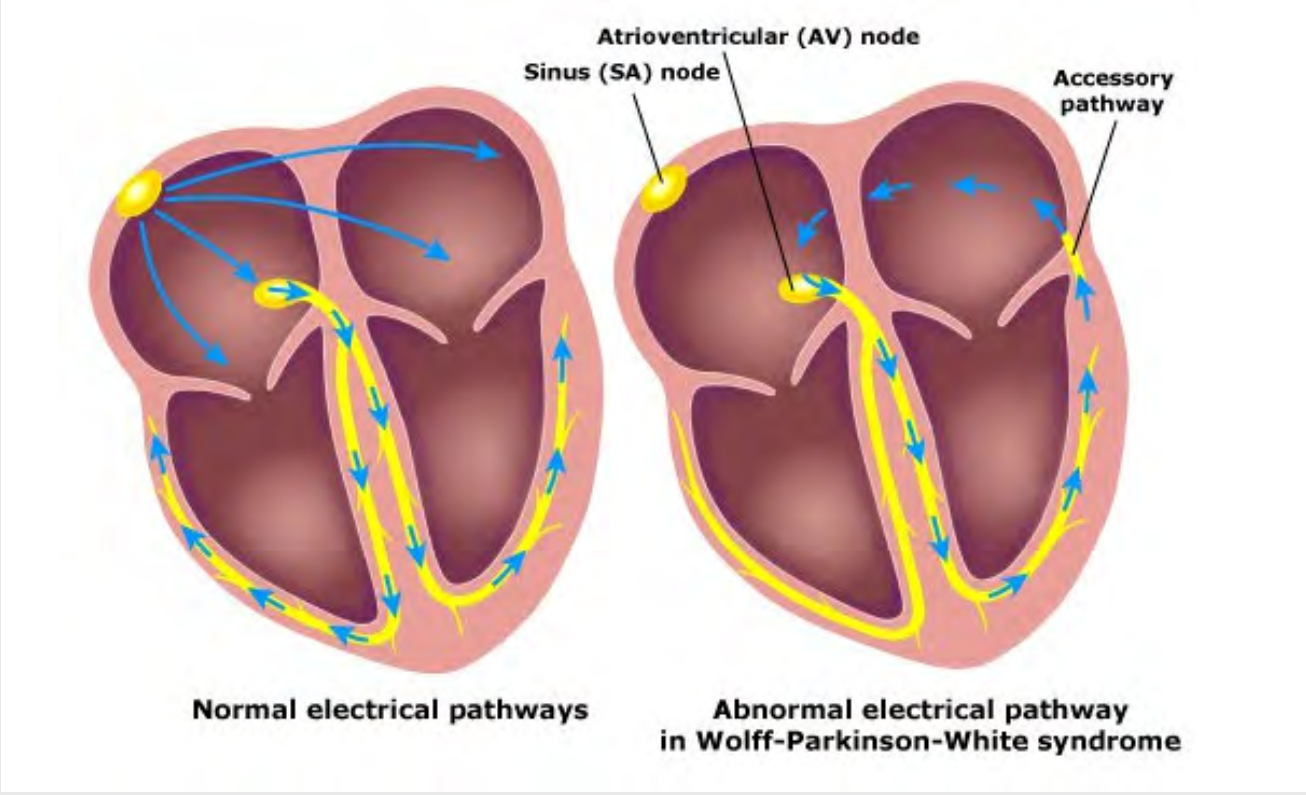


Fig. 8-14: *Wolff Parkinson white syndrome*

Pathophysiology of Atrial Flutter

The most common, type 1 atrial flutter, is caused by a reentrant loop-type arrhythmia with an origin in the right atrium that passes around the tricuspid valve. Type 2 atrial flutter may have an origin in the left or right atrium, pulmonary veins (similar to atrial fibrillation), or the mitral valve annulus.

A reentrant loop-type arrhythmia is characterized as a depolarization signal that moves in a tight circle through the conducting fibers of the heart, resulting in rapid uncontrolled contractions. In atrial flutter, this reentry circuit is limited to the atria. Both type 1 and type 2 atrial flutter require a conduction block; only one of every 2 or 3 contraction signals passes through the AV node, resulting in a ventricular contraction.

Clinical Features of Atrial Flutter

The acute symptoms of atrial flutter are regular palpitations. This is usually well tolerated in a healthy heart in a healthy patient. **However, if patients are deconditioned or suffer from underlying heart disease they may develop symptoms including:**

- Shortness of breath
- Chest pain
- Lightheadedness
- Dizziness
- Nausea
- Feelings of impending doom

A prolonged course of atrial flutter may result in heart failure. Symptoms include:

- Exertional breathlessness
- Edema
- Orthopnea
- Chest pain

Diagnostic of Atrial Flutter

ECG

An electrocardiograph is usually sufficient to diagnose atrial flutter. On ECG, the atrial heart rate of 250–350 bpm (type 1) or 350–450 bpm (type 2) are expressed by P waves. The P waves will have a distinct **saw-tooth shape** and are sometimes called f-waves or **'flutter waves'.** Saw-tooth flutter waves in ECG leads II, III, aVF are sufficient to diagnose atrial flutter type 1. If the flutter waves are upright, the reentry circuit runs clockwise. If the flutter waves are inverted, the reentry circuit loop is counterclockwise (more common). Additionally, QRS complexes are narrow as the ectopic beat originates in the atria. Finally, the atrial and ventricular heart rates will be at a constant ratio. A 2:1 or 3:1 ratio of P waves to QRS complexes is common. Occasionally, the heart rate is too fast to identify saw-tooth flutter waves. **An adenosine infusion** will slow the conduction velocity at the AV node, reducing the ventricular heart rate and increasing the number of observable repeating P waves. This may ease diagnosis. Alternatively, a vagal maneuver may provide the same diagnostic assistance. The most commonly used vagal maneuver in a clinical setting is the Valsalva maneuver.

Echocardiogram

A transthoracic echocardiogram will be part of the standard workup for atrial flutter. This procedure will evaluate the left and right atria and help rule out cardiomyopathy, pericarditis, and valvular heart disease. Additionally, a transesophageal echocardiogram will likely be performed to detect thrombi formation in the the left atrium. Atrial flutter and atrial fibrillation both allow thrombi formation in the left atria that may result in cerebral embolism.

Differential Diagnoses of Atrial Flutter

Atrial flutter should be differentiated from other causes of narrow complex irregular tachycardia:

- Atrial fibrillation
- Atrial tachycardia
- Multifocal atrial tachycardia

Treatment of Atrial Flutter

Treatment of atrial flutter is similar to that of atrial fibrillation. Several options are available, such as rate control, rhythm control, and ablation. In addition, as there is a risk of thrombus formation, anticoagulation therapy must be considered.

Anticoagulation

Atrial flutter of less than 48-hour duration does not require anticoagulation therapy. Anticoagulation is recommended for atrial flutter episodes of unknown duration or those lasting greater than 48 hours, and is required for at least 3 weeks.

Anticoagulation options include:

- Heparin
- Warfarin: maintain an INR of 2–3
- Novel oral anticoagulants (dabigatran, apixaban, and rivaroxaban)

Cardioversion

Cardioversion can be done using either:

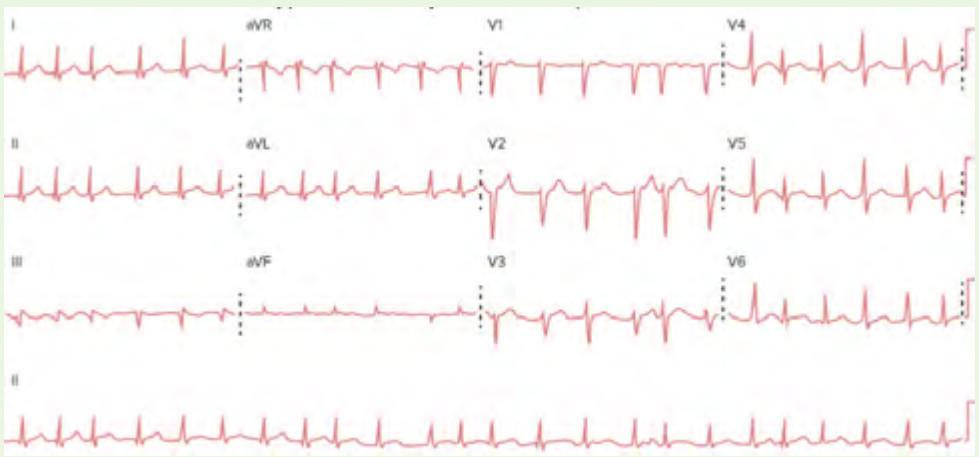
1. Electrical conversion: Uses a **jolt of electricity to reset the heart** and restore a regular rate and rhythm.
2. Pharmacologic conversion: Involves the use of medications (See atrial fibrillation).

If there is no spontaneous cardioversion after medical therapy, electrical cardioversion can be performed (if > 48 hours, after 3–4 weeks of anticoagulation therapy).

Prognosis of Atrial Flutter

Atrial flutter is considered an unstable rhythm that may progress to atrial fibrillation or revert to sinus rhythm. Tachycardia-induced cardiomyopathy may occur if the ventricular rate remains elevated for a prolonged period of time and should be corrected early in the disease process. Additionally, thrombus formation is a concern with atrial flutter or atrial fibrillation. Treatment with catheter ablation is very well tolerated and rarely results in relapse.

Review Questions



Test your knowledge:
Arrhythmia
START QUIZ
FIND MORE QUESTIONS

Question 8.4: A 58-year-old woman comes to the emergency department with difficulty breathing and an unpleasant feeling of her "heart racing" for the past 3 days. She adds that she lost weight despite good appetite in the last 7 weeks and is anxious most of the times with difficulty in sleeping at night. She smokes 10 cigarettes per day for the past 15 years. Her blood pressure is 100/55 mm Hg, her temperature is 36.5 °C (97.7 °F), and her pulse is irregular has a rate of 140–150/min. On physical examination, she looks thin, frail, and rather anxious. Her palms are sweaty and there are fine tremors on the extension of both hands. She has a palpable smooth thyroid mass. Examination of the eyes shows bilateral exophthalmos. An electrocardiogram is obtained and shown. Which of the following has a strong positive correlation with the same type of heart rhythm that this patient has?

Fig. Q. 8.4

A. Digoxin blood level

B. PR interval

C. QT interval

D. Age

E. Amiodarone blood level

Correct answer: 8.4D

Multifocal Atrial Tachycardia (MAT)

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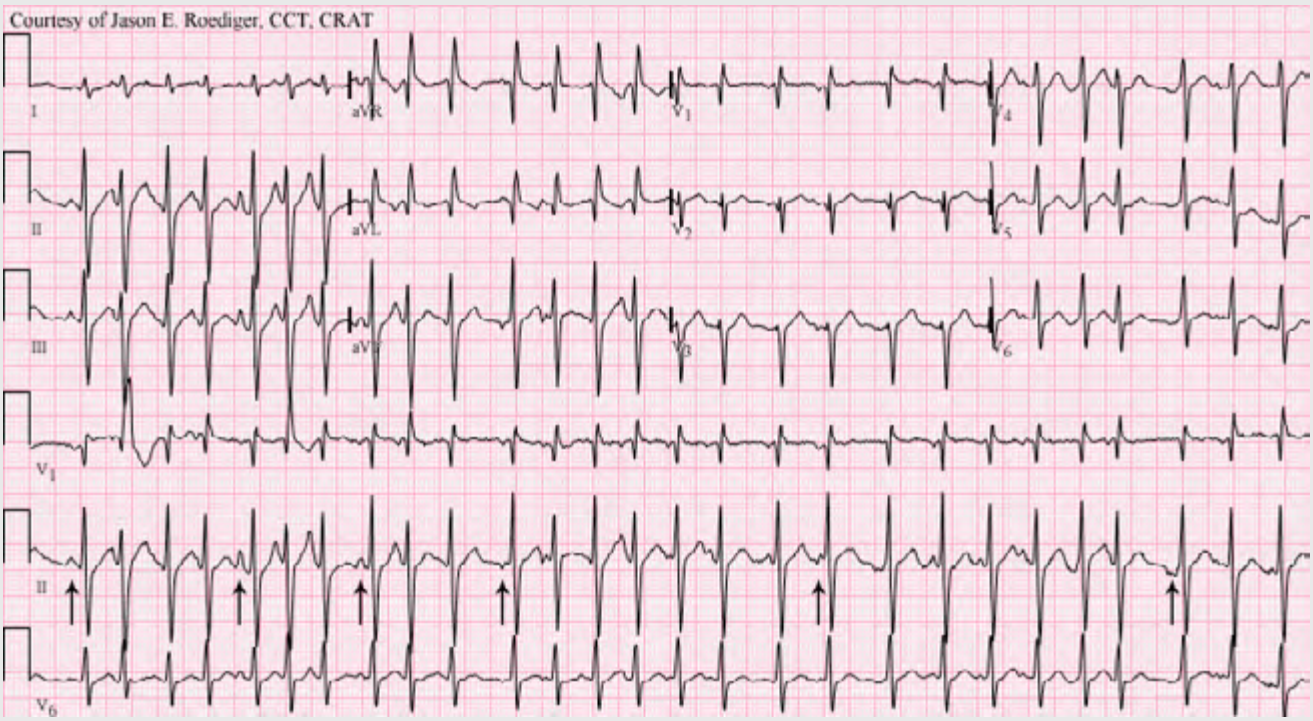


Fig. 8-16: Multifocal atrial tachycardia

Definition of MAT

Multifocal atrial tachycardia is an **atrial** arrhythmia characterized by 3 **or more different P-wave morphologies.**

Pathophysiology of MAT

As the electrical signal passes from the SA node through the walls of the atria, it causes their contraction; the signal slows down allowing the atria to contract before the ventricles. This delay is demonstrated as the PR interval in the ECG. Due to focal pacemaker abnormalities, multiple ectopic atrial pacemakers fire, leading to tachycardia. Rapid abnormal P waves can be seen preceding QRS complexes. The ectopic pacemakers can be located in the left or right atrium. In the former case, it is most often close to the sinoatrial node at a structure called the 'crista terminalis'; if in the left atrium, it is located most commonly near the site of the pulmonary vein. The source of the arrhythmia can be detected with good reliability by 12-lead ECG monitoring.

Etiology of MAT

A multifocal atrial tachycardia implies that **several areas of the heart emit electrical signals simultaneously**. This results in a **greatly increased heart rate**, between 100 and 250 bpm. It occurs commonly in the following cases:

- COPD due to exposure to lung irritants
- Congestive heart failure
- Pulmonary embolism
- Hypertensive heart diseases
- Hyperthyroidism
- Alcohol ingestion
- Electrolyte disturbances (hypokalemia)

Clinical Features of MAT

Patients affected by multifocal atrial tachycardia can be asymptomatic or they can present with complaints of palpitations, irregular heart rate, fatigue, angina, dyspnea, lightheadedness, and syncope. If symptoms occur, they manifest sporadically. The most common symptoms are **palpitations and fainting**.

Diagnostics of MAT

ECG

There are some diagnostic features associated with multifocal atrial tachycardia:

- Greater than 100 bpm (usually 100–250 bpm)
- ECG reveals multiple P wave morphologies
- At least 3 distinct P wave morphologies in the same lead
- If less than 100 bpm = wandering atrial pacemaker

ECG holter monitor

Patient can be monitored over 24 hours while carrying out routine activities to record any abnormal arrhythmias using this device.

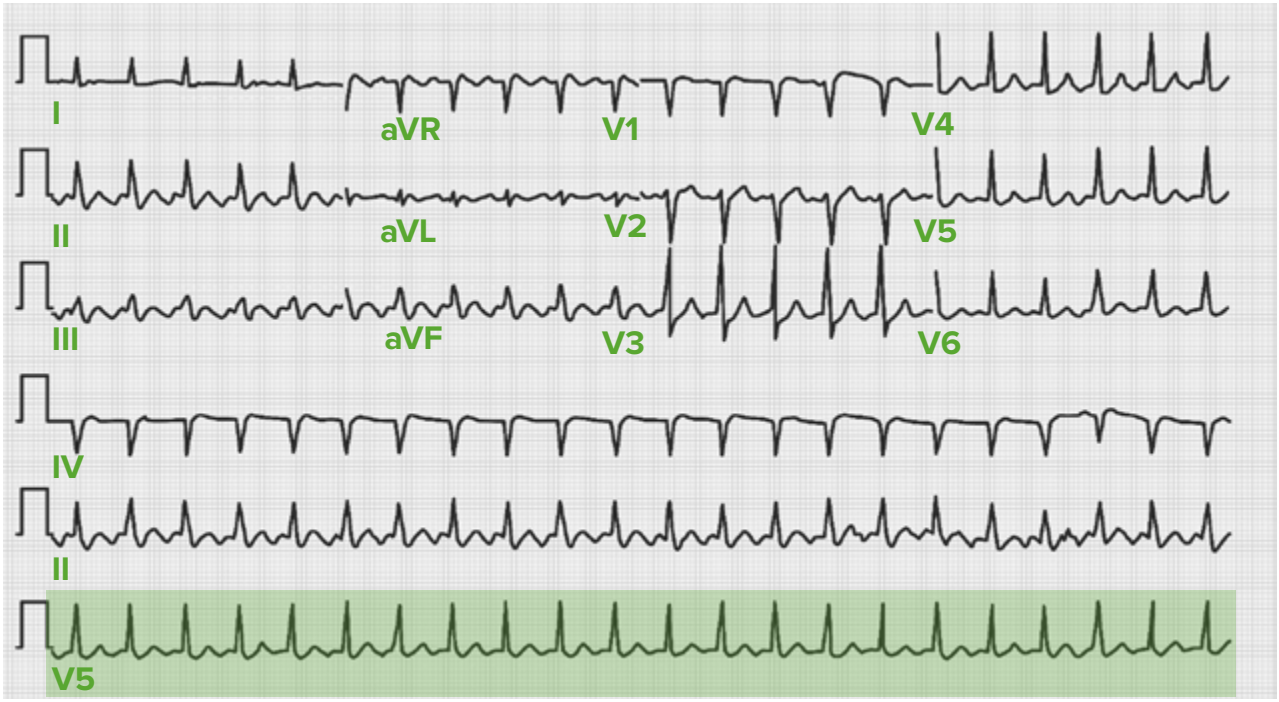


Fig. 8-17: ECG recording of multifocal atrial tachycardia

Treatment of MAT

The first step in the management of multifocal atrial tachycardia is to treat the **underlying cause**, which may include:

1. Stop any precipitating drugs, such as theophylline.
2. **Electrolytes disturbances should be corrected**, such as magnesium and potassium.

Heart rate controlling drugs

Several drugs can be used to control heart rate based on indications and contraindications, such as:

1. Calcium channels blockers
2. Beta-blockers
3. Amiodarone

Invasive procedure

People with uncontrollable multifocal atrial tachycardia may be treated with **atrioventricular ablation of the tissues** that send signals of contraction and implantation of a **permanent pacemaker**.

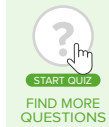
Prognosis of MAT

The symptoms of multifocal atrial tachycardia can be properly controlled as long as the underlying condition causing the high heartbeat is controlled. There are **several long term complications** associated with multifocal atrial tachycardia that may develop over time, such as tachycardia-induced cardiomyopathy.

The natural course of multifocal atrial tachycardia is a spontaneous resolution within weeks or months. For cases requiring medical treatment, this can be terminated after that period. Long term prognosis is good, with no late recurrence.

Note:
Cardioversion is ineffective since the arrhythmia is frequently recurrent.

Review Questions



Test your knowledge:
Arrhythmia

Question 8.5: A 68-year-old male comes to the emergency department accompanied by his wife because of difficulty breathing and chest tightness for 3 days. He also has a productive cough with excessive amounts of green sputum. He has a chronic obstructive pulmonary disease for the past 10 years but says that this time, the cough and the sputum are different compared to his baseline. He took 2 doses of nebulized albuterol and ipratropium at home but that did not relieve his symptoms completely. He has a 50-pack-year smoking history and drinks alcohol occasionally. His vital signs include a blood pressure of 110/60 mm Hg, a temperature of 37.2 °C (98.9 °F), respiratory rate of 26/min, irregular radial pulse at a rate of 110–120/min, and oxygen saturation of 88 %. On physical examination, the patient looks drowsy, crepitations on both sides of the chest are heard, and heart sounds are irregular. Chest X-ray shows hyperinflation of both lungs and flattened diaphragms. An ECG is ordered and shown. Which of the following is the best initial treatment for this patient arrhythmia?

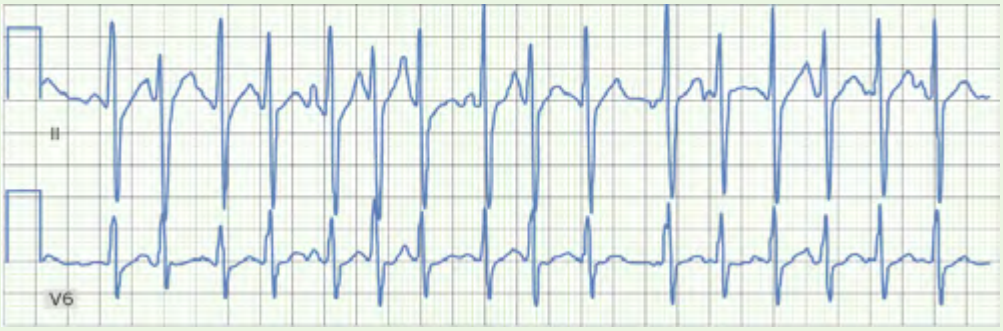


Fig. Q. 8.5

A. Diltiazem

B. Reversing bronchoconstriction and electrolyte correction

C. Synchronised cardioversion

D. Catheter ablation of the cavotricuspid isthmus (CTI)

E. Metoprolol

Correct answer: 8.5B

Wolff-Parkinson-White (WPW) Syndrome

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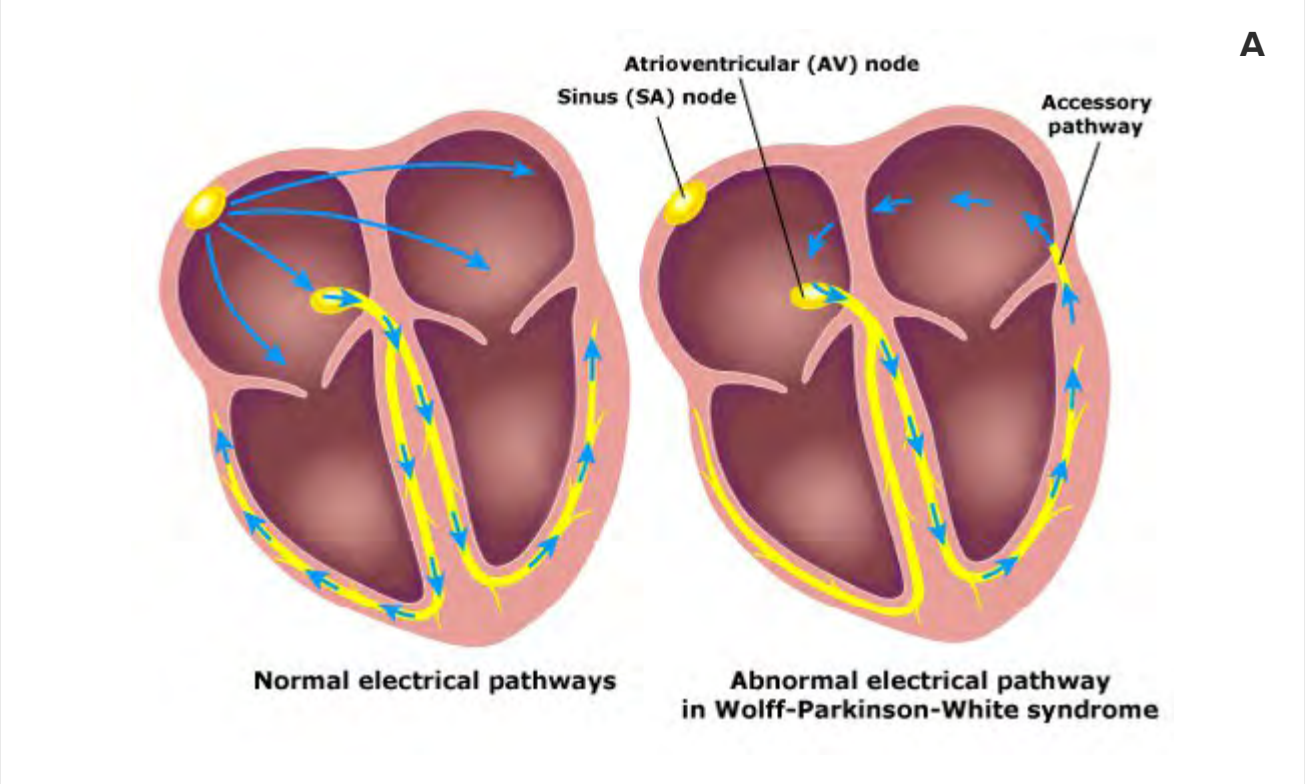


Fig. 8-18: (A) Wolff-Parkinson-White syndrome (B) WPW syndrome ECG

Definition of WPW

Wolff-Parkinson-White syndrome (WPW), also known as bypass tract or pre-excitation syndrome, is characterized by attacks of tachycardia due to the existence of alternative electrical pathways directly connecting the atria and ventricles, bypassing the AV node. The prognosis and long-term outcome of WPW is very good after proper treatment.

Epidemiology of WPW

The prevalence of WPW syndrome and pattern is **less than 1 % of the population** with the WPW pattern being 100 times more common than WPW syndrome. The difference between both will be discussed later in this eBook.

Pathophysiology of WPW

Normally, **both atria and ventricles are electrically isolated, where the discharged electrical impulses move from the SA node in the right atrium to the ventricles via the atrioventricular node** (AV) and the His-Purkinje system.

Fig. 8-19: *A characteristic delta wave seen in a patient with WPW. Note short PR interval.*

AV conduction is through the AV bypass tract (bundle of Kent), an anatomical accessory pathway (AP) which conducts the impulses from atria to ventricles. This directly causes earlier ventricular activation than when activated by the AV node (pre-excitation). As a result, a short PR interval is seen on an ECG recording. This accessory pathway is congenital in origin, and results from the failure of resorption of the myocardial syncytium at the annulus fibrosus during fetal development.

- About 75 % of the AP can conduct the impulses in both directions (anterograde and retrograde) between the atrium and ventricle.
- About 35 % of APs are only able to conduct impulses retrograde from the ventricle to the atrium and are so-called ‘concealed’ accessory pathways. Most of these are left-sided, which don’t create a delta wave or WPW pattern on the ECG, but are still able to support reentrant tachycardia.
- About 25 % of APs only conduct impulses anterograde from the atria to the ventricles.

The mechanism of unidirectional conduction of impulses along the accessory pathway in either **anterograde** or **retrograde** direction remains undetermined.

WPW is simply a pre-excitation syndrome, it can be associated with some types of arrhythmias discussed in this eBook, and with hypertrophic cardiomyopathy and Ebstein‘s anomaly of the tricuspid valve (lithium toxicity).

Anatomy of accessory atrioventricular pathways

Based on electrophysiological studies, accessory atrioventricular pathways are located anywhere along the AV ring or in the interventricular septum. The most frequently documented locations are:

- 50 % → Left lateral
- 30 % → Posteroseptal
- 10 % → Right anteroseptal
- 10 % → Right lateral

WPW pattern and WPW syndrome

Patients with an accessory pathway (AP) can be described as having either WPW pattern or WPW syndrome based on the absence or the presence of arrhythmias respectively.

Wolff-Parkinson-White pattern

This term is applied to a patient with ECG findings of pre-excitation in the **absence of symptomatic arrhythmias.**

Wolff-Parkinson-White syndrome

This term is applied to a patient with ECG findings of pre-excitation and **symptomatic arrhythmias**. In either situation, anterograde conduction of the impulses, from the atria to ventricles through an AP, will result in earlier activation or pre-excitation of part of the ventricles.

Classification of WPW

Arrhythmias associated with WPW

WPW syndrome can be associated with either:

1. **Tachycardias requiring an accessory pathway for initiation and maintenance**

   Atrioventricular Reentrant Tachycardia (AVRT): Occurs when the heart has a circuit which consists of 2 pathways: Normal AV conduction system and the AV accessory pathway, where both are linked by tissue. If there are adequate differences in conduction time and refractoriness between the normal conducting system and the bypass tract, premature impulse from the atrium of the ventricle can initiate reentry. The main 2 types of this arrhythmia in WPW syndrome are **orthodromic and antidromic AVRT.**

2. **Tachycardias not requiring an accessory pathway for initiation and maintenance**

   The heart consists of an accessory pathway, but this is not involved in the initiation of the arrhythmia and includes: **Atrioventricular Nodal Reentrant Tachycardia (AVNRT)**, ventricular tachycardia and **ventricular fibrillation.** Patients with accessory pathways are at risk of atrial fibrillation. If the AP rapidly conducts the impulses retrograde from the atrium to the ventricle in a patient with AF, a rapid ventricular response would occur which may result in ventricular fibrillation.

Clinical Features of WPW

The vast majority of patients with WPW pattern are **asymptomatic**, while a **small percentage have arrhythmias** (for example, AF with rapid ventricular response) and thus WPW syndrome. Patients with a WPW syndrome and developed arrhythmia can present with any of the following manifestations:

- Palpitations
- Lightheadedness and/or dizziness
- Syncope or presyncope
- Chest pain
- Sudden cardiac death

Diagnostics of WPW

WPW pattern

Diagnosis of WPW pattern requires only **ECG** which shows characteristic findings.

WPW syndrome

Diagnosis of WPW syndrome involves the **identification of WPW pattern on surface ECG** of a patient who develops arrhythmia, especially in young adults presenting with paroxysmal arrhythmia.

ECG findings

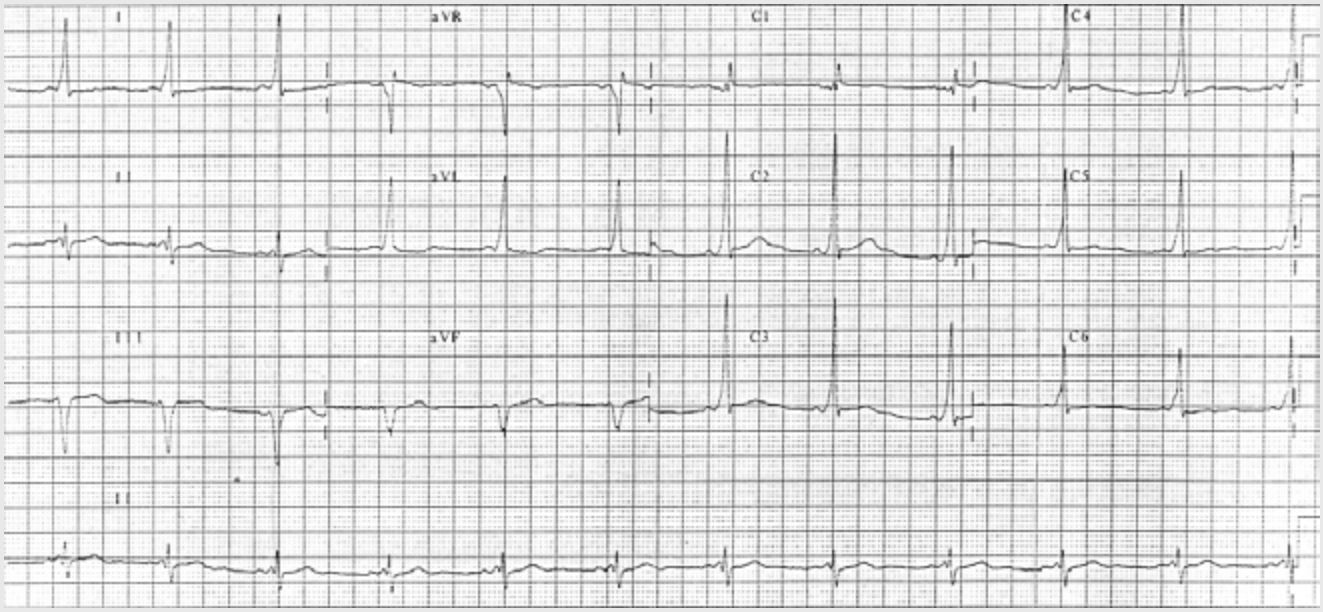


Fig. 8-20: A 12-lead ECG demonstrating Wolff-Parkinson-White syndrome with characteristic delta waves.

The main feature of AV accessory pathway is **pre-excitation**, where the ventricles are activated by direct activation of the myocardium throughout the accessory pathway; the ventricles are therefore activated earlier than expected after atrial depolarization, resulting in:

- **Shortening of the PR interval (less than 0.12 seconds)**, occurs as a result of rapid AV conduction via the accessory pathway, bypassing the AV node.
- **Delta wave**, which arises because the initial stages of ventricular depolarization are slowed and the QRS complex upstroke is slurred. This is due to the slowing of conduction from muscle fiber to muscle fiber, otherwise referred to as slow muscle fiber conduction velocity.
- **Widening of the QRS complex.**

Concealed APS

As mentioned before, in about 35–50% of patients accessory pathways conduct one-way impulses retrograde from the ventricle to the atrium. In this condition, the AP manifests only during sustained tachycardia. Concealed AP can be identified by the time, and by how the atrium is activated during tachycardia:

- **P wave follows the ventricular depolarization and a short RP wave interval** can be seen.
- Sometimes APs conducts impulses retrograde very slowly, which may result in a longer retrograde conduction, and developing a **longer RP interval during tachycardia** (long RP tachycardia).

Treatment of WPW

Patients with Wolff-Parkinson-White syndrome are treated because they either have:

1. Symptomatic arrhythmia
2. Risk of arrhythmia, for example, pre-excited atrial fibrillation, or atrial flutter with a rapid ventricular response

Asymptomatic

Asymptomatic WPW pattern doesn't require treatment.

Symptomatic

In case of symptomatic WPW syndrome, treatment should be aimed at **preventing the rapid ventricular response** if the patient manifests with pre-excitation and AF in order to avoid atrial fibrillation.

- **Unstable patients:** Treatment of choice is synchronized electrical cardioversion if patient is hemodynamically unstable.
- **Stable patients:** Stable patients with WPW should be treated with Procainamide infusion at a dose of 15 mg/kg which will slow the rapid ventricular response and may correct the AF.

Note:
AV nodal blocking agents (calcium channel blockers, beta-blockers, adenosine, digoxin and amiodarone) are contraindicated in patients with WPW!

Long term management of WPW

Long term management of WPW includes medical treatment to control recurrent palpitations and catheter radiofrequency ablation.

Medical treatment

Patients with atrial fibrillation (AF) and rapid ventricular response should receive class IA or IC antiarrhythmic drugs, such as quinidine, flecainide or propafenone, to slow conduction through the accessory pathway (AP) and increase its refractory period.

Catheter radiofrequency ablation

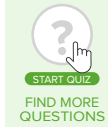
Definitive treatment is with ablation of the accessory pathway.

Catheter ablation therapy appears to be **effective in more than 90 % of patients** in the treatment of WPW syndrome regardless of age.

It is indicated in patients with a history of:

1. Recurrent symptomatic SVT episodes
2. Incessant SVT
3. Heart rates > 200 beats/min with SVT

Review Questions



Test your knowledge:
Arrhythmia

Question 8.6: A 32-year-old man comes to the urgent care clinic because of rapid pulsations in his chest, shortness of breath, and lightheadedness for the past 2 hours. He never had such symptoms before and does not have any chronic health condition. He drinks alcohol socially but does not smoke. His vital signs include a blood pressure of 100/60 mm Hg and a regular pulse of 140/min. An ECG is ordered and the result is shown (picture 1). The patient is given adenosine intravenously and his symptoms stop. A repeat ECG 1 hour later shows the following (picture 2). Which of the following is the cause of the patient's problem?

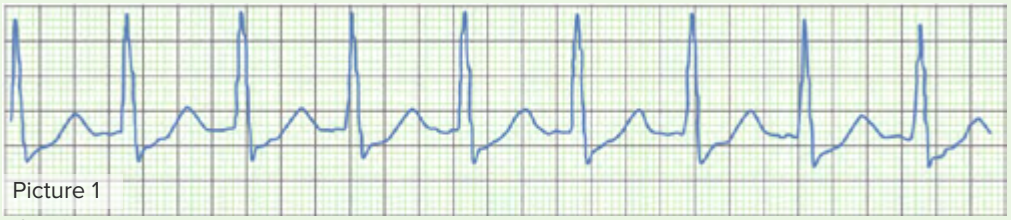


Fig. Q. 8.6.1

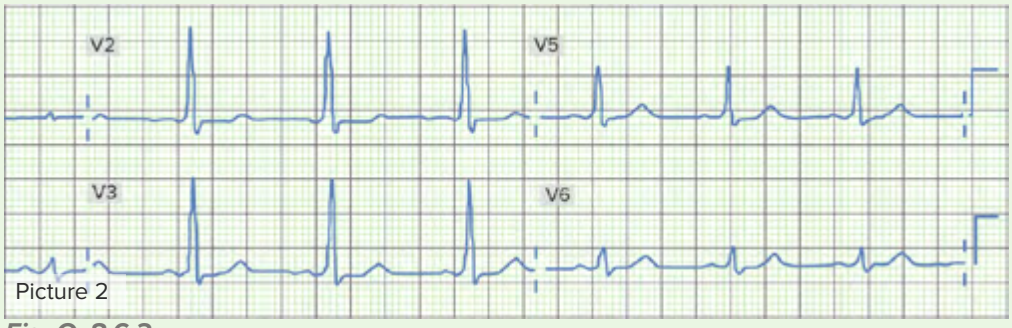


Fig. Q. 8.6.2

A. Anemia

B. Atrioventricular reentrant tachycardia from accessory conduction pathway

C. Premature ventricular complex

D. Intense emotional episodes

Correct answer: B

Ventricular Tachycardia (VT)

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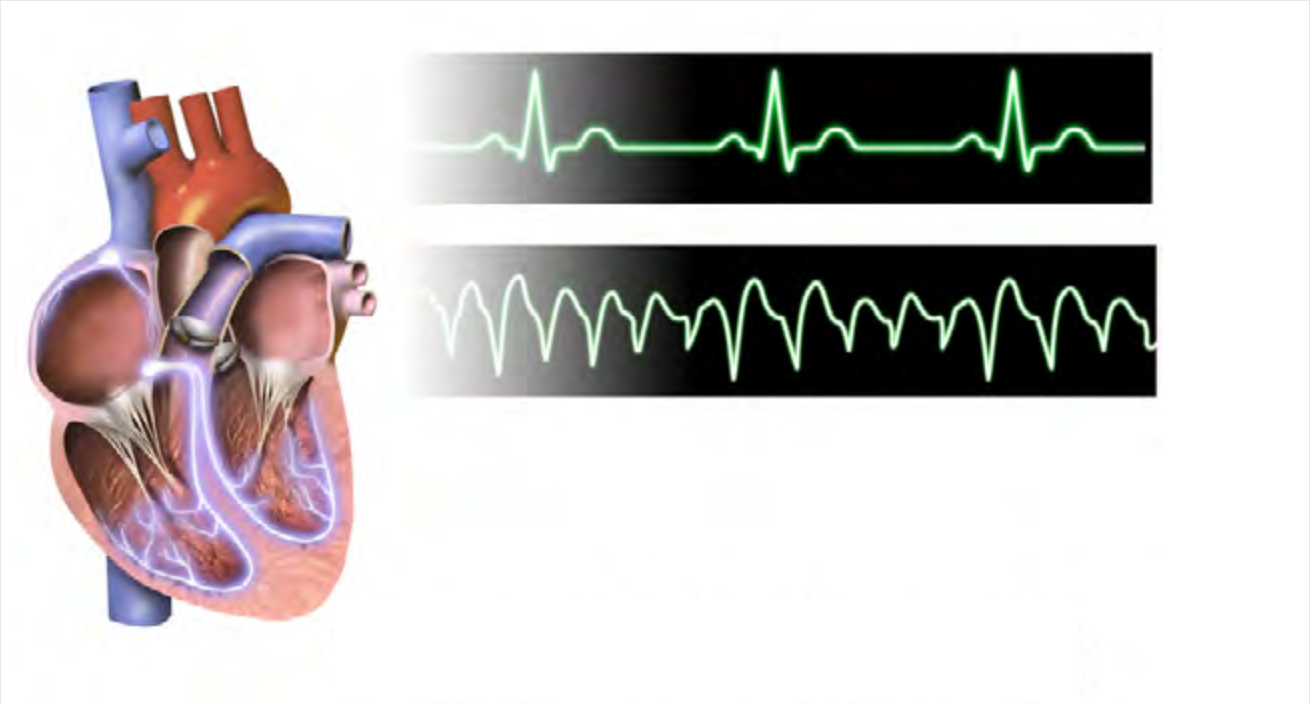

Fig. 8-21: Ventricular tachycardia

Definition of VT

Ventricular tachyarrhythmia (VT) is a life-threatening arrhythmia characterized by a broad QRS complex (> 120 ms) and tachycardia (HR > 120 bpm), resulting in palpitations, syncope, and sudden cardiac death.

Epidemiology of VT

VT makes up **about half the cardiac mortality rate** in the United States. **Incidence increases with age**, as the incidence of coronary artery disease increases. Half of all deaths due to coronary artery disease are caused by VF. VF is found **more frequently in men** than in women; however, torsades de pointes is more frequently found in women.

Classification of VT

Based on duration of VT

- **Non-sustained VT**: Short, lasting less than 30 seconds.
- **Sustained VT**: Longer than 30 seconds.

Based on the origin of the ectopic beat

- **Monomorphic ventricular tachycardia**: Repeatedly originates in the same place.
- **Polymorphic ventricular tachycardia**: Ectopic beat arises in different locations around the ventricle, such as in **torsades de pointes**.

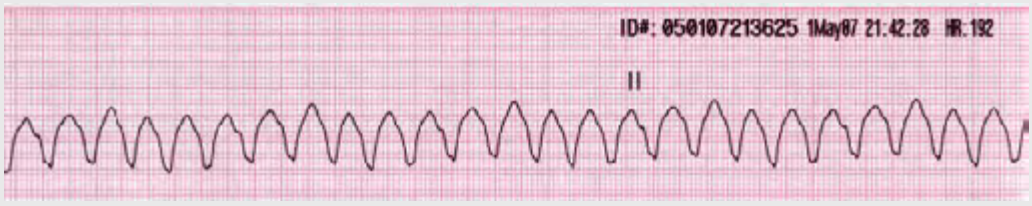

Fig. 8-22: Monomorphic ventricular tachycardia

Monomorphic ventricular tachycardia

Monomorphic ventricular tachycardia is a **simple, rapid heart rate with an ectopic beat** originating in the ventricles. The ectopic beat is constant, and the QRS wave on ECG will be abnormal but consistent. There is a risk of **hemodynamic collapse** and **sudden cardiac death** in all patients with ventricular tachycardia.

Ventricular tachycardia is further divided into ventricular tachycardia with a pulse, and pulseless ventricular tachycardia. In **pulseless tachycardia**, the heart rate is too rapid and the rhythm too uncoordinated to pump blood. This condition should be treated like ventricular fibrillation. Advanced cardiac life support measures should be started immediately, including cardiac monitoring, oxygen, medication, and cardioversion if necessary.

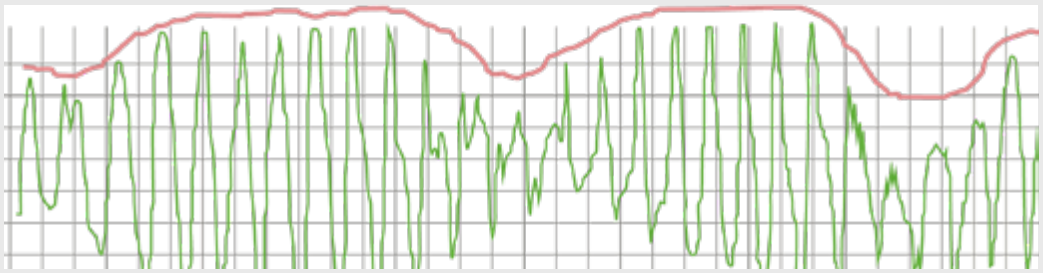

Fig. 8-23: Polymorphic tachycardia (torsades de pointes). The red line shows the characteristic 'twist' around the isoeclectric baseline.

Polymorphic ventricular tachycardia

Polymorphic ventricular tachycardia **(torsades de pointes)** is a ventricular tachyarrhythmia with a **rapidly changing rate and rhythm**. The rate can change between 150–250 bpm and the amplitude also changes when observed by ECG. This arrhythmia may spontaneously revert to normal or progress into ventricular fibrillation.

Torsades de pointes is closely associated with a prolonged QT interval due to abnormal ion regulation in the cardiac muscles of the heart; any medications and genetic disorders that result in prolonged or delayed repolarization may result in early afterdepolarization and torsades de pointes.

Note:
Torsades de pointes is a life-threatening polymorphic VT that appears to twist around the isoelectric line. Best initial medical treatment is IV magnesium sulfate.

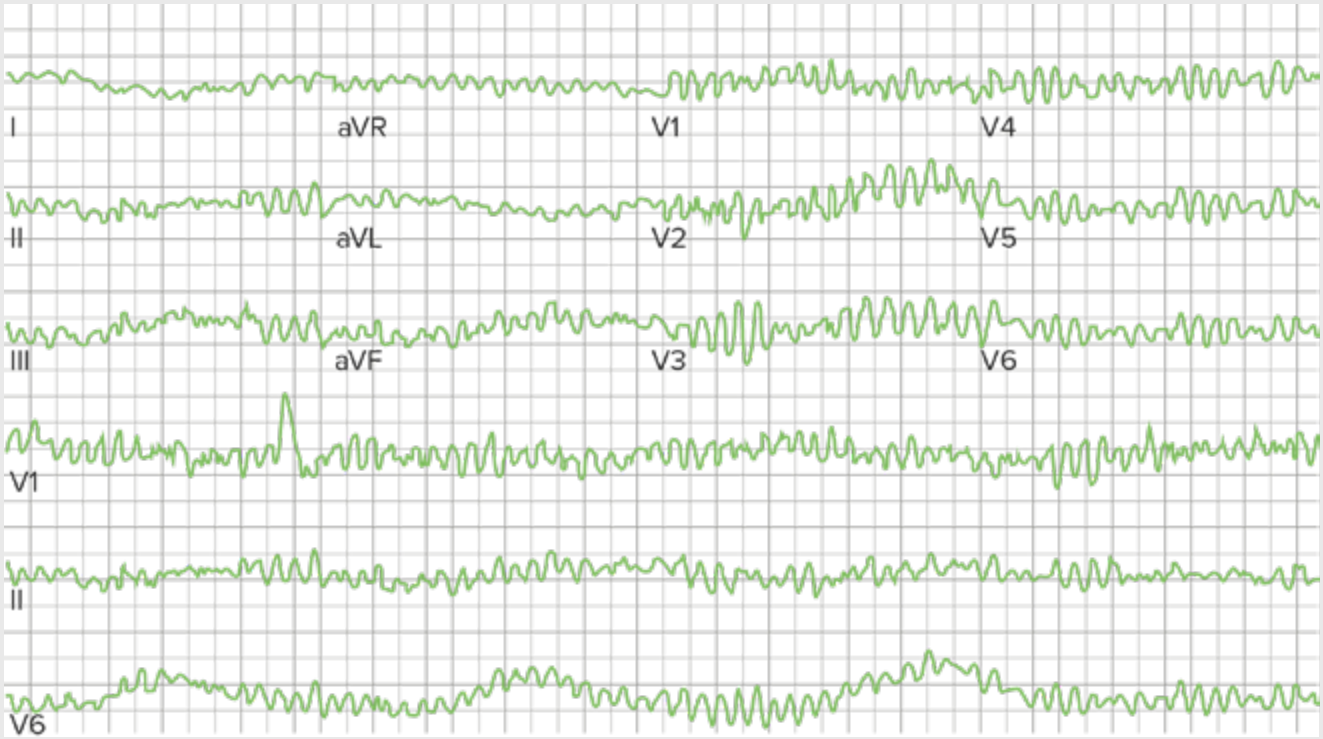

Fig. 8-24: Ventricular fibrillation

Ventricular fibrillation (VF)

Ventricular fibrillation is a more severe ventricular tachyarrhythmia due to disorganized, uncoordinated ventricular contractions that result in immediate hemodynamic collapse. Death is likely within minutes unless advanced cardiac life support measures are started immediately.

ECG characteristics of VF

- Fibrillatory baseline, usually > 300 bpm
- Indiscernible QRS complexes
- No atrial P waves

Etiology of VT

Coronary artery disease and MI

The most common cause of VT is **ischemic heart disease**, often after an MI. Scar formation via surgery or infiltrative cardiomyopathy due to systemic inflammatory diseases such as sarcoidosis, amyloidosis, and hemochromatosis also increase the risk for VT. Coronary artery disease is a major risk factor for VF, and extensive coronary artery occlusion is the most common pathologic finding. Restoring coronary artery flow has demonstrated a reduced risk for VF.

Non-ischemic cardiomyopathy

Dilated cardiomyopathy increases the risk for VF. It is the most common type of non-ischemic cardiomyopathy and is associated with ventricular remodeling and an increased ventricular volume. **Hypertrophic cardiomyopathy** is frequently related to a genetic disorder (autosomal dominant) and also increases the risk of VF. Hypertrophic cardiomyopathy is the most common cause of ventricular fibrillation in patients under 30 years old. **Takotsubos** cardiomyopathy increases the risk for developing torsades de pointes. Takotsubos (broken heart syndrome) is associated with acute heart wall weakness and severe stress.

Long QT

Some patients have a naturally long QT interval. The QT interval is measured on an ECG strip from the start of the Q wave to the end of the T wave and represents the **depolarization and repolarization of the ventricles of the heart**. Certain medications can also prolong the QT interval (tricyclic antidepressants, phenotiazines, quinidine, procainamide, disopyramide, fluoroquinilone antibiotics, azithromycin, antifungals (azoles), and psychiatric medications such as haloperidol, methadone, and ziprasidone). A prolonged QT interval can result in polymorphic ventricular tachycardia and torsades de pointes. Other conditions can prolong the QT interval such as hypothyroidism. It is also common in type 1 diabetes.

Electrolyte imbalance

Electrolyte imbalance can lead to arrhythmias anywhere in the heart. The heart is most sensitive to low levels of **potassium** (hypokalemia), **calcium** (hypocalcemia), and **magnesium** (hypomagnesemia).

Digitalis toxicity

Digitalis toxicity may result from excess use or an abnormal reaction to the drug and increases the risk of developing monomorphic ventricular tachycardia.

Ventricular tachyarrhythmias are **abnormal** and **potentially deadly** arrhythmias. They are caused by an abnormal ectopic contraction in the ventricle. The condition may be benign if the ectopic signal is regular and stationary, and cardiac output is maintained; however, if the signal moves around the ventricle or if the rate changes rapidly, this arrhythmia could quickly result in cardiovascular collapse and death. Ischemic change following coronary artery disease or a myocardial ischemic event is the most common cause of VT due to scar formation.

The normal electrical signal slows as it passes through the scar tissue. This pause allows the surrounding ventricle to repolarize. The slowed signal then depolarizes the repolarized ventricular tissue before the supraventricular signal has a chance to pass through the ventricular conduction fibers. The ectopic beat causes the ventricle to beat rapidly (greater than 100 bpm) and **out of sequence with the atria**. The result is a **drop in cardiac output** and, potentially, sudden death. If the rapid ventricular contraction rate is tolerated, then arrhythmia may cause cardiomyopathy over time.

Clinical Features of VT

Symptoms include:

- Dizziness and syncope secondary to decreased CO
- Palpitations
- Lightheadedness
- May lead to ventricular fibrillation and cardiac arrest
- Sudden cardiac death, especially during ventricular fibrillation

In torsades de pointes, the patient is unconscious and at severe risk of sudden cardiac death.

Pathophysiology of VT

These symptoms often cause the patient to become anxious and agitated. Hypoperfusion to the brain may result in lethargy or coma. Additionally, the patient may describe a sensation of fullness in the neck and difficulty breathing as the venous blood pools and venous pressure increases. On physical exam, patients with VT will present with **tachycardia**. Due to low cardiac output, they may also present with **hypotension and tachypnea**. VT is also associated with cannon A waves. In this condition, the atria and ventricle contract at the same time, producing a strong pressure wave against the mitral and tricuspid valves of the heart. The wave may be visible as it passes up the jugular vein.

Other symptoms include jaw pain and cough. Other conditions may also produce a cannon A wave including pulmonary hypertension and complete heart block (third-degree AV block). There may be some short-term or permanent physical changes after VT has been converted to a sinus rhythm. Displacement of the point of maximal impulse is possible. Any structural heart changes that result in valve disease may produce a murmur. An S3 gallop may also develop.

Diagnostics of VT

Ventricular tachyarrhythmias are **potentially life-threatening**. If VT is a concern, advanced cardiac life support measures should be activated while making the diagnosis.

ECG

An electrocardiogram and physical findings are sufficient to diagnose VT. ECG signs of VT are:

- > 3 consecutive PVCs
- Wide complex tachycardia (QRS > 120 msec)
- AV dissociation (P waves independent of QRS)
- Fusion beats, precordial concordance
- Appearance is typically different to usual RBBB and LBBB patterns

Laboratory studies

Measure electrolytes for abnormally high or low levels, especially **potassium, calcium, and magnesium**. Test blood for **medications** that may prolong QT or induce VT, such as digoxin or tricyclic antidepressants. Test for recreational **drugs** such as cocaine and methamphetamines. Evaluate the heart for damage by measuring cardiac **enzymes** including troponin I and troponin T.

Differential Diagnoses of VT

Differential diagnosis of wide-complex tachycardia

- Ventricular tachycardia (VT): Any wide complex tachycardia is a VT until proven otherwise.
- Pacemaker rhythm: wide complex ECG with artificial spikes.
- SVT with conductive aberrations.

Differentiating SVT with aberrations from VT

- SVT has narrow-complex tachycardia with P waves preceding each QRS.
- AV dissociation (P waves independent of QRS) favors VT.

Treatment of VT

Short term

Ventricular tachycardia may result in hemodynamic collapse and requires **life-saving measures** to restore normal sinus rhythm. Sustained VT requires immediate intervention:

Unstable patient

Immediate cardioversion with DC shock:

- Synchronized DC shock: If VT with pulse.
- Non-synchronized defibrillation: If pulseless VT.

In left ventricular dysfunction, cardioversion should be carried out with amiodarone or lidocaine; these antiarrhythmics are preferred because they will not exacerbate left heart failure, while procainamide may.

Stable patient

If patient is stable, give IV amiodarone or lidocaine, but failure to convert may require immediate electrical cardioversion. If ventricular tachycardia is the result of digitalis toxicity treat with anti-digitalis antibody and cardiovert to normal sinus rhythm. In torsades de pointes, **IV magnesium sulfate** should be administered, along with immediate electrical cardioversion.

Long term

The goal of long-term treatment is to prevent ventricular tachycardia with the most effective and conservative treatment available. Treatment options include medication **(antiarrhythmics), ablation**, and an **implantable cardioverter-defibrillator.** Additionally, evaluate the QT interval and remove and change medications that may unnecessarily prolong it.

Cardiovert it if unstable!

Antiarrhythmics: amiodarone, procainamide, sotalol

If regular and monomorphic, consider adenosine instead

Fig. 8-25: *Treating VT*

Prognosis of VT

Prognosis is dependent on several characteristics but is usually determined by left heart function. Patients with ventricular tachycardia and left heart dysfunction are much more likely to suffer from hemodynamic collapse and sudden cardiac death.

Review Questions

Question 8.7: A 72-year-old man is taken to the Emergency Room after he loses consciousness. According to his wife, he suddenly started complaining about fluttering in his chest, lightheadedness and started sweating heavily while walking to the grocery store. A minute later, he turned gray, lost consciousness, and collapsed onto the ground. Past medical history is significant for a prior anterior wall myocardial infarction 2 years back complicated by severe left ventricular systolic dysfunction. His blood pressure is 80/50 mmHg, temperature is 36.7 °C and carotid pulse is not palpable. ECG is shown. Cardiopulmonary resuscitation is initiated and the patient is cardioverted to sinus rhythm with an external defibrillator. The patient regains consciousness. There was no antecedent chest discomfort. Cardiac enzymes are negative and serum electrolytes are normal. Which of the following is the best next step for this patient?

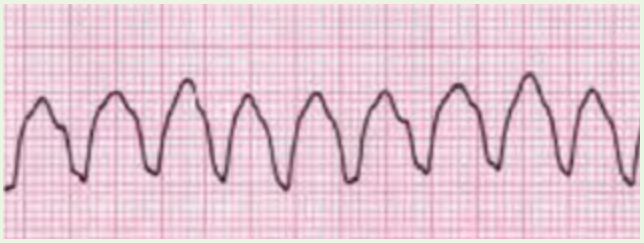

Fig. Q. 8.7

A. Intravenous metoprolol

B. Intravenous magnesium sulphate

C. Implantable cardioverter defibrillator

D. Intravenous adenosine

E. Temporary or permanent cardiac pacing

Correct answer: 8.7C

Chapter 9:
Common Vascular Disorders

Aortic Dissection (AD)

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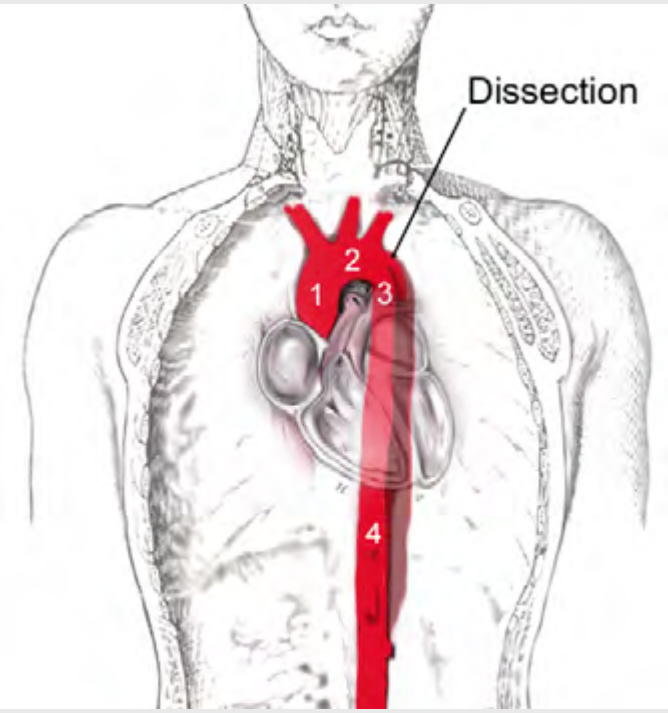

Fig. 9-01: Dissection of the descending aorta (3), which starts from the left subclavian artery and extends to the abdominal aorta (4). The ascending aorta (1) and aortic arch (2) are not involved.

Definition of AD

Aortic dissection is an emergent condition characterized by tears in the innermost layer (tunica intima) of the aorta and leading to the separation of tunica intima and tunica media, with the formation of a new false channel. This creates pressure on the layers of blood vessels that forcibly separates them, causing severe pain, characteristically known as tearing pain. This is a serious medical emergency as it can partially occlude branches of the aorta and reduce blood flow to the rest of the body, resulting in insufficient supply of blood and nutrients to the vital organs. In severe cases, the aorta can rupture and cause rapid death.

Epidemiology of AD

Aortic dissection is a rare condition in which new cases are reported at a rate of 2–3.5 per 100,000 people every year. It is more common in men than women as 65 % of all dissections are reported in males. 50 % of cases of aortic dissection in women are reported in pregnant women under the age of 40 years (rare).

People aged 40–70 years are more likely to develop this condition, and account for almost 75 % of dissections. Its peak incidence occurs at 50–65 years of age. Dissections that occur at 30–40 years of age are usually associated with genetic predisposition and/or connective tissue diseases such as Marfan syndrome. 90 % of cases occur in males with hypertension between the ages of 40 and 60 years. It is more common in Afro-Caribbean people than Caucasians, as is hypertension. Asians have the lowest incidence.

Etiology of AD

Acquired causes

- Hypertension
- **Atherosclerosis**
- Blunt chest trauma (e.g car accidents, although these are deceleration injuries that more commonly cause aortic transection, which is the laceration of all 3 layers of the aorta) or iatrogenic trauma (during catheterization or intra-aortic balloon pump counterpulsation)
- Pregnancy, especially third trimester and postpartum
- **Syphilis** (tertiary stage) as this causes vasculitis with aortic involvement
- **Amphetamines and cocaine use**
- Cardiac surgery – especially aortic valve replacement, as aortic regurgitation can cause dilation and aortic wall weakening

Congenital causes

- Genetic disease/connective tissue abnormalities that affect the aorta; affect the structure and function of connective tissue/proteins (e.g. collagen and elastin) in the walls of the aorta – **Marfan syndrome** (more likely to be proximal dissections), **Ehler-Danlos syndrome**
- **Turner syndrome** (causes aortic root dilation)
- Bicuspid aortic valve increases the chance of ascending aortic dissection
- Coarctation of the aorta

High-yield:

Hypertension is the most common cause of ascending aortic aneurysm.

70 % of patients with aortic dissection have uncontrolled high blood pressure.

Classification of AD

There are several systems of classification for aortic dissection based on anatomy or duration of onset of symptoms.

Stanford classification

The Stanford classification is the most commonly used in aortic dissection.

Mnemonic:

Stanford A = Affects ascending aorta

Stanford B = Begins beyond brachiocephalic vessels

Type A 70–75 %	Type B 25–30 %
• Ascending aorta +/– aortic arch, possibly descending aorta. • Can involve the aortic valve.	• Descending aorta or the aorta (distal to the left subclavian artery) without involvement of the ascending aorta.
• Requires primary surgical treatment.	• Generally treated conservatively by controlling blood pressure and heart rate. • Surgery is indicated in complicated cases only.

DeBakey system

In contrast, the **DeBakey system** is based on anatomy:

Type 1: 60 %	Type 2: 30–35 %	Type 3: 10–15 %
Origin – ascending aorta, extends to the aortic arch and often beyond. Most lethal and often seen in patients < 65.	Origin – ascending aorta and is confined to this region.	Origin – descending aorta – rarely moves proximally, but common distally. Elderly patients with hypertension and atherosclerosis.

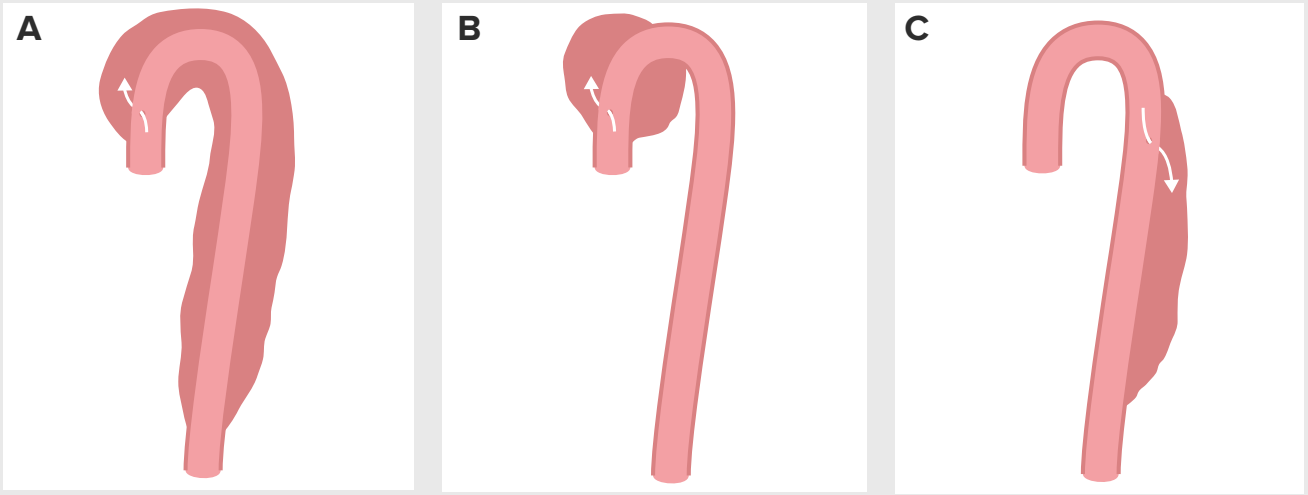

Fig. 9-02: *(A) DeBakey Type 1. (B) DeBakey Type 2. (C) DeBakey Type 3.*

Pathophysiology of AD

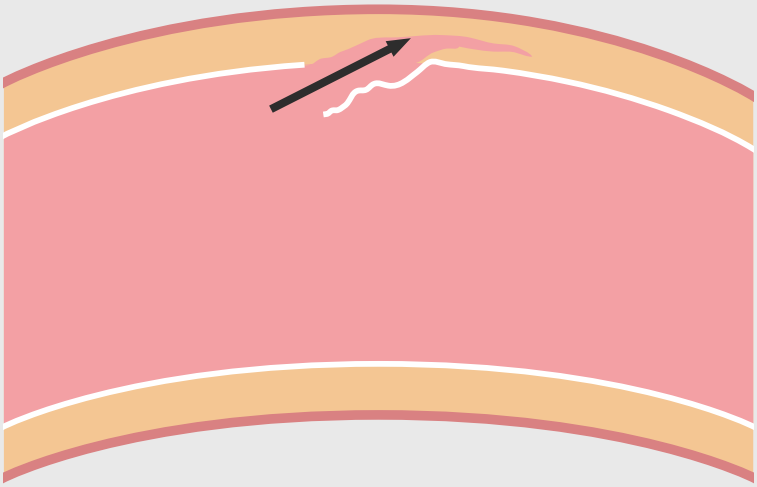

Fig. 9-03: *Schematic showing aortic*

In aortic dissection, blood enters the intima from the media layers. The high pressure exerted by blood tears the media apart in a laminated plane. The plane is usually located between the inner 2/3rd and the outer 1/3rd. The dissection can extend proximally and/or distally for variable distances. This establishes a connection between the media and intima through a false lumen.

Most dissections originate in the ascending aorta, usually within 10 cm of the aortic valve. These tears are commonly 1–5 cm long and are transverse or oblique in orientation, with rough edges.

- **Antegrade dissection** – spreads towards the iliac bifurcation and sometimes all the way down to the iliac and femoral arteries.
- **Retrograde dissection** – spreads towards the aortic root and heart.

Sometimes, the dissection can spread through the intima, media, and adventitia causing external rupture. This results in huge internal bleeding, or cardiac tamponade should the dissection extend not through the adventitia but into the pericardial sac and form a hemopericardium. Both scenarios are life-threatening and can rapidly lead to death.

When the blood enters the intima and tears through the media, it creates a **false lumen**. The **true lumen** is the natural physiological lumen of the vessel. Between these two layers is a layer of intima known as the **intimal flap**. As stated above, the false lumen may recanalize into the true lumen.

There are different types of aortic dissection. 65 % originate in the **ascending aorta**, 10 % in the aortic arch, and 20 % occur in the **descending thoracic aorta** (distal to the **ligamentum arteriosum**).

The reasons why an intimal tear occurs are unknown. It can occur as a result of intimal ischemia from increased shear forces due to hypertension, or due to genetic connective tissue diseases such as **Marfan syndrome**. In Marfan, the collagen and elastin within the media are degenerative, unstructured, and dysfunctional – causing **cystic medial necrosis** (as discussed below).

In approximately 10 % of cases, there is no evidence of an intimal tear. These dissections may be caused by bleeding within the medial layer of the vessel resulting in a **secondary aortic dissection**.

Genetic disease implications

- Marfan syndrome is a connective tissue disorder which involves the misfolding of **fibrillin-1**. This is a protein that forms elastic tissue and plays a role in signaling. One such role includes binding to **TGF-beta**; inappropriate functioning of the mutated fibrillin-1 causes an accumulation of TGF-beta in various tissues, including the aorta, and resulting in weakened tissue with abnormal structure and function.
- **Ehlers-Danlos syndrome** is a genetic condition characterized by insufficient production and processing of **collagen**, (an essential protein involved in tissue structure). This can lead to weakened **vessel walls** that are more prone to develop an aneurysm.

Pathology

Lesions associated with aortic dissection

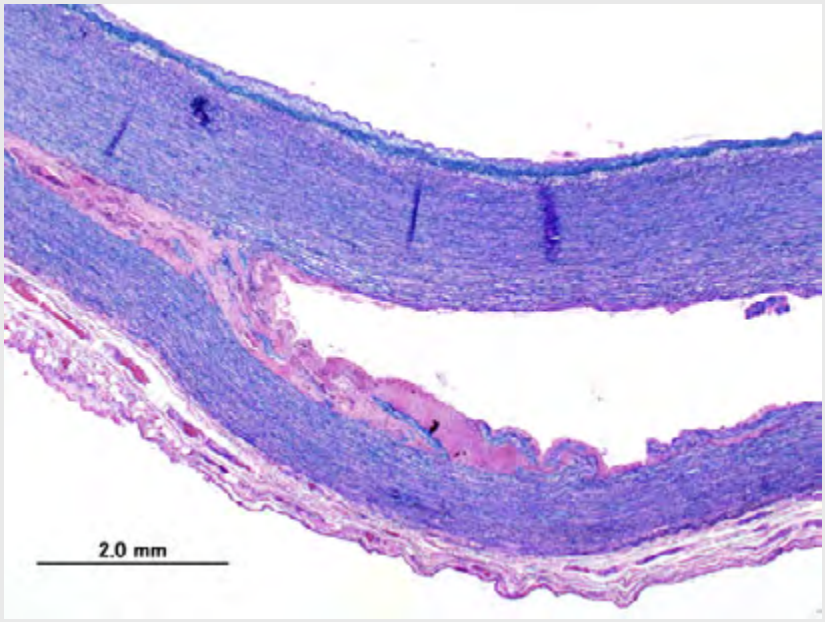

Fig. 9-04: Histopathological image of dissecting aneurysm of thoracic aorta in a patient without evidence of Marfan trait. The damaged aorta was surgically removed and replaced by an artificial vessel. Victoria blue & HE stain.

The most commonly identified lesion within the aortic wall is **cystic medial degeneration** – a decrease in smooth muscle, necrosis, fragmentation of elastic tissue, and deposition of a proteoglycan-rich extracellular matrix. Cystic medial degeneration is usually related to a genetic disease such as **Marfan syndrome**. There may be further evidence of atherosclerosis and abnormal connective tissue structure in genetic conditions. Inflammation is absent. Dissection can also occur when no identifiable histological lesions are present and can be spontaneous.

Clinical Features of AD

Symptoms and signs

Thoracic aortic dissection should be considered in all patients with **chest pain**. This pain usually has the following **characteristics**:

- **Site:** Chest pain depends on the location of dissection (can mimic myocardial infarction pain). This pain occurs as a result of to the interruption of blood flow to the coronary arteries causing ischemia (usually when arch or root are affected). Pain is usually more sudden and severe at onset when compared to MIs. Dissection is painless in 10 % of patients.
- **Onset:** Sudden.
- **Character:** Excruciating tearing/ripping pain (tearing pain between the shoulder blades is usually associated with descending aortic dissection).
- **Radiation:** To the back and/or between the shoulders. Can radiate to the neck or jaw (usually occurs with arch dissection which spreads into the branches of the aorta).
- **Severity:** Usually excruciating (can be mild in some cases).

The following **neurological symptoms** can be responsible for the presenting complaint (20 %):

- **Syncope** (hypovolemia, arrhythmia, increased vagal tone)
- Altered mental status
- Stroke (CVA) – hemiparesis or hemiplegia with hemianesthesia
- Change in sensation (tingling, paresthesia, pain) and motor function (weakness) can occur if peripheral nerves are affected by the lack of blood supply
- Hoarseness due to compression of laryngeal nerve

Additionally, other types of **symptoms** may occur **alongside aortic dissection**.

- **Cardiovascular symptoms:** There may be acute severe aortic valve compromise leading to secondary congestive left heart failure. This leads to orthopnoea and dyspnea.
- **Hypertension:** Underlying hypertension or an increase in circulating catecholamines.
- **Hypotension:** Poor prognostic sign as may be the result of cardiac tamponade, hypovolemia or increased vagal tone.
- Symptoms of **esophageal compression**: Dysphagia.
- Abdominal pain: With abdominal aorta involvement.
- **Flank pain:** With renal artery involvement.
- Symptoms of **systemic disease**(s): Patients may have established disease(s) associated with aortic dissection and could therefore have symptoms of peripheral vascular disease, infection, Marfan syndrome, or Ehler-Danlos syndrome.

Signs

The following list comprises the **most common signs of aortic dissection**:

- Blood pressure that is unequal in both arms, usually with a difference of > 20 mmHg between left and right arms (20 % do not) due to dissection obstructing the branches of the aorta
- **Aortic regurgitation** characterized by bounding (collapsing/water hammer) pulse, wide pulse pressure, murmurs (diastolic)
- Signs of congestive heart failure secondary to acute severe aortic valve dysfunction leading to orthopnoea, dyspnea, elevated JVP, and bibasal crackles
- Possibly **unconsciousness**
- **Cardiac tamponade** characterized by distension of jugular veins, hypotension, pulsus paradoxus, Kussmaul's sign
- SVC obstruction (rare) that can lead to **SVC syndrome**
- Signs of **stroke** – e.g., body leaning to one side due to hemiparesis
- Patient in shock: cold, clammy, pale, tachycardia, tachypnea
- **Horner's syndrome** may be present due to compression of the cervical sympathetic chain
- Numbness and tingling in the upper and lower limbs due to peripheral ischemia
- New diastolic murmur and/or asymmetrical pulses
- Signs of hemothorax may be present if the dissection ruptures into the pleura – rapid shallow breaths, sharp pleuritic pain
- **Acute arterial insufficiency** in the lower or upper limbs, as indicated by weak pulses, pallor, low body temperature, loss of sensation – paraesthesia, paralysis
- Signs of connective tissue disorders such as Marfan and Ehlers-Danlos syndrome signs

Complications of AD

Aortic dissection might cause the following complications:

- **Hypotension and** shock (hypovolemic) that can eventually lead to death due to exsanguination (blood loss)
- Permanent **disability** from stroke (CVA)
- **Acute aortic regurgitation** leading to proximal dissection spreading to the sinus of Valsalva and aortic root.
- Pulmonary edema related to acute aortic valve regurgitation
- Pericardial tamponade due to blood in the pericardial sac (hemopericardium)
- **Myocardial ischemia** due to reduction in blood flow to the coronary arteries
- **Aortic insufficiency**
- **Myocardial infarction**
- **Global ischemia** e.g. mesenteric, bowel, renal, spinal cord, visceral ischemia/infarction
- **Compression** of anatomical structures including esophagus, SVC, ganglia (sympathetic chain causing Horner's syndrome), airway, and left recurrent laryngeal nerve (hoarseness and vocal cord paralysis).
- **Aortic aneurysm**

Diagnosis of AD

Diagnosis of aortic dissection needs to be rapid and accurate. Diagnosis should be suspected from the history and physical examination as previously discussed.

Investigations

Investigations are used to diagnose and reveal the site of the intimal tear and extent of dissection.

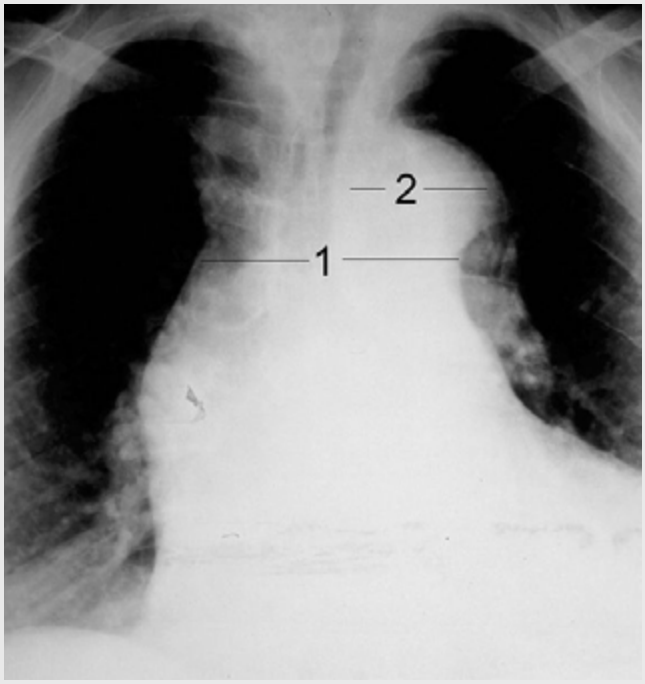

Fig. 9-05: Chest radiograph of aortic dissection type Stanford A.

Chest radiograph

- Initial imaging that shows mediastinal widening > 8 mm.
- Pleural effusions may be visible
- Calcium sign – the calcified intima is separated from the outer aortic soft-tissue border by 1 cm (rare)
- Obliteration of the aortic knob

Transoesophageal Echocardiogram (TEE)

- High sensitivity and specifically for hemo-dynamically unstable patients
- Fast, minimally invasive, and can be used in unstable patients, renal insufficiency and contrast allergy
- Can determine whether valves or ostia of the coronary arteries are involved
- Does not provide a full view, hence MRI is recommended

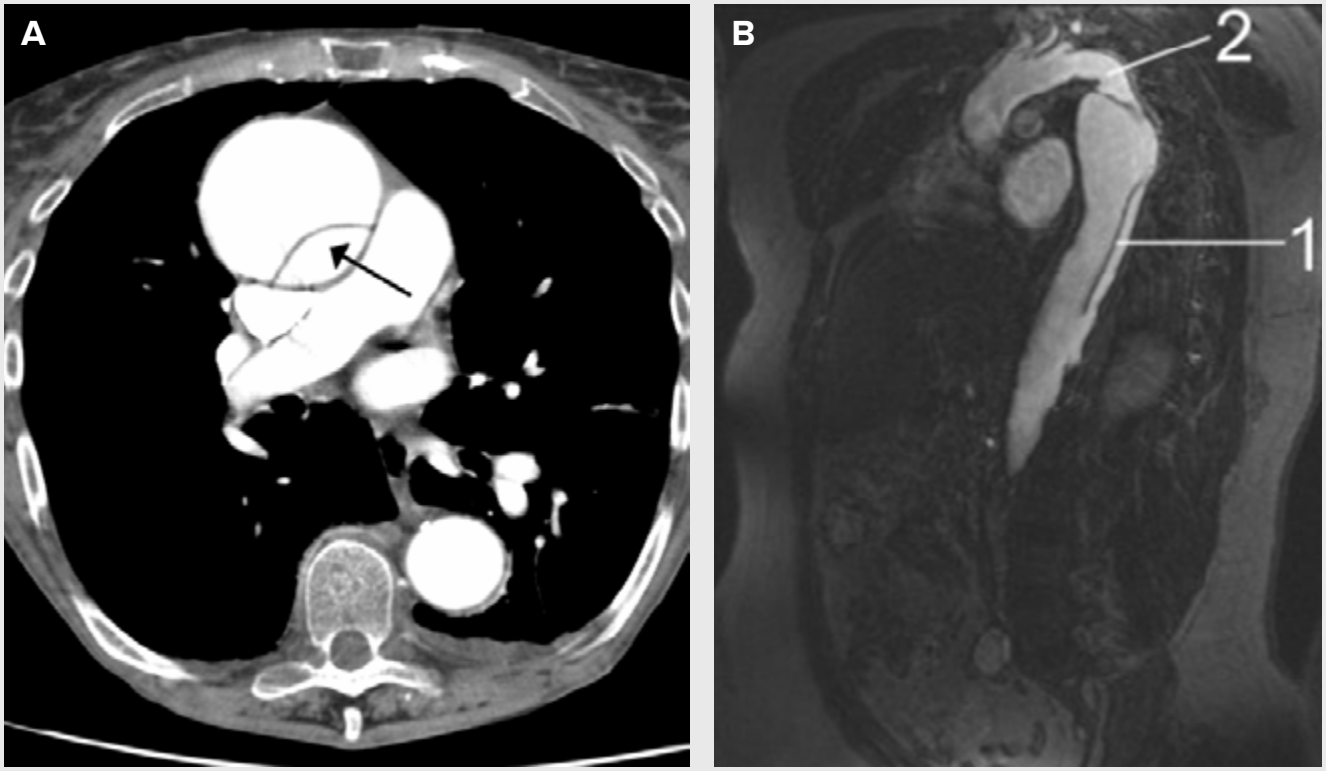

Fig. 9-06: (A) CT scan of an aortic dissection. (B) MRT scan of aortic dissection.

CT Scan

- Non-invasive, rapid and accurate test that can give a 3D view of the aorta – especially useful for surgical interventions
- Used in stable patients
- Injected iodinated contrast medium used
- Very sensitive and specific investigation
- Unable to diagnose site of intimal tear

MRI

- Gold standard for detection and assessment.
- Sensitivity and specificity of 98 %
- Used if contrast-enhanced CT is contraindicated in stable patients
- Can create a 3D reconstruction and determine the intimal tear location (unlike CT scans) and extent of the dissection
- Noninvasive
- No iodinated contrast needed
- Quantifies the level of aortic insufficiency
- May only be available at larger hospitals
- Takes longer than CT scans and may therefore be less useful

Differential Diagnoses of AD

Myocarditis, myocardial infarction, aortic aneurysmal rupture, and mechanical chest pain are the main differential diagnoses.

Treatment of AD

Acute Stanford type A (DeBakey 1+2) Acute ascending aortic dissection	Surgery > medical
Acute Stanford type B (DeBakey 3) Descending aortic dissection	Medical > surgical

Early treatment

Beta-blockers given via intravenous route are the first-line early treatment of AD. Aim to decrease the heart rate to 60 bpm. The next step is to control hypertension which can be achieved with beta-blockers alone or with an add-on therapy of nitroprusside or calcium channel blockers. IV labetalol, esmolol, and propranolol are the most commonly used beta-blockers in this setting.

Surgery

Surgery is mandatory and life saving in acute dissection of type A wherein **fatal outcome is imminent without** intervention. Surgery carries risk due to proximity to the heart and the significance of the aorta. The surgical procedure aims to remove the damaged section of the aorta and repair the false lumen to prevent entry of blood. The intimal tear is therefore removed.

Surgery can be carried out via open surgery (indicated for ascending aortic dissection) or endovascularly (indicated mainly for descending aortic dissection). Surgery can replace the damaged aorta with a tube graft (Dacron graft) and/or repair the damaged aortic valve if it is implicated in the aortic dissection.

Prognosis of AD

Acute Aortic dissection has a high mortality rate, 40 % at time of presentation. Of the remaining 60 %, 1 % die every hour; this highlights the importance of rapid diagnosis and referral for surgical repair (or medical treatment if indicated). The surgery itself is extremely high risk with a mortality of 5–20 %.

Ascending aortic dissections have a much worse prognosis in comparison to

Note:
Type A aortic distension is treated by open surgery or endoscopy through replacement of the damaged aorta with a tube graft.

Type B aortic distension is treated by beta-blockers, vasodilators, or calcium channel blockers.

Note:
Initial treatment should be beta-blockers before vasodilators to avoid reflex tachycardia.

Beta-blockers lower the heart rate, reducing shearing forces with the aorta.

descending thoracic aortic dissections.

There are **risk factors** which affect the postoperative prognosis:

- Increased preoperative evaluation time
- Older age
- Aneurysm leakage
- Cardiac tamponade
- Pre-existing heart pathology (MI, coronary artery disease)
- Previous stroke
- Shock
- Kidney failure (acute/chronic)

Screening of AD

High-risk individuals such as those with a family history of collagen-disease or AD should be screened, especiallyif they develop hypertension.

Review Questions

Test your knowledge:
Aortic Dissection

Question 9.1: A 58-year-old man presents to the emergency department with severe chest pain and uneasiness. He says that symptoms onset acutely half an hour ago while he was watching television. He describes the pain as being 8/10 in intensity, sharp in character, localized to the center of the chest and retrosternal, and radiating to the back and shoulders. The patient denies any associated change in the pain with breathing or body position. He says he has associated nausea but denies any vomiting. He denies any recent history of fever, chills, or chronic cough. His past medical history is significant for hypertension, hyperlipidemia, and diabetes mellitus for which he takes lisinopril, hydrochlorothiazide, simvastatin, and metformin. He reports a 30-pack-year smoking history and has 1–2 alcoholic drinks during the weekend. Family history is significant for hypertension, hyperlipidemia, and an ST elevation myocardial infarction in his father and paternal uncle. His blood pressure is 220/110 mm Hg in the right arm and 180/100 mm Hg in the left arm. On physical examination, the patient is diaphoretic. Cardiac exam reveals a grade 2/6 diastolic decrescendo murmur loudest over the left sternal border. Remainder of the physical examination is normal. The chest radiograph shows a widened mediastinum. The ECG reveals non-specific ST segment and T wave changes. Intravenous morphine and beta-blockers are started. Which of the following is the most likely diagnosis in this patient?

A. Aortic dissection

B. Pulmonary embolism

C. Acute myocardial infarction

D. Myocarditis

E. Aortic regurgitation

Question 9.2: A 63-year-old man presents to the emergency department with a sudden onset of excruciating chest pain which he describes as tearing. He has been diagnosed with essential hypertension 20 years ago but he is not compliant with his medications. On physical examination, his temperature is 37.1 °C (98.78 °F), heart rate is 95/min, and blood pressure is 195/90 mm Hg in the right arm and 160/80 mm Hg in the left arm. Pulses are absent in the right leg and diminished in the left. Chest X-ray shows widened mediastinum. Which of the following is the next best step?

A. CT Scan

B. Intravenous sodium nitroprusside

C. Surgery

D. D-dimer

E. Intravenous ultrasound

Correct answers: 9.1A, 9.2A

Peripheral Artery Disease (PAD)

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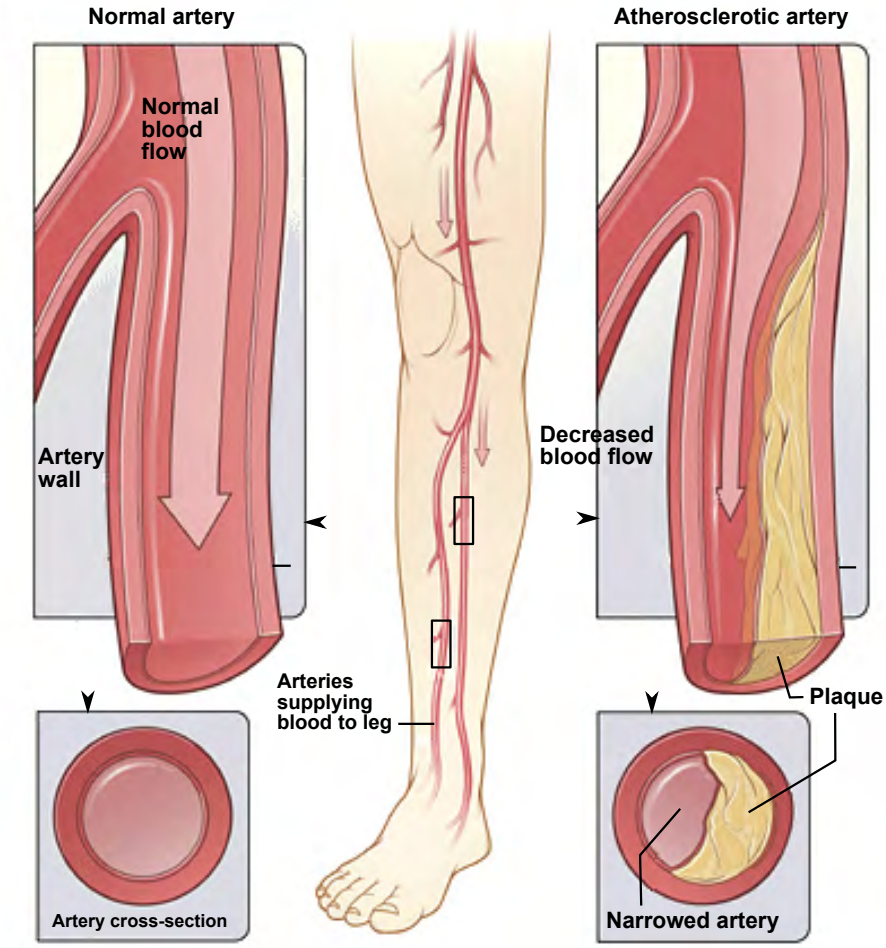

Fig. 9-07: Peripheral Arterial Disease (PAD)

Definition of PAD

Peripheral artery occlusive disease is a chronic disease characterized by narrowing of arterial circulatory vessels in the extremities due to depositions of plaques in blood vessels. Plaques are substances that are composed of fat, calcium, cholesterol, and fibrous tissues.

Chronic atherosclerotic processes lead to **arterial stenosis,** resulting in the complete occlusion of the arteries at a later stage. The resulting hypoperfusion leads to pain in the extremities which is described as intermittent claudication with walking, which is also the primary symptom of the disease.

By definition, acute peripheral artery occlusive disease also falls under PAD and involves the complete blockage of an **arterial vessel**. It may occur suddenly due to embolic incidents, or as a complication of PAD.

Epidemiology of PAD

The prevalence of PAD increases with age, starting from the age of 40, and affects 15–21 % of people over 70 years of age. Studies conducted in 2014 show that the prevalence of PAD in those under 40 years of age is less than 1 %. Males and females are equally affected.

Etiology of PAD

In 85–95 % of the cases, peripheral artery occlusive disease is caused by atherosclerotic placques. These plaques are deposits on the arterial walls that consist of lipids, connective tissue, thrombi, or calcium on the arterial walls. Atherosclerosis, by definition, involves the entire arterial wall, but is often referred to as atherosclerosis of the tunica intima. In terms of clinical use, both expressions are used interchangeably and practically synonymous.

The primary risk factors for atherosclerosis are the following:

- Nicotine abuse
- Diabetes mellitus
- Arterial hypertension
- Dyslipidemia
- Obesity or overweight
- Physical inactivity
- Chronic renal failure

In less than 5 % of cases, PAD is a result of recurrent emboli, **thrombotic aneurysms**, compartment syndrome, or **vascular injury**.

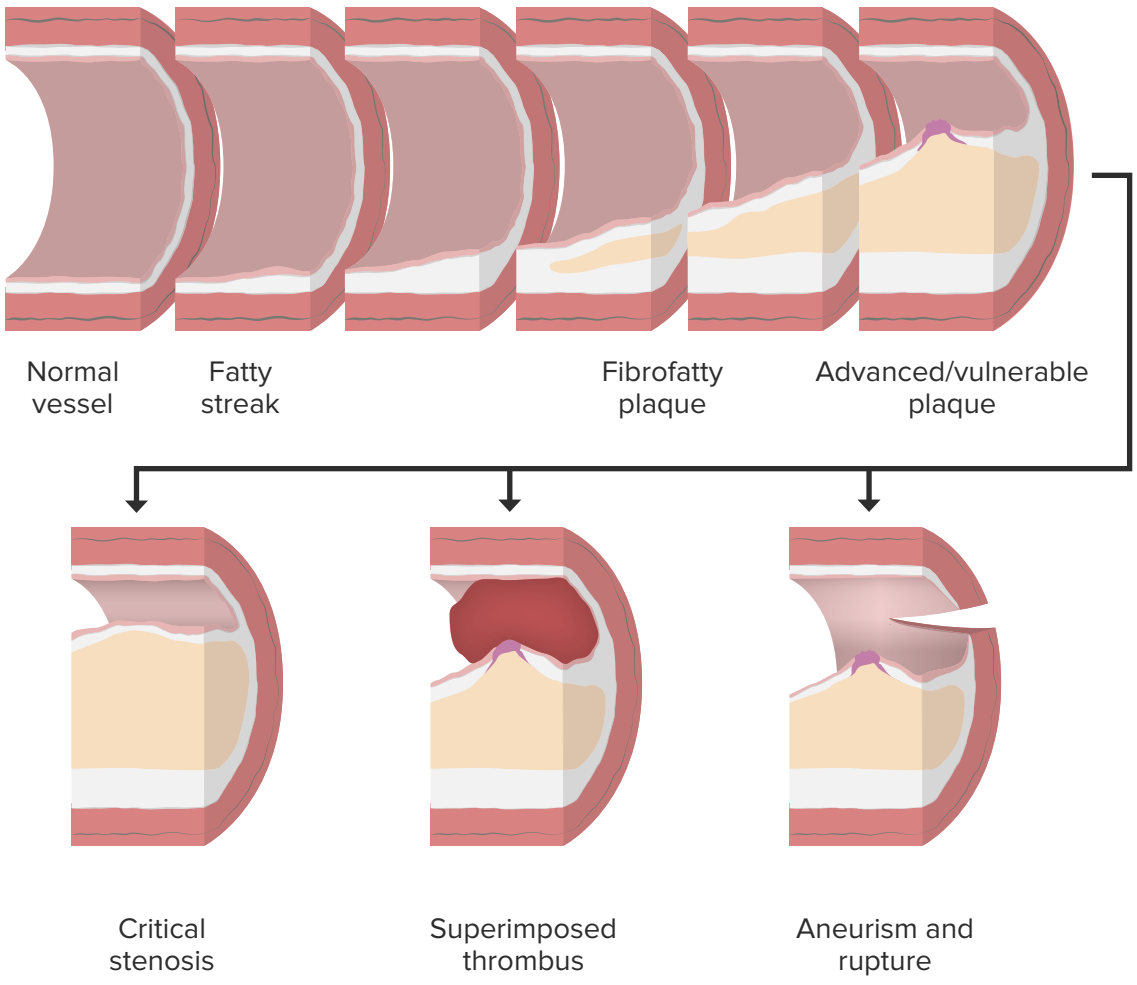

Fig. 9-08: Atherosclerosis disease progression.

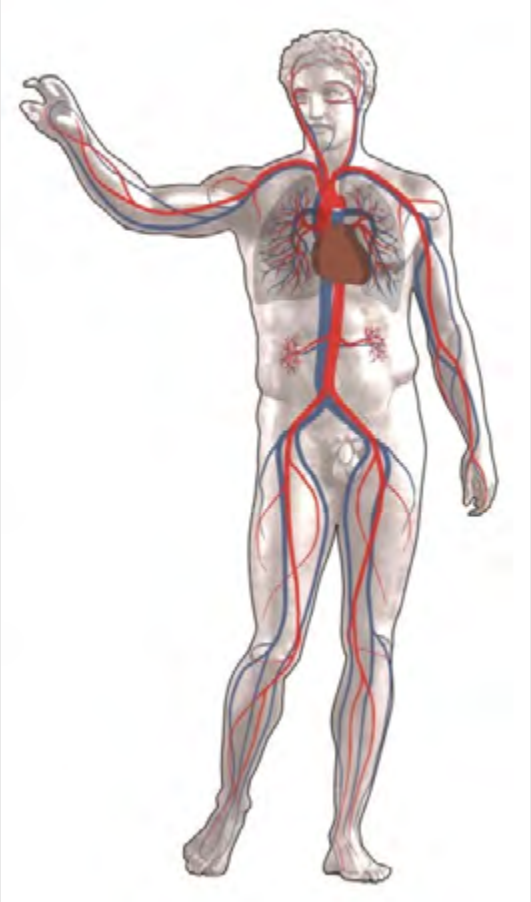

Fig. 9-09: The human circulatory system. Red indicates oxygenated blood, blue indicates deoxygenated blood.

Clinical Features of PAD

The primary symptom of PAD is pain occurring with physical activity, typically located distally to the **stenotic vessel**. Pain causes patients to often come to a halt when walking and the symptom is referred to as **intermittent claudication** (latin for the 'occasional limp').

Typically, claudication is relieved after a pause during walking.

The body is generally able to overcome a small stenosis through collateral circulation. The full panel of symptoms does not appear until stenosis has reached more than 90 % – this actually explains the extremely high percentage of asymptomatic PAD patients. Diminished circulation constitutes fertile ground for ulcers, healing disorders, necrosis, or gangrene in the affected areas.

Cassification based on stenosis location and symptom:

Stenosis location	Symptoms
Aortoiliac type	Aortic bifurcation syndrome, buttocks, thighs
Femoral type	Shanks
Shank/peripheral type	Feet

Symptoms of acute arterial occlusion

When the disease has reached late-stage, a complete blockage of the artery is possible. This acute **peripheral arterial occlusion**, can lead to acute ischemia of the extremities, possibly resulting in necrosis of the tissues of the feet and loss of the affected extremity through surgical amputation; acute ischemia of the extremities is potentially life-threatening.

Significant hypoperfusion in the extremities causes symptoms that can be synopsized with the mnemonic of 'the 6 P's' rule according to Pratt, a mnemonic all medical students should be familiar with.

1. Pain
2. Pulselessness
3. Pallor
4. Paresthesia
5. Paralysis
6. Poikilothermia

In order to diagnose PAD, a physician needs to go through a multi-level assessment of the patient's medical history, physical examination, and imaging. A medical history and physical examination can determine the first indications of PAD and also help to classify the disease.

History

The patient should be asked about the circumstances under which symptoms appeared in full detail. This means asking about the duration of the pain, its location, its quality, and the distances they are able to walk. Questions related to risk factors of the underlying atherosclerosis and diseases connected to it (like coronary heart disease) should also be asked. Nicotine abuse, diabetes mellitus, hypercholesterolemia, arterial hypertension, and dyslipidemia are assessed as the most important risk factors.

Physical examination

Decreased blood flow in the affected extremity can be detected early by inspection. It is important to note the quality of the skin. A pale color, lower temperature and increased sweat production are indications of diminished perfusion. Look for visible lesions or complications such as **ulcers, necrosis**, or **moist gangrene**. Auscultation of the assumed-to-be-affected artery must be done if possible. In severe stenosis with an occlusion of over 60–70 % a **systolic murmur** can be heard.

Since many patients have asymptomatic PAD, clinical diagnosis is made possible with palpation of the foot pulses (comparison of the 2), or determination of the **ankle-brachial index**. A treadmill ergometer is also helpful to determine the distances deemed by a patient as “walkable” and to assess the severity of the disease.

The Ratschow positioning test is a non-invasive test that involves maneuvering the position of the feet, and is used to diagnose PAD. The patient is made to lie on their back, the legs are lifted to a 90 degrees angle, and then returned to a sitting position. In this positioning test, a physician can visually assess the blood circulation and venous filling, where assessment results are totally dependent upon how much time is needed before the feet regain their normal color.

Ankle-brachial index

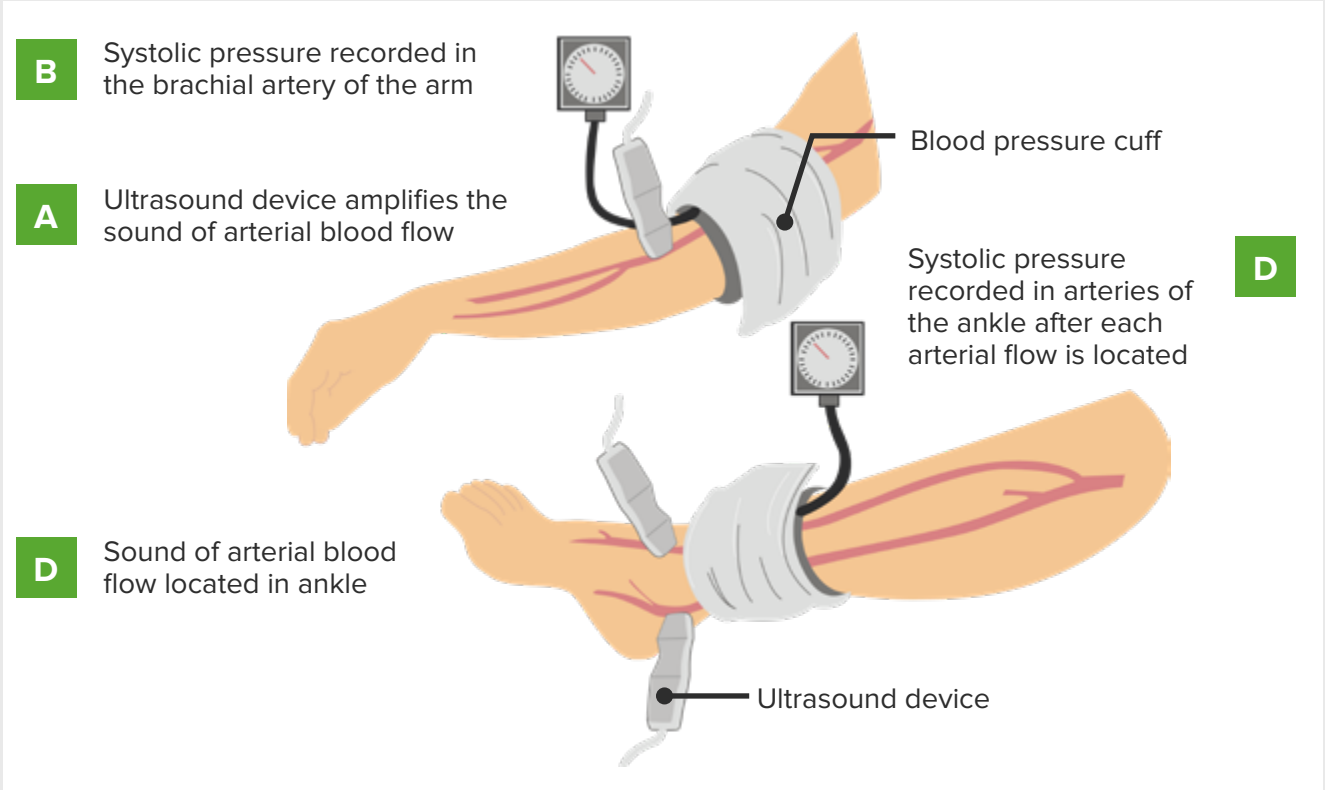

Fig. 9-10: Measuring the ankle-brachial index.

The ankle-brachial index (ABI) is a Doppler pressure measurement and is expressed via the ratio of blood pressure at the ankle to blood pressure in the upper arm. The test requires 10–15 minutes.

Characterization	Value
Normal value	0.9–1.2
Mild PAD	0.75–0.9
Moderate PAD	0.5–0.75
Severe PAD	< 0.5

Classification of PAD

Based on the symptoms, PAD is classified in stages which also constitute criteria for its proper treatment plan.

Stage	Characteristics	Therapy plan
Stage I	Symptom-free	
Stage II	Pain during physical activity. IIa: distances walked without pain > 200 m. IIb: distances walked without pain < 200 m.	Intermittent claudication, no acute danger to the extremities yet.
Stage III	Ischemic rest pain	
Stage IV	Necrosis, gangrene, ulcers. IVa: dry necrosis, trophic disorders. IVb: infected necrosis, moist gangrene.	Indication for systemic therapeutic action, otherwise danger for (partly) losing the extremity. 1 year mortality rate lies between 20–40 %.

Diagnostics of PAD

Imaging in PAD

When ABI measurement is above 1.3, non invasive methods are performed in order to confirm the diagnosis of PAD and locate the stenosis. First-choice options include various non-invasive imaging methods.

- **Color-flow Doppler sonography:** Allows for reliable conclusions concerning the extent and location of the stenosis.
- **Digital Subtraction Angiography (DSA):** Constitutes the gold-standard test for diagnosis.
- **Magnetic Resonance angiography (MR-angiography):** Gold standard for intervention. Allows for comprehensive depiction of the vascular system, helps in difficult differential diagnoses, and is mandatory before performing any operative procedure.
- **CT-angiography with contrast material:** Useful when indicated, e.g., in case of an **aortic aneurysm.**
- Duplex ultrasonography: Evaluates the status of PAD.

Differential Diagnoses of PAD

The differential diagnosis should primarily debate whether the patient's symptoms actually have an arterial cause, or if there is an alternative causality for symptoms arising with physical activity. Other possible causes for this clinical picture might be:

- Arteriopathies
- Venous disorders
- Neuralgias
- Neurologic conditions
- Degenerative/inflammatory joint diseases

Treatment of PAD

Treatment of PAD focuses on 4 chief aims:

1. Improving the ability to walk longer distances without pain, so that the patient's quality of life is significantly enhanced.
2. Impeding the progression of atherosclerosis.
3. Lowering the secondary risk of cardiac and cerebral events, such as a myocardial infarction or stroke.
4. Preservation of the extremities under all possible circumstances and avoidance of amputation.

Treatment strategies for PAD can be:

- Conservative
- Medicinal
- Interventional
- Operative

Conservative treatment

Important general measures include keeping the feet at a lower level than that of the heart, taking good and regular care of the feet, and avoiding cold temperatures, infections, and trauma, especially in the last stages of the condition. Next, and one of the most important therapeutic measures, is treatment of atherosclerosis risk factors. One of the first steps a physician must take is to advise the patient to quit smoking. This should be followed by medical control of blood sugar levels, lowering LDL-cholesterol, and restoration of normal blood pressure.

Medical treatment

1. All patients should receive long term antiplatelet therapy such as aspirin, clopidogrel, or ticagrelor as this reduces mortality and morbidity.
2. Patient should receive lipid-lowering agents (statins).
3. Antihypertensive and antidiabetic medications to control risk factors.
4. PDE inhibitors (cilostazol) are used if conservative measures fail to control the symptoms.

High-yield:
Cilostazol acts as a vasodilator and antiplatelet agent.

Minimally invasive intervention

Invasive measures are indicated for stages III/IV, with an aim to avoid amputation of an extremity. Performing a **Percutaneous Transluminal Angioplasty** (PTA) with/without stent insertion allows dilation of the affected vessel by way of a balloon catheter.

Surgery

Operative procedures include:

1. **Thromboendarterectomy,** during which the thrombus is extracted through the vascular wall.
2. Bypass surgery wherein an **autologous vein**, usually the **great saphenous vein**, is used to bypass the stenosis.

Complications of PAD

If left untreated, and in progressive stages, PAD can cause several complications due to hypoperfusion of the tissues. These include healing disorders, wound infections, and even sepsis. An acute arterial occlusion of an extremity can lead to necrosis and amputation. Furthermore, PAD patients run a higher risk of atherosclerotic secondary diseases, such as myocardial infarctions and strokes.

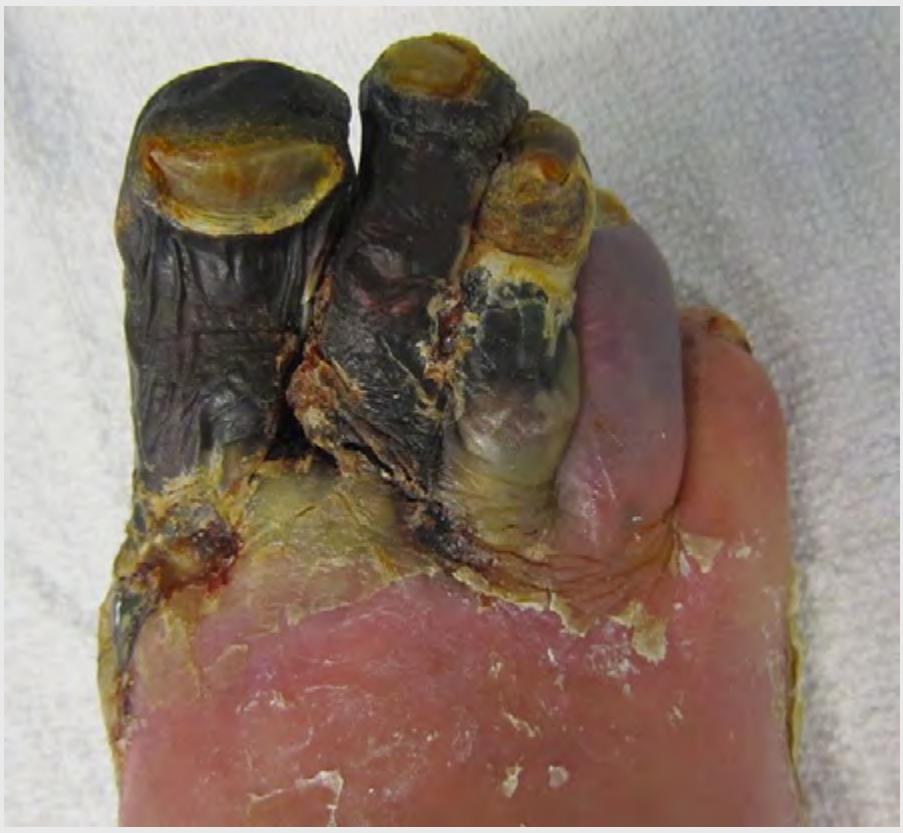

Fig. 9-11: *Gangrene of the 1st to 4th toes of the right foot in person with diabetes.*

Note:

Indications of revascularization:

1. *Critical limb ischemia*
2. *Failure of conservative and medical treatment*
3. *Physical disability due to claudication*
4. *Good anatomy with high-chance of success*

Review Questions

Question 9.3: A 59-year-old man presents to his primary care physician complaining of leg pain with exertion for 6 months. He notices that he has calf cramping on both sides when walking. He states that it is worse on his right calf than his left and that it goes away when he stops walking. He has type 2 diabetes mellitus for 15 years and is not compliant with his medications. He has smoked 20–30 cigarettes daily for the past 30 years. On examination, the femoral pulses are diminished on both sides. Which of the following is the most likely cause of this patient's condition?

A. Joint degeneration

B. Narrowing of the spinal canal

C. Venous thrombosis

D. Atherosclerosis

E. Segmental arterial occlusions due to non-atherosclerotic vasculitis

Question 9.4: A 75-year-old man comes to the emergency department because of pain in his left thigh and left calf for the past 3 months. The pain occurs at rest, increases by walking, and mildly improved by hanging his foot off the bed. He has hypertension for 25 years and type 2 diabetes mellitus for 30 years. He has smoked 30–40 cigarettes per day for the past 45 years. On examination, femoral, popliteal, and dorsalis pedis pulses are faint on both sides. The patient's foot is shown in the image. Which of the following is the most likely diagnosis?

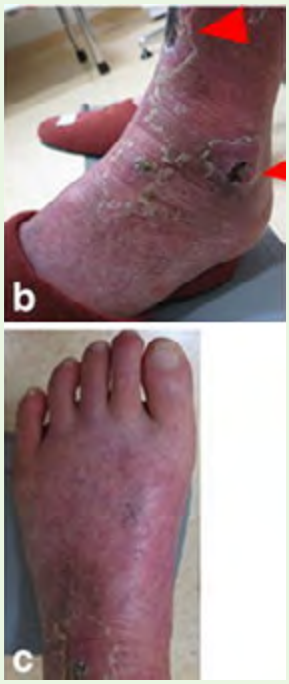

Fig. Q. 9.3

A. Critical limb ischemia

B. Venous ulcer

C. Raynaud's phenomenon

D. Pseudogout

E. Cellulitis

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Chapter 8: Arrhythmia

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Chapter 9: Common Vascular Disorders

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