DIABETES MELLITS

dr.ammar khalid

➢ What is Diabetes mellitus?

It is a group of metabolic disorders characterized by hyperglycemia due to

1. **Absolute absence of insulin secretion, OR**
2. **Impaired insulin secretion and /or insulin resistance.**

Each of the above will leads to, abnormal metabolism of carbohydrates, proteins & lipids, in addition to significant changes in water and electrolyte homeostasis.

-

➢ Clinical Physiology of glucose metabolism.

Blood glucose is tightly regulated and maintained within a narrow range to ensure a continuous supply of glucose (fuel) especially to the brain (cannot store glycogen or triglyceride and the blood–brain barrier is impermeable to fatty acids.)
After ingestion of carbohydrates, normal blood glucose levels are maintained by insulin which is secreted from pancreatic β cells into the portal circulation in response to a rise in blood glucose (β cells are sensitive to glucose concentrations in the blood) through the following

:

-1Suppression of hepatic glucose production

2- Stimulation of hepatic glucose uptake

-3Stimulation of glucose uptake by peripheral tissues.

The other important regulator of normal blood glucose levels is glucagon, secreted from alpha cells into the portal circulation in response to a drop in blood glucose; it will regulate the glucose level by increasing hepatic glucose output through

1. **Gluconeogenesis (the process of producing glucose from non-carbohydrate sources as proteins, lipids and pyruvate.).**
2. **Glycogenolysis (Glycogen breakdown**

➢ What are the types of diabetes?

Aetiological classification of diabetes mellitus

1 Type 1 diabetes

- **Immune-mediated 1A**
- **Idiopathic 1B.**

2 Type 2 diabetes.

3 Secondary and other specific types of diabetes.

a. Genetic defects of β-cell function e.g. (Monogenic diabetes mellitus or maturity onset diabetes of the young (MODY.))

b. Genetic defects of insulin action

c.Pancreatic disease, e.g. pancreatitis, pancreatectomy, cystic fibrosis, haemochromatosis.

d.Excess endogenous production of hormonal antagonists to insulin (Endocrinopathies), e.g.

Growth hormone as acromegaly.

Glucocorticoids as Cushing's syndrome.

Glucagon as glucagonoma.

Catecholamines as phaeochromocytoma.

Thyroid hormones as thyrotoxicosis.

e.Drug-induced e.g. corticosteroids, thiazide diuretics, phenytoin and many others.

f.Uncommon forms of immune-mediated diabetes e.g. immunodysregulation polyendocrinopathy X syndrome.

g. Associated with genetic syndromes e.g. Down's syndrome; Klinefelter's syndrome; Turner's syndrome; Friedreich's ataxia; Myotonic dystrophy.

-4Gestational diabetes.

Type 1 diabetes ()10-15%

Pathology It is due to the destruction of insulin-secreting β cells in the pancreatic islets of Langerhans, leading to absolute insulin deficiency.

It is of two types

-1Immune-mediated Type 1 A, which is a T cell-mediated autoimmune disease.

2- Idiopathic Type 1 B. unknown cause, non immune mechanisms.

Progressive loss of β cell function takes place over a period of months to years.
Diabetes and its classical symptoms, occurs only when 80–90% of β cells has been lost, at which time symptoms will develop acutely, and the condition is often diagnosed in an emergency setting as Ketoacidosis.
Islet cell antibodies are present before the clinical presentation of type I diabetes, their detection can be useful in confirming a diagnosis of type 1 diabetes.
Type 1 diabetes is associated with other autoimmune disorders, including thyroid disease, coeliac disease,Addison's disease, pernicious anaemia and vitiligo.

Genetic predisposition

Environmental predisposition

Genetic susceptibility is a prerequisite for type 1 diabetes ,

others

1. **Viruses, include mumps, Coxsackie B4, retroviruses, rubella (in utero), cytomegalovirus and Epstein–Barr virus.**
2. **Specific drugs or chemicals.**

3 **Dietary constituents. Nitrosamines (found in smoked and cured meats) and coffee.**

Bovine serum albumin a major constituent of cow's milk, given early in infancy,

4 **The hygiene hypothesis. It has been proposed that reduced exposure to microorganisms in early childhood limits maturation of the immune system and increases susceptibility to autoimmune disease.**

Type 2 DM ()85-90%

Is characterized by

-1Impaired insulin secretion and/or insulin resistance,
2- Increased hepatic glucose production,
3 Abnormal fat metabolism (both 2 and 3 are due to increased glucagon secretion to provide glucose in response to false signal from the body of glucose deficiency.)

Genetic Considerations

The disease is polygenic and multifactorial. There are more than 65 genes involved; these genes are responsible for β-cell function and regulation.
The concordance of type 2 diabetes in identical twins is between 70 and 100%, they also have a strong +ve family history, (Type 2 has a strong genetic component more than type .)1

Environmental factors such as

1 Age. Over 70% of all cases of diabetes occur after the age of 50 years.
2 Obesity particularly visceral or central, Diabetes increases tenfold in people with a body mass index of more than 30 kg/m.2
3Sedentary lifestyle, urbanization and unhealthy diet. 4- Economic development.

- **What goes wrong in diabetes?**

Pathophysiology

Type2 diabetes

In the early stages, glucose tolerance remains near-normal, despite insulin resistance, because the pancreatic beta cells compensate by increasing insulin output.
As the disease progress, these cells are unable to sustain the hyperinsulinemic state in susceptible individuals, and this decline in insulin secretion continues associated with an increase in glucagon secretion leading to hepatic glucose production and lipolysis, and so overt diabetes occur.

Type1 diabetes

In type 1 diabetes there is an absolute insulin deficiency, so the above abnormal mechanisms will occur more rapidly and will end up in unrestrained lipolysis and proteolysis, weight loss and ketoacidosis, which is characteristic of type 1 diabetes, (blood glucose inspite of being high, can't be utilized without insulin so glucagon secretion increase to provide other source of energy.)

Other types of diabetes

Monogenic diabetes mellitus: maturity onset diabetes of the young (MODY)

LADA

Latent autoimmune diabetes of adults, or slow onset type 1 diabetes or diabetes type

Diabetes in Pregnancy

This includes, 1. Overt diabetes (type 1 and 2) and 2. GDM, It is recommended that diabetes diagnosed at the initial prenatal visit (i.e. before 24-28 wks) is classified as "overt" diabetes.

Gestational Diabetes Mellitus (GDM)

Gestational diabetes occur in the second half of pregnancy (24-28 wks) in susceptible women, when there is an increased tissue insulin resistance due to the increased oestrogens, progestogens and in particular, human placental lactogen (hPL.)
The resulting maternal hyperglycemia drives fetal hyperinsulinemia, which in turn increase fetal growth, resulting in increased birth weight (macrosomia), and neonatal hypoglycemia. Most women revert to normal glucose tolerance after delivery but have an increased risk (35–60%) of developing DM in the next 10–20 years.

Terms frequently used

- **Honeymoon phase**

Is a transient phase that may occur in some patients with type 1 diabetes in the first 1 or 2 years of onset, during which glycemic control is achieved with no insulin or with lesser doses. It is due to endogenous insulin production from residual beta cells which then disappears as the autoimmune process destroys these remaining cells.

- **Stress hyperglycemia**

In some people, an abnormal blood glucose results is observed under conditions which impose a burden on the pancreatic β cells, e.g. during pregnancy, sever infection, myocardial infarction, or during treatment with diabetogenic drugs such as corticosteroids plus any other severe stress.
This 'stress hyperglycemia' usually disappears after the acute illness has resolved. However, blood glucose should be remeasured, and follow up is needed because they are more susceptible for development of future overt diabetes.

➢ What are the classical symptoms of hyperglycemia?

Polyuria /Polydipsia/ Polyphagia/ Weight loss and emaciation/ tiredness and easy fatigability/ Nausea, vomiting/ blurred vision/ slow healing infections and fever/ impotence in men…etc.

Each may or may not be present depending on the type and stage of diabetes.

➢ How do patients with diabetes present?

Type 1 diabetics Usually develop symptoms over a short (acute) period of time, and the condition is often diagnosed in an emergency setting as Ketoacidosis, or sometimes may present with the classical symptoms that not responding to conventional treatment or may present with severe abdominal pain and fever leading to misdiagnosis of acute abdomen.

Type 2 diabetes Usually develop the symptoms above over a long period of time, and the condition is often diagnosed or present for the first time with complications or more commonly diagnosed incidentally during a routine lab testing.

Others give a long history of fatigue, with or without 'osmotic symptoms' (thirst and polyuria). In some the presentation is late and pancreatic β-cell failure has reached an advanced stage of insulin deficiency so weight loss, and sever osmotic symptoms.

Many patients stay undiagnosed (25-50%).

Summary of the classical features of type 1 and type 2 diabetes

Features	Type 1	Type 2
Age at onset	Usually < 40 yrs	Usually > 50 yrs
Duration of symptoms	Days to Weeks	Months to yrs
Body weight	Normal or low	Obese
Auto antibodies	+ve in 80–90%	Negative
Complications at diag	No	25%
Family history of DM	Uncommon	Common

➢ How diabetes is diagnosed?

- **In a patient with classical symptoms (symptomatic) of hyperglycemia one of the following is enough to reach a diagnosis**
  1- A1C ≥ 6.5%. OR
  2 FPG ≥ 126 mg/dL (7.0 mmol/L) OR
  3 Random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).
- **If a patient is asymptomatic with +ve single test, it is preferable to repeate the same test for confirmation.**

- **Diagnosis of GDM**

At 24–28 weeks of gestation women with risk factors not previously diagnosed with overt diabetes should perform.
OGTT, after an overnight fast of at least 8 hrs. Diagnosis of GDM is made when any one of the following plasma glucose values is exceeded:

- **Fasting: ≥92 mg/dL (5.1 mmol/L) OR**
- **1 h: ≥ 180 mg/dL (10.0 mmol/L) OR**
- **2 h: ≥ 153 mg/dL (8.5 mmol/L)**

Prediabetes

Impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) or both.
It importance is that although these glucose levels are below diabetes range, they carry a high risk for the future development of diabetes and Cardiovascular disease, because it is usually associated with

- **Obesity**
- **Dyslipidemia and**
- **Hypertension.**

Criteria for the diagnosis of Prediabetes

1- -FPG 100 mg/dL (5.6mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG) OR
2- 2-h Post Glucose in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL(11.0 mmol/L) (IGT) OR
3- -HbA1C 5.7–6.4%

INVESTIGATIONS USED IN THE MANAGMENY OF DIABETES

1- Urine testing

a.Glucose Urine for glucose test is only a screening test because of the individual variation in renal threshold for glucose. The most frequent other causes of glycosuria is a low renal threshold, which is common during pregnancy and in young people (old people have high renal threshold).

b.Protein Microalbuminuria or proteinuria, in the absence of urinary tract infection, is an important indicator of diabetic nephropathy.

c.Ketones Ketonuria may be found in people who have been fasting or exercising strenuously, repeated vomiting also, but if associated with hyperglycemia, the diagnosis of diabetic ketoacidosis is strongly considered.

2- Blood testing

a- Glucose Blood glucose levels depend on whether the patient has eaten recently, so it is important to consider the circumstances in which the blood sample was taken. FBS is measured after over night 8-12 hrs of fasting.
Glucose concentrations are lower in venous than arterial or capillary (finger prick) blood. Whole blood glucose concentrations are lower than plasma concentrations because red blood cells contain relatively little glucose.
Venous plasma values are usually the most reliable test for diagnostic purposes.

b.Ketones Measures the major ketone in blood during diabetic ketoacidosis (DKA), beta-hydroxybutyrate (β-OHB).
Blood ketone monitoring is useful in monitoring resolution of DKA.

c.Glycated hemoglobin Glycated haemoglobin provides an accurate and objective measure of glycaemic control integrated over a period of (120 days), HbA1c is most sensitive to changes in glycaemic control occurring in the month before measurement. In Iraq HbA1c values are reported in (%), other value not used here is the mmol/mol. HbA1c is diminished in anemia, pregnancy, and may be difficult to interpret with some assay methods in patients who have uremia or a haemoglobinopathy.

Prevention of diabetes

- **Can we prevent diabetes?**

Yes, type 2 diabetes is preventable by screening for people with high risk of developing diabetes as (Family history. Obesity (BMI ≥ 25 kg/m^2), Physical inactivity, Hypertension, Dyslipidemia, history of GDM….etc) then start

1Intensive changes in lifestyle (healthy diet and exercise for at least 30 min/day five times/week) in individuals with IGT (prediabetes) will prevent or delay the development of type 2 DM by 58% regardless of age, sex, or ethnic group.
2Also metformin and other drugs are also being used but there is still a lot of debate about the cost and side effects. They will prevent or delay diabetes by 31% compared to placebo.

MANAGEMENT OF DIABETES

Cornerstones of Diabetes Management are

- **Healthy eating (Diet)/ Exercise / Monitoring / Medication / Education**

Goals of management inc

1.Maintain as near-normal blood glucose levels as possible.
2- Eliminate symptoms related to hyperglycemia,

3 Reduce the short and long-term complications,
4 Allow the patient to achieve as normal lifestyle as possible

The target level of glycemic control should be individualized for each patient, according to

- **Patient's age,**
- **Presence and severity of complications,**
- **Presence of other medical co morbidities,**
- **Patient preference, co operation and understanding.**

Diet

Recommended dietary constituents
• Carbohydrate: 45–60%/ Sucrose: up to 10% (high fibers).
• Fat (total): < 35%
Polyunsaturated: < 10%/ Monounsaturated: 10–20%/ Saturated: < 10%
• Protein: 10–15% (do not exceed 1 g/kg body weight/day)
• Fruit/vegetables: 5 portions daily. 1 portion = 80 g.

Exercise

All patients with diabetes should achieve a significant level of physical activity. This can include walking, gardening, swimming or cycling.
Adults (18–64 year) should achieve a weekly minimum of 2.5 hours of moderate-intensity exercise or 75 minutes of vigorous-intensity exercise, or a combination.
Older adults should also follow these guidelines as far as their abilities allow.

Pharmacological therapy

- **In type 2 diabetes mellitus the care of individuals should include treatment of diabetes complications and conditions associated as (obesity, hypertension, dyslipidemia, and cardiovascular disease).**

Type 2 diabetes

In patients with newly diagnosed type 2 diabetes with sever symptoms and/or high blood glucose or A1C, consider initiating insulin therapy or insulin secretagogues' immediately, otherwise follow these steps

Oral antidiabetic agents

1- Biguanides

Decrease fasting blood glucose./ Decrease post-prandial blood glucose/ Decrease plasma insulin./ Don't effect body weight / No risk of hypoglycaemia.

Metformin is the only biguanide now available. It is widely used as first-line therapy for type 2 diabetes, irrespective of body weight.

The main side-effects are, 25% of patients develop diarrhoea, abdominal cramps, bloating and nausea.

Classically considered an 'insulin sensitizer' because it lowers insulin levels, reduces hepatic glucose production, increase glucose uptake, and has effects on intestinal glucose uptake and utilization.
Is usually introduced at low dose (500 mg twice daily) to minimize the risk of gastrointestinal side effects.

2 Sulphonylureas

Decrease fasting blood glucose./ Decrease post-prandial blood glucose./ Increase plasma insulin / Increase body weight / Increase risk of hypoglycaemia.

Sulphonylureas are 'insulin secretagogues',

3 Meglitinides

(e.g. repaglinide and nateglinide) short-acting 'insulin secretagogues', sulphonylurea like drugs.

The main adverse effects of sulphonylurea and sulphonylurea like drugs are weight gain and hypoglycaemia.
There are a number of Sulphonylureas, as gliclazide, glibenclamide (also known as glyburide), glimepiride and glipizide.

4 Alpha-glucosidase inhibitors

Little effect on fasting blood glucose / Decrease post-prandial blood glucose/ Decrease Plasma insulin / No effect on Body weight/ No Risk of hypoglycaemia.

The α-glucosidase inhibitors delay carbohydrate absorption in the gut.
The main side-effects are flatulence, abdominal bloating and diarrhoea.

5 Thiazolidinedione

Decrease of fasting blood glucose / Decrease post-prandial blood glucose/ Decrease Plasma insulin / Increase Body weight/ No Risk of hypoglycaemia.

TZDs enhance the actions of endogenous insulin, in part directly (in the adipose cells) and indirectly (by altering release of 'adipokines', which alter insulin sensitivity in the liver).

TZDs results in an increase in fat mass and body weight.

Rosiglitazone, increase the risk of myocardial infarction and was withdrawn in 2010. The other is pioglitazone, which does not appear to increase the risk of myocardial infarction but it does exacerbate cardiac failure by causing fluid retention, it increases the risk of bone fracture, and possibly bladder cancer.

6 Incretin-based therapies:

i. DPP-4 inhibitors

Decrease Fasting blood glucose /Decrease Post-prandial blood glucose/ Increase insulin with eating only /No effect on Body weight/No Risk of hypoglycaemia.

The DPP-4 inhibitors (gliptins), prevent the breakdown and enhance concentrations of endogenous GLP-1 and GIP. Oral tablets.

ii. GLP-1 analogues

Decrease Fasting blood glucose/ Decrease Post-prandial blood glucose/Increase insulin with eating only.

7- The sodium, glucose transporter 2 (SGLT2) inhibitor,

Decrease Fasting blood glucose/ Decrease Post-prandial blood glucose/Decrease Plasma insulin/ Decrease Body weight/ No Risk of hypoglycaemia.

Glucose is filtered freely in the renal glomeruli and reabsorbed in the proximal tubules. SGLT2 is involved in reabsorption of glucose. So inhibition of the SGLT2 results in approximately 25% of the filtered glucose not being reabsorbed, with consequent glycosuria.

The glycosuria may result in increased urinary tract and genital fungal infections.

Insulin therapy

Types of insulin

1- Human recombinant DNA insulin

2- Human insulin analogues

.

Treatment of GDM

1- Dietary and life style modification,
2- Metformin or glibenclamide.
3- Insulin may be required, especially in the later stages of pregnancy, OR if the maternal blood glucose is not well controlled by the first 2.
The aim is to maintain near-normal blood glucose levels whilst avoiding hypoglycaemia throughout their pregnancy.
Women with established diabetes before pregnancy, should, achieve excellent glycaemic control before becoming pregnant. In addition, high-dose folic acid (5 mg, daily) should be given before conception to reduce the risk of neural tube defects.
Hyperglycemia early in pregnancy can adversely affect fetal development, including cardiac, renal and skeletal malformations.

Complicatio of DM:
1-Hypoglycemia
2-Diabetic ketoacidosis

.

Chronic Complications of DM

Chronic complications can be divided into vascular and nonvascular complications.

1. Vascular

a. Microvascular

- **Eye disease**

  Retinopathy (nonproliferative /proliferative) / Macular edema

- **Neuropathy**

  Sensory and motor (mono- and polyneuropathy) / Autonomic

- **Nephropathy**

b- Macrovascular

- **Coronary heart disease**
- **Peripheral arterial disease**
- **Cerebrovascular disease**

2Nonvascular complications include Gastrointestinal (gastroparesis, diarrhea), Cataracts and Glaucoma. Periodontal disease, Hearing loss, Dermatological features, Infections.

Eye Complications

It needs 4-7 years history of uncontrolled DM to develop, Classified into two stages:

1- Nonproliferative

2 Proliferative

Renal Complications

Microalbuminuria is an important early indicator of nephropathy,

Diabetic Neuropathy

Diabetic neuropathy occurs after >10years. Types
1- polyneuropathy, 2-mononeuropathy, 3- autonomic neuropathy.

1 **Polyneuropathy**

2 **Autonomic Neuropathy**

GIT:

Dysphagia.

Abdominal fullness due to parasympathetic dysfunction and hyperglycemia , both

Genitourinary:

a. Diabetic cystopathy - U.T.I is treated by {intermittent self-catheterization}

b.Male Impotence, and retrograde ejaculation. Impotence (Erectile dysfunction) is Female sexual dysfunction (reduced sexual desire, dyspareunia, reduced vaginal lubrication).

Pseudomotor: result from sympathetic nervous system dysfunction.

Vasomotor:

a. Cold feet.

b. Dependent edema.

c.Bullous formation.

G. Diabetic foot:

-

PULMONARY TUBERCULOSIS

Definition:

- Pulmonary tuberculosis (TB) is a highly contagious disease caused by a bacteria known as *Mycobacterium tuberculosis*.
- TB generally affects the lungs, but it also can invade other organs of the body, like the brain, kidneys, and lymphatic system.

Mycobacterium Tuberculosis (MTB)

- The My. Tuberculosum bacteria causes MTB
- It is an airborne infection

MTB affects areas of high O_2 tension:

- The Lungs:
  - The Hilum is most affected in Children
  - The Apex is most affected in Adults
- The Kidneys
- The Growing Bones
- The lungs are most commonly affected

How TB Spreads

- TB bacteria are spread through the air from one person to another when a person with TB disease of the lungs or throat coughs, speaks, or sings.

TB is NOT spread by:

Shaking someone's hand.

Sharing food or drink.

Touching bed linens or toilet seats.

Sharing toothbrushes.

Kissing.

- When a person breathes in TB bacteria, the bacteria can settle in the lungs and begin to grow. From there, they can move through the blood to other parts of the body, such as the kidney, spine, and brain.
- TB disease in the lungs or throat can be infectious.
- TB in other parts of the body, such as the kidney or spine, is usually not infectious.

Latent TB Infection and TB Disease

- Not everyone infected with TB bacteria becomes sick.

A- LATENT TB INFECTION:

TB bacteria can live in the body without making disease.

People with latent TB infection:

*Have no symptoms

* Don't feel sick

*Can't spread TB bacteria to others

* Usually have a positive TB skin test reaction or positive TB blood test

* May develop TB disease if they do not receive treatment for latent TB infection.

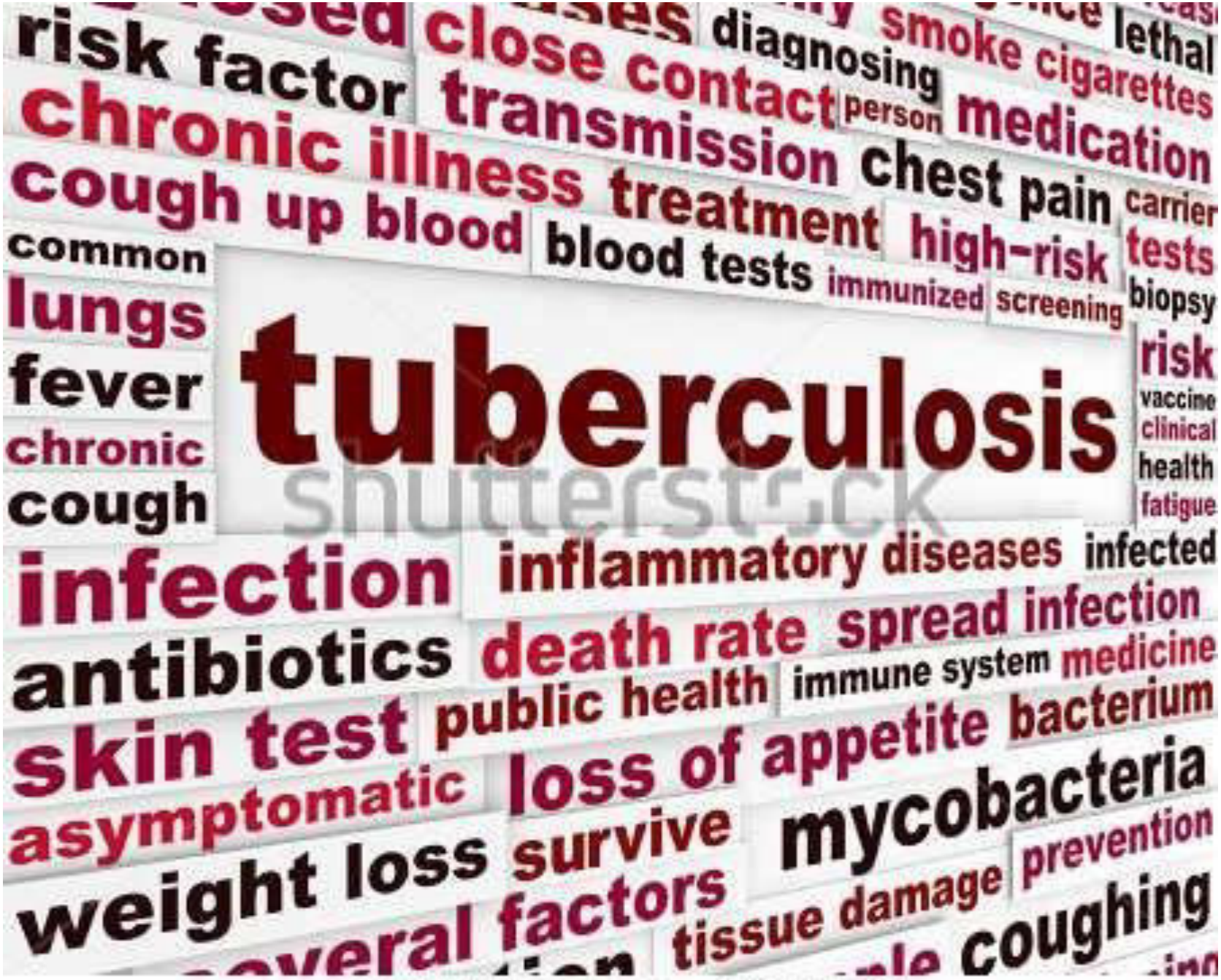
B-TB Disease:

- TB bacteria become active if the immune system can't stop them from growing.
- People with TB disease are sick.
- They may also be able to spread the bacteria to people .
- Some people develop TB disease soon after becoming infected (within weeks) before their immune system can fight the TB bacteria.
- Other people may get sick years later when their immune system becomes weak for another reason.

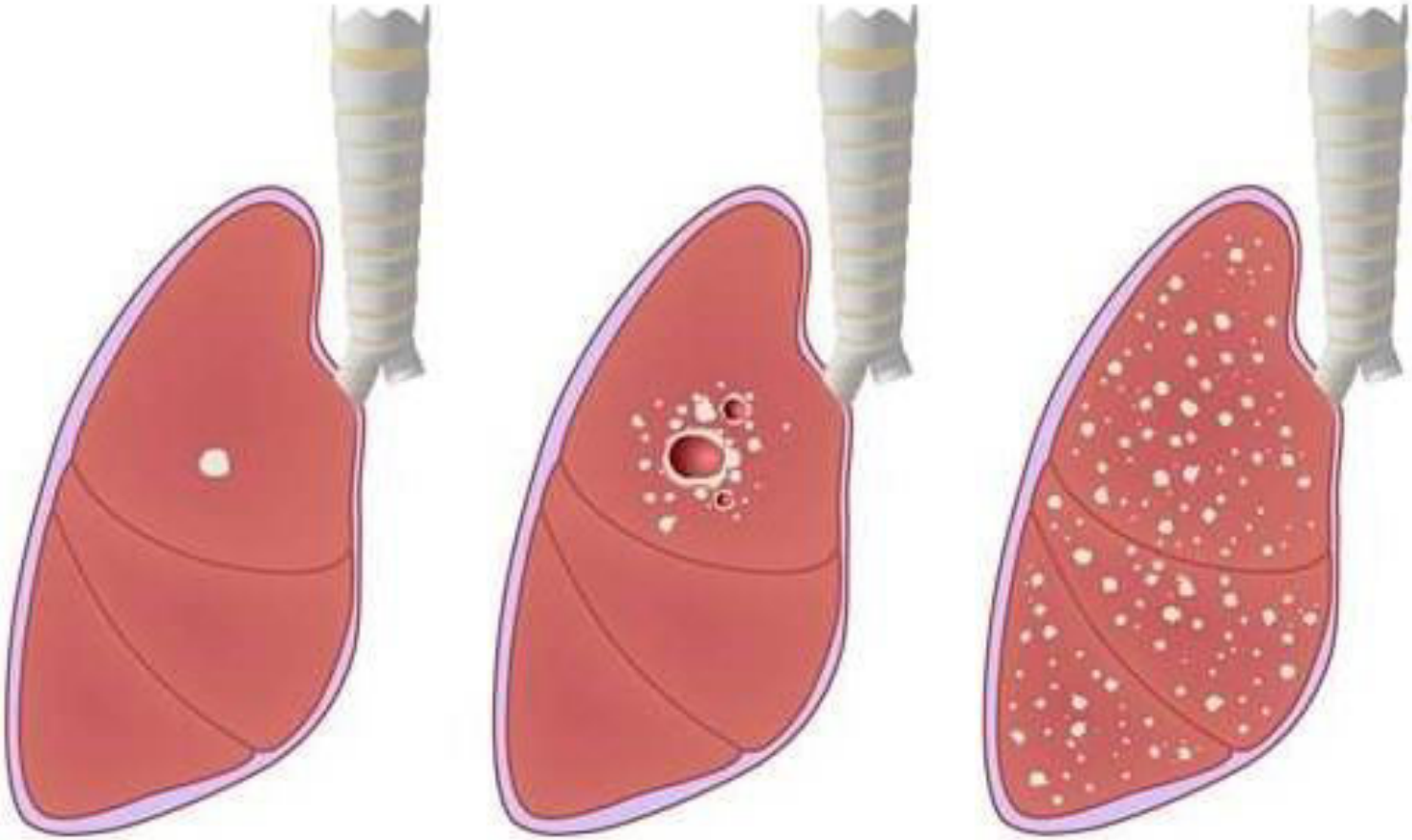
Especially those with HIV infection, the risk of developing TB disease is much higher than for people with normal immune systems.

TB Disease

- A Person with TB Disease
  Has symptoms that may include
  A bad cough that lasts 3 weeks or longer
  Pain in the chest
  Coughing up blood or sputum
  Weakness or fatigue
  Weight loss
  No appetite
  Chills
  Fever
  Sweating at night



Tuberculosis



Latent infection

Cavitary tuberculosis

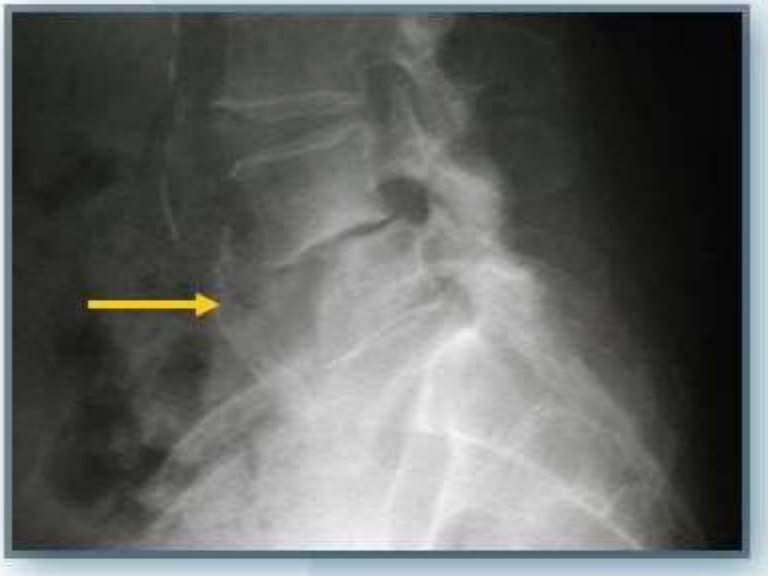
Miliary tuberculosis

Tuberculosis

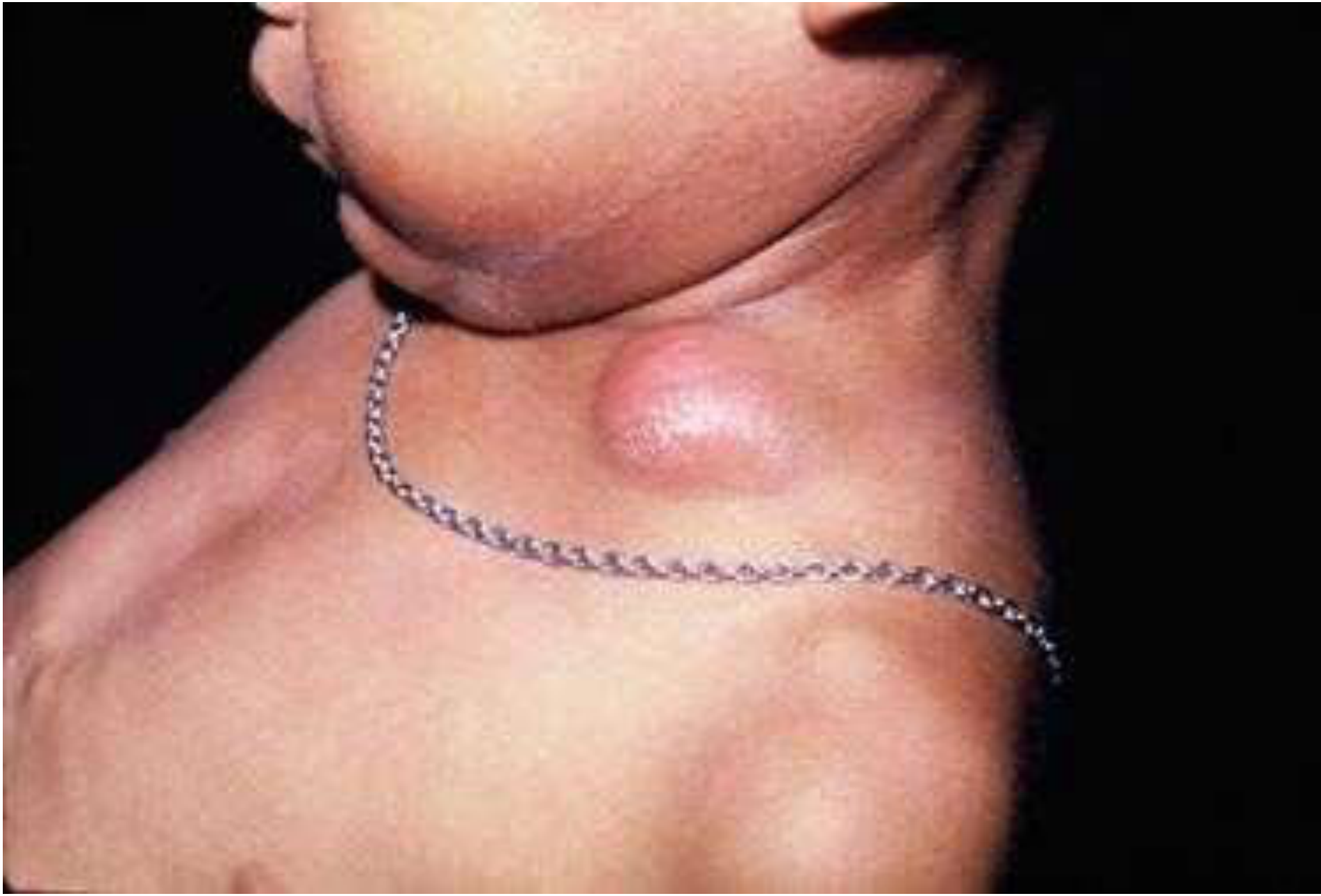
- Etiology/Pathophysiology
  - Tubercle bacillus (Mycobacterium tuberculosis)
  - Chronic pulmonary and extrapulmonary infectious disease
  - Inhalation of droplet containing tubercle bacillus
  - Infection
    - Presence of mycobacteria in the tissue of a person who has no s/s of TB
    - Positive TB skin test
    - 10% will become active disease
  - Active Disease
    - S/S of TB are present
  - NOT easily transmitted
    - Most inhaled TB organisms are destroyed by the upper resp. system

Can this be TB? Extrapulmonary

54-year-old man with three months of focal low-back pain



- "Pott's disease"
- Signs and symptoms of extrapulmonary TB are site specific
- Sampling of extrapulmonary sites for smear, culture, and histopathology may confirm diagnosis



Risk Factors

- Weakened immune system
- Contact with someone with active TB
  - Caring for active TB patients
  - Living or working in crowded conditions with someone with active TB
    - e.g., prisons, nursing homes, homeless shelters
- Poor access to healthcare
- Alcohol or drug abuse
- Travel to places where TB is endemic
- Being born in a country where TB is endemic
- Some medications for rheumatoid arthritis

Signs & Symptoms

- A bad cough that lasts 3 weeks or longer
- Chest pain
- Coughing up blood or sputum (phlegm from deep inside the lungs)

Other symptoms of TB disease are

- weakness or fatigue
- weight loss
- no appetite
- chills
- fever
- sweating at night
- Symptoms of TB disease in other parts of the body depend on the area affected.

Testing for TB Infection

There are two types of tests for TB infection: the TB skin test and the TB blood test:

1-The TB skin test :

- Is also called the Mantoux tuberculin skin test (TST). The TB skin test is performed by injecting a small amount of fluid (called tuberculin) into the skin on the lower part of the arm.
- A person given the tuberculin skin test must return within 48 to 72 hours to have a trained health care worker look for a reaction on the arm.
- The result depends on the size of the raised, hard area or swelling.

Positive skin test: This means the person's body was infected with TB bacteria. Reading the result of a TB skin test

Additional tests are needed to determine if the person has latent TB infection or TB disease.

- **Negative skin test:** This means the person's body did not react to the test, and that latent TB infection or TB disease is not likely.


TUBERCULOS

2-TB blood tests :

are also called interferon-gamma release assays or IGRAs. Two TB blood tests are approved by the U.S. Food and Drug Administration (FDA) the QuantiFERON®-TB Gold In-Tube test (QFT-GIT) and the T-SPOT®.TB test (T-Spot).

•**Positive TB blood test:** This means that the person has been infected with TB bacteria. Additional tests are needed to determine if the person has latent TB infection or TB disease.
•**Negative TB blood test:** This means that the person's blood did not react to the test and that latent TB infection or TB disease is not likely.

TB blood tests are the preferred TB test for:

•People who have received the TB vaccine bacille Calmette-Guérin (BCG).

•People who have a difficult time returning for a second appointment to look for a reaction to the TST.

Who Should be Tested

- People who have spent time with someone who has TB disease.
- People from a country where TB disease is common (most countries in Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia)
- People who live or work in high-risk settings (for example: correctional facilities, long-term care facilities or nursing homes, and homeless shelters)
- Health-care workers who care for patients at increased risk for TB disease
- Infants, children and adolescents exposed to adults who are at increased risk for latent tuberculosis infection or TB disease
- People with HIV infection
- People who became infected with TB bacteria in the last 2 years
- People who inject illegal drugs

- People who were previously vaccinated with BCG may receive a TB skin test to test for TB infection.
- Vaccination with BCG may cause a false positive reaction to a TB skin test.
- A positive reaction to a TB skin test may be due to the BCG vaccine itself or due to infection with TB bacteria.
- TB blood tests (IGRAs), unlike the TB skin test, are not affected by prior BCG vaccination and are not expected to give a false-positive result in people who have received BCG.
- TB blood tests are the preferred method of TB testing for people who have received the BCG vaccine.

Diagnosis of TB Disease

1-Medical History :

TB disease should be suspected in persons who have any of the following symptoms:

- Unexplained weight loss
- Loss of appetite
- Night sweats
- Fever
- Fatigue

If TB disease is in the lungs (pulmonary), symptoms may include:

- Coughing for longer than 3 weeks
- Hemoptysis (coughing up blood)
- Chest pain

Diagnosis of TB Disease

- Clinicians should ask about the patient's history of TB exposure, infection, or disease. It is also important to consider demographic factors (e.g., country of origin, age, ethnic or racial group, occupation) that may increase the patient's risk for exposure to TB or to drug-resistant TB.
- Also, clinicians should determine whether the patient has medical conditions, such as HIV infection or diabetes, that increase the risk of latent TB infection progressing to TB

Diagnosis of TB Disease

2. Physical Examination

- A physical exam can provide valuable information about the patient's overall condition and other factors that may affect how TB is treated, such as HIV infection or other illnesses.

3. Test for TB Infection

- The Mantoux tuberculin skin test (TST) or the TB blood test can be used to test for *M. tuberculosis* infection. Additional tests are required to confirm TB disease.

Diagnosis of TB Disease

4. Chest Radiograph •

- A posterior-anterior chest radiograph is used to detect chest abnormalities. Lesions may appear anywhere in the lungs and may differ in size, shape, density, and cavitation.
- These abnormalities may suggest TB, but cannot be used to definitively diagnose TB.
- *However, a chest radiograph may be used to rule out the possibility of pulmonary TB in a person who has had a positive reaction to a TST or TB blood test and no symptoms of disease.*

Diagnosis of TB Disease

5. Diagnostic Microbiology

- The presence of acid-fast-bacilli (AFB) on a **sputum smear** or other specimen often indicates TB disease.
- Acid-fast microscopy is easy and quick, but it does not confirm a diagnosis of TB because some acid-fast-bacilli are not *M. tuberculosis*.
- Therefore, a **culture** is done on all initial samples to confirm the diagnosis. (
- A positive culture for *M. tuberculosis* confirms the diagnosis of TB disease. Culture examinations should be completed on all specimens, regardless of AFB smear results.

Diagnosis of TB Disease

6. Drug Resistance

- For all patients, the initial *M. tuberculosis* isolate should be tested for drug resistance.
- It is crucial to identify drug resistance as early as possible to ensure effective treatment.
- Drug susceptibility patterns should be repeated for patients who do not respond adequately to treatment or who have positive culture results despite 3 months of therapy.

Deciding When to Treat Latent TB infection

Treatment of latent TB infection should be initiated after the possibility of TB disease has been excluded.

Groups Who Should be Given High Priority for Latent TB Infection Treatment

- People with a positive IGRA result or a TST reaction of 5 or more millimeters
- HIV-infected persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Organ transplant recipients
- Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)

- People with a positive IGRA result or a TST reaction of 10 or more millimeters.

•Recent immigrants (< 5 years) from high-prevalence countries.

• Injection drug users

•Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities).

• Mycobacteriology laboratory personnel.

•Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories.

Drugs	Duration	Interval	Comments
Isoniazid	9 months	Daily	•Preferred treatment for:Persons living with HIV •Children aged 2-11 •Pregnant Women (with pyridoxine/vitamin B6 supplements)
		Twice weekly*	•Preferred treatment for: Pregnant Women (with pyridoxine/vitamin B6 supplements)
Isoniazid	6 months	Daily	
		Twice weekly*	

Treatment for TB Disease

TB disease can be treated by taking several drugs for 6 to 9 months.

There are 10 drugs currently approved by the U.S. Food and Drug Administration (FDA) for treating TB.

The first-line anti-TB agents that form the core of treatment regimens are:

- Isoniazid (INH)
- Rifampcin (RIF)
- Ethambutol (EMB)
- Pyrazinamide (PZA)

Drug-Resistant TB

- drug-resistant TB occurs when bacteria become resistant to the drugs used to treat TB.
- Drug-resistant TB (DR TB) is spread the same way that drug-susceptible TB is spread.
- Drug-resistant TB is more common in people who :

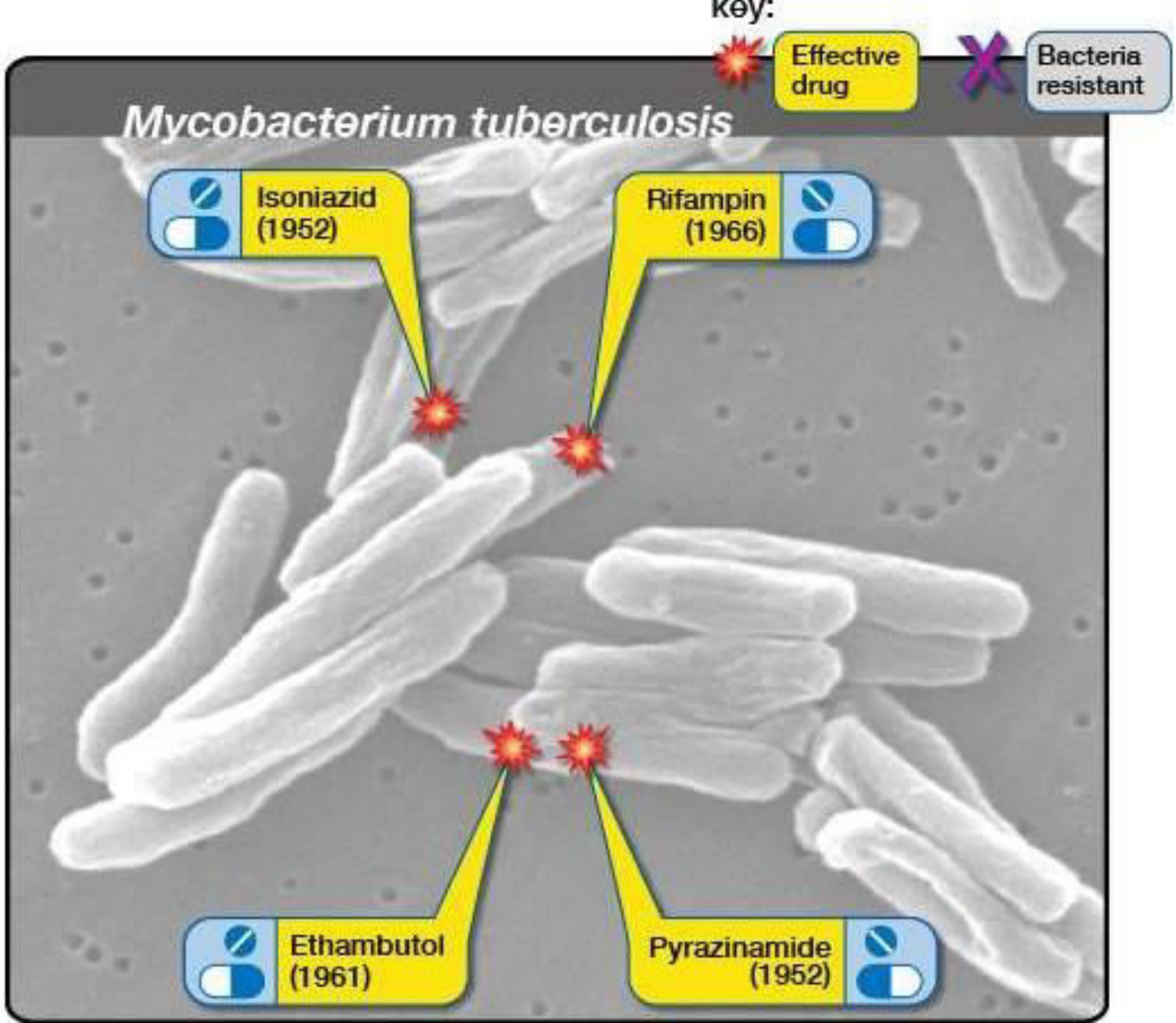
1- Do not take their TB drugs regularly.

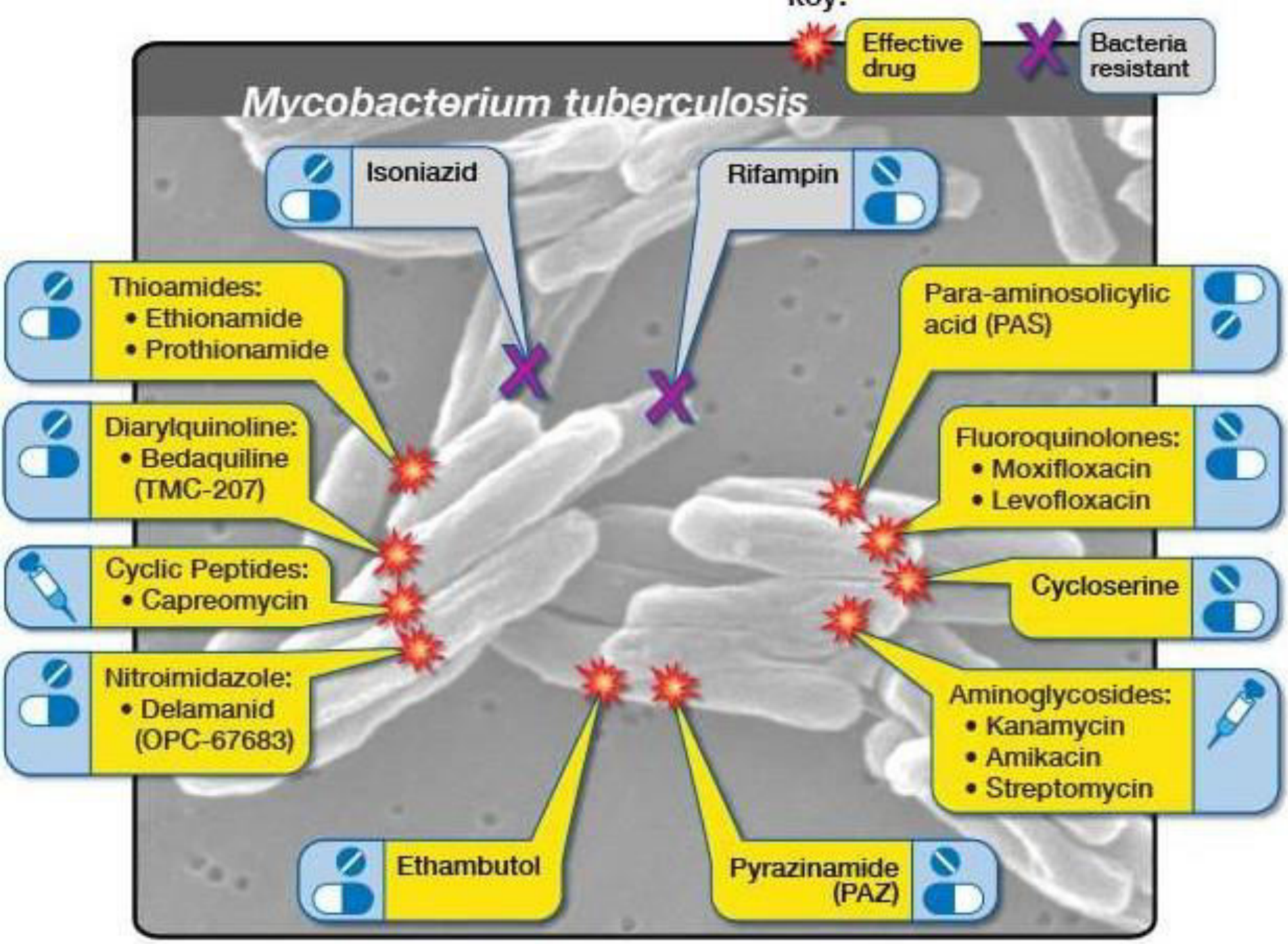
2- Do not take all of their TB drugs.

3- Develop TB disease again, after being treated for TB disease in the past.

4- Come from areas of the world where drug-resistant TB is common.

5- Have spent time with someone known to have drug-resistant TB disease.


key:
Effective drug
Bacteria resistant
Mycobacterium tuberculosis
Isoniazid (1952)
Rifampin (1966)
Ethambutol (1961)
Pyrazinamide (1952)


Effective drug
Bacteria resistant
Mycobacterium tuberculosis
Isoniazid
Rifampin
Thioamides:
• Ethionamide
• Prothionamide
Para-aminosolicylic acid (PAS)
Diarylquinoline:
• Bedaquiline (TMC-207)
Fluoroquinolones:
• Moxifloxacin
• Levofloxacin
Cyclic Peptides:
• Capreomycin
Cycloserine
Nitroimidazole:
• Delamanid (OPC-67683)
Aminoglycosides:
• Kanamycin
• Amikacin
• Streptomycin
Ethambutol
Pyrazinamide (PAZ)

CONCLUSION

- TB IS TREATABLE AND CURABLE DISEASE IF DIAGNOSED AND TREATED EARLILY.

THANK YOU

THE THYROID GLAND

Objectives

By the end of this lecture the student should be able to

1. Determine the etiology and establish the differential diagnosis of thyrotoxicosis,
2. Describe the clinical manifestations and discuss the management of Grave's disease, toxic multinodular goiter and toxic solitary thyroid adenoma
3. Define and manage briefly thyroid storm and subclinical thyrotoxicosis.

Case scenario

A 27 years old female presented with few weeks history of palpitation, weight loss inspite of good appetite, always felling hot and irregular small in amount menses.

1. What do you think the patient has?
2. Enumerate the types of this condition.
3. Which one of them is the most common?
4. What investigation you need to consolidate your diagnosis?
5. How are you going to treat her?

Presenting problems in thyroid disease

Thyroid disorders may present with or without enlargement of the thyroid gland (goiter), the thyroid gland may be

- **Nodular (single or multiple) or Diffuse.**
- **They may be euthyroid, hypothyroid or hyperthyroid.**

Diagnosis of thyroid disease

I)The medical history and physical exam are important parts of the evaluation of thyroid problems, focusing on the eyes, skin, heart, and neurologic findings.

II) Blood tests

1.Thyroid-stimulating hormone (TSH): TSH is usually regarded as the most useful investigation of thyroid function.

When there is an excess of thyroid hormone in the blood, as in hyperthyroidism, the TSH is suppressed or undetected (due to negative feedback), and the opposite is true for hypothyroidism.

TSH may take several weeks to 'catch up' with changes in T4 and T3 levels after treatment, so for follow up you need T4 and T3 levels.

Circadian rhythm of TSH secretion is present but the variation is small so it can be assessed from a single blood sample and does not require any stimulation or suppression.

2. T3 and T4: T4 can be regarded as a pro-hormone, since it has a

- **Longer half-life in the blood than that of T3 (approximately 1 week compared with approximately 18 hours),**
- **T4 binds and activates thyroid hormone receptors less effectively than T3.**
- **T4 can be converted to the inactive metabolite, reverse T3 (rT3 is metabolically inactive).**
- **T3 is four times more potent than T4.**

So T4 acts as a steady, supply that can be converted to the more potent hormone T3 as needed.

More than 99% of T3 and T4 circulate in plasma, bound to transport proteins, mainly thyroxin-binding globulin (TBG), and to a lesser extent transthyretin, and albumin.

It is the unbound or free hormones which diffuse into tissues and exert the metabolic actions as

- **Increased metabolic rate**
- **Adrenergic action, e.g. on the heart rate, gut motility and CNS activation**
- **Bone demineralization, Osteoporosis.**
- **Cellular differentiation.**

➢ **Thyroxine (T4): High T4 usually indicates hyperthyroidism and Low T4 indicates hypothyroidism.**

➢ **Triiodothyronine (T3): High T3 indicates hyperthyroidism and Low T3 indicates hypothyroidism.**

TSH	T4	T3	Most likely interpretation(s)
Undetectable Or Low	Raised	Raised	Primary thyrotoxicosis
Undetectable Or Low	Normal	Raised	Primary T3-toxicosis
Undetectable Or Low	Normal	Normal	Subclinical thyrotoxicosis
Undetectable Or inappropriatly Normal	Low	Low	Secondary hypothyroidism
Mildly elevated 5–20 mU/L	Normal	Normal	Subclinical hypothyroidism
Elevated > 20 mU/L Elevated	Low Raised	Low Raised	Primary hypothyroidism Non-compliance with treatment– recent 'loading' dose. Secondary thyrotoxicosis4
Undetectable Or Low	Raised	Low or Normal	Non-thyroidal illness (sick euthyroid)

3.TSH receptor antibody (TRAb) is an IgG antibody that can cross the placental barrier. TRAb auto antibodies are most closely associated with disease pathogenesis of Graves' thyrotoxicosis. TRAb can be stimulatory (Thyroid-stimulating immunoglobulin (TSI)), causing Graves' thyrotoxicosis, or sometimes as an antagonists (TRAb -blocking antibodies), causing hypothyroidism.

TSI, is also known as a long-acting-thyroid-stimulator independent of the normal feedback, it is present in Grave's disease mainly (+ve in 80–95%), the sensitivity and specificity for the diagnosis of Grave's disease are >90%.
It may also be +ve in 10–20% of patients with Autoimmune hypothyroidism especially TRAb -blocking antibodies.

4.Thyroid peroxidase Antibody (TPO): This antibody is present in patients with Autoimmune hypothyroidism (+ve in 90–100 %), and may also be +ve in 50–80% of patients with Grave's disease.
Also may be +ve in normal population, multinodular goitre, transient thyroiditis so less sensitive and less specific.

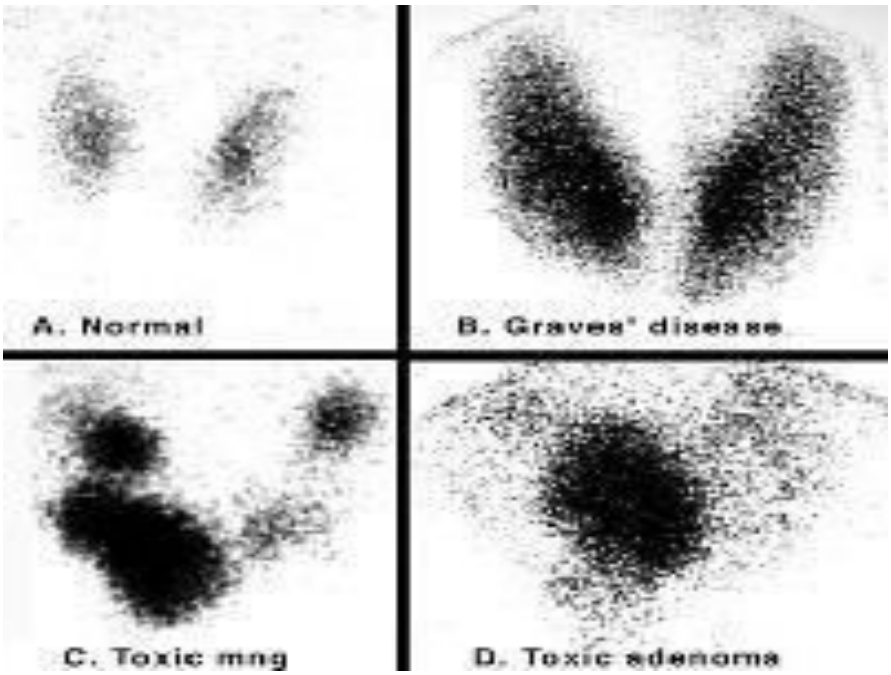
5.Thyroglobulin Antibody(Tg): is +ve in normal population, grave's disease, multinodular goitre, transient thyroiditis, so less sensitive and less specific.
The role of both TPO and Tg in the disease pathogenesis is less well established.

III)Thyroid ultrasound: Thyroid ultrasound helps to determine the size, surface, number and types of nodules in the thyroid gland.
It can discriminate the diffuse goitre of Graves' disease from the irregular enlargement of a multinodular goitre or a solitary nodule.
This test can also detect if there are enlarged parathyroid glands or lymph nodes.

IV)Nuclear thyroid scan: During this scan radioactive ^{123}I or ^{99m}technetium, is used and then an imaging study of the thyroid is done.

- **Increased uptake with thyrotoxic function test, indicates hyperthyroidism,**
- **While low uptake and a hypothyroid function test indicates hypothyroidism.**

- **Low-uptake with a thyrotoxic function test, indicates thyrotoxic phase of transient thyroiditis or iatrogenic thyrotoxicosis.**
  This test should not be performed on women who are pregnant.
  ^{99m}technetium scans, are quicker to perform with a lower dose of radioactivity, and provide a higher-resolution image.



V)Fine-needle aspiration: 21-gauge needle, usually making several passes through different parts of the nodule, and sent for histopathological study.

VI) Computerized axial tomography (CT) scan: is occasionally used to look for the extent of a goiter into the upper chest or to look for narrowing or displacement of the trachea.

Thyrotoxicosis

Is a condition caused by an excess of thyroid hormones from any cause.

Hyperthyroidism is a condition in which an overactive thyroid gland is producing excessive amount of thyroid hormones.

Causes pf Thyrotoxicosis

The most common causes are Graves' disease, toxic multinodular goiter and toxic Solitary thyroid adenoma (nodule) respectively.

Other less common causes are shown below

Thyroiditis • Subacute (de Quervain's) • Post-partum	**Iodide-induced** • Drugs (amiodarone) • Radiographic contrast media • Iodine prophylaxis programme
Extrathyroidal source of thyroid hormone • Factitious thyrotoxicosis • Struma ovarii	**TSH-induced** • TSH-secreting pituitary adenoma • Choriocarcinoma and hydatidiform mole • Follicular carcinoma

Graves' Disease

Is the most common cause of hyperthyroidism (about 80%). In this condition, the thyroid gland is under te control TSI the TSH has lost the ability of normal control.

Graves' disease is 5 times more common among women than men.

Grave's disease is considered an autoimmune disease, and antibodies are found in the blood.

These antibodies include TRAb (TSI antibodies), thyroid peroxidase antibodies (TPO), and TRAb -blocking antibodies.

The triggers for Grave's disease include: stress/smoking/radiation to the neck, medications, and infectious organisms such as viruses.

Functioning Adenoma

A single nodule becomes "autonomous" and does not respond to pituitary regulation via TSH and produces thyroid hormones independently.

The toxic solitary nodule is the cause of less than 5% of all cases of thyrotoxicosis. The nodule is a follicular cell adenoma, which autonomously secretes excess thyroid hormones and inhibits endogenous TSH secretion with subsequent atrophy of the rest of the thyroid gland.

Most patients are females and over 40 years of age.
Although many nodules are palpable, the diagnosis can be made with certainty only by isotope scanning.
^{131}I is highly effective and is an ideal treatment since the atrophic cells surrounding the nodule do not take up iodine and so receive little or no radiation. For this reason, permanent hypothyroidism is unusual. A surgical hemithyroidectomy is an alternative.

Toxic Multinodular Goiter

Multinodular goiter (nontoxic) becomes "autonomous" and does not respond to pituitary regulation via TSH and produces thyroid hormones independently.

Excessive intake of thyroid hormones(Iatrogenic thyrotoxicosis)

Taking too much thyroid hormone medication is actually quite common. Excessive doses of thyroid hormones frequently go undetected due to the lack of follow-up of patients taking their thyroid medicine.
Other persons may be abusing the drug in an attempt to achieve other goals.

Abnormal secretion of TSH

A tumor in the pituitary gland may produce an abnormally high secretion of TSH, this leads to excessive signaling to the thyroid gland to produce thyroid hormones. This condition is very rare and can be associated with other abnormalities of the pituitary gland.

Excessive iodine intake

An excess of iodine may cause Iodine-induced hyperthyroidism or hypothyroidism, and is usually seen in patients who already have an underlying abnormal thyroid gland. Certain medications, such as amiodarone, which is used in the treatment of heart problems, contain a large amount of iodine and may be associated with thyroid function abnormalities.

Clinical manifestations of Thyrotoxicosis

The most common symptoms are weight loss with a normal or increased appetite, heat intolerance, sweating, palpitations, tremor and irritability. In patients older than 70 years, the typical signs and symptoms may be absent and only present with irregular heart rhythms and heart failure

Other symptoms are

Common	Less common
Dyspnea, fatigue, emotional lability	Osteoporosis Diarrhoea, steatorrhoea Angina Ankle swelling psychosis Muscle weakness Periodic paralysis Pruritus, alopecia Amenorrhoea/oligomenorr-hoea/Infertility/ Loss of libido, impotence
Rare Vomiting Apathy Anorexia Exacerbation of asthma	

Signs

Common signs for thyrotoxicosis are Weight loss, Tremor
Palmar Erythema, Sinus tachycardia, lid retraction and lid lag.
All causes of thyrotoxicosis can cause lid retraction and lid lag, due to potentiation of sympathetic innervations of the levator palpebrae muscles.

Other signs are

Less common	Rare
	Gynaecomastia
Atrial fibrillation	Spider naevi
Systolic hypertension/ increased pulse pressure	Onycholysis
Cardiac failure	Pigmentation
Hyper-reflexia/clonus	
Proximalmyopathy	

Signs characteristic of Graves' disease: Grave's disease only may be associated with

1. **Ophthalmopathy, which includes**
   Periorbital edema, conjunctival irritation, exophthalmos and diplopia.
   Ophthalmopathy can occur before, after, or at the same time of hyperthyroidism.
   The degree of ophthalmopathy is worsened in those who smokes or treated by radiation. The course of the eye disease is often independent of the thyroid disease, and steroid therapy may be necessary to control the inflammation. In addition, surgical intervention may be required.
2. **Thyroid Acropachy (rare periosteal hypertrophy, indistinguishable from finger clubbing)**
3. **Thyroid Dermopathy (Pretibial Myxedema) This skin condition is rare and is due to deposition of glycosaminoglycans in the dermis of the lower legs causing nonpitting edema, which is usually associated with erythema and thickening of the skin, without pain or pruritus that appears on the shins of the legs and tops of the feet.**

4. **Thyroid Bruit.**

Diagnosis of Thyrotoxicosis

- **Clinical manifestations and signs**
- **Investigations**

The first-line investigations are serum T3, T4 and TSH.
The main tool for detection of hyperthyroidism is measurement of the TSH level. Which is low or undetectable except in secondary hyperthyroidism.

- **Measurement of TSH receptor antibodies (TRAb, elevated in Graves' disease).**
- **Others if needed as U. S and isotope scanning,**
- **Other none specific Investigations as**
  ECG may demonstrate sinus tachycardia or atrial fibrillation.
  High bl.sugar, …… etc .

Treatment

The options for treating hyperthyroidism include:

1. **Treating the symptoms**
2. **Antithyroid drugs**
3. **Radioactive iodine**
4. **Surgery** **1.Treating the symptoms**

By beta-blockers to decrease rapid heart rate and if used in high doses (only Propranalol), it decrease peripheral T4 to T3 conversion.

2. Antithyroid Drugs

There are two main antithyroid drugs available for use, methimazole and propylthiouracil (PTU). These drugs block production of thyroid hormones in the thyroid. PTU also blocks peripheral conversion of T4 to T3.
The major risk of these medications is occasional suppression of white blood cells production by the bone marrow (agranulocytosis).
It is important for patients to know that if they develop a fever, a sore throat, or any signs of infection while taking methimazole or propylthiouracil, they should see a doctor immediately.
The actual risk of developing agranulocytosis is less than 1%
long-term Antithyroid therapy is only used for Graves' disease, since this disease may actually go into remission in 40%-70% after 1-2y of treatment.
Relapse of Graves' dis after stopping treatment is most likely in the 1st year.
If a patient does relapse, antithyroid drug therapy can be restarted for a longer period, or radioactive iodine or surgery may be considered.

3. Radioactive Iodine

^{131}I is used to ablate a hyperactive gland.
It is the treatment of choice for

- **Recurring Graves' disease,**
- **Patients with severe cardiac involvement,**
- **Multinodular goiter or solitary toxic adenomas,**
- **Patients who cannot tolerate antithyroid drugs.**

It takes 8 to 12 weeks for the thyroid to become normal after therapy.
Since iodine is only picked up by thyroid cells, the destruction is local, and there are no widespread side effects with this therapy.
Not used in pregnancy and breast-feeding. and used with caution in patients with Graves' eye disease since eye disease may worsen after therapy.

Permanent hypothyroidism is the major complication of this form of treatment.

4. Surgery is appropriate for:

- **Pregnant patients in 2nd trimester.**
- **Children who have major adverse reactions to Antithyroid drugs.**
- **Patients with very large thyroid glands and in those who have symptoms from compression of tissues adjacent to the thyroid, such as difficulty swallowing, hoarseness, and shortness of breath.**

The major complication of surgery is disruption of the surrounding tissue, including the

- **Nerves supplying the vocal cords**
- **Parathyroid glands**

Thyroid Crises (Thyroid storm)

Thyroid storm is an acute form of hyperthyroidism that results from either unrecognized untreated or inadequately treated severe hyperthyroidism. It is a rare medical emergency, which has a mortality of 10% despite early recognition and treatment.

Precipitated by infection, trauma, surgery, or any other stressful condition

Present with severe symptoms of hyperthyroidism with one or more of the following: fever, agitation confusion, psychosis, coma, tachycardia or atrial fibrillation, cardiovascular collapse and shock.

Treatment of Thyroid Storm

- **Patients should be rehydrated**
- **Give propranolol, either orally (80 mg 4 times daily) or intravenously (1–5 mg 4 times daily). It helps in controlling adrenergic symptoms and also reduces the peripheral conversion of T4 to T3 (propranolol only in high doses).**
- **Sodium ipodate (500 mg per day orally) will restore serum T3 levels to normal in 48–72 hours (inhibits the release of thyroid hormones, and reduces the peripheral conversion of T4 to T3).**
- **Dexamethasone (2 mg 4 times daily) also reduces the peripheral conversion of T4 to T3.**

- **Oral carbimazole 40–60 mg daily should be given to inhibit the synthesis of new thyroid hormone.**
- **If the patient is unconscious or uncooperative, carbimazole can be administered rectally with good effect.**

Subclinical thyrotoxicosis

Serum TSH is undetectable or very low, and serum T3 and T4 are at the upper end of the normal range.
This is most often found in older patients with multinodular goitre.
These patients are at increased risk of atrial fibrillation and osteoporosis, and hence the consensus view is that they have mild thyrotoxicosis and require therapy, usually with ^{131}I.
Otherwise, annual review is essential, as the conversion rate to overt thyrotoxicosis is onlt about 5% each year.

THE THYROID GLAND

Hypothyroidism

Hypothyroidism is a state of thyroid hormone deficiency.
Occurs at any age but is particularly common among the elderly,
10% of women and 6% of men older than 65years are affected.
In all age group women are 6 times more frequently affected than men.
It is either Primary or secondary.

Causes:

The most common cause of

1. Primary hypothyroidism is

- **Autoimmune disease that usually results from Hashimoto's thyroiditis.**

2. The 2nd most common cause is post-therapeutic hypothyroidism as,

- **Following ^{131}I ,**
- **Surgical treatment of thyrotoxicosis and goiter**
- **Overtreatment with antithyroid drugs. Both**

above accounts for over 90% of causes, others causes are

Transient thyroiditis • Subacute (de Quervain's) thyroiditis • Post-partum thyroiditis	**Iodine deficiency, e.g. in mountainous regions If iodine deficiency is severe,**
	Congenital • Dyshormonogenesis • Thyroid aplasia
Infiltrative Amyloidosis/Riedel's thyroiditis/sarcoidosis etc.	

3. Secondary hypothyroidism occurs when the hypothalamus produces insufficient thyrotropin-releasing hormone (TRH) or the pituitary produces insufficient TSH.

Clinical features of hypothyroidism

Symptoms and signs of primary hypothyroidism are often subtle and insidious.

It may manifest atypically in the elderly as confusion, anorexia, weight loss, incontinence, and decreased mobility.

Hypothyroidism of a long duration, leads to the infiltration of many body tissues by

- **Mucopolysaccharides,**
- **Hyaluronic acid,**
- **proteoglycan as dermatan sulfate,**

Resulting in

- **A low-pitched voice, slurred speech due to a large tongue,**
- **Poor hearing,**
- **Compression of the median nerve at the wrist (carpal tunnel synd with paresthesias of the hands).**
- **Infiltration of the dermis gives rise to non pitting edema (myxedema), which is most marked in the skin of the hands, feet, face and eyelids. Resulting in periorbital and facial puffiness with dull facial expression combined with facial pallor.**

Facial pallor is due to

- **Vasoconstriction or**
- **Anemia (B12 or iron deficiency),**
- **Or a lemon-yellow tint of the skin caused by Carotenemia.**

Other symptoms are

Common	Less common
Weight gain Cold intolerance Fatigue, Somnolence, Dry skin, Dry hair, Menorrhagia.	Constipation, Hoarseness of voice, Carpal tunnel syndrome, Alopecia, Muscle stiffness Deafness, Depression, Infertility.
Rare Psychosis (myxedema madness)/ Galactorrhoea/Impotence	

Clinical signs are

com	mon
Weight gain Hoarse voice Facial features: • Purplish lips/ Malar flush • Periorbital oedema and eyelids droop due to decreased adrenergic drive	• Loss of lateral eyebrows • Anemia • lemon-yellow tint • Erythema ab igne • Bradycardia • Hypertension • Delayed relaxation of reflexes • Dermal myxedema
Rare Ileus/ascites/Pericardial and pleural effusions /Cerebellar ataxia/Myotonia	

Investigations

- In Primary hypothyroidism, the serum T4 is low and TSH is elevated, usually in excess of 20 mU/L.
- Measurements of serum T3 are unhelpful since they do not discriminate reliably between euthyroidism and hypothyroidism.
- Measurement of thyroid peroxidase antibodies although +ve in many different etiologies is some times helpful.

Other non-specific abnormalities are

- Raised serum enzymes: creatine kinase, aspartate aminotransferase, lactate dehydrogenase (LDH)
- Hypercholesterolemia
- Anemia: normochromic normocytic or macrocytic
- Hyponatremia
- ECG classically demonstrates sinus bradycardia with low-voltage complexes and ST segment and T-wave changes.

Treatment

Is with Levothyroxine (T4) replacement.

- **In patients with known ischemic heart disease and elderly, thyroid hormone replacement should be introduced at low dose 25 µg per day, and increased very slowly, to finally reach maintenance dose of 100–150 µg per day.**
- **In younger patients, it is safe to initiate levothyroxine at a higher dose 100 µg per day.**
- **Aim to maintain serum TSH within the reference range, and to achieve this, the serum T4 should be in the upper normal range.**
- **Levothyroxine (T4) has a half-life of 7 days so it should always be taken as a single daily dose.**
- **At least 6 weeks should pass before repeating thyroid function tests and adjusting the dose, usually by 25 µg/day.**
- **Measure thyroid function every 1–2 years once the dose of T4 is stabilized.**
- **Patients feel better within 2–3 weeks. Reduction in weight and periorbital puffiness occurs quickly, but the restoration of skin and hair texture and resolution of any effusions may take 3–6 months.**

Situations where an increase in the dose of T4 is necessary are

1 Pregnancy

Increases concentration of serum thyroxine-binding globulin, require an increase in the dose of levothyroxine of approximately 25–50 µg. Inadequate maternal T4 therapy may be associated with impaired cognitive development in an unborn child.

2 Malabsorption

3 Drugs

•Drugs that Increase T4 clearance: Phenobarbital, phenytoin, carbamazepine, rifampicin, sertraline, chloroquine.

•Drugs Interfere with intestinal T4 absorption: colestyramine, calcium carbonate …..etc.

SUBCLINICAL HYPOTHYROIDISM

Is elevated serum TSH (TSH > 4.5 mU/L and <20 mU/L) in patients with absent or minimal symptoms of hypothyroidism and normal serum levels of free T4.

It is relatively common; occurs in more than 15% of elderly women and 10% of elderly men.

In patients with serum TSH > 10 and <20 mU/L, there is a high likelihood of progression to overt hypothyroidism. These patients are also more likely to have hypercholesterolemia and atherosclerosis. They should be treated with T4, even if they are asymptomatic.

For patients with TSH levels between 4.5 and 10 mU/L, use of T4 is reasonable if symptoms of early hypothyroidism (eg, fatigue, depression) are present, therapy is also indicated in pregnant women and who plan to become pregnant to avoid effects of hypothyroidism on the pregnancy and fetal development.

If no treatment is needed then repeat the measurement after 3 months, then an annual measurement of serum TSH and free T4 to assess progress of the condition.

Non-thyroidal illness ('sick euthyroidism')

This presents with a low serum TSH, raised T4 and normal or low T3, in a patient with systemic illness who doesn't have clinical evidence of thyroid disease.

These abnormalities are due to

- **Decreased peripheral conversion of T4 to T3,**
- **Altered levels of binding proteins and their affinity for thyroid hormones,**
- **Reduced secretion of TSH.**

Myxedema coma (Tutorial)

The condition usually occurs in patients with long-standing, undiagnosed hypothyroidism and is usually precipitated by infection, cerebrovascular disease, heart failure, trauma, or drug therapy.

It has a 50% mortality rate and needs urgent treatment.

Pathophysiology

long-standing hypothyroidism is associated with reduced metabolic rate and decreased oxygen consumption, which affects all body systems resulting in

- **Hypothermia,**
- **Cardiac contractility is impaired, leading to reduced stroke volume, low cardiac output, bradycardia, hypotension and pericardial effusions.**
- **Respiratory depression (Central), Hypoventilation with CO2 retention.**
- **Brain function is affected by**
  - **Reduction in oxygen delivery**
  - **Decreased glucose utilization**
  - **Reduced cerebral blood flow.**

Rapid diagnosis based on clinical judgment, history, and physical examination is imperative, because death is likely without rapid treatment. So treatment must begin before biochemical confirmation of the diagnosis.

Treatment

- **Maintenance of adequate airway is crucial, since most patients have depressed mental status with respiratory failure. Mechanical ventilation is usually required during the first 36-48 hours.**
- **Intravenous injection of 20 µg triiodothyronine(T3) three times daily until there is sustained clinical improvement.**
- **Or an intravenous loading dose of 300-600 micrograms of levothyroxine (T4) followed by a daily intravenous dose of 50-100 micrograms.**
- **Corticosteroids are also given, because the possibility of central (2ndry) hypothyroidism usually cannot be initially ruled out.**
- **Treat hypothermia with passive rewarming using ordinary blankets and a warm room. Active rewarming using external devices carries a risk of vasodilatation and worsening hypotension and should be avoided.**
- **The precipitating factor should be rapidly treated.**

Goiter

A common thyroid problem, affecting about 5% of the population that present as a lump in the neck or sometimes present with acute painful enlargement of the thyroid.

There are 3 main types

1- Diffuse goiter

2 Multinodular goitre

3 Solitary nodule.

1- Diffuse goitre

A- Simple goitre This form of goitre usually presents between the ages of 15 and 25 years.

It occurs sporadically and is of unknown etiology.

The goitre is soft and symmetrical and the thyroid is enlarged to 2-3 times its normal size.

There is no tenderness, no lymphadenopathy, no bruit.

T3,T4 and TSH are normal and no thyroid autoantibodies.

A diffuse goitre rarely needs further treatment, and in most cases the goitre regresses, unless it is very large and causing cosmetic symptoms or compression of other local structures (resulting in stridor or dysphagia).

Thyroxine therapy is sometimes justified in an attempt to shrink the goitre.

In some, however, the stimulus that caused the thyroid enlargement persists and, as a result of recurrent episodes of hyperplasia and involution during the following 10–20 years, the gland becomes multinodular with areas of autonomous function (Multinodular goitre).

2- Multinodular goitre

Patients with thyroid enlargement in the absence of thyroid dysfunction or positive autoantibodies (i.e. 'simple goitre') may progress to develop thyroid nodules. These nodules with time grows at a varying rate and secrete thyroid hormone 'autonomously', thereby suppressing TSH-dependent growth and function in the rest of the gland. Ultimately, complete suppression of TSH occurs in about 25% of cases, with T4 and T3 levels often within the normal range (subclinical thyrotoxicosis) but sometimes elevated (toxic multinodular goitre).

Management

- **If the goitre is small and non toxic, no treatment is necessary, but only annual follow up.**
- **Partial thyroidectomy is indicated for large Goiters.**

- **Thyroxine therapy is of no benefit in shrinking multinodular goitres and may simply aggravate any associated thyrotoxicosis.**

3- Solitary thyroid nodule

It is important to determine whether the nodule is benign or malignant. It is rarely possible to make this distinction on clinical grounds alone, the presence of the following increase the suspicion,

- **Cervical lymphadenopathy**
- **Presenting in childhood or adolescence,**
- **Past history of head and neck irradiation,**
- **Presenting in the elderly.**

Investigations

Serum T3, T4 and TSH should be measured in all patients with a solitary thyroid nodule.
The finding of undetectable TSH is very suggestive of a benign autonomously functioning thyroid follicular adenoma (Toxic adenoma), the diagnosis can be confirmed by thyroid isotope scanning which will show hot nodule in Toxic adenoma and Cold nodule in euthyroid nodule.
The most useful investigation is fine needle aspiration of the nodule. Cytological examination can differentiate benign (80%) from definitely malignant or indeterminate nodules (20%).
Of these 20%, about 25–50% are confirmed as cancer at surgery.

Management

Solitary nodules in which cytology either is inconclusive or shows malignant cells are treated by surgical excision.
Benign euthyroid lesions are sometimes excised, if they are growing, but the majority of patients can be reassured without treatment. Benign toxic nodules is mentioned before.

Thyroiditis (Self Study)

A- Permanent thyroiditis

i- Hashimoto's thyroiditis

Thyroiditis refers to an inflammation of the thyroid.
It is characterised by Permanent destructive lymphoid infiltration of the thyroid, leading to a varying degree of fibrosis and thyroid enlargement. Hashimoto's thyroiditis increases in incidence with age and affects approximately 3.5 per 1000 women and 0.8 per 1000 men each year. Many present with a small or moderately sized diffuse goitre, which is characteristically firm or rubbery in consistency. It is sometimes impossible to differentiate it from simple goitre by palpation alone. Around 25% of patients are hypothyroid at presentation. In the remainder, serum T4 is normal and TSH normal, but these patients are at risk of developing overt hypothyroidism in the future years.
Anti-thyroid peroxidase antibodies are present in the serum in more than 90% of patients with Hashimoto's thyroiditis.
Thyroxine therapy is indicated as a treatment for hypothyroidism, and also to shrink an associated goitre.

B- Transient thyroiditis is of many types

i. Sub acute (de Quervain's) thyroiditis

In its classical painful form, subacute thyroiditis is a transient inflammation of the thyroid gland occurring after infection with Coxsackie, mumps or adenoviruses.
There is pain in the region of the thyroid that radiate to the angle of the jaw and the ears, and is made worse by swallowing,
coughing and movement of the neck. The thyroid is usually palpably enlarged and tender. Systemic upset (fever…..etc) is common. Affected patients are usually females aged 20–40 years.

ii. Silent thyroiditis

Is an other form of transient thyroiditis, it is Painless. Can also occur after viral infection and in patients with underlying autoimmune disease.

iii. Drug-induced thyroiditis

Transient thyroiditis that can be precipitated by drugs, including interferon-α and lithium. Symptoms continue as long as the drug is taken.

iv. Acute thyroiditis (also called suppurative thyroiditis)

Transient thyroiditis caused by bacteria or other infectious organisms. Symptoms include a painful thyroid, generalized illness and occasionally symptoms of mild hypothyroidism. Symptoms improve after treatment of the infectious cause.

v. Post-partum thyroiditis

The maternal immune response, which is modified during pregnancy to allow survival of the fetus, is enhanced after delivery and may unmask previously unrecognized auto antibodies that attack the thyroid after delivery of a child. Symptoms of thyroid dysfunction are rare . However, symptomatic thyrotoxicosis presenting for the first time within 12 months of childbirth is likely to be due to post-partum thyroiditis and the diagnosis is confirmed by no radioisotope uptake. The clinical course and treatment are similar to painless subacute thyroiditis. Post-partum thyroiditis tends to recur after subsequent pregnancies and eventually patients progress over a period of years to permanent hypothyroidism.

In most types of Transient thyroiditis, inflammation in the thyroid gland occurs and is associated with release of stored thyroid hormones, with damage to follicular cells and impaired synthesis of new thyroid hormones. As a result, T4 and T3 levels are raised for 4–6 weeks until the stored thyroid hormones is depleted. Then, there is usually a period of hypothyroidism of variable severity until follicular cells recover and normal thyroid function is restored within 4–6 months. During this time there is no radioisotope uptake, because the damaged follicular cells are unable to trap iodine and because TSH secretion is suppressed.

The pain usually respond to simple non-steroidal anti-inflammatory drugs. Occasionally, it may be necessary to prescribe prednisolone 40 mg daily for 3–4 weeks.

The thyrotoxicosis is mild and treatment with a β-blocker is usually adequate. Antithyroid drugs are of no benefit because thyroid hormone synthesis is impaired rather than enhanced. Careful monitoring of thyroid function and symptoms is required so that thyroxine can be prescribed temporarily in the hypothyroid phase.

PULMONARY TUBERCULOSIS

Objectives

- To know definition of TB.
- Way of transmission , types of TB.
- To cover clinical presentation of TB.
- How can make diagnosis of TB.
- How can manage patients with TB.
- To know types of Anti.TB drugs resistant,presentation & diagnosis.

- 26 years old male presented with history of dry cough of more than 3 months with low grade fever, night sweating, loss of appetite.
- He have history of contact with tuberculosis patient.
- Q1: What's defferntional diagnosis .
- Q2: Who can proved diagnosis.
- Q3: Who can treated this patients.

Definition:

- Pulmonary tuberculosis (TB) is a highly contagious disease caused by a bacteria known as *Mycobacterium tuberculosis*.
- TB generally affects the lungs, but it also can invade other organs of the body, like the brain, kidneys, and lymphatic system.

Mycobacterium Tuberculosis (MTB)

- The My. Tuberculosum bacteria causes MTB
- It is an airborne infection

MTB affects areas of high O_2 tension:

- The Lungs:
  - The Hilum is most affected in Children
  - The Apex is most affected in Adults
- The Kidneys
- The Growing Bones
- The lungs are most commonly affected

How TB Spreads

- TB bacteria are spread through the air from one person to another when a person with TB disease of the lungs or throat coughs, speaks, or sings.

TB is NOT spread by:

Shaking someone's hand.

Sharing food or drink.

Touching bed linens or toilet seats.

Sharing toothbrushes.

Kissing.

- When a person breathes in TB bacteria, the bacteria can settle in the lungs and begin to grow. From there, they can move through the blood to other parts of the body, such as the kidney, spine, and brain.
- TB disease in the lungs or throat can be infectious.
- TB in other parts of the body, such as the kidney or spine, is usually not infectious.

Latent TB Infection and TB Disease

- Not everyone infected with TB bacteria becomes sick.

A- LATENT TB INFECTION:

TB bacteria can live in the body without making disease.

People with latent TB infection:

*Have no symptoms

* Don't feel sick

*Can't spread TB bacteria to others

* Usually have a positive TB skin test reaction or positive TB blood test

* May develop TB disease if they do not receive treatment for latent TB infection.

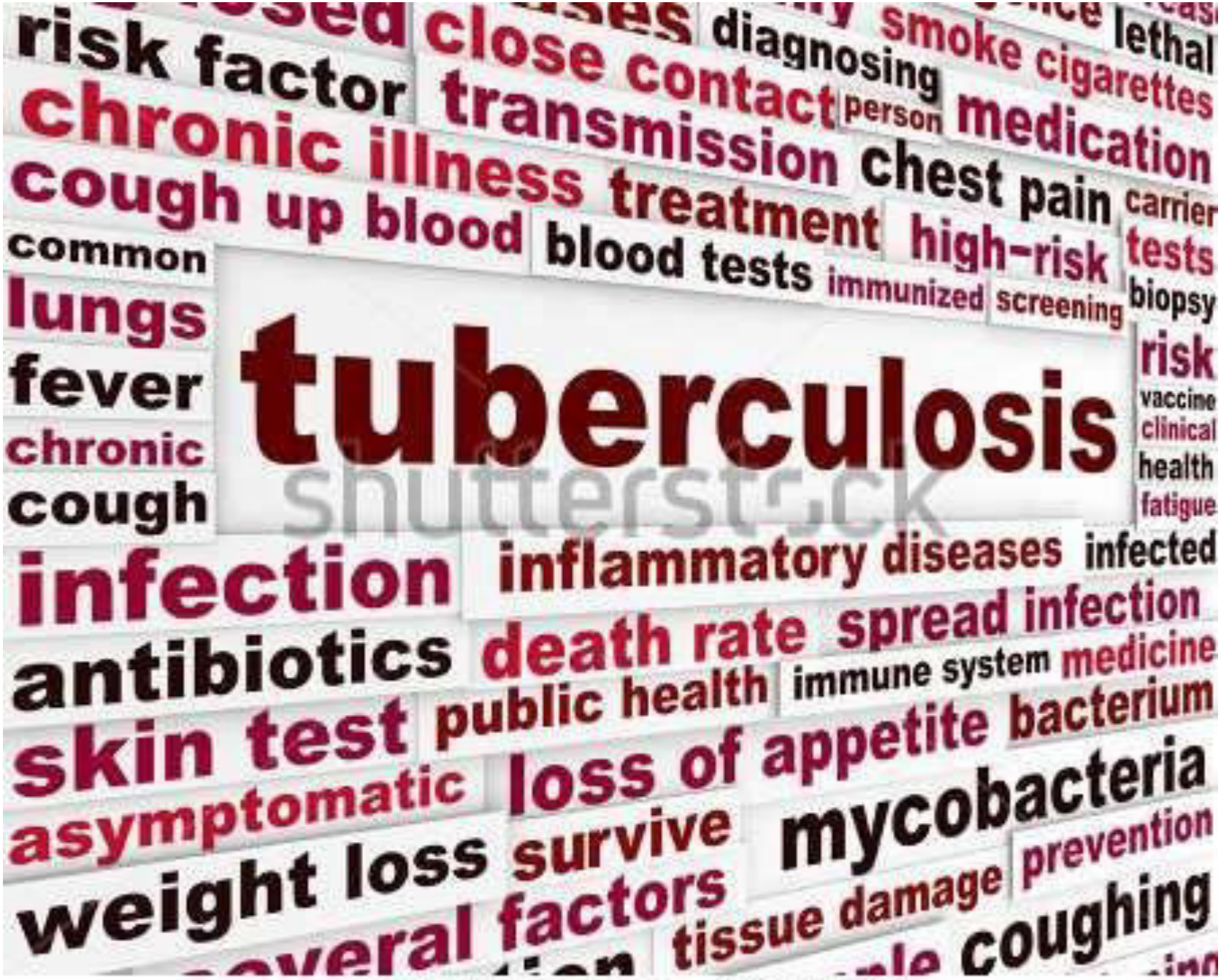
B-TB Disease:

- TB bacteria become active if the immune system can't stop them from growing.
- People with TB disease are sick.
- They may also be able to spread the bacteria to people .
- Some people develop TB disease soon after becoming infected (within weeks) before their immune system can fight the TB bacteria.
- Other people may get sick years later when their immune system becomes weak for another reason.

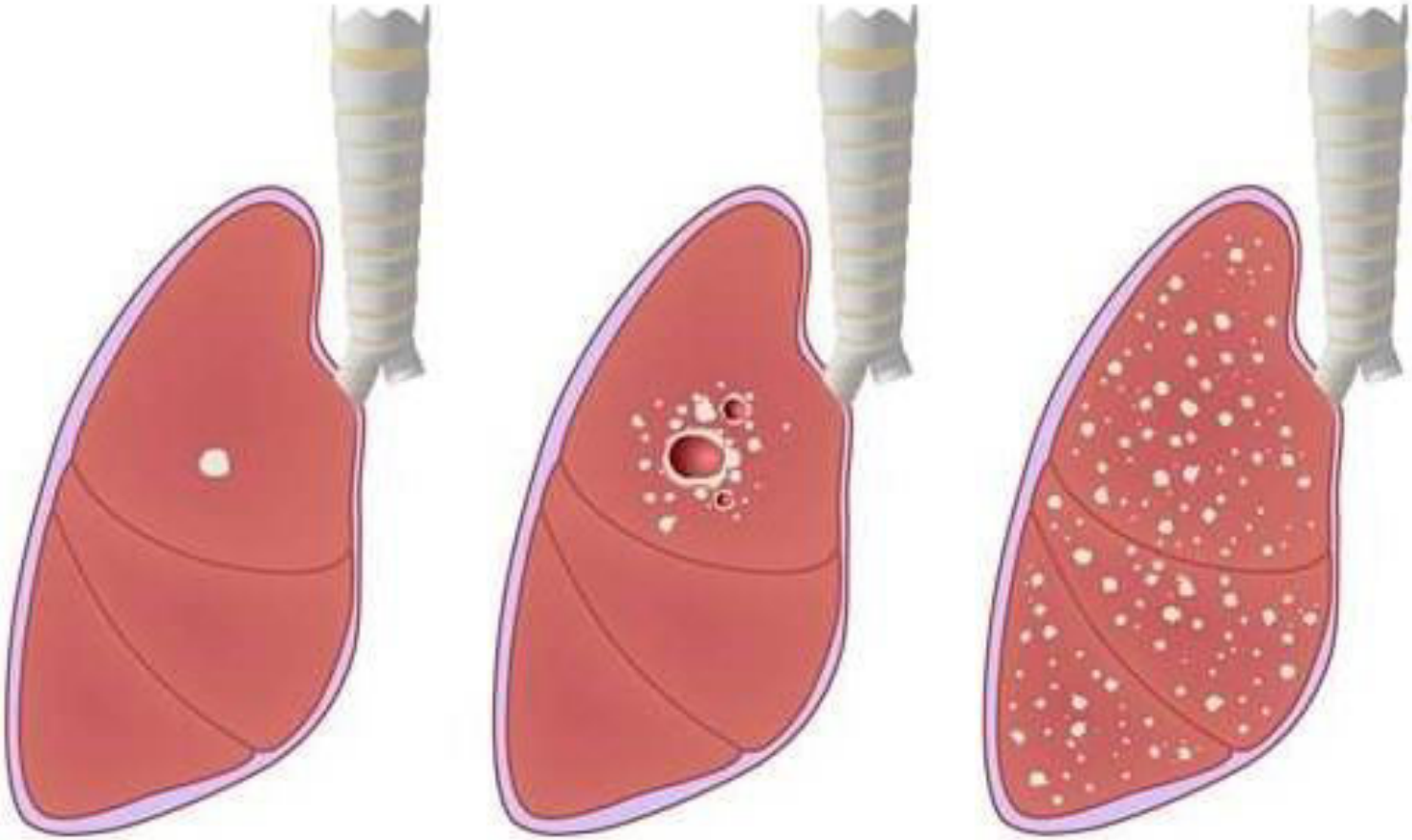
Especially those with HIV infection, the risk of developing TB disease is much higher than for people with normal immune systems.

TB Disease

- A Person with TB Disease
  Has symptoms that may include
  A bad cough that lasts 3 weeks or longer
  Pain in the chest
  Coughing up blood or sputum
  Weakness or fatigue
  Weight loss
  No appetite
  Chills
  Fever
  Sweating at night



Tuberculosis



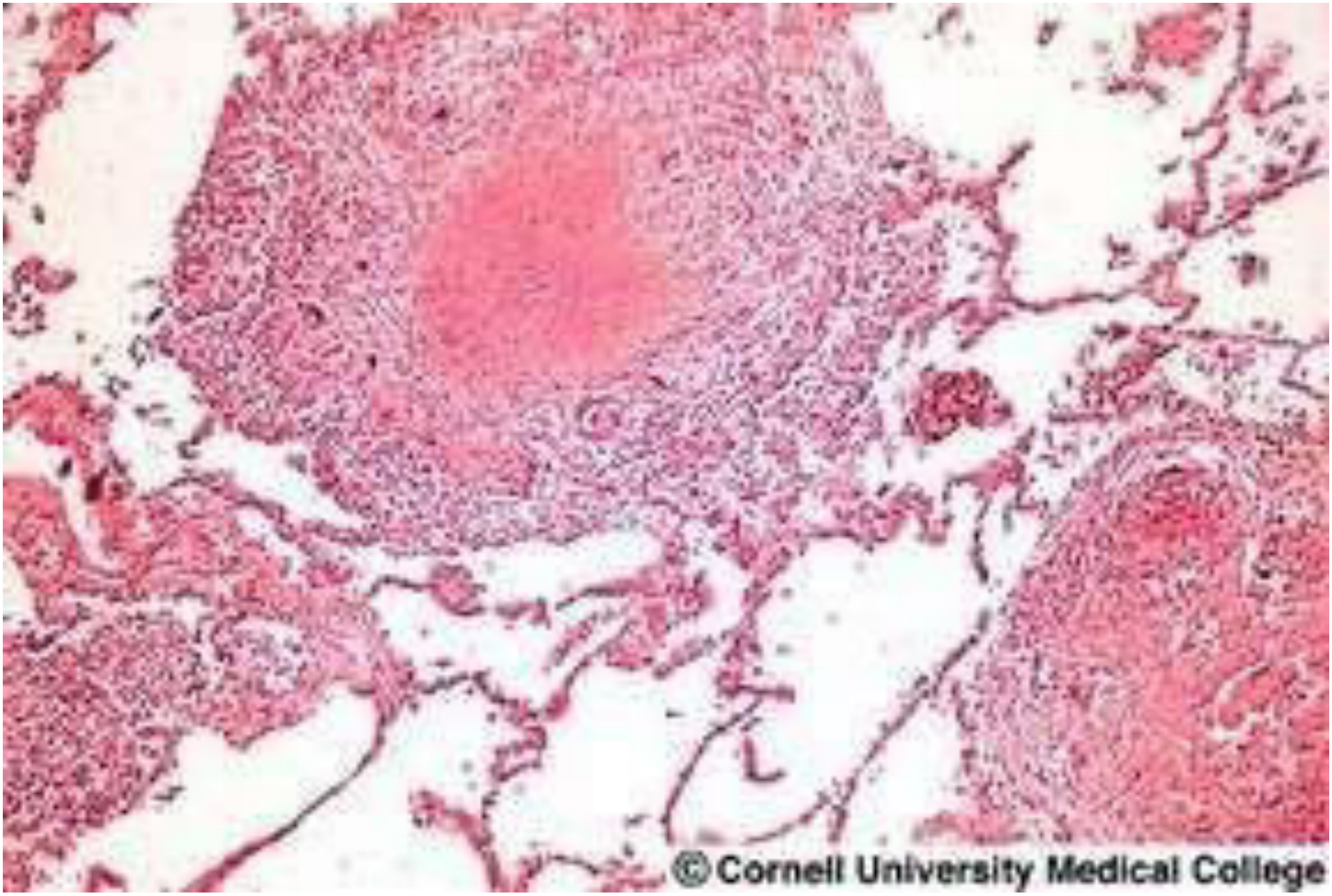
Latent infection

Cavitary tuberculosis

Miliary tuberculosis

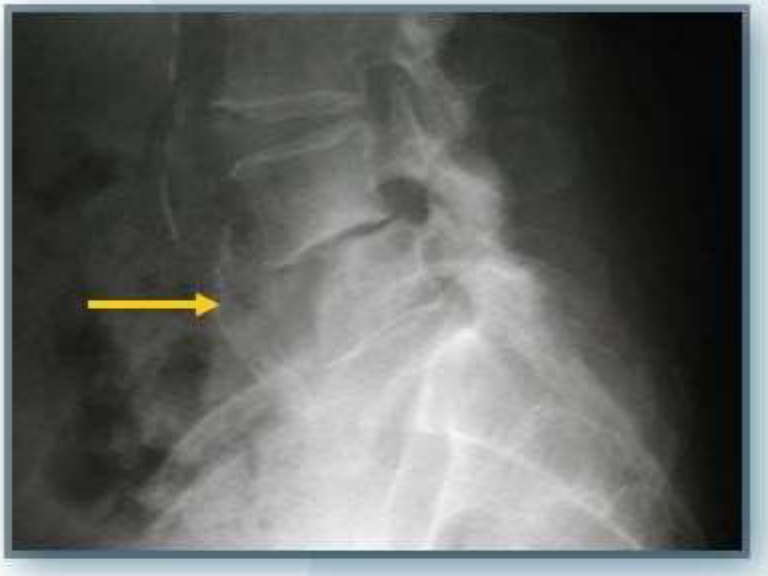
Tuberculosis

- Etiology/Pathophysiology
  - Tubercle bacillus (Mycobacterium tuberculosis)
  - Chronic pulmonary and extrapulmonary infectious disease
  - Inhalation of droplet containing tubercle bacillus
  - Infection
    - Presence of mycobacteria in the tissue of a person who has no s/s of TB
    - Positive TB skin test
    - 10% will become active disease
  - Active Disease
    - S/S of TB are present
  - NOT easily transmitted
    - Most inhaled TB organisms are destroyed by the upper resp. system

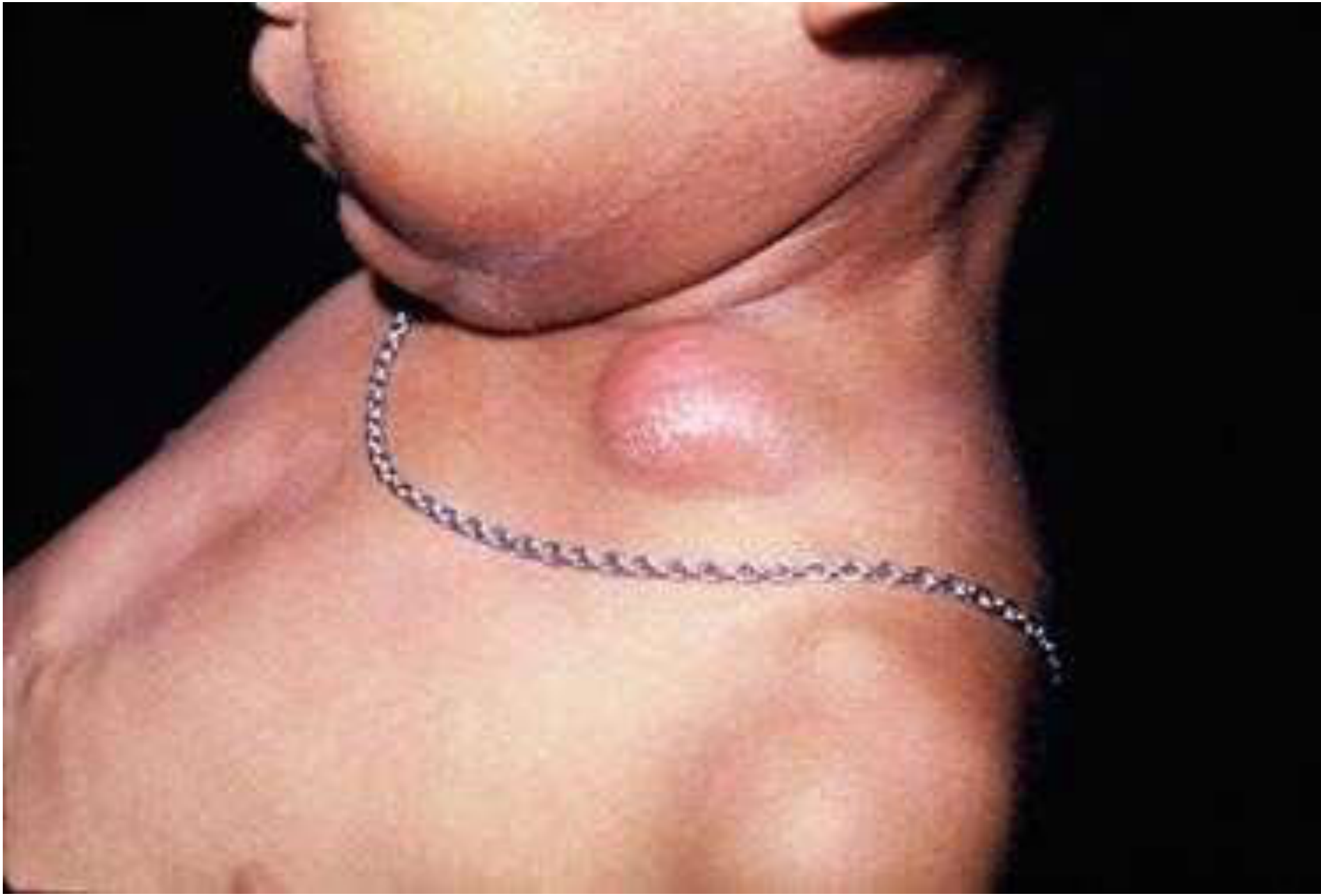

© Cornell University Medical College

Can this be TB? Extrapulmonary

54-year-old man with three months of focal low-back pain

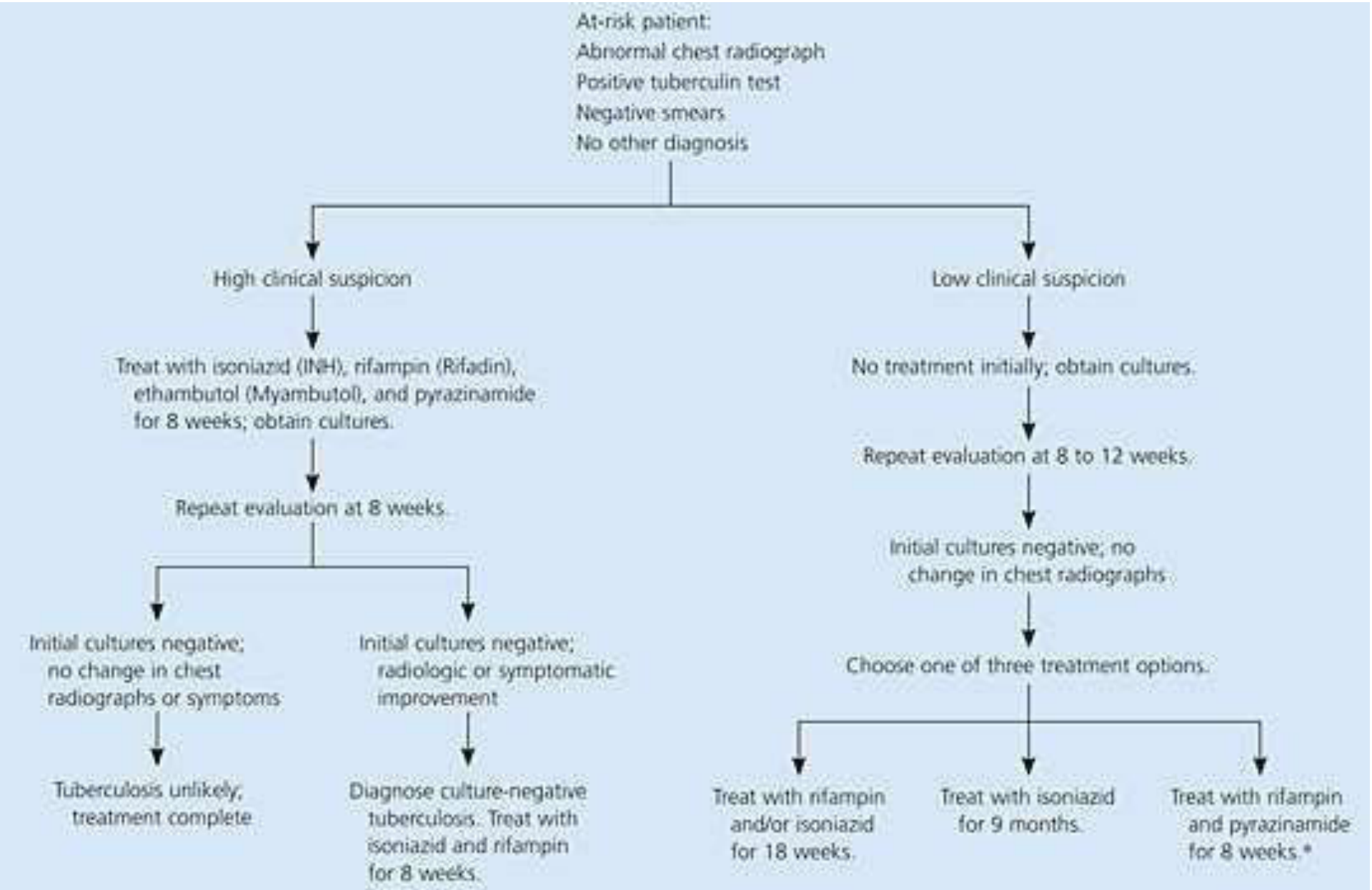


- "Pott's disease"
- Signs and symptoms of extrapulmonary TB are site specific
- Sampling of extrapulmonary sites for smear, culture, and histopathology may confirm diagnosis



Risk Factors

- Weakened immune system
- Contact with someone with active TB
  - Caring for active TB patients
  - Living or working in crowded conditions with someone with active TB
    - e.g., prisons, nursing homes, homeless shelters
- Poor access to healthcare
- Alcohol or drug abuse
- Travel to places where TB is endemic
- Being born in a country where TB is endemic
- Some medications for rheumatoid arthritis



*—*The eight-week regimen of rifampin and pyrazinamide should be used only in patients who are not likely to complete a longer course of therapy and who can be monitored closely.*

Signs & Symptoms

- A bad cough that lasts 3 weeks or longer
- Chest pain
- Coughing up blood or sputum (phlegm from deep inside the lungs)

Other symptoms of TB disease are

- weakness or fatigue
- weight loss
- no appetite
- chills
- fever
- sweating at night
- Symptoms of TB disease in other parts of the body depend on the area affected.

Testing for TB Infection

There are two types of tests for TB infection: the TB skin test and the TB blood test:

1-The TB skin test :

- Is also called the Mantoux tuberculin skin test (TST). The TB skin test is performed by injecting a small amount of fluid (called tuberculin) into the skin on the lower part of the arm.
- A person given the tuberculin skin test must return within 48 to 72 hours to have a trained health care worker look for a reaction on the arm.
- The result depends on the size of the raised, hard area or swelling.

Positive skin test: This means the person's body was infected with TB bacteria. Reading the result of a TB skin test

Additional tests are needed to determine if the person has latent TB infection or TB disease.

- **Negative skin test:** This means the person's body did not react to the test, and that latent TB infection or TB disease is not likely.


TUBERCULOS

2-TB blood tests :

are also called interferon-gamma release assays or IGRAs. Two TB blood tests are approved by the U.S. Food and Drug Administration (FDA) the QuantiFERON®-TB Gold In-Tube test (QFT-GIT) and the T-SPOT®.TB test (T-Spot).

•**Positive TB blood test:** This means that the person has been infected with TB bacteria. Additional tests are needed to determine if the person has latent TB infection or TB disease.
•**Negative TB blood test:** This means that the person's blood did not react to the test and that latent TB infection or TB disease is not likely.

TB blood tests are the preferred TB test for:

•People who have received the TB vaccine bacille Calmette-Guérin (BCG).

•People who have a difficult time returning for a second appointment to look for a reaction to the TST.

Who Should be Tested

- People who have spent time with someone who has TB disease.
- People from a country where TB disease is common (most countries in Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia)
- People who live or work in high-risk settings (for example: correctional facilities, long-term care facilities or nursing homes, and homeless shelters)
- Health-care workers who care for patients at increased risk for TB disease
- Infants, children and adolescents exposed to adults who are at increased risk for latent tuberculosis infection or TB disease
- People with HIV infection
- People who became infected with TB bacteria in the last 2 years
- People who inject illegal drugs

- People who were previously vaccinated with BCG may receive a TB skin test to test for TB infection.
- Vaccination with BCG may cause a false positive reaction to a TB skin test.
- A positive reaction to a TB skin test may be due to the BCG vaccine itself or due to infection with TB bacteria.
- TB blood tests (IGRAs), unlike the TB skin test, are not affected by prior BCG vaccination and are not expected to give a false-positive result in people who have received BCG.
- TB blood tests are the preferred method of TB testing for people who have received the BCG vaccine.

Testing During Pregnancy

- There is a greater risk to a pregnant woman and her baby if TB disease is not diagnosed and treated.
- TB skin testing is considered both valid and safe throughout pregnancy.
- TB blood tests also are safe to use during pregnancy.

Diagnosis of TB Disease

1-Medical History :

TB disease should be suspected in persons who have any of the following symptoms:

- Unexplained weight loss
- Loss of appetite
- Night sweats
- Fever
- Fatigue

If TB disease is in the lungs (pulmonary), symptoms may include:

- Coughing for longer than 3 weeks
- Hemoptysis (coughing up blood)
- Chest pain

Diagnosis of TB Disease

- Clinicians should ask about the patient's history of TB exposure, infection, or disease. It is also important to consider demographic factors (e.g., country of origin, age, ethnic or racial group, occupation) that may increase the patient's risk for exposure to TB or to drug-resistant TB.
- Also, clinicians should determine whether the patient has medical conditions, such as HIV infection or diabetes, that increase the risk of latent TB infection progressing to TB

Diagnosis of TB Disease

2. Physical Examination

- A physical exam can provide valuable information about the patient's overall condition and other factors that may affect how TB is treated, such as HIV infection or other illnesses.

3. Test for TB Infection

- The Mantoux tuberculin skin test (TST) or the TB blood test can be used to test for *M. tuberculosis* infection. Additional tests are required to confirm TB disease.

Diagnosis of TB Disease

4. Chest Radiograph •

- A posterior-anterior chest radiograph is used to detect chest abnormalities. Lesions may appear anywhere in the lungs and may differ in size, shape, density, and cavitation.
- These abnormalities may suggest TB, but cannot be used to definitively diagnose TB.
- *However, a chest radiograph may be used to rule out the possibility of pulmonary TB in a person who has had a positive reaction to a TST or TB blood test and no symptoms of disease.*

Diagnosis of TB Disease

5. Diagnostic Microbiology

- The presence of acid-fast-bacilli (AFB) on a **sputum smear** or other specimen often indicates TB disease.
- Acid-fast microscopy is easy and quick, but it does not confirm a diagnosis of TB because some acid-fast-bacilli are not *M. tuberculosis*.
- Therefore, a **culture** is done on all initial samples to confirm the diagnosis. (
- A positive culture for *M. tuberculosis* confirms the diagnosis of TB disease. Culture examinations should be completed on all specimens, regardless of AFB smear results.

Diagnosis of TB Disease

6. Drug Resistance

- For all patients, the initial *M. tuberculosis* isolate should be tested for drug resistance.
- It is crucial to identify drug resistance as early as possible to ensure effective treatment.
- Drug susceptibility patterns should be repeated for patients who do not respond adequately to treatment or who have positive culture results despite 3 months of therapy.

Deciding When to Treat Latent TB infection

Treatment of latent TB infection should be initiated after the possibility of TB disease has been excluded.

Groups Who Should be Given High Priority for Latent TB Infection Treatment

- People with a positive IGRA result or a TST reaction of 5 or more millimeters
- HIV-infected persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Organ transplant recipients
- Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)

- People with a positive IGRA result or a TST reaction of 10 or more millimeters.

•Recent immigrants (< 5 years) from high-prevalence countries.

• Injection drug users

•Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities).

• Mycobacteriology laboratory personnel.

•Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories.

Drugs	Duration	Interval	Comments
Isoniazid	9 months	Daily	•Preferred treatment for:Persons living with HIV •Children aged 2-11 •Pregnant Women (with pyridoxine/vitamin B6 supplements)
		Twice weekly*	•Preferred treatment for: Pregnant Women (with pyridoxine/vitamin B6 supplements)
Isoniazid	6 months	Daily	
		Twice weekly*	

Treatment for TB Disease

TB disease can be treated by taking several drugs for 6 to 9 months.

There are 10 drugs currently approved by the U.S. Food and Drug Administration (FDA) for treating TB.

The first-line anti-TB agents that form the core of treatment regimens are:

- Isoniazid (INH)
- Rifampcin (RIF)
- Ethambutol (EMB)
- Pyrazinamide (PZA)

TB Treatment in Pregnancy

Diagnosis	Treatment
Latent TB Infection	•Isoniazid (INH) daily or twice weekly for 9 months, with pyridoxine (vitamin B6) supplementation
TB Disease	•The preferred initial treatment regimen is INH, rifampin (RIF), and ethambutol (EMB) daily for 2 months, followed by INH and RIF daily, or twice weekly for 7 months (for a total of 9 months of treatment). •Streptomycin should not be used because it has been shown to have harmful effects on the fetus. •Pyrazinamide (PZA) is not recommended to be used because its effect on the fetus is unknown

Drug-Resistant TB

- drug-resistant TB occurs when bacteria become resistant to the drugs used to treat TB.
- Drug-resistant TB (DR TB) is spread the same way that drug-susceptible TB is spread.
- Drug-resistant TB is more common in people who :

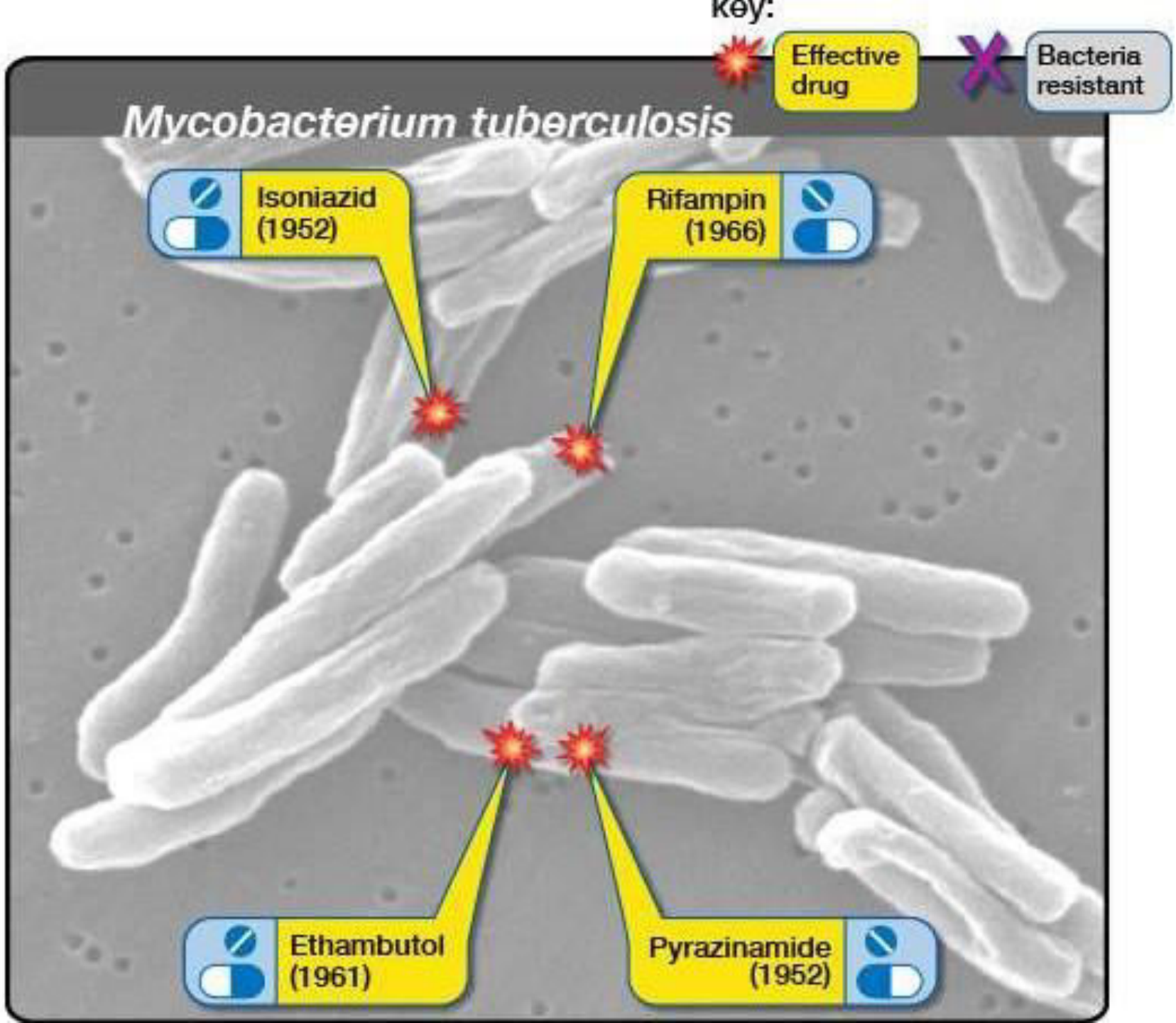
1- Do not take their TB drugs regularly.

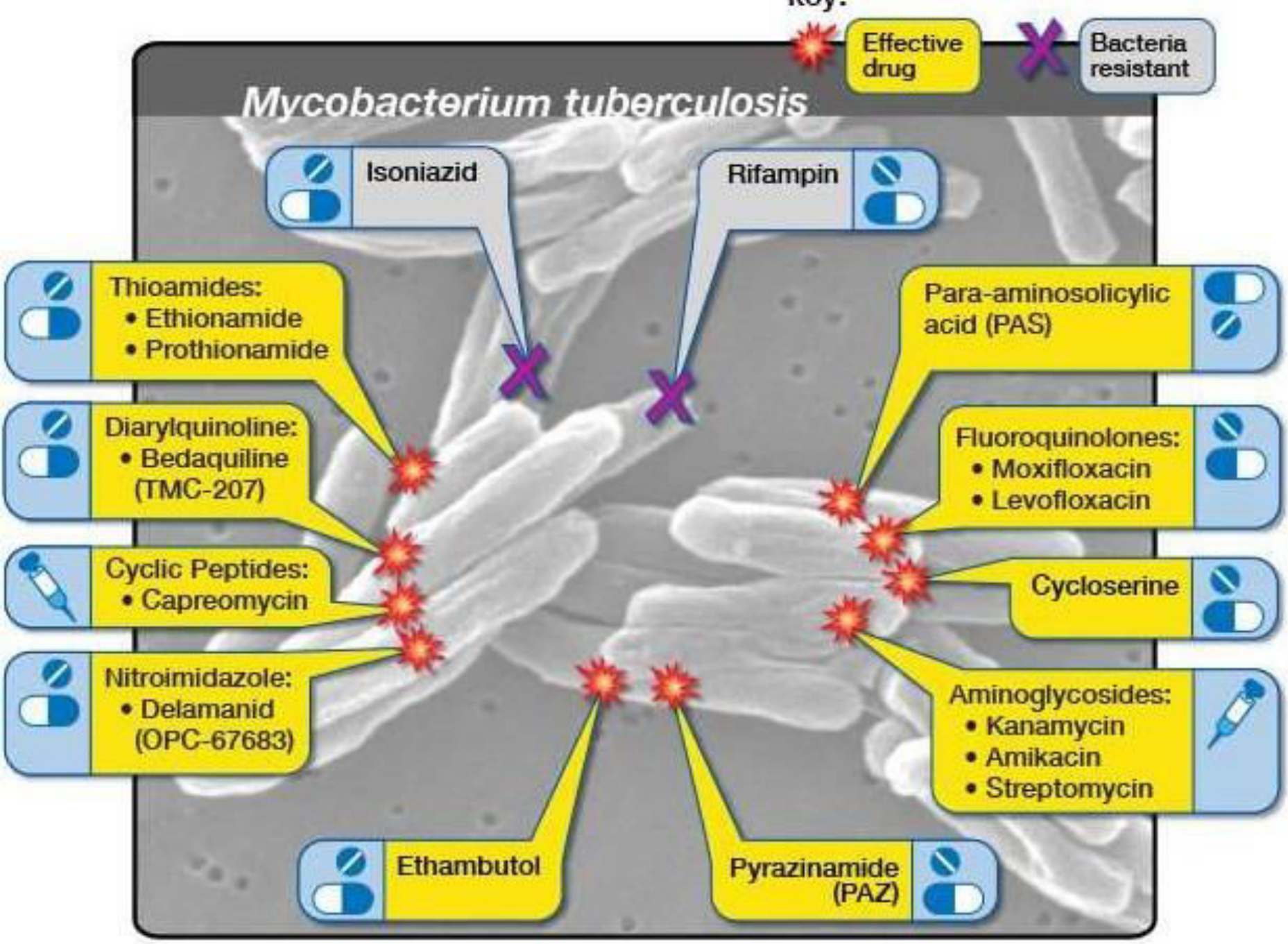
2- Do not take all of their TB drugs.

3- Develop TB disease again, after being treated for TB disease in the past.

4- Come from areas of the world where drug-resistant TB is common.

5- Have spent time with someone known to have drug-resistant TB disease.


key:
Effective drug
Bacteria resistant
Mycobacterium tuberculosis
Isoniazid (1952)
Rifampin (1966)
Ethambutol (1961)
Pyrazinamide (1952)


Effective drug
Bacteria resistant
Mycobacterium tuberculosis
Isoniazid
Rifampin
Thioamides:
• Ethionamide
• Prothionamide
Para-aminosolicylic acid (PAS)
Diarylquinoline:
• Bedaquiline (TMC-207)
Fluoroquinolones:
• Moxifloxacin
• Levofloxacin
Cyclic Peptides:
• Capreomycin
Cycloserine
Nitroimidazole:
• Delamanid (OPC-67683)
Aminoglycosides:
• Kanamycin
• Amikacin
• Streptomycin
Ethambutol
Pyrazinamide (PAZ)

Unite to End TB

EACH YEAR, WE RECOGNIZE WORLD TB DAY ON MARCH 24

CONCLUSION

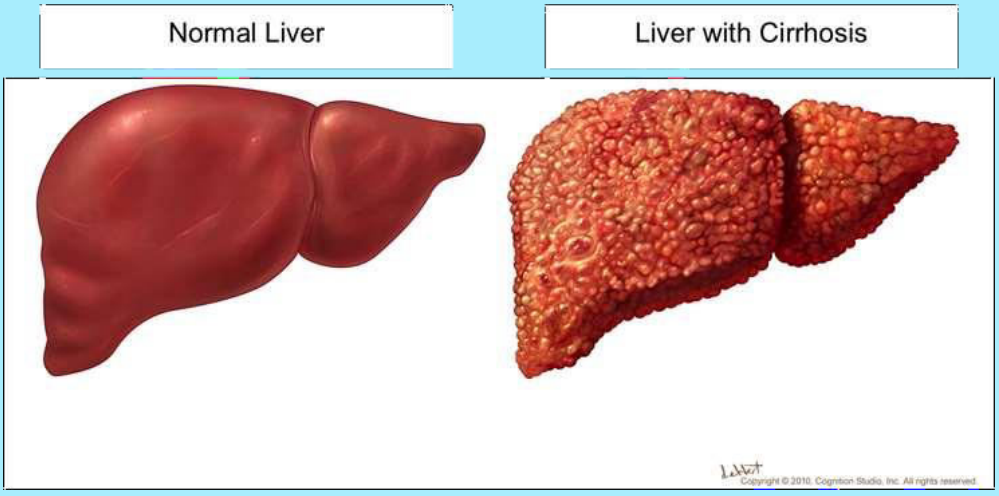
- TB IS TREATABLE AND CURABLE DISEASE IF DIAGNOSED AND TREATED EARLILY.

THANK YOU

Cirrhosis & Its Sequelae

Dr.

Ammar Khalid A



2016

Definition:

It's the final stage of any chronic liver disease, is a diffuse process characterized by fibrosis and conversion of normal architecture to structurally abnormal nodules. These "regenerative" nodules lack normal lobular organization and are surrounded by fibrous tissue.

Cirrhosis can be classified by its status as compensated or decompensated.

Decompensated cirrhosis is defined by the presence of ascites, variceal bleeding, encephalopathy, or jaundice.

Epidemiology:

The prevalence of chronic liver disease or cirrhosis worldwide is estimated to be **100 (range, 25 to 400) per 100,000** subjects.

According to the WHO, about **800,000** people die of cirrhosis annually.

The **12th** leading cause of death overall.

Chronic liver disease and cirrhosis are the seventh leading cause of death in the United States in individuals between 25 and 64 years of age.

PATHOLOGY

Liver Fibrosis/Cirrhosis

In response to injury, hepatic stellate cells become activated, secrete extracellular matrix they become contractile hepatic myofibroblasts.

Collagen deposition in the space of Disse. leads to defenestration of the sinusoidal endothelial cells ("capillarization" of the sinusoids), decreased sinusoidal diameter.

CLINICAL MANIFESTATIONS

The clinical manifestations of cirrhosis range widely from an asymptomatic patient with no signs of chronic liver disease to a patient who is confused and jaundiced and has severe muscle wasting and ascites.

The natural history of cirrhosis is characterized by an initial phase, termed *compensated cirrhosis, followed by a rapidly progressive* phase marked by the development of complications of portal hypertension or liver dysfunction (or both), termed *decompensated cirrhosis.*

In the compensated phase, identified for the development of varices or ascites.

As the disease progresses, portal pressure increases, portal hypertensive gastrointestinal (GI) bleeding, encephalopathy, and jaundice.

Transition from a compensated to a decompensated stage occurs at a rate of approximately 5 to 7% per year.

Compensated Cirrhosis

cirrhosis is mostly asymptomatic , Nonspecific fatigue, decreased libido, or sleep disturbances.

About 40% of patients with compensated cirrhosis have esophageal varices.

Decompensated Cirrhosis

ascites, variceal hemorrhage, jaundice, hepatic encephalopathy, or any combination of these findings.

Ascites, which is the most frequent sign of decompensation, is present in 80% of patients with decompensated cirrhosis.

Variceal Hemorrhage

present in approximately 50% of patients with newly diagnosed cirrhosis.

The prevalence of varices correlates with the severity of liver disease and ranges from 40% in Child A cirrhotic patients to 85% in Child C cirrhotic patients.

The incidence of a first variceal hemorrhage in patients with small varices is about 5% per year, whereas medium and large varices bleed at a rate of approximately 15% per year.

Ascites

Occurs at a rate of 7 to 10% per year.

The most frequent symptoms associated with ascites are increased abdominal girth.

Hepatorenal syndrome

Hepatic Encephalopathy

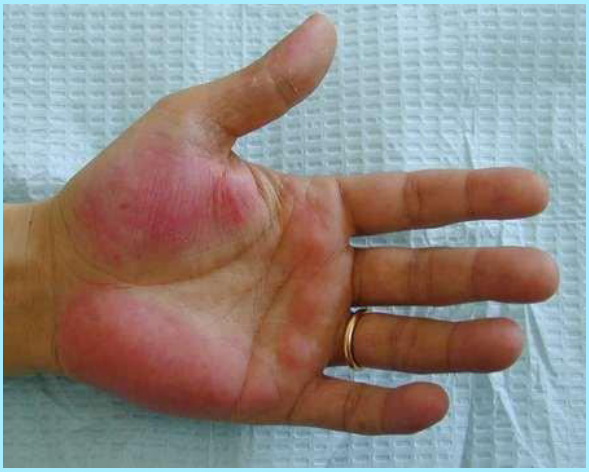
Occurs at a rate of approximately 2 to 3% per year.

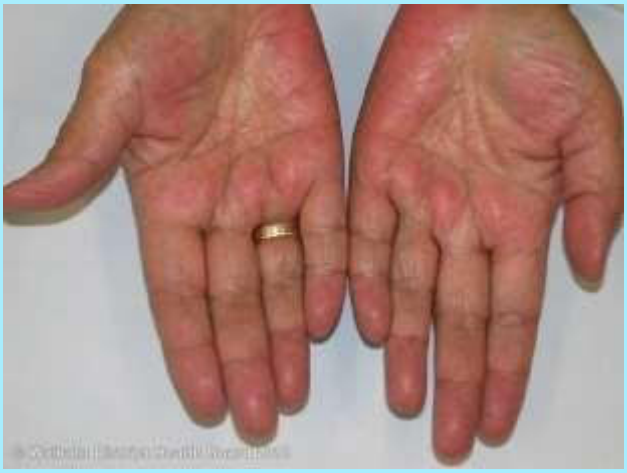
Gradual onset and rarely fatal.

Clinically, it is characterized by alterations in consciousness and behavior ranging from inversion of the sleep-wake pattern and forgetfulness ; to confusion, bizarre behavior, to lethargy to coma.

On physical examination, a distal tremor, asterixis Additionally, sweet-smelling breath, a characteristic termed fetor hepaticus.

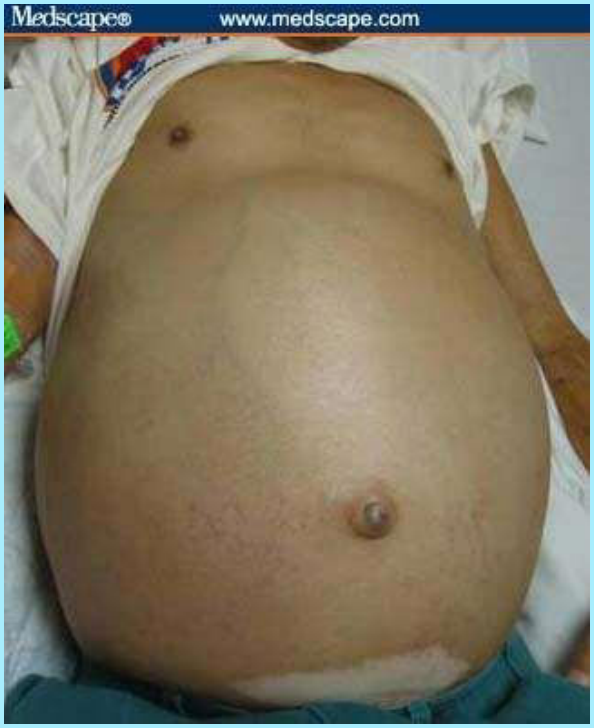
Palmar erythema



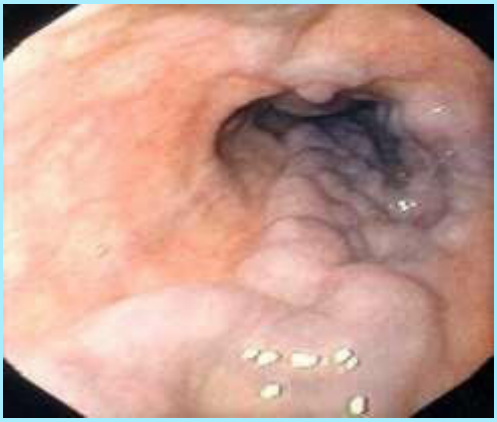


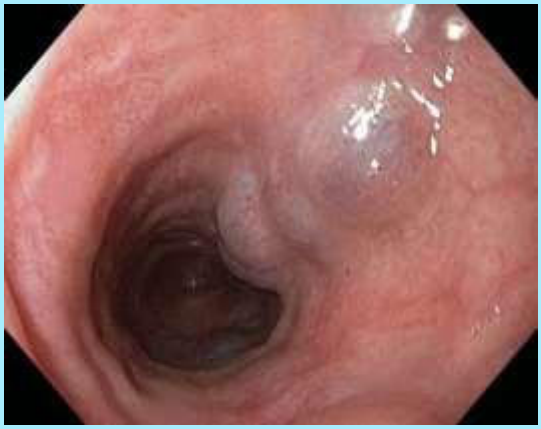
Dupuytren's contracture

Ascites

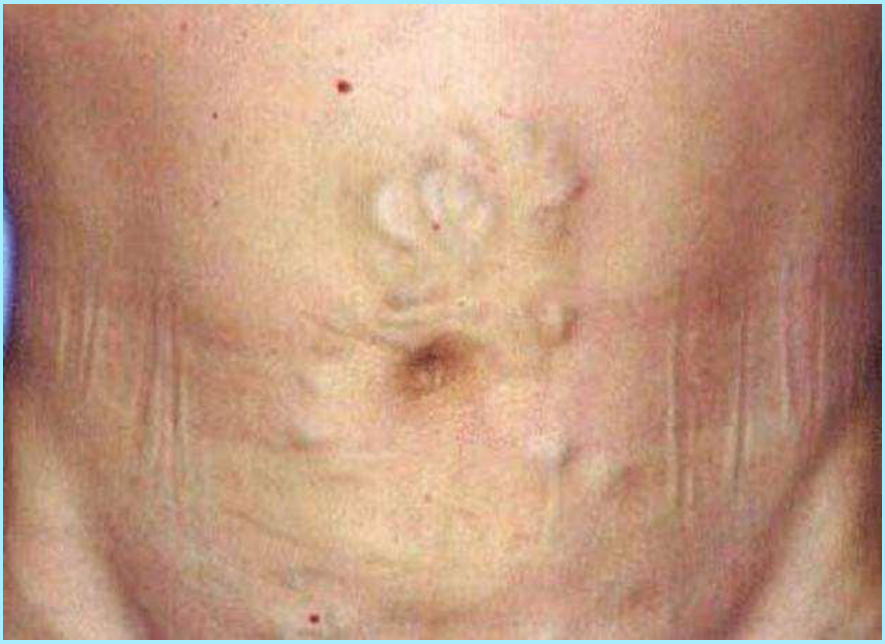


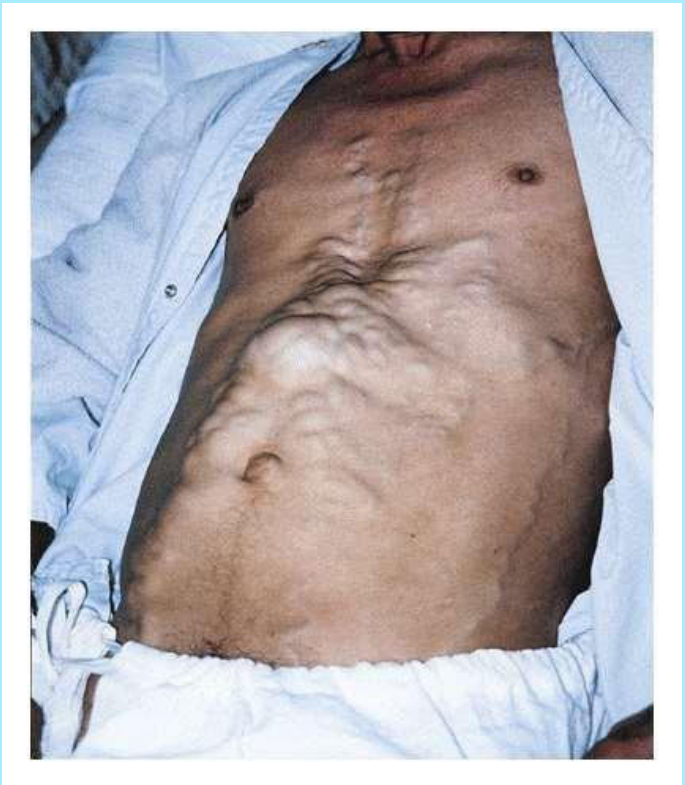
Esophageal varices





Caput medusae





DIAGNOSIS

The diagnosis of cirrhosis should be considered in any patient with chronic liver disease.

In asymptomatic patients with *compensated cirrhosis,* diagnosis may often require histologic confirmation by liver biopsy, which is the "gold standard" for the diagnosis of cirrhosis.

In patients with symptoms or signs of chronic liver disease, confirmed noninvasively by imaging studies without the need for liver biopsy.

Physical Examination

Stigmata of cirrhosis consist of muscle atrophy, spider angiomas, palmar erythema , Males may have hair loss, gynecomastia, and testicular atrophy.

Petechiae and ecchymoses may be present as a result of thrombocytopenia or a prolonged prothrombin time, Dupuytren's contracture.

A pathognomonic feature of cirrhosis is small right liver lobe, with a span of less than 7 cm on percussion, and a palpable left lobe that is nodular with increased consistency. Splenomegaly may also be present and is indicative of portal hypertension. Collateral circulation on the abdominal wall (caput medusae).

Laboratory Tests

subtle abnormalities in serum levels of albumin or bilirubin or elevation of the international normalized ratio.

low platelet count, abnormal levels of aspartate aminotransferase, γ-glutamyl transpeptidase.

Imaging Studies

Computed tomography, ultrasound, and magnetic resonance imaging.

Findings consistent with cirrhosis include nodular contour of the liver, a small liver with or without hypertrophy of the left or caudate lobe, splenomegaly, and in particular, identification of intraabdominal collateral vessels indicative of portal hypertension .

Transient elastography: measures liver stiffness .

In *decompensated cirrhosis, detection of ascites, variceal bleeding, or* encephalopathy in the setting of chronic liver disease essentially establishes the diagnosis of cirrhosis, so a liver biopsy is not necessary.

Complications of Cirrhosis

Varices and Variceal Hemorrhage

Upper GI endoscopy the main method for diagnosing varices and variceal hemorrhage.

Varices are classified as small (straight, minimally elevated veins above the esophageal mucosal surface), medium (tortuous veins occupying less than one third of the esophageal lumen), or large (occupying more than one third of the esophageal lumen).

Ascites

The most common cause of ascites is cirrhosis, which accounts for 80% of cases. Diagnostic paracentesis is a safe procedure , Ultrasound guidance should be used in patients in whom percussion cannot locate the ascites. The fluid should always be evaluated for albumin , polymorphonuclear (PMN) blood cell count, bacteriologic cultures, cytology, glucose and lactate dehydrogenase levels ,smear and culture for acid-fast bacilli.

The serum-ascites albumin gradient useful in the differential diagnosis of ascites. The serum-ascites albumin gradient correlates with sinusoidal pressure and will therefore be elevated (>1.1 g/dL) in patients in whom the source of ascites is the hepatic sinusoid (e.g., cirrhosis or cardiac ascites).

Hepatorenal Syndrome

characterized by maximal peripheral vasodilation ,maximal activation of hormones that cause the retention of sodium and water and intense vasoconstriction of renal arteries. Ascites unresponsive to diuretics is universal, and dilutional hyponatremia is almost always present.

Spontaneous Bacterial Peritonitis

Diagnostic paracentesis should be performed in any patient with symptoms or signs of spontaneous bacterial peritonitis.

Spontaneous bacterial peritonitis is often asymptomatic

The diagnosis of spontaneous bacterial peritonitis is established by an ascitic fluid PMN count greater than 250/mm3. Bacteria can be isolated from ascitic fluid in only 40 to 50% of cases. Spontaneous bacterial peritonitis is mostly a monobacterial infection, usually with gram-negative enteric organisms. Anaerobes and fungi very rarely causes.

Hepatic Encephalopathy

The diagnosis based on the history and physical examination.

There is poor correlation between the stage of hepatic encephalopathy and ammonia blood levels.

Hepatopulmonary Syndrome and Portopulmonary Hypertension

The diagnostic criteria for hepatopulmonary syndrome are arterial hypoxemia with a Pao2 of less than 80 mm Hg or an alveolar arterial oxygen gradient of greater than 15 mm Hg, along with evidence of pulmonary vascular shunting on contrast echocardiography.

Portopulmonary hypertension is diagnosed by the presence of mean pulmonary arterial pressure higher than 25 mm Hg on right heart catheterization, provided that pulmonary capillary wedge pressure is less than 15 mm Hg.

TREATMENT

Treatment of cirrhosis should ideally be aimed at interrupting or reversing fibrosis.

Treatment of compensated cirrhosis is currently directed at preventing the development of decompensation by

(1) treating the underlying liver disease (e.g., antiviral therapy for hepatitis C or B) to reduce fibrosis and prevent decompensation;
(2) avoiding factors that could worsen liver disease, such as alcohol and hepatotoxic drugs; and
(3) screening for varices (to prevent variceal hemorrhage) and for hepatocellular carcinoma (to treat at an early stage).

Varices and Variceal Bleeding

Reducing portal pressure. Nonselective β-adrenergic blockers (propranolol, nadolol) reduce portal pressure by producing

splanchnic vasoconstriction and decreasing portal venous inflow. 1- Propranolol should be titrated to produce a resting heart rate of about 50 to 55 beats per minute.

Endoscopic variceal ligation.

Endoscopy should be repeated every 2 to 3 years in patients with no varices, every 1 to 2 years in patients with small varices.

The most effective specific therapy for the control of active variceal hemorrhage is the combination of a vasoconstrictor with endoscopic therapy. Safe vasoconstrictors include terlipressin, and the somatostatin analogues ,octreotide, which is used as a 50-µg intravenous bolus followed by an infusion at 50 µg/hour.

The next best results (rebleeding rates of about 22%) are obtained with the combination of nonselective β-blockers (propranolol or nadolol), with or without isosorbide mononitrate, and endoscopic variceal ligation.

Transjugular intrahepatic portosystemic shunt (TIPS), should be used in patients whose variceal bleeding has persisted.

Ascites

Salt restriction and diuretics constitute the mainstay of management of ascites. Dietary sodium intake should be restricted to 2 g/day.

Spironolactone, should be started at a dose of 100 mg/day to a maximal effective dose of 400 mg/day.

Furosemide, at an escalated dose from 40 to 160 mg/day.

The goal is weight loss of 1 kg in the first week and 2 kg/week subsequently.

In the 10 to 20% of patients with ascites who are refractory to diuretics,

large-volume paracentesis, aimed at removing all or most of the fluid,

plus albumin at a dose of 6 to 8 g intravenously per liter of ascites removed.

In patients requiring frequent large-volume paracentesis (more than twice per month), polytetrafluoroethylene-covered TIPS

- stents should be considered.

Hepatorenal Syndrome

The mainstay of therapy is liver transplantation.

Terlipressin, plus albumin.

use of terlipressin, which at a dose 0.5 to 2.0 mg intravenously every 4 to 6 hours.

The most used combination is octreotide (100 to 200 µg subcutaneously three times a day) plus midodrine.

Spontaneous Bacterial Peritonitis

Empirical antibiotic therapy with an intravenous third-generation cephalosporin. the minimal duration of therapy should be 5 days. Repeat diagnostic paracentesis should be performed 2 days after starting antibiotics.

,The renal dysfunction associated with spontaneous bacterial peritonitis can be prevented by the intravenous administration of albumin, Albumin has been used at a dose of 1.5 g/kg of body weight at diagnosis.

Hepatic Encephalopathy

Treating the precipitating factor and reducing the ammonia level. Precipitating factors include infections, overdiuresis, GI bleeding, a high oral protein load, and constipation. Narcotics and sedatives contribute to hepatic encephalopathy by directly depressing brain function.

lactulose (15 to 30 mL) orally twice daily or orally administered nonabsorbable antibiotics such as neomycin, metronidazole (250 mg two to four times per day), or rifaximin (550 mg two times per day). Switching dietary

- protein from an animal source to a vegetable source may be beneficial.

Pulmonary Complications

Hepatopulmonary syndrome The only viable treatment is liver transplantation .

PROGNOSIS

The 10-year survival rate of patients who remain in a compensated stage is approximately 90%, whereas their likelihood of decompensation is 50% at 10 years.

Four clinical stages of cirrhosis:

Stage 1 patients without varices or ascites, the mortality rate is about 1% per year.

Stage 2 patients, or those with varices but without ascites or bleeding, have a mortality rate of about 4% per year.

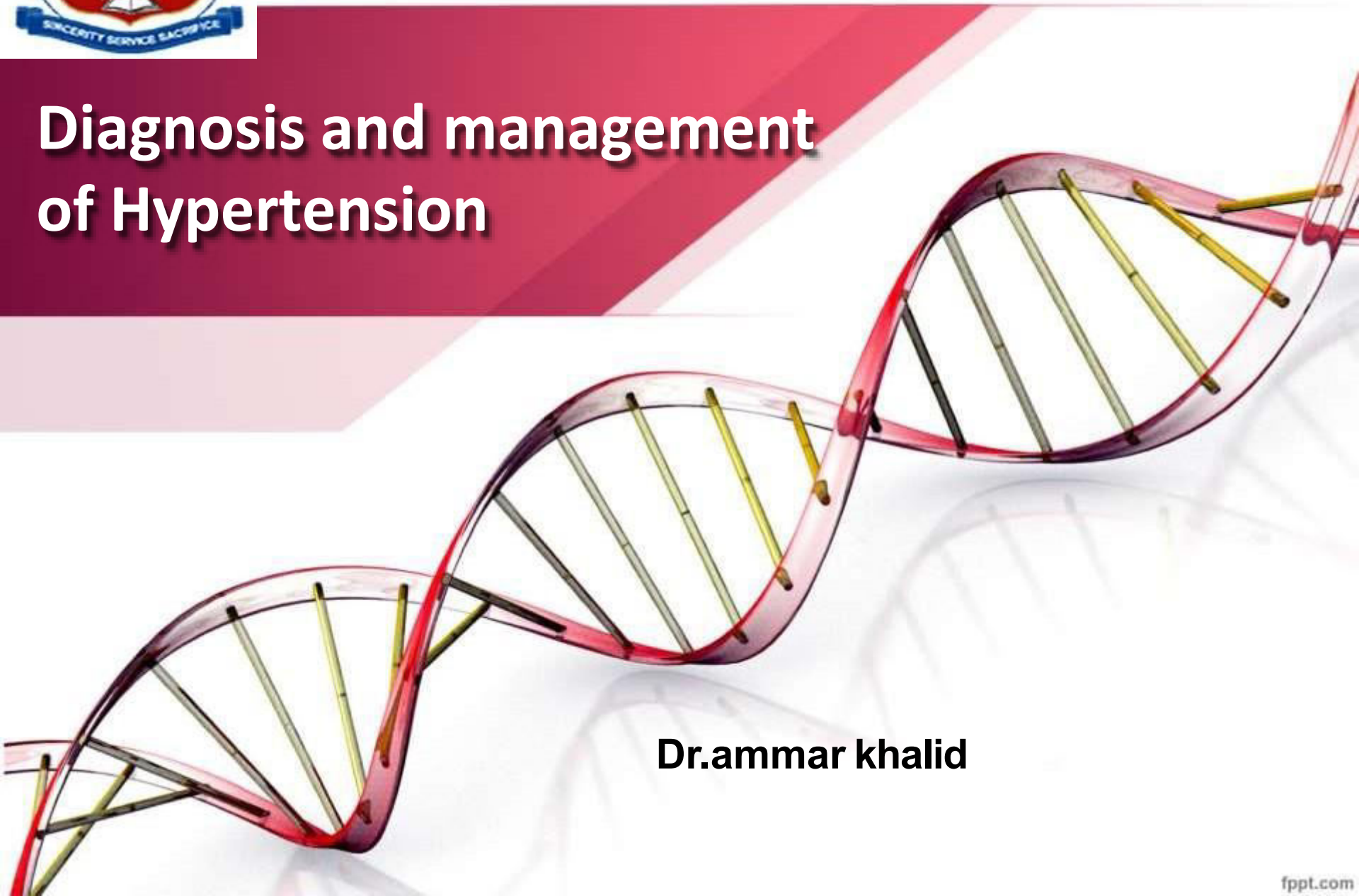
Stage 3 patients have ascites with or without esophageal varices that have never bled; their mortality rate while remaining in this stage is 20% per year.

Stage 4 patients, or those with portal hypertensive GI bleeding with or without ascites, have a 1-year mortality rate of 57%, with nearly half of these deaths occurring within 6 weeks after the initial episode of bleeding.

Hepatocellular carcinoma develops at a fairly constant rate of 3% per year..

Thank You

Diagnosis and management of Hypertension



Dr.ammar khalid

- WHY HYPERTENSION IS IMPORTANT ?

AGENDA

- Definition
- Causes
- Diagnosis
- Treatment
- Questions

Hypertension is defined as systolic blood pressure (SBP) of 140 mmHg or greater, diastolic blood pressure (DBP) of 90 mmHg or greater, or taking antihypertensive medication.

VI JNC, 1997

Types of hypertension

- Primary
- Secondary
- Isolated systolic
- Pseudo hypertension
- White coat hypertension
- Mask hypertension
- Pregnancy induce hypertension
- Resistance hypertension

- Essential hypertension
- 95%
- No underlying cause
- Secondary hypertension
- Underlying cause

Causes of Secondary Hypertension

- Renal
  - Parenchymal
  - Vascular
  - Others
- Endocrine
- Miscellaneous
- Unknown

Classification

Blood Pressure Classification

BP Classification	SBP mmHg		DBP mmHg
Normal	<120	and	<80
Prehypertension	120–139	or	80–89
Stage 1 Hypertension	140–159	or	90–99
Stage 2 Hypertension	≥160	or	≥100

Incidence in India

- 25% of urban population and 10 % of rural population suffer from hypertension
- 70% of all hypertensive patients are stage I hypertension
- 12% of all hypertensive suffer from isolated systolic hypertension

Who are at risk ?

Hypertension: Predisposing factors

- Advancing Age
- Sex (men and postmenopausal women)
- Family history of cardiovascular disease
- Sedentary life style & psycho-social stress
- Smoking ,High cholesterol diet, Low fruit consumption
- Obesity & wt. gain
- Co-existing disorders such as diabetes, and hyperlipidaemia
- High intake of alcohol

Haemodynamic Pattern in Hypertension

Young : ↑ BP = ↑CO X TPR

Elderly : ↑ BP = ↓ CO X ↑ ↑ TPR

Aetiology of Systemic Hypertension

Secondary HTN (05%)

A. Renal (80%)	• AGN • CGN, • CPN, • Polycyst. K.D	• Renal Artery stenosis
B. Endocrine	• Adrenal	• Primary aldosteronism • Cushing's syndrome • Pheochromocytoma
	• Acromegaly	
	• Exogenous hormone	• Oral contraceptive • Glucocorticoids
	• Hypothyroidism & • Hyperparathyroidism	

Continue…

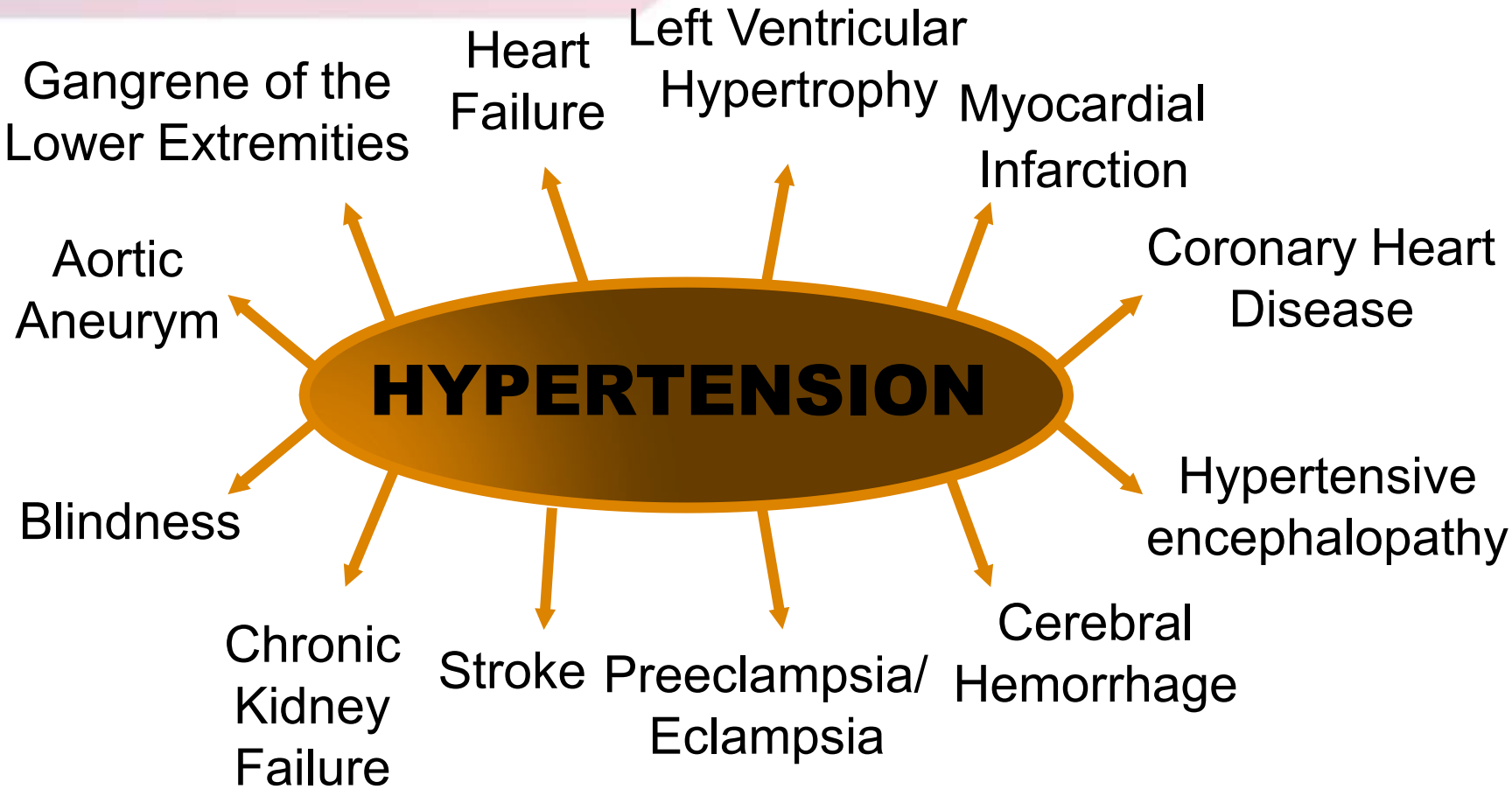
Aetiology of Systemic Hypertension

Others

- Coarctation of the aorta
- Pregnancy Induced HTN (Pre-eclampsia)
- Sleep Apnea Syndrome.

Why to treat ?

Diseases Attributable to Hypertension



Adapted from Dustan HP et al. Arch Intern Med. 1996; 156: 1926-1935

Target Organ Damage

- Heart
  - Left ventricular hypertrophy
  - Angina or myocardial infarction
  - Heart failure
- Brain
  - Stroke or transient ischemic attack
- Chronic kidney disease
- Peripheral arterial disease
- Retinopathy

CVD Risk

- The BP relationship to risk of CVD is continuous, consistent, and independent of other risk factors.

- Prehypertension signals the need for increased education to reduce BP in order to prevent hypertension.

Diagnosis

Clinical manifestations

- No specific complains or manifestations other than elevated systolic and/or diastolic BP (Silent Killer)
- Morning occipital headache
- Dizziness
- Fatigue
- In severe hypertension, epistaxis or blurred vision

Self-Measurement of BP

- Provides information on:
  1. Response to antihypertensive therapy
  2. Improving adherence with therapy
  3. Evaluating white-coat HTN

- Home measurement of >135/85 mmHg is generally considered to be hypertensive.

- Home measurement devices should be checked regularly.

Measuring Blood Pressure

- Patient seated quietly for at least 5minutes in a chair, with feet on the floor and arm supported at heart level

- An appropriate-sized cuff (cuff bladder encircling at least 80% of the arm)

- At least 2 measurements

Continue…

Measuring Blood Pressure

- Systolic Blood Pressure is the point at which the first of 2 or more sounds is heard
- Diastolic Blood Pressure is the point of disappearance of the sounds (Korotkoff 5th)

Continue…

Measuring Blood Pressure

- Ambulatory BP Monitoring – information about BP during daily activities and sleep.
- Correlates better than office measurements with target-organ injury.

Continue…

Laboratory Tests

- Routine Tests
  - Electrocardiogram
  - Urinalysis
  - Blood glucose,
  - Serum potassium, creatinine, or the corresponding estimated GFR, and calcium
  - Lipid profile, after 9- to 12-hour fast, that includes high-density and low-density lipoprotein cholesterol, and triglycerides
- Optional tests
  - Measurement of urinary albumin excretion or albumin/creatinine ratio
- More extensive testing for identifiable causes is not generally indicated unless BP control is not achieved

How to treat ?

Treatment Overview

- Goals of therapy
- Lifestyle modification
- Pharmacologic treatment
- Algorithm for treatment of hypertension
- Follow up and monitoring

Goals of Therapy

- **Reduce Cardiac and renal morbidity and mortality.**
- **Treat to BP <140/90 mmHg or BP <130/80 mmHg in patients with diabetes or chronic kidney disease.**

Non pharmacological Treatment of hypertension

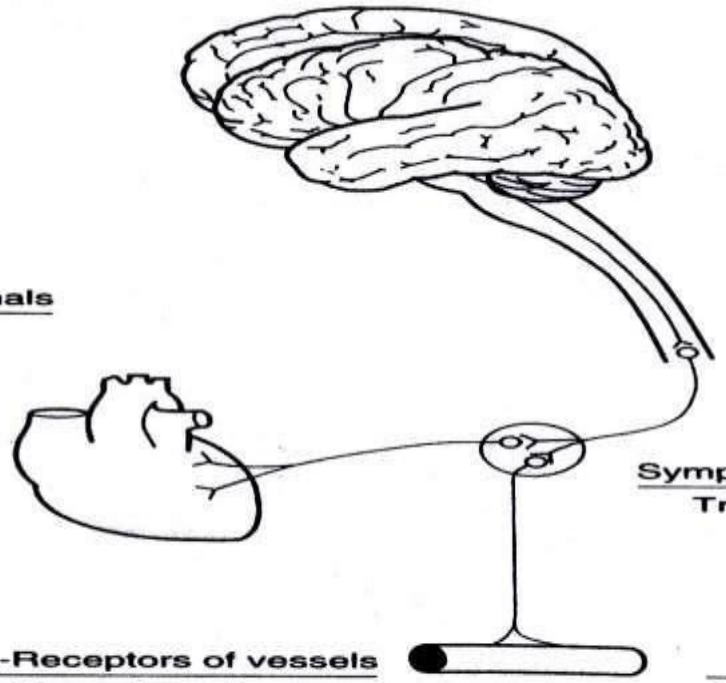
Life style modifications

- Lose weight, if overweight
- Increase physical activity
- Reduce salt intake
- Stop smoking
- Limit intake of foods rich in fats and cholesterol
- increase consumption of fruits and vegetables
- Limit alcohol intake

Lifestyle Modification

Modification	Approximate SBP reduction (range)
Weight reduction	5–20 mmHg / 10 kg weight loss
Adopt DASH eating plan	8–14 mmHg
Dietary sodium reduction	2–8 mmHg
Physical activity	4–9 mmHg
Moderation of alcohol consumption	2–4 mmHg

Antihypertensive Drugs



Vasomotor center
Methyldopa
Clonidine
Guanabenz
Guanfacine

Sympathetic nerve terminals
Guanethidine
Guanadrel
Reserpine

β-Receptors of heart
Propranolol and other β-blockers

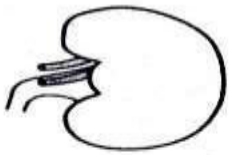
Sympathetic ganglia
Trimethaphan

Angiotensin receptors of vessels
Losartan and other angiotensin receptor blockers

α-Receptors of vessels
Prazosin and other α_1-blockers

Vascular smooth muscle
Hydralazine
Minoxidil
Nitroprusside
Diazoxide
Verapamil and other calcium channel blockers
Fenoldopam

Kidney tubules
Thiazides, etc



β-Receptors of juxtaglomerular cells that release renin
Propranolol and other β-blockers

Angiotensinogen → (Renin) → Angiotensin I → (Angiotensin-converting enzyme) → Angiotensin II

Captopril and other ACE inhibitors

ARB

Continue....

Drug therapy for hypertension

Class of drug	Example	Initiating dose	Usualmaintenance dose
Diuretics	Hydrochlorothiazide	12.5 mg o.d.	12.5-25 mg o.d.
β-blockers	Atenolol	25-50 mg o.d.	50-100 mg o.d.
Calcium channel blockers	Amlodipine	2.5-5 mg o.d.	5-10 mg o.d.
α-blockers	prazosin	2.5 mg o.d	2.5-10mg o.d.
ACE- inhibitors	ramipril	1.25-5 mg o.d.	5-20 mg o.d.
Angiotensin-II receptor blockers	Losartan	25-50 mg o.d.	50-100 mg o.d.

Diuretics

Example: **Hydrochlorothiazide**

- Act by decreasing blood volume and cardiac output
- Decrease peripheral resistance during chronic therapy
- Drugs of choice in elderly hypertensives

Side effects-

- Hypokalaemia
- Hyponatraemia
- Hyperlipidaemia
- Hyperuricaemia (hence contraindicated in gout)
- Hyperglycaemia (hence not safe in diabetes)
- Not safe in renal and hepatic insufficiency

Beta blockers

Example: **Atenolol, Metoprolol, nebivolol,**

- Block β_1 receptors on the heart
- Block β_2 receptors on kidney and inhibit release of renin
- Decrease rate and force of contraction and thus reduce cardiac output
- Drugs of choice in patients with co-existent coronary heart disease

Side effects-

- lethargy, impotency, bradycardia
- Not safe in patients with co-existing asthma and diabetes
- Have an adverse effect on the lipid profile

Calcium channel blockers

Example: **Amlodipine**

- Block entry of calcium through calcium channels
- Cause vasodilation and reduce peripheral resistance
- Drugs of choice in elderly hypertensives and those with co-existing asthma
- Neutral effect on glucose and lipid levels

Side effects

Flushing, headache, Pedal edema

ACE inhibitors

Example: **Ramipril, Lisinopril, Enalapril**

- Inhibit ACE and formation of angiotensin II and block its effects
- Drugs of choice in co-existent diabetes mellitus, Heart failure

Side effects-

dry cough, hypotension, angioedema

Angiotensin II receptor blockers

Example: **Losartan**

- Block the angiotensin II receptor and inhibit effects of angiotensin II
- Drugs of choice in patients with co-existing diabetes mellitus

Side effects-

safer than ACEI, hypotension,

Alpha blockers

Example: **prazosin**

- Block α-1 receptors and cause vasodilation
- Reduce peripheral resistance and venous return
- Exert beneficial effects on lipids and insulin sensitivity
- Drugs of choice in patients with co-existing BPH

Side effects-

Postural hypotension,

Antihypertensive therapy: Side-effects and Contraindications

Class of drugs	Main side-effects	Contraindications/ Special Precautions
Diuretics Anuria (e.g. Hydrochloro-thiazide)	Electrolyte imbalance, total and LDL cholesterol levels, ↓ HDL cholesterol levels, glucose levels, uric acid levels	Hypersensitivity,
β-blockers (e.g. Atenolol) Conduction Diabetes, cardiac	Impotence, Bradycardia, Fatigue	Bradycardia, disturbances, Asthma, Severe failure

Algorithm for Treatment of Hypertension

Lifestyle Modifications

Not at Goal Blood Pressure (<140/90 mmHg)
(<130/80 mmHg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Without Compelling Indications

Stage 1 Hypertension
(SBP 140–159 or DBP 90–99 mmHg)
Thiazide-type diuretics for most.
May consider ACEI, ARB, BB, CCB,
or combination.

Stage 2 Hypertension
(SBP ≥160 or DBP ≥100 mmHg)
2-drug combination for most (usually
thiazide-type diuretic and
ACEI, or ARB, or BB, or CCB)

With Compelling Indications

Drug(s) for the compelling indications
Other antihypertensive drugs (diuretics,
ACEI, ARB, BB, CCB)
as needed.

Not at Goal Blood Pressure

Optimize dosages or add additional drugs
until goal blood pressure is achieved.
Consider consultation with hypertension specialist.

Choice of Drug

Condition	Preferred drugs	Other drugs that can be used	Drugs to be avoided
Asthma	Calcium channel blockers	α-blockers/Angiotensin-II receptor blockers/Diuretics/ ACE-inhibitors	β-blockers
Diabetes mellitus	α-blockers/ACE inhibitors/ Angiotensin-II receptor blockers	Calcium channel blockers	Diuretics/ β-blockers
High cholesterol levels	α-blockers	ACE inhibitors/ A-II receptor blockers/ Calcium channel blockers	β-blockers/ Diuretics
Elderly patients (above 60 years)	Calcium channel blockers/Diuretics	β-blockers/ACE-inhibitors/Angiotensin-II receptor blockers/α- blockers	
BPH	α-blockers	β-blockers/ ACE inhibitors/ Angiotensin-II receptor blockers/ Diuretics/ Calcium channel blockers	

Antihypertensive therapy: Side-effects and Contraindications (Contd.)

Class of drug	Main side-effects	Contraindications/ Special Precautions
Calcium channel blockers (e.g. Amlodipine, Diltiazem)	**Pedal edema, Headache**	**Non-dihydropyridine CCBs (e.g diltiazem)– Hypersensitivity, Bradycardia, Conduction disturbances, CHF, LV dysfunction.**
α-blockers (e.g. prazosin)	**Postural hypotension**	**Hypersensitivity**
ACE-inhibitors (e.g. Lisinopril)	**Cough, Hypotension, Angioneurotic edema**	**Hypersensitivity, Pregnancy, Bilateral renal artery stenosis**
Angiotensin-II receptor blockers (e.g. Losartan)	**Headache, Dizziness**	**Hypersensitivity, Pregnancy, Bilateral renal artery stenosis**

Condition	Preferred Drugs
• Pregnancy	• Nifedipine, labetalol, hydralazine, beta-blockers, methyldopa, prazosin
• Coronary heart disease	• Beta-blockers, ACE inhibitors, Calcium channel blockers
• Congestive heart failure	• ACE inhibitors, beta-blockers

1999 WHO-ISH guidelines

Causes of Resistant Hypertension

- Improper BP measurement
- Excess sodium intake
- Inadequate diuretic therapy
- Medication
  - Inadequate doses
  - Drug actions and interactions (e.g., (NSAIDs), illicit drugs, sympathomimetics, OCP)
  - Over-the-counter drugs and some herbal supplements
- Excess alcohol intake
- Identifiable causes of HTN

take home message ----------

- Hypertension is a major cause of morbidity and mortality, and needs to be treated
- It is an extremely common condition; however it is still under-diagnosed and undertreated
- Hypertension is easy to diagnose and easy to treat
- Aim of the management is to save the target organ from the deleterious effect
- Besides pharmacology we have other choices and one has to be acquainted with that choice
- Life style modification should always be encouraged in all Hypertensive patients

Any questions?

Que 1) Life style intervention for management of hypertension includes all except:

a) Regular aerobic activity 30 min /day
b) Salt intake to <6 gm./day
c) Attain and maintaining BMI >25k/m^2
d) Diets rich in fruits and vegetables and restricted content of saturated fats
e) Moderation of alcohol consumption

Que 2) Hypertension management is helpful in the prevention of all except:

a) Coronary heart disease
b) Heart failure
c) Chronic kidney disease
d) Deep venous thrombosis
e) Cerebrovascular disease

Que 3) Isolated systolic hypertension is common in:

a) Young
b) Elderly
c) Pregnancy
d) Blacks

Que 4) Antihypertensive agent recommended for the protection of cardiovascular diseases is:

a) Calcium channel blockers
b) Diuretics
c) ACE inhibitors
d) Alpha antagonists
e) Central sympatholytic

Que 5) Angiotensin Receptor Blockers play Reno protective effect through all except:

a) Decreasing proteinuria
b) Decreasing intraglomerular pressure
c) Preventing endothelial dysfunction
d) Inhibiting conversion of angiotensin-I to angiotensin –II
e) Blocking the angiotesin mediated renal remodelling

Que 6) which of the following is the side effect of ACE inhibitors:

a) Hyperkalaemia
b) Hypercalcemia
c) Hyperglycaemia
d) Hypertension
e) Hypermagnesemia

Que 7) Calcium channel blockers cause all except:

a) Pedal oedema
b) Flushing
c) Hyperkalaemia
d) Headache

Que 8) : Safest drug for hypertension in pregnancy is:

a) ACE inhibitors
b) Angiotensin receptor blockers
c) Diuretic
d) Methyldopa

Que9) the first line antihypertensive in diabetic patients is:

a) Diuretics
b) Angiotensin converting enzyme inhibitors
c) Beta blockers
d) Calcium channel blockers

Que10) which of the following antihypertensive agent is contraindicated in congestive cardiac failure:

a) ACE inhibitors
b) Angiotensin receptor blockers
c) Beta blockers
d) Diuretics
e) NSAID

CHROINIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Dr. Ammar

GOLD Definition

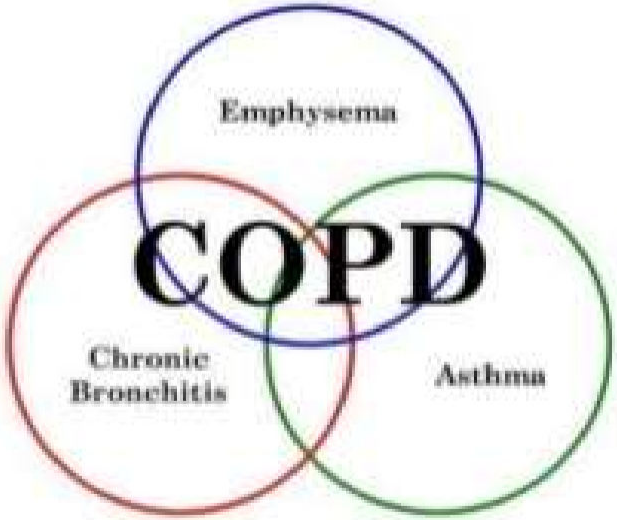
- COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.

- Exacerbations and comorbidities contribute to the overall severity in individual patients.

GOLD 2013

Definition : Airflow Limitation

- The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person



Global initiative for chronic obstructive pulmonary disease updated 2013

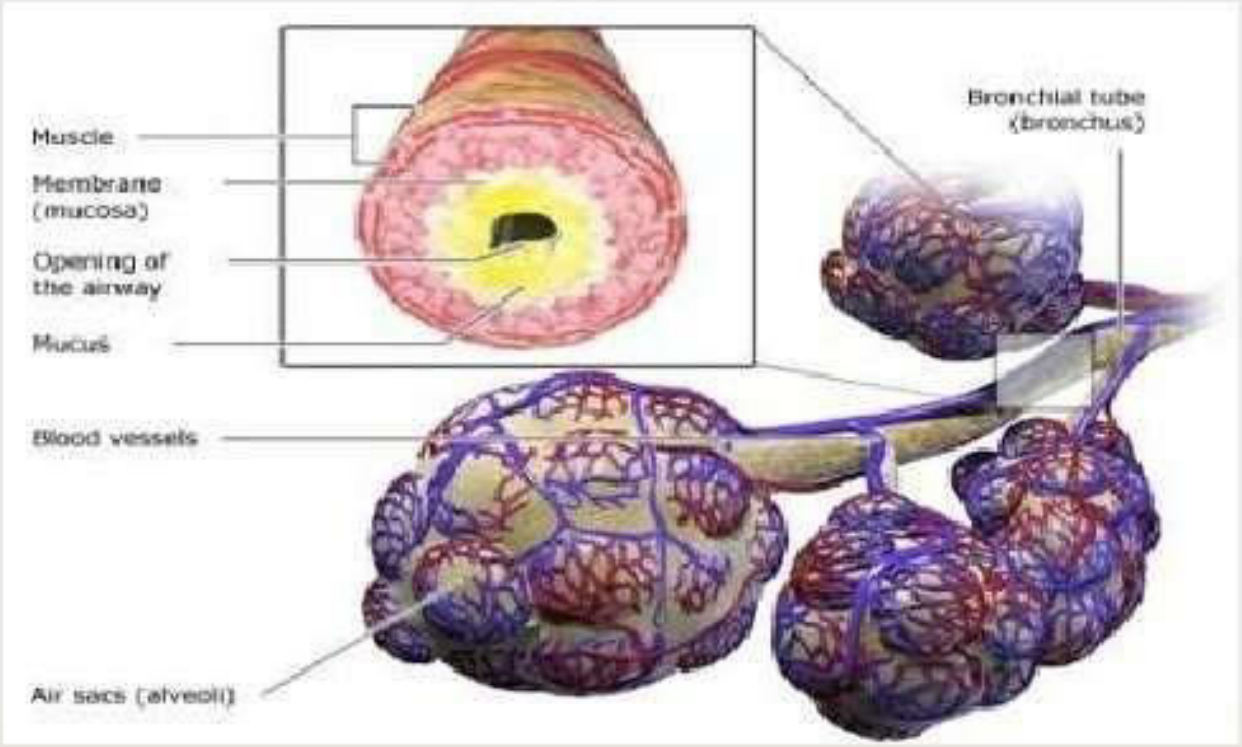
Definitions

- **Emphysema** pathological term which is destruction of the gas exchanging surfaces of the lung (alveoli).

- **Chronic bronchitis** is the presence of cough and sputum production for at least 3 months in each of two consecutive years.

What does COPD do?

- COPD causes airway narrowing, inflammation and mucous production.



Primary Symptoms

- Chronic Bronchitis
  - Chronic cough
  - Shortness of breath
  - Increased mucus
  - Frequent clearing of throat
- Emphysema
  - Chronic cough
  - Shortness of breath
  - Limited activity level

EMPHYSEMA

- Severe dyspnea
- Cough after dyspnea
- Scant sputum
- Less frequent infections
- Terminal RF
- $PaCO_2$ 35-40 mmHg
- PaO_2 65-75 mmHg
- Hematocrit 35-45%
- DLCO is decreased
- Cor pulmonale rare.

CHRONIC BRONCHITIS

1. Mild dyspnea
2. Cough before dyspnea starts
3. Copious, purulent sputum
4. More frequent infections
5. Repeated resp. insufficiency
6. $PaCO_2$ 50-60 mmHg
7. PaO_2 45-60 mmHg
8. Hematocrit 50-60%
9. DLCO is not that much ↓
10. Cor pulmonale common

SPIROMETRY

- Decreased FEV_1
- Decreased FVC
- FEV_1 < 80%
- FEV_1 ÷ FVC < 70%
- Post bronchodilator – no change in FEV_1
- PEF is decreased
- FET – is prolonged
- V Max - decreased

CLINICAL SIGNS

- Physical exam may be negative
- Hyper-inflated chest, Barrel chest
- Wheeze or quite breathing
- Pursed lip / accessory muscles resp.
- Peripheral edema
- Cyanosis, ↑ JVP
- Cachexia
- Cough, wheeze, dyspnea, sputum

PHYSICAL EXAMINATION

- Large, barrel-shaped chest.
- Prominent accessory respiratory muscles in neck.
- Low, flat diaphragm causing costal margin retractions on inspiration.
- Diminished breath sounds, distant heart sounds.
- Prolonged expiration with generalized wheezing predominantly on expiration.

PHYSICAL EXAMINATION (CONTD).

- Depressed liver, which is not enlarged.
- The 'blue bloater' type of COPD patient may also have:

  Cyanosis at rest or mild exertion.

  Oedema of ankles

  Crackles at lung bases.

  Loud second heart sound in pulmonary area (difficult to hear in COPD).
- The 'pink puffer' type of COPD patient may also have:-.

  expiratory pursed-lip breathing, thin body build and tendency to lean forward over a support to assist breathing.

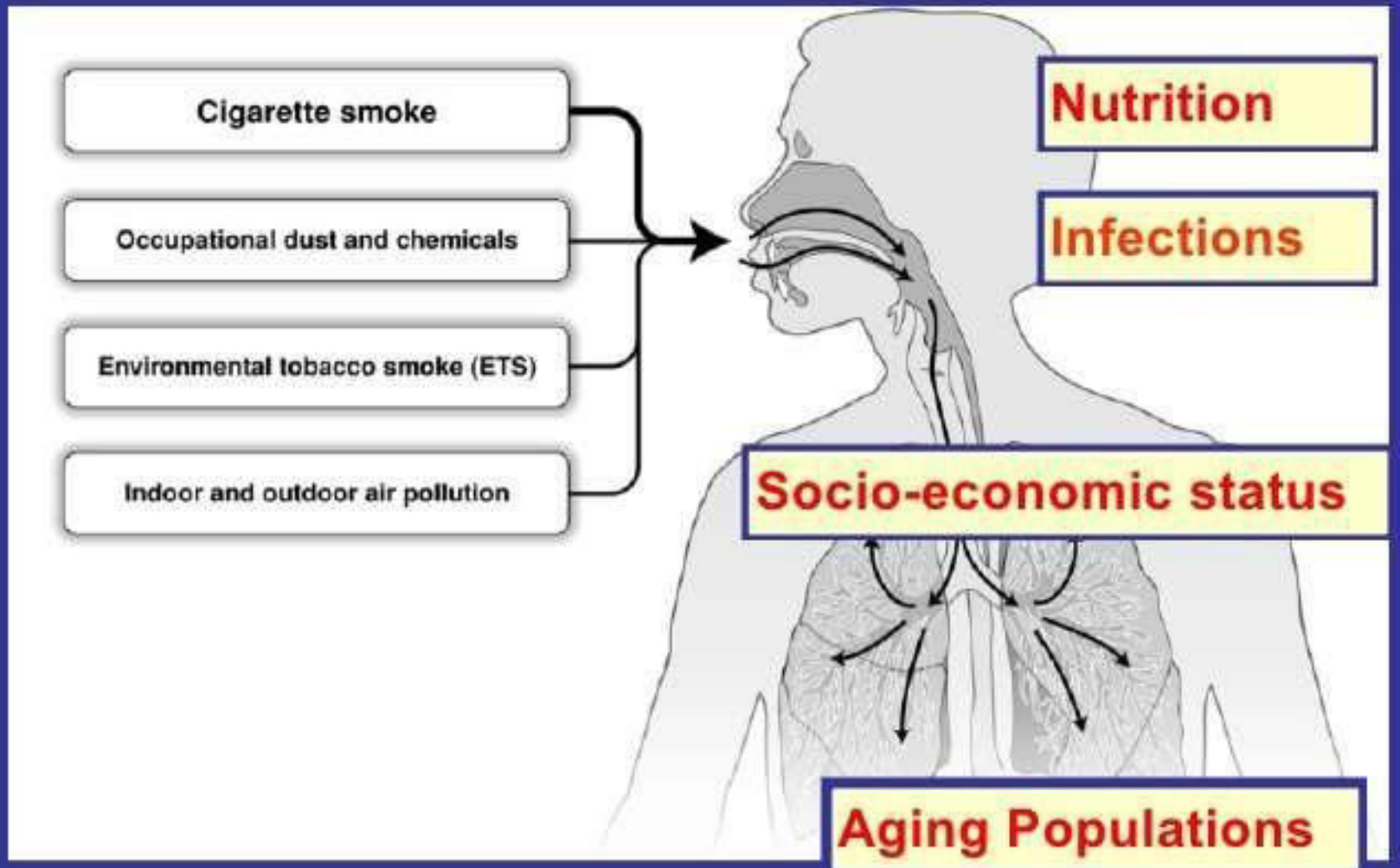
What can cause COPD?

- Smoking is the primary risk factor
  - Long-term smoking is responsible for 80-90 % of cases
    - Smoker, compared to non-smoker, is 10 times more likely to die of COPD
- Prolonged exposures to harmful particles and gases from:
  - Second-hand smoke,
  - Industrial smoke,
  - Chemical gases, vapors, mists & fumes
  - Dusts from grains, minerals & other materials

Other Risk Factors for COPD

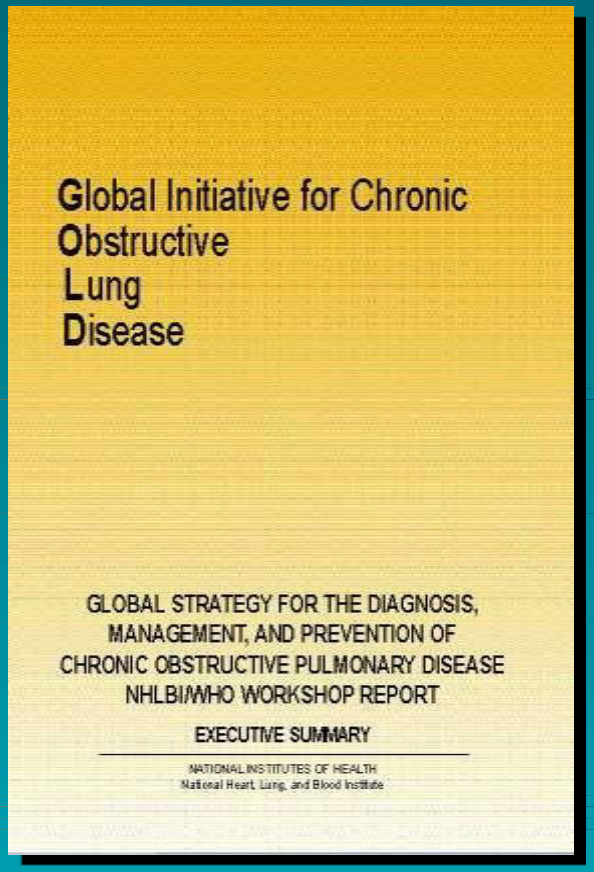
- History of childhood respiratory infections
- Genetic makeup
- Increasing age

Risk Factors for COPD



Treatment Guidelines For COPD

Four Components of COPD Management



1. Assess and monitor disease
2. Reduce risk factors
3. Manage stable COPD
   - Education
   - Pharmacologic
   - Non-pharmacologic
4. Manage exacerbations

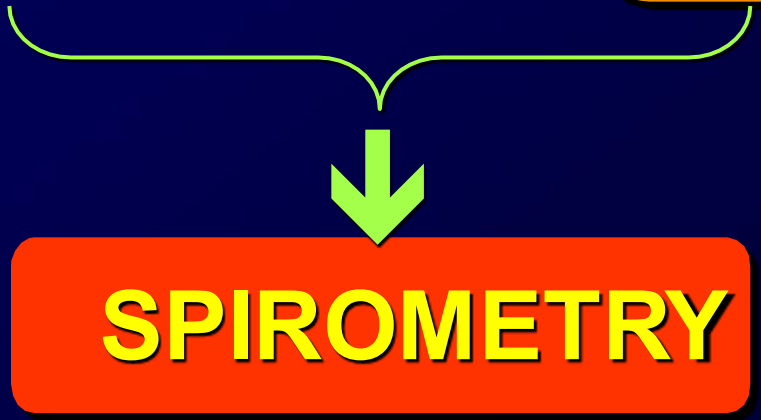
Diagnosis of COPD

SYMPTOMS

- cough
- sputum
- dyspnea

EXPOSURE TO RISK FACTORS

- tobacco
- occupation
- indoor/outdoor pollution



Factors Determining Severity Of Chronic COPD

- Severity of symptoms
- Severity of airflow limitation
- Frequency and severity of exacerbations
- Presence of complications of COPD
- Presence of respiratory insufficiency
- Co morbidity
- General health status
- Number of medications needed to manage the disease

Reduce Risk Factors Key Points

- Reduction of total personal exposure to tobacco smoke, occupational dusts and chemicals, and indoor and outdoor air pollutants are important goals to prevent the onset and progression of COPD.

- Smoking cessation is the single most effective-and cost-effective- intervention to reduce the risk of developing COPD and stop its progression.

Manage Stable COPD
Key Points

- Bronchodilator medications are central to the symptomatic management of COPD. They are given on an as-needed basis or on a regular basis to prevent or reduce symptoms.

- The principal bronchodilator treatments are anticholinergics, Beta$_2$-agonists theophylline, and a combination of these drugs.

Manage Stable COPD Key Points

- Regular treatment with inhaled glucocortico-steroids should only be prescribed for symptomatic COPD patients with a documented spirometric response to glucocorticosteroids or in those with an FEV_1 < 50% predicted and repeated exacerbations requiring treatment with antibiotics and/or oral glucocorticosteroids.

Manage Stable COPD
Key Points

- Chronic treatment with systemic glucocortico-steroids should be avoided because of an unfavorable benefit-to-risk ratio.

- All COPD-patients benefit from exercise training programs, improving with respect to both exercise tolerance and symptoms of dyspnea and fatigue.

Manage Stable COPD Key Points

- The long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival.

Stage (2003 update)	0 At risk	I Mild	II Moderate	III Severe	IV Very severe
Pre-bronchodilator FEV_1 (% predicted)	Normal	>80%	50–80%	30–50%	<30%

- Avoidance of risk factors **SMOKING CESSATION**
- Influenza vaccination

Short-acting bronchodilator if needed

- Add regular treatment with one or more long-acting bronchodilators, including tiotropium
- Pulmonary rehabilitation

Add regular treatment with inhaled corticosteroids if repeated exacerbations

- Long-term oxygen therapy (LTOT) if respiratory failure
- Consider surgical options

Based on GOLD global strategy (2003)
For clinical definitions of stages, refer to Figures 1.3 and 3.15

Cholinergic Constriction in COPD

- In COPD, cholinergic constriction is the dominant mechanism of airway obstruction
- Anticholinergics specifically target cholinergic constriction, therefore they are a logical treatment option in COPD

Criteria for COPD Exacerbation:

1. Increase dyspnea
2. Increase in sputum production
3. Change of sputum color
4. Fever

Manage Exacerbations
Key Points

- Exacerbations of respiratory symptoms requiring medical intervention are important clinical events in COPD.

- The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution, but the cause of about one-third of severe exacerbations cannot be identified.

Manage Exacerbations
Key Points

- Inhaled bronchodilators (anticholinergics and/or $Beta_2$-agonists), theophylline, and systemic, preferably oral, glucocortico-steroids are effective for the treatment of COPD exacerbations (Evidence A).

Manage Exacerbations
Key Points

- Patients experiencing COPD exacerbations with clinical signs of airway infection (e.g., increased volume and change of color of sputum, and/or fever) may benefit from antibiotic treatment.

Manage Exacerbations
Key Points

- Noninvasive intermittent positive pressure ventilation (NIIPPV) in acute exacerbations improves blood gases and pH, reduces in-hospital mortality, decreases the need for invasive mechanical ventilation and intubation, and decreases the length of hospital stay.

Nutritional Supplementation

- Energy-dense supplements in divided doses: 1000 KCAL is optimal

Carbohydrate- rich liquid

Protein 1.5 mg\kg

Minerals and vitamins

Efficacy

- Short term 2-3 weeks:Excellent response in body weight and respiratory muscle function and exercise capacity
- Long term: Poor response
- Doctor fault
- Patient fault
- Disease fault

What Is an Exacerbation, and Why Are They Important?

- Definition: a sustained worsening of the patient's symptoms from his or her usual stable state that is beyond normal day-to-day variation and acute in onset
  - Onset usually over 1 to 3 days
  - Term should not be used for other acute processes occurring in a COPD patient

Conclusions

- The Prevalence de COPD is between 10 - 15 %.
- Most patients have not been diagnosed.
- Cigarette smoking and biomass are major risk factors for the disease.
- Co-morbid conditions prevalence are increasing.
- COPD is a disease of younger patie nts, and increased number of women.
- Different therapies including smoking cessation, and pharmacotherapy impact the disease.

THANK YOU

Small intestinal colonic disorders

Diarrhea

- Passage of more than 200 g of stool daily.
- Decrease in stool consistency and an increase stool frequency(>3 time /day) and volume
- Wide range of severity from mild to severe with stool urgency and incontinence

Diarrhea

Must be distinguished

- Pseudodiarrhea

  (proctitis, IBS)

- Fecal incontinence

Classify as

- Acute diarrhea
- Chronic diarrhea

Acute diarrhea

- Acute diarrhea (<2weeks)
- This is extremely common
- Causes :
- Infection: 90%
- Short lived 10 days
- bacteria, their toxins, viruses or parasites

Acute diarrhea

- Pathphysiology
- Toxins

  Preformed staph toxins

  Enterotoxine vibrio cholera

  Cytotoxine E.coli
- Mucosal invasion salmonella
- Mucosal attachment giardia

Acute diarrhea

- Bacteria

Campylobacter spp.
Clostridium difficile
Escherichia coli
Enterotoxigenic
Enteroinvasive
Enterohemorrhagic
Salmonella spp.
Shigella spp.

Acute diarrhea

- Viruses
  - Adenovirus
  - Norovirus
  - Rotavirus
- Parasites or Protozoa
  - Entamoeba histolytica
  - Giardia lamblia
  - Microsporidia
  - Cryptosporidia
  - Cyclospora

Acute diarrhea

- Drugs
  - Antibiotics
  - Cytotoxic drugs
  - PPIs and laxative
  - NSAIDs
- Food allergies soya, peanut, egg
- Poisoning (organphosphorus)
- Acute Ischemia bowel
- Initial present. of chronic diarrhea

Acute diarrhea

Management

- Conservative
  - Oral fluid
  - IV fluid
  - Antipyretic
  - antispasmodic
- Antibiotics

  Empirical in moderate to severe diarrhea

  (ciprofloxacin plus metronidazole)

Acute diarrhea

Indications for evaluation(GSE and culture and toxine) and Abs treatment

- Severe prolonged
- bloody diarrhea
- Fever 38.5° C, duration > 48 h without improvement
- Recent antibiotic use
- New community outbreaks
- Severe abdominal pain in patients >50 y.
- Elderly (70 years)
- Immunocompromised patients.
- Co morbidity

Acute diarrhea

Persistent diarrhea > 2weeks

- *Giardia*
- *C. difficile*
- *E. histolytica*
- *Campylobacter*
- *Non infectious*

Investigation

- Stool examination and culture
- sigmoidoscopy with biopsies
- upper endoscopy with duodenal aspirates and biopsies

Chronic diarrhea

- Duration >4 weeks
- Prevalence 2-7%
- Classified to

  volume (large vs. small),

  pathphysiology (secretory vs. osmotic)

  stool characteristics (watery vs. fatty vs. inflammatory)

  small vs. large intestinal

Chronic diarrhea

Fatty diarrhea

MalabsorP	Mesenteric schemia Mucosal diseases(lymphoma celiac disease,giardiasis) Short bowel syndrome Small intestinal bacterial overgrowth
Maldigest	Inadequate bile acid Pancreatic exocrine insufficiency
	lymphatic obstruction

Chronic diarrhea

Watery Diarrhea

Osmotic

Carbohydrate malabsorption

primary lactase deficiency

secondary to mucosal dis.

Osmotic laxatives

Chronic diarrhea

Secretory

Carcinoid syndrome

Gastrinoma

VIPoma

Somatostatinoma

Villous adenoma in colon

Addison's disease

Pheochromocytoma

Medullary carcinoma thyroid

bowel resection (Ileal bile acid malabsorption

Chronic diarrhea

(secretory vs. osmotic)

- Large volume stool
- No response to fasting
- No abdominal pain
- No anion gap(<50 mosmo/l)

  (290 mosmol/kg)-[2 x (fecal sodium + potassium concentration)].

Chronic diarrhea

Inflammatory

IBD (U.colitis, crohn disease)

Ulcerative jejunoileitis

Microscopic colitis

Radiation colitis

Ischemic colitis

Eosinophilic Gastroenteritis

tuberculosis ileitis

Chronic diarrhea

Disordered motility

Hyperthyroidism

Postvagotomy diarrhea

Medications and toxins

Laxative abuse

Acid-reducing agents

Antibiotics

Antineoplastic agents

Heavy metals arsinate

Chronic diarrhea

Evaluation of chronic diarrhea

Most important steps for characterizing the type of the diarrhea are the history, examination and GSE

History

onset, duration, pattern

stool characteristics.

fever, weight loss, abdominal pain night diarrhea

responding to fasting

medications, surgery

family history of IBD or sprue

Chronic diarrhea

Examination

Malabsorption features

weigt loss,anaemia, edema

bone pain

Inflammatory bowel disease features

anaemia, mouth ulcer

Abdominal mass or tenderness

Mucocutaneous features

erythema nodosum

flushing

oral ulcers

Chronic diarrhea

Investigation

CBC and ESR

GSE

S. electrolytes

S. ca and ph

S. albumin and globulin

Chronic diarrhea
Exclude medication and surgery

Stool blood and pus

Features of malabsorption
Fatty foul smell stool
Nutritional deficiency

Watery
No abdominal pain
no respond to fasting

Watery
Abdominal bloating
Respond to fasting
Increase with milk

Colonoscopy with biopsy

Small bowel image
Endoscope biopsy

Osmotic gap
CT abdomen
Hormonal assessment

Trial of dietary exclusion
Stool PH

If normal small bowel
Consider pancreatic insufficiency

CT abdomen
Pancreatic function assessment

Chronic diarrhea

Treatment

- Fluid and electrolyte repletion
- Antidiarrhea
  - Diphenoxylate
  - loperamide
- Treatment of specific etiology
  - cholestyramine for bile acid diarrhea
  - octriotide for neuroendocrine diarrhea
  - Clonidin for diabetic diarrhea

Constipation

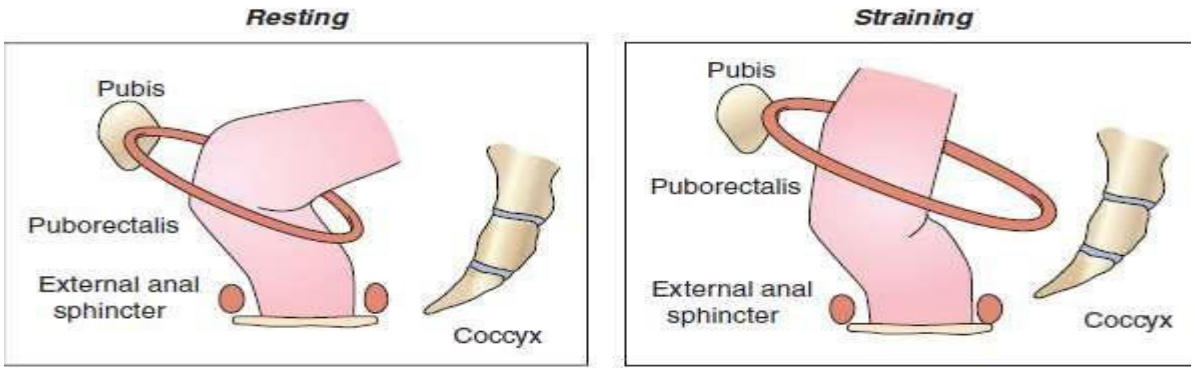
Defined as infrequent passage(< 3 bowel motions per week) of hard stools.

Patients may also complain of straining, a sensation of incomplete evacuation and abdominal discomfort.

Prevalence 10-20%

Constipation

- During defecation, sacral parasympathetic nerves relax puborectalis muscle, facilitating the straightening of the rectoanal angle
- Distention of the rectum results in transient relaxation of the internal anal sphincter via intrinsic and reflex sympathetic innervation.
- As sigmoid and rectal contractions increase the pressure within the rectum, the rectosigmoid angle opens by 15 %
- Voluntary relaxation of the external anal sphincter permits the evacuation of feces
- evacuation process can be augmented by an increase in intraabdominal pressure created by the Valsalva



Constipation

Gastrointestinal disorders

Dietary

Lack of fiber and/or fluid intake

Motility

Irritable bowel syndrome

Chronic intestinal pseudo-obstruction

(slow-transit constipation)

Hirschsprung's disease

Constipation

Slow transit constipation

- is characterized by the reduced motility of the large intestine, caused by abnormalities of the enteric nerves. The unusually slow passage of waste through the large intestine leads to chronic constipation
- functional colonic disorder represents ~15 to 30% of constipated patients
- Slow transit constipation can be diagnosed with a complete history, physical exam, and a battery of specific diagnostic studies

Constipation

Structural

Colonic carcinoma

Diverticular disease

Defecation problems

Disorders of rectal evacuation

- Pelvic floor dysfunction
- descending perineum syndrome; rectal mucosal prolapse; rectocele

Painful anal disease

Crohn's disease

fissures, hemorrhoids

Constipation

Non-gastrointestinal disorders

Drugs

- Opiates
- Anticholinergics
- Calcium antagonists
- Iron supplements
- Aluminium-containing antacids

Neurological

- Multiple sclerosis
- Spinal cord lesions
- Cerebrovascular accidents

Constipation

Metabolic/endocrine

- Hypercalcaemia
- Hypothyroidism

Others

- Any serious illness with immobility, especially in the elderly
- Depression

Constipation

Approach to the Patient

History

- Frequency (e.g., fewer than three bowel movements per week)
- consistency (lumpy/hard)
- excessive straining,
- prolonged defecation time
- digitate the anorectum
- diet and medication history

Constipation

- The onset, duration

  neonatal onset Hirschsprung‘s

- Recent change in bowel activity

  colonic carcinoma.

- Associated symptoms such as rectal bleeding, pain and weight loss is important

Constipation

Physical examination

Search for general medical disorders

Signs of intestinal obstruction

Abdominal and rectal examination

Investigate

basic tests: serum calcium, potassium, and thyroid hormone levels.

Barium enema

- less costly
- identifies colonic dilatation

Constipation

Sigmoidoscopy plus barium enema or colonoscopy alone

- weight loss
- rectal bleeding
- Anemia
- patients >40 years (recent)

Constipation

- Tests physiologic function of the colon and pelvic floor

  – Measurement of Colonic Transit
  – Anorectal and Pelvic Floor Tests
    Anorectal manometry(rectal and sphinicter pressure)
    Defecography

Constipation

Treatment

- Trial of dietary fiber

  chronic constipation

  no alarm features

  normal basic tests

- If No response consider evaluation of the colon by colonoscopy and Barium study

- If No pathology consider potent laxatives osmotic, and stimulant laxatives

Constipation

- Disabling symptoms

  specialist referral for investigation of possible dysmotility and pschycolgical assessment.

- According to the finding in the physiological test:
- slow-transit constipation

1. long time trial of potent laxative

2. Surgery

Laparoscopic colectomy with ileorectostomy

- Evacuation disorder
- pelvic floor retraining (biofeedback)

THANKS

ASTHMA

Dr. Ammar.

The Definition

- Asthma is a chronic inflammatory disease of the airways characterized by hyper-responsiveness of the tracheo-bronchial tree to a multiplicity of stimuli.
- Asthma is manifested physiologically by widespread narrowing of the air passages which may be reversed spontaneously or in response to treatment.
- Clinically asthma is manifested by paroxysms of dyspneoa, cough, & wheezing.

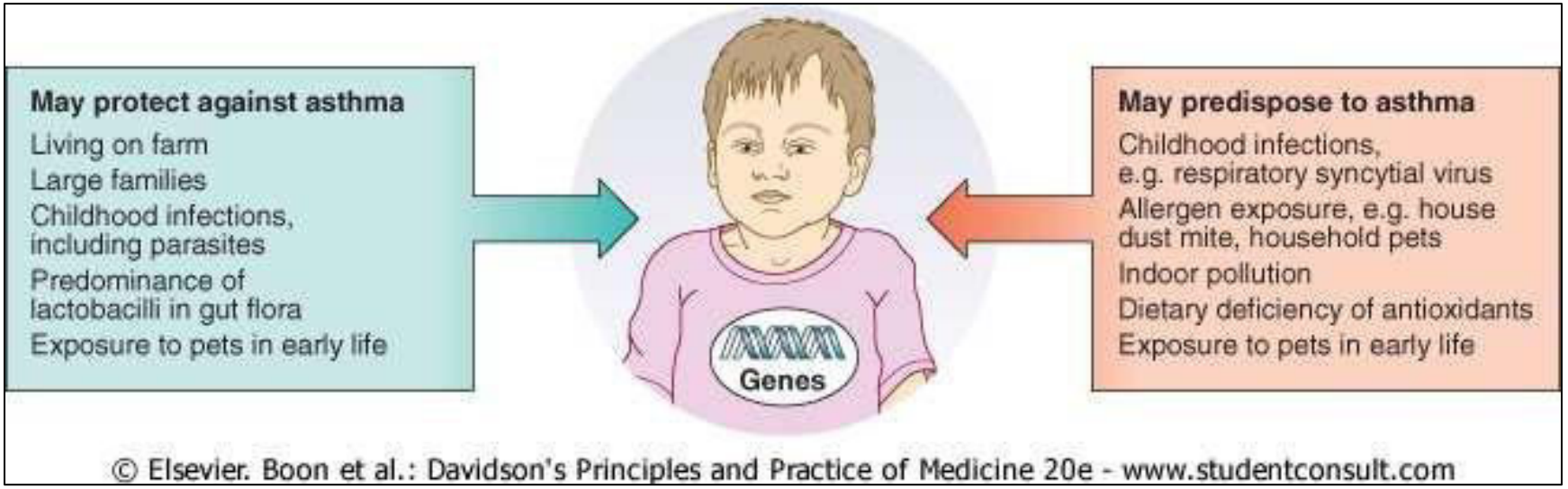
Harrison Text book of Internal Medicine

Etiology of Asthma

- Asthma is a heterogeneous disease with genetic and environmental factors playing a role.
- Environmental factors include viruses, occupational exposure and allergens playing a role in both the initiation and continuation of the disease.
- Henry Salter in 1860 suggested “distinct traces of inheritance are seen in 2 cases out of 5.
- Many studies now suggest that first degree relatives have a 20-25% chance of developing Asthma.

Harrison Text Book of Internal Medicine

Aetiology


May protect against asthma
Living on farm
Large families
Childhood infections, including parasites
Predominance of lactobacilli in gut flora
Exposure to pets in early life
Genes
May predispose to asthma
Childhood infections, e.g. respiratory syncytial virus
Allergen exposure, e.g. house dust mite, household pets
Indoor pollution
Dietary deficiency of antioxidants
Exposure to pets in early life
© Elsevier. Boon et al.: Davidson's Principles and Practice of Medicine 20e - www.studentconsult.com

Classification Of Asthma

1. Allergic Asthma (atopic)(extrinsic)

- It is often associated with a personal \family history of allergic disease + increased level of IgE in serum \positive response to provocation test .

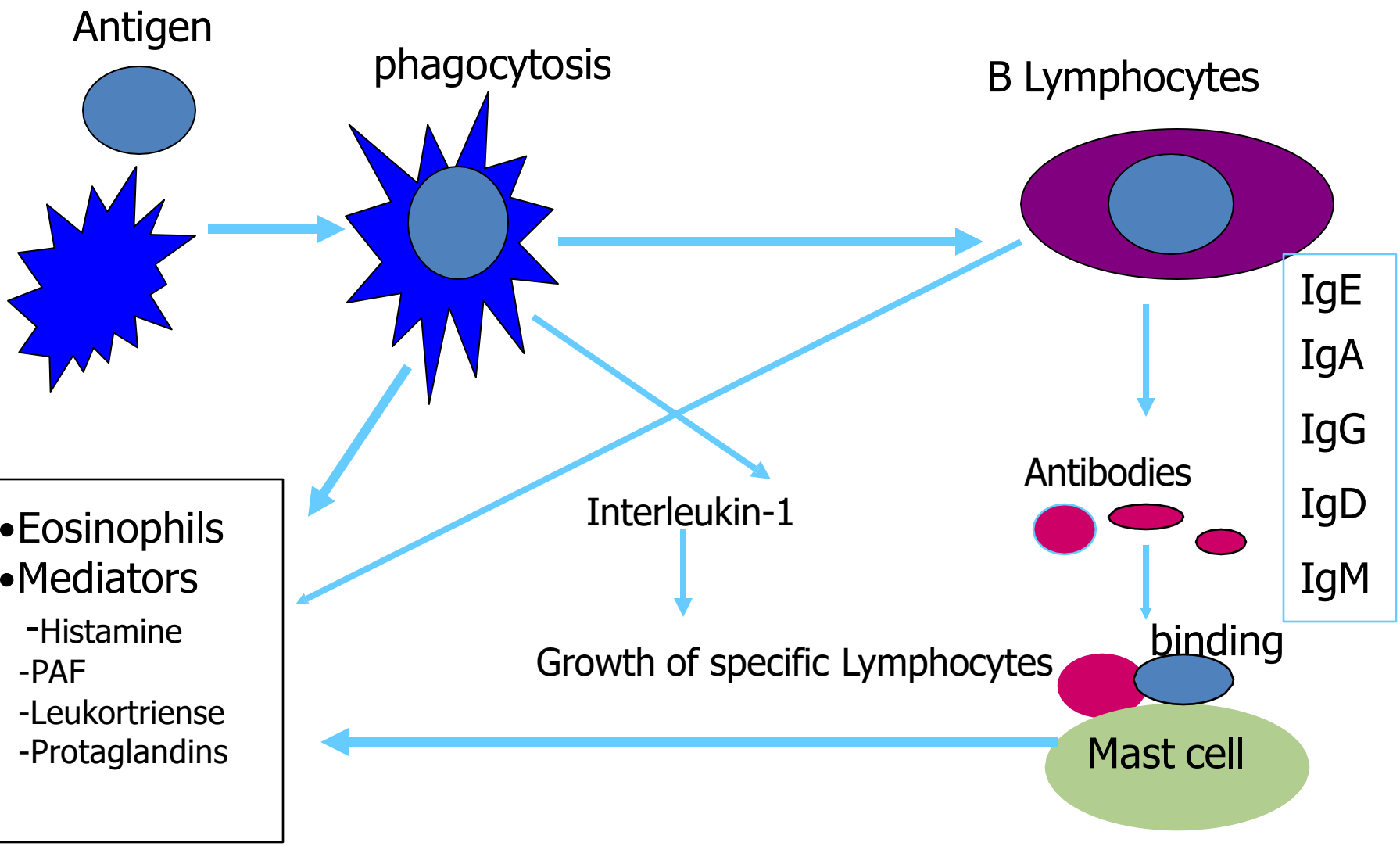
-It is usually early –onset & typically episodic .

2. Idiosyncratic Asthma (non- atopic) (intrinsic):

3. Many patients have disease not fit clearly into either of the above (mixed group).

Harrison Text book of Internal Medicine

Asthma mechanism- role of inflammatory cells



GINA 2004

Mediators

- Histamine
- Leukotriens
- Prostaglandins
- Thromboxane
- PAF
- Bradykinins
- Tachykinins
- Endothelins and others.

Mediators released produce an intense , immediate inflammatory reaction involving :

1. Bronchoconstruction
2. Vascular congestion
3. Edema formation
4. Increased mucus production
5. Impaired mucociliary transport.
6. Structural changes (fibrosis , smooth muscle hyperplasia , angiogenesis ,mucus hyperplasia)

Stimuli That Incite Asthma

1.Allergens.
2.Pharmacologic Stimuli.
3.Environment & Air Pollution..
4.Occupational Factors.
5.Infections.
6.Exercise..
7.Emotional.

Coexisting conditions that can aggravate asthma :

1. Rhinitis 2. sinusitis 3. GERD .

Allergens

- Most of the allergens that provoke asthma are airborne.
- Immune mechanisms appear to be causally related to the development of asthma in 25-35% of all cases & contributory in ~ another third.
- Important allergen such as house dusts mites, cat's allergen & pets ,cockroach allergen.
- Smoking increase the risk of asthma by about 4 times.

What Makes Asthma Worse?

- Allergens
  - Warm-blooded pets (including dogs, cats, birds, and small rodents)
  - House dust mites
  - Cockroaches
  - Pollens from grass and trees
  - Molds (indoors and outdoors)

Environmental Control in Asthma

eliminate these "mobile allergen bearing units"

Aspirin-sensitive asthma

- Aspirin & other NSAID can result in asthma exacerbation in some (~10%) patients , most of such patients have severe Asthma & nasal polyps. The affected patients develop rhinorrhea & nasal congestion .
- They may benefit from leukotriene modifying agents and other drugs e.g. B- blockers .

Infections

- Respiratory infections are the most common stimuli that evoke acute exacerbations of asthma.
- Viruses & not bacteria are the major stimuli.
- In children RCV & par influenza virus are most important.
- In older children & adult , rhinovirus & influenza virus are the commonest .

- Workers most commonly reported to occupational asthma schemes .

* Paint sprays
* Welders
* Chemical workers
* Timber workers
* Bakers & pastry-makers
* Food processing
* Animal handlers
* Nurses

Nocturnal asthma

- Occurrence of asthma symptoms at night or early morning
- Circadian rhythm
- Exposure to triggers at day time leads to broncho-spasm at night
- Sleep Apnea?
- Sinusitis ?
- GERD ?
- Increase venous return?

Clinical Presentation Of Asthma

1. Triad of **cough + dyspnea + wheezing** (in up to90%) usually episodic .
2. Dry cough : It may be the sole presentation (cough-variant asthma) , as many as 30-50% in children who complaint from chronic cough will developed wheeze (75%) in the next 5-7 years & 13% of adult >50 years .
3. Exertional dyspnea.
4. Asymptomatic .

Davidson Text book of Internal Medicine

Clinical features in adults that influence the probability of asthma

- MORE THAN ONE OF THE FOLLOWING SYMPTOMS :

Wheeze , breathlessness , chest tightness , & cough , particularly if :

* symptoms worse at night\ early morning
* symptoms in response to exercise , allergens & cold air .
* symptoms after taking aspirin or B-blockers.

From BTS 2008

Clinical features cont.

- History of atopic disorders .
- Family history of asthma or atopic disorders.
- Widespread wheeze on auscultation .
- Otherwise unexplained low FEV1 or PEF .
- Otherwise unexplained peripheral eosinophilia .

From BTS 2008

Differential Diagnosis Of Asthma

COMMON :

1. Acute bronchitis
2. Aspiration(foreign body)
3. Bronchial stenosis
4. Cardiac failure
5. Chronic bronchitis
6. Cystic fibrosis
7. Eosinophilic pneumonias

D. Dx (cont.)

Uncommon :

1. Airway obstruction e.g. external or internal
2. Carcinoid syndrome
3. Pulmonary embolism
4. Systemic vasculitis
5. Endobronchial sarcoid
6. Systemic mastocytosis.

Management Of Asthma

1. Patients education :

Patients & their parents (children)should be educated for :

1. The nature of the disease
2. the deference between reliever & controller .
3. proper using of the inhaler .
4. the uses of a peak flow meter .
5. about corticosteroids

Management cont.

2. Avoidance of precipitating factors:

Desensitization :

There is little evidence of its benefit in asthma ,
& there is attendant risk .

Davidson Text Book of Internal Medicine

Classification of Asthma Severity

CLASSIFY SEVERITY Clinical Features Before Treatment	Symptoms	Nighttime Symptoms	PEF
STEP 4 Severe Persistent	Continuous Limited physical activity	Frequent	<60% predicted Variability >30%
STEP 3 Moderate Persistent	Daily Use b_2-agents daily Attacks affect activity	>1 time week	>60%- <80% predicted Variability >30%
STEP 2 Mild Persistent	>1 time a week but <1 time a day	>2 times a months	<80% predicted Variability 20-30%
STEP 1 Intermittent	<1 time a week Asymptomatic and normal PEF between attacks	<2 times a month	³80% predicted Variability <20%

The presence of one of the features of severity is sufficient to place a patient in that category.

GINA 2004

3-Management of chronic Asthma

Step 1 :

In patients with mild to moderate asthma (occasional use of inhaled short –acting B2 agonist (ISABA) e.g. salbutamol, terbutaline

Step 2 :

When the pat. use ISABA more than once daily .

ISABA used as required + regular inhaled steroids (ICS).

e.g. beclomethasone ; budesonide (up to 800 mcg\d) or fluticasone (up to 400 mcg \ d).

- Or leukotriene modifier .

Davidson's Text Book of Internal Medicine

Management cont.

Step 3:

1 Medium- high dose of ICS (800-2000 mcg|d) + ISABA or

2 Low dose of ICS + long – acting B2 – agonist e.g. salmeterol ; formoterol or

3 Low dose of ICS + leukotriene modifier .

Step 4 :

Like step 3 plus one or more of :

a. Leukotriene receptor antagonist.

b. Inhaled ipratropium bromide or oxitropium.

c. Long –acting oral B2 – agonist .

d. Sodium cromoglycate or nedocromili.

Davidson's Text Book of Internal Medicine

Management cont.

Step 5:

When a patient in exacerbations of asthma .

Short courses of `**rescue**` oral corticosteroids (30-60mg\d of prednisolone) often required .

Indications for `rescue` courses include:

1. Symptoms & PEF progressively worsening day by day
2. PEF < 60%
3. Onset or worsening of sleep disturbance.
4. Persistence of morning until midday.
5. Symptoms severe enough to require nebulised or injected bronchodilators

Davidson's Text Book of Internal Medicine

Clinical Control of Asthma

No (or minimal)* daytime symptoms

No limitations of activity

No nocturnal symptoms

No (or minimal) need for rescue medication

Close to Normal lung function

No exacerbations

---

* *Minimal = twice or less per week*

GINA 2004

Why don’t patients comply with treatment?

Drug factors

- Difficulties with inhaler devices
- Too complex regimen e.g multiple doses or multiple drugs
- Side effects
- Cost of medication
- Dislike of medication(taste, odour or shape)
- Distant health services and pharmacies

Non drug factors

- Misunderstanding or lack of instructions
- Dissatisfaction with health care professionals
- Poor supervision, training or follow-up
- Inappropriate expectations
- underestimation of severity
- Cultural issues
- Fear of addiction
- Attitude toward ill health
- religious issues

Management of acute severe asthma :

A-Features of acute severe asthma:

1. PEF 33-50 % of predicted (< 200 l\ min)
2. Respiratory rate > 25 \ min
3. Heart rate > 110 \ min
4. Inability to complete sentences in one breath.

B-Features of Life- threatening asthma :

1. PEF < 100 L\min
2. SaO2 < 92% or PaO2 < 8 Kpa (60 mmHg)
3. Normal PaCO2
4. Silent chest .
5. Cyanosis
6. Feeble respiratory effort
7. Bradycardia or arrhythmias
8. Hypotension
9. Exhaustion
10. Confusion
11. Coma

C-Near- fatal Asthma :

Raised PaCO2 &\or requiring mechanical ventilation

GINA 2014

Treatment of acute severe Asthma:

1. Oxygen therapy :

High concentration to maintain SaO2 > 92%

2. Inhaled bronchodilators: (high dose)

a. short- acting B2 –agonist (metered dose inhaler through a spacer or nebulizer e.g. salbutamol.

b. Ipratropium bromide (provide additional effect)

Davidson's Text Book of Internal Medicine

3. Systemic corticosteroids :

Oral prednisolone 30-60 mg \d or I.V. Hydrocortisone 200mg initially

4. Other :

I.V. Fluids (if the patients dehydrated)

potassium supplementation

5. Subsequent management :

A. I.V. magnesium 1.2- 2.0 g \ 20 min

B. I.V. aminophylline

C. I.V. leukotriene receptor antagonist .

Davidson's Text Book of Internal Medicine

Indications for assisted ventilation

1. Coma
2. Respiratory arrest
3. Deterioration of ABG

   $PaO_2 < 8$ Kpa

   Pa $CO_2 > 6$ kpa

   low PH

4. Exhaustion ; confusion ; drowsiness

Asthma in pregnancy

* Asthma during pregnancy has unpredictable course:
  1\3 improve ; 1\3 worsen.
* It represents the greater danger to the fetus :
  - intrauterine growth restriction & low birth weight.
  - preterm birth .
  - high perinatal mortality.
  - neonatal hypoxia .
- Uncontrolled asthma associated with more maternal :

  Hypertension ; hyperemesis ; pre-eclampsia ; vaginal bleeding ; complicated labour .

Davidson's Text Book of Internal Medicine

Asthma in pregnancy (cont):

Good safety for:

B2- agonist; inhaled steroids; theophyllines; oral prednisolone & chromones .

Oral leukotriene receptor antagonist should not be stopped in women have previously controlled before pregnancy .

Women on prednisolone > 7.5 mg / d should receive hydrocortisone 100 mg 6-8 h during labour.

Davidson's Text Book of Internal Medicine

Asthma in pregnancy (cont):

* Prostaglandin F2 alpha may induce bronchospasm !!

* During breastfeeding medication can be used normally.

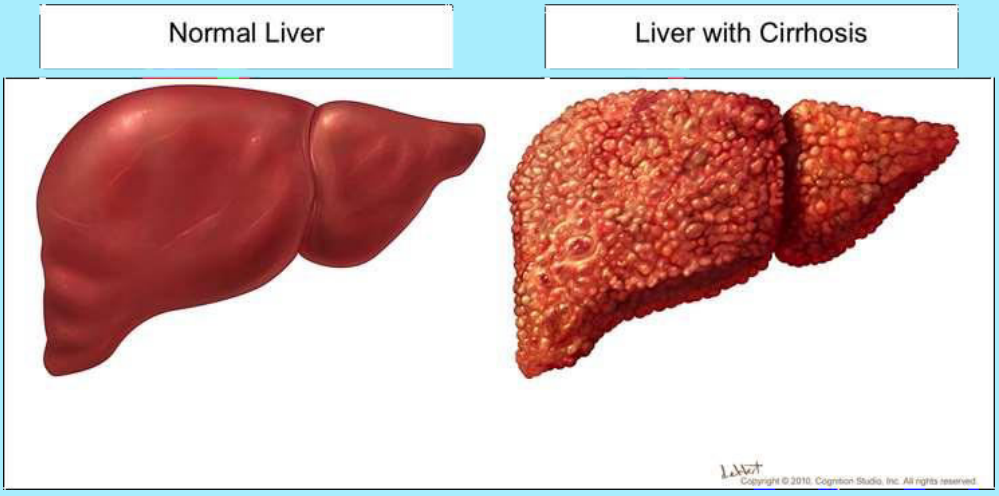
Davidson's Text Book of Internal Medicine

Thank You

Cirrhosis & Its Sequelae

Dr.

Ammar Khalid A



2016

Definition:

It's the final stage of any chronic liver disease, is a diffuse process characterized by fibrosis and conversion of normal architecture to structurally abnormal nodules. These "regenerative" nodules lack normal lobular organization and are surrounded by fibrous tissue.

Cirrhosis can be classified by its status as compensated or decompensated.

Decompensated cirrhosis is defined by the presence of ascites, variceal bleeding, encephalopathy, or jaundice.

Epidemiology:

The prevalence of chronic liver disease or cirrhosis worldwide is estimated to be **100 (range, 25 to 400) per 100,000** subjects.

According to the WHO, about **800,000** people die of cirrhosis annually.

The **12th** leading cause of death overall.

Chronic liver disease and cirrhosis are the seventh leading cause of death in the United States in individuals between 25 and 64 years of age.

PATHOLOGY

Liver Fibrosis/Cirrhosis

In response to injury, hepatic stellate cells become activated, secrete extracellular matrix they become contractile hepatic myofibroblasts.

Collagen deposition in the space of Disse. leads to defenestration of the sinusoidal endothelial cells ("capillarization" of the sinusoids), decreased sinusoidal diameter.

CLINICAL MANIFESTATIONS

The clinical manifestations of cirrhosis range widely from an asymptomatic patient with no signs of chronic liver disease to a patient who is confused and jaundiced and has severe muscle wasting and ascites.

The natural history of cirrhosis is characterized by an initial phase, termed *compensated cirrhosis, followed by a rapidly progressive* phase marked by the development of complications of portal hypertension or liver dysfunction (or both), termed *decompensated cirrhosis.*

In the compensated phase, identified for the development of varices or ascites.

As the disease progresses, portal pressure increases, portal hypertensive gastrointestinal (GI) bleeding, encephalopathy, and jaundice.

Transition from a compensated to a decompensated stage occurs at a rate of approximately 5 to 7% per year.

Compensated Cirrhosis

cirrhosis is mostly asymptomatic , Nonspecific fatigue, decreased libido, or sleep disturbances.

About 40% of patients with compensated cirrhosis have esophageal varices.

Decompensated Cirrhosis

ascites, variceal hemorrhage, jaundice, hepatic encephalopathy, or any combination of these findings.

Ascites, which is the most frequent sign of decompensation, is present in 80% of patients with decompensated cirrhosis.

Variceal Hemorrhage

present in approximately 50% of patients with newly diagnosed cirrhosis.

The prevalence of varices correlates with the severity of liver disease and ranges from 40% in Child A cirrhotic patients to 85% in Child C cirrhotic patients.

The incidence of a first variceal hemorrhage in patients with small varices is about 5% per year, whereas medium and large varices bleed at a rate of approximately 15% per year.

Ascites

Occurs at a rate of 7 to 10% per year.

The most frequent symptoms associated with ascites are increased abdominal girth.

Hepatorenal syndrome

Hepatic Encephalopathy

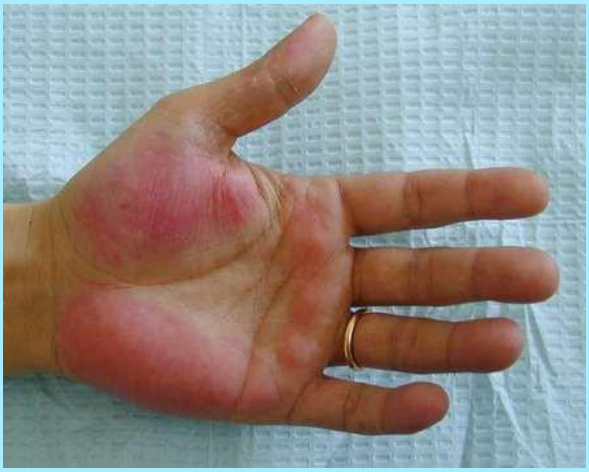
Occurs at a rate of approximately 2 to 3% per year.

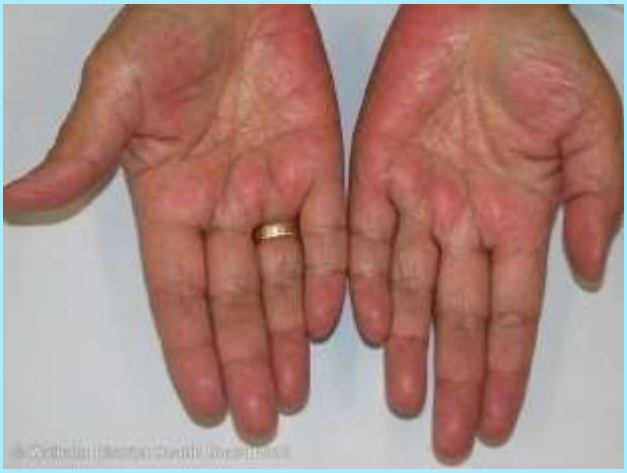
Gradual onset and rarely fatal.

Clinically, it is characterized by alterations in consciousness and behavior ranging from inversion of the sleep-wake pattern and forgetfulness ; to confusion, bizarre behavior, to lethargy to coma.

On physical examination, a distal tremor, asterixis Additionally, sweet-smelling breath, a characteristic termed fetor hepaticus.

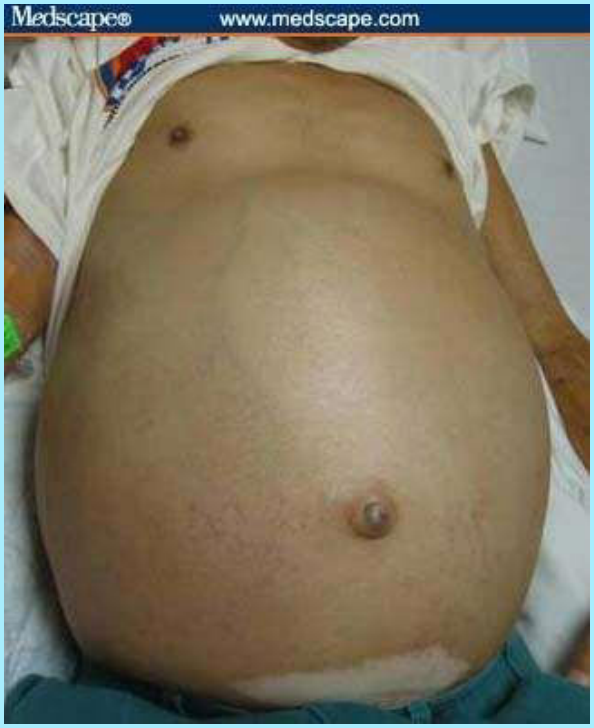
Palmar erythema



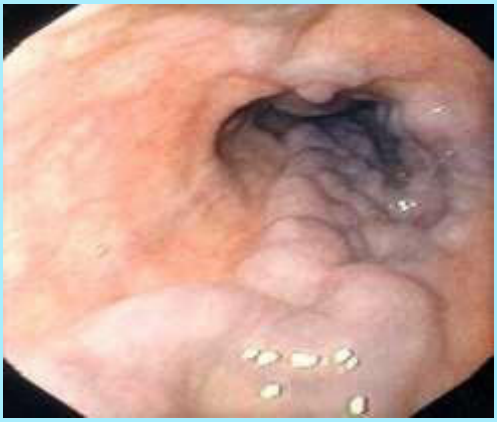


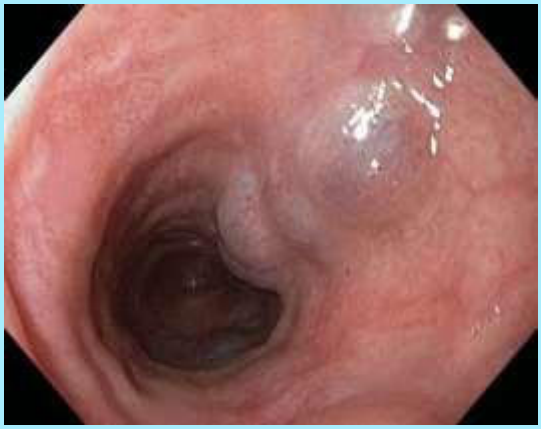
Dupuytren's contracture

Ascites

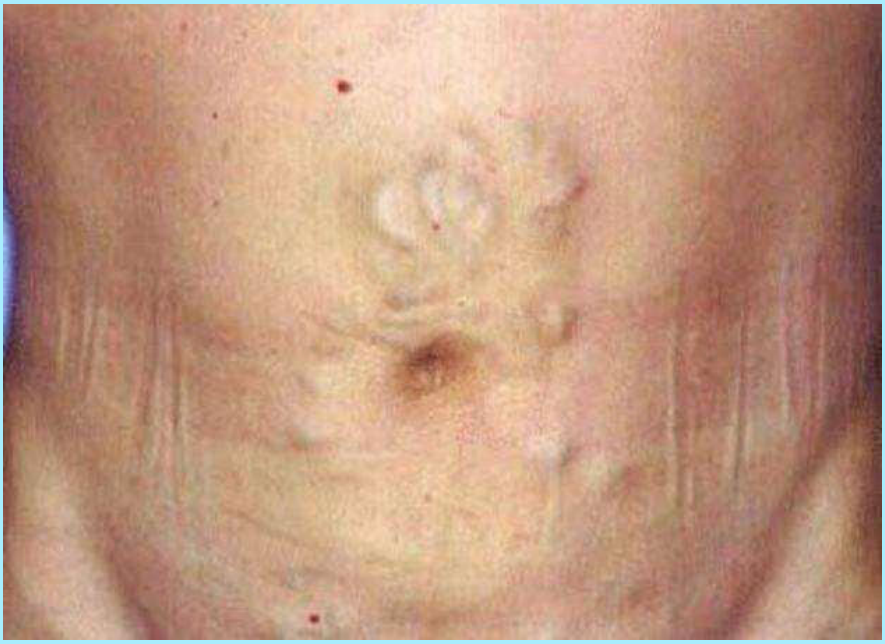


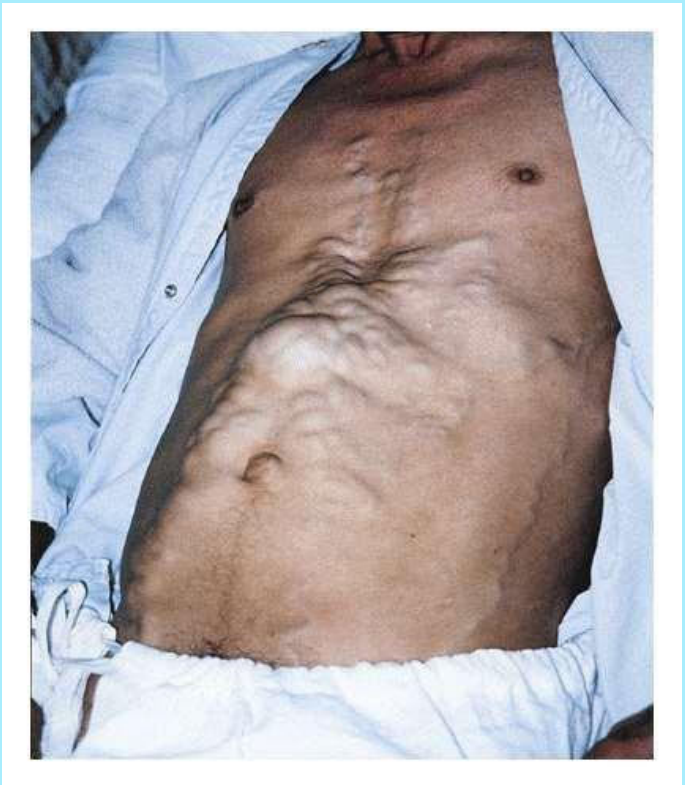
Esophageal varices





Caput medusae





DIAGNOSIS

The diagnosis of cirrhosis should be considered in any patient with chronic liver disease.

In asymptomatic patients with *compensated cirrhosis,* diagnosis may often require histologic confirmation by liver biopsy, which is the "gold standard" for the diagnosis of cirrhosis.

In patients with symptoms or signs of chronic liver disease, confirmed noninvasively by imaging studies without the need for liver biopsy.

Physical Examination

Stigmata of cirrhosis consist of muscle atrophy, spider angiomas, palmar erythema , Males may have hair loss, gynecomastia, and testicular atrophy.

Petechiae and ecchymoses may be present as a result of thrombocytopenia or a prolonged prothrombin time, Dupuytren's contracture.

A pathognomonic feature of cirrhosis is small right liver lobe, with a span of less than 7 cm on percussion, and a palpable left lobe that is nodular with increased consistency. Splenomegaly may also be present and is indicative of portal hypertension. Collateral circulation on the abdominal wall (caput medusae).

Laboratory Tests

subtle abnormalities in serum levels of albumin or bilirubin or elevation of the international normalized ratio.

low platelet count, abnormal levels of aspartate aminotransferase, γ-glutamyl transpeptidase.

Imaging Studies

Computed tomography, ultrasound, and magnetic resonance imaging.

Findings consistent with cirrhosis include nodular contour of the liver, a small liver with or without hypertrophy of the left or caudate lobe, splenomegaly, and in particular, identification of intraabdominal collateral vessels indicative of portal hypertension .

Transient elastography: measures liver stiffness .

In *decompensated cirrhosis, detection of ascites, variceal bleeding, or* encephalopathy in the setting of chronic liver disease essentially establishes the diagnosis of cirrhosis, so a liver biopsy is not necessary.

Complications of Cirrhosis

Varices and Variceal Hemorrhage

Upper GI endoscopy the main method for diagnosing varices and variceal hemorrhage.

Varices are classified as small (straight, minimally elevated veins above the esophageal mucosal surface), medium (tortuous veins occupying less than one third of the esophageal lumen), or large (occupying more than one third of the esophageal lumen).

Ascites

The most common cause of ascites is cirrhosis, which accounts for 80% of cases. Diagnostic paracentesis is a safe procedure , Ultrasound guidance should be used in patients in whom percussion cannot locate the ascites. The fluid should always be evaluated for albumin , polymorphonuclear (PMN) blood cell count, bacteriologic cultures, cytology, glucose and lactate dehydrogenase levels ,smear and culture for acid-fast bacilli.

The serum-ascites albumin gradient useful in the differential diagnosis of ascites. The serum-ascites albumin gradient correlates with sinusoidal pressure and will therefore be elevated (>1.1 g/dL) in patients in whom the source of ascites is the hepatic sinusoid (e.g., cirrhosis or cardiac ascites).

Hepatorenal Syndrome

characterized by maximal peripheral vasodilation ,maximal activation of hormones that cause the retention of sodium and water and intense vasoconstriction of renal arteries. Ascites unresponsive to diuretics is universal, and dilutional hyponatremia is almost always present.

Spontaneous Bacterial Peritonitis

Diagnostic paracentesis should be performed in any patient with symptoms or signs of spontaneous bacterial peritonitis.

Spontaneous bacterial peritonitis is often asymptomatic

The diagnosis of spontaneous bacterial peritonitis is established by an ascitic fluid PMN count greater than 250/mm3. Bacteria can be isolated from ascitic fluid in only 40 to 50% of cases. Spontaneous bacterial peritonitis is mostly a monobacterial infection, usually with gram-negative enteric organisms. Anaerobes and fungi very rarely causes.

Hepatic Encephalopathy

The diagnosis based on the history and physical examination.

There is poor correlation between the stage of hepatic encephalopathy and ammonia blood levels.

Hepatopulmonary Syndrome and Portopulmonary Hypertension

The diagnostic criteria for hepatopulmonary syndrome are arterial hypoxemia with a Pao2 of less than 80 mm Hg or an alveolar arterial oxygen gradient of greater than 15 mm Hg, along with evidence of pulmonary vascular shunting on contrast echocardiography.

Portopulmonary hypertension is diagnosed by the presence of mean pulmonary arterial pressure higher than 25 mm Hg on right heart catheterization, provided that pulmonary capillary wedge pressure is less than 15 mm Hg.

TREATMENT

Treatment of cirrhosis should ideally be aimed at interrupting or reversing fibrosis.

Treatment of compensated cirrhosis is currently directed at preventing the development of decompensation by

(1) treating the underlying liver disease (e.g., antiviral therapy for hepatitis C or B) to reduce fibrosis and prevent decompensation;
(2) avoiding factors that could worsen liver disease, such as alcohol and hepatotoxic drugs; and
(3) screening for varices (to prevent variceal hemorrhage) and for hepatocellular carcinoma (to treat at an early stage).

Varices and Variceal Bleeding

Reducing portal pressure. Nonselective β-adrenergic blockers (propranolol, nadolol) reduce portal pressure by producing

splanchnic vasoconstriction and decreasing portal venous inflow. 1- Propranolol should be titrated to produce a resting heart rate of about 50 to 55 beats per minute.

Endoscopic variceal ligation.

Endoscopy should be repeated every 2 to 3 years in patients with no varices, every 1 to 2 years in patients with small varices.

The most effective specific therapy for the control of active variceal hemorrhage is the combination of a vasoconstrictor with endoscopic therapy. Safe vasoconstrictors include terlipressin, and the somatostatin analogues ,octreotide, which is used as a 50-µg intravenous bolus followed by an infusion at 50 µg/hour.

The next best results (rebleeding rates of about 22%) are obtained with the combination of nonselective β-blockers (propranolol or nadolol), with or without isosorbide mononitrate, and endoscopic variceal ligation.

Transjugular intrahepatic portosystemic shunt (TIPS), should be used in patients whose variceal bleeding has persisted.

Ascites

Salt restriction and diuretics constitute the mainstay of management of ascites. Dietary sodium intake should be restricted to 2 g/day.

Spironolactone, should be started at a dose of 100 mg/day to a maximal effective dose of 400 mg/day.

Furosemide, at an escalated dose from 40 to 160 mg/day.

The goal is weight loss of 1 kg in the first week and 2 kg/week subsequently.

In the 10 to 20% of patients with ascites who are refractory to diuretics,

large-volume paracentesis, aimed at removing all or most of the fluid,

plus albumin at a dose of 6 to 8 g intravenously per liter of ascites removed.

In patients requiring frequent large-volume paracentesis (more than twice per month), polytetrafluoroethylene-covered TIPS

- stents should be considered.

Hepatorenal Syndrome

The mainstay of therapy is liver transplantation.

Terlipressin, plus albumin.

use of terlipressin, which at a dose 0.5 to 2.0 mg intravenously every 4 to 6 hours.

The most used combination is octreotide (100 to 200 µg subcutaneously three times a day) plus midodrine.

Spontaneous Bacterial Peritonitis

Empirical antibiotic therapy with an intravenous third-generation cephalosporin. the minimal duration of therapy should be 5 days. Repeat diagnostic paracentesis should be performed 2 days after starting antibiotics.

,The renal dysfunction associated with spontaneous bacterial peritonitis can be prevented by the intravenous administration of albumin, Albumin has been used at a dose of 1.5 g/kg of body weight at diagnosis.

Hepatic Encephalopathy

Treating the precipitating factor and reducing the ammonia level. Precipitating factors include infections, overdiuresis, GI bleeding, a high oral protein load, and constipation. Narcotics and sedatives contribute to hepatic encephalopathy by directly depressing brain function.

lactulose (15 to 30 mL) orally twice daily or orally administered nonabsorbable antibiotics such as neomycin, metronidazole (250 mg two to four times per day), or rifaximin (550 mg two times per day). Switching dietary

- protein from an animal source to a vegetable source may be beneficial.

Pulmonary Complications

Hepatopulmonary syndrome The only viable treatment is liver transplantation .

PROGNOSIS

The 10-year survival rate of patients who remain in a compensated stage is approximately 90%, whereas their likelihood of decompensation is 50% at 10 years.

Four clinical stages of cirrhosis:

Stage 1 patients without varices or ascites, the mortality rate is about 1% per year.

Stage 2 patients, or those with varices but without ascites or bleeding, have a mortality rate of about 4% per year.

Stage 3 patients have ascites with or without esophageal varices that have never bled; their mortality rate while remaining in this stage is 20% per year.

Stage 4 patients, or those with portal hypertensive GI bleeding with or without ascites, have a 1-year mortality rate of 57%, with nearly half of these deaths occurring within 6 weeks after the initial episode of bleeding.

Hepatocellular carcinoma develops at a fairly constant rate of 3% per year..

Thank You

Complications Of ACS Arrhthymias

- **Common**
- **Usually transient**
- **Needs no action apart from close observation**

Unless they are causing

1 haemodynamic compromise ie Hypotension

2 Or carry a bad prognostic implication such late onset Ventricular Tachycardia (VT)

Arrhythmias in ACS VT and VF

- **Ventricular Fibrillation (VF)**

  Can occurs spontaneously

  or complicates Ventricular Tachycardia (VT)

- **The major mode of death before hospitalization**
- **Early VF has no bad prognosis**
- **Treatment ;- Defibrillate promptly**

Ventriculat Tachycardia VT

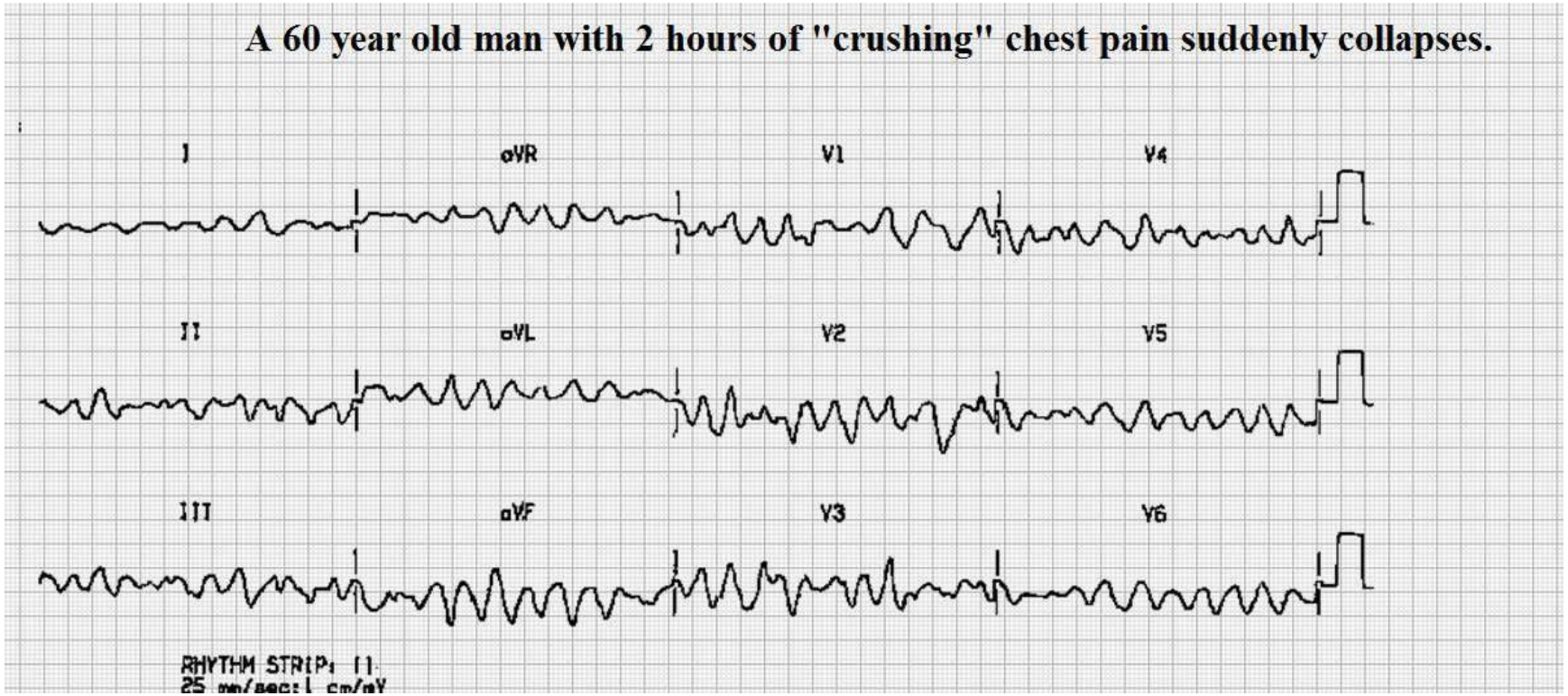
1 Slow VT is frequent good sign of reperfusion; called Idioventricular rhythm. It is self limiting. No RX

2 Other VT must Defibrillate promptly

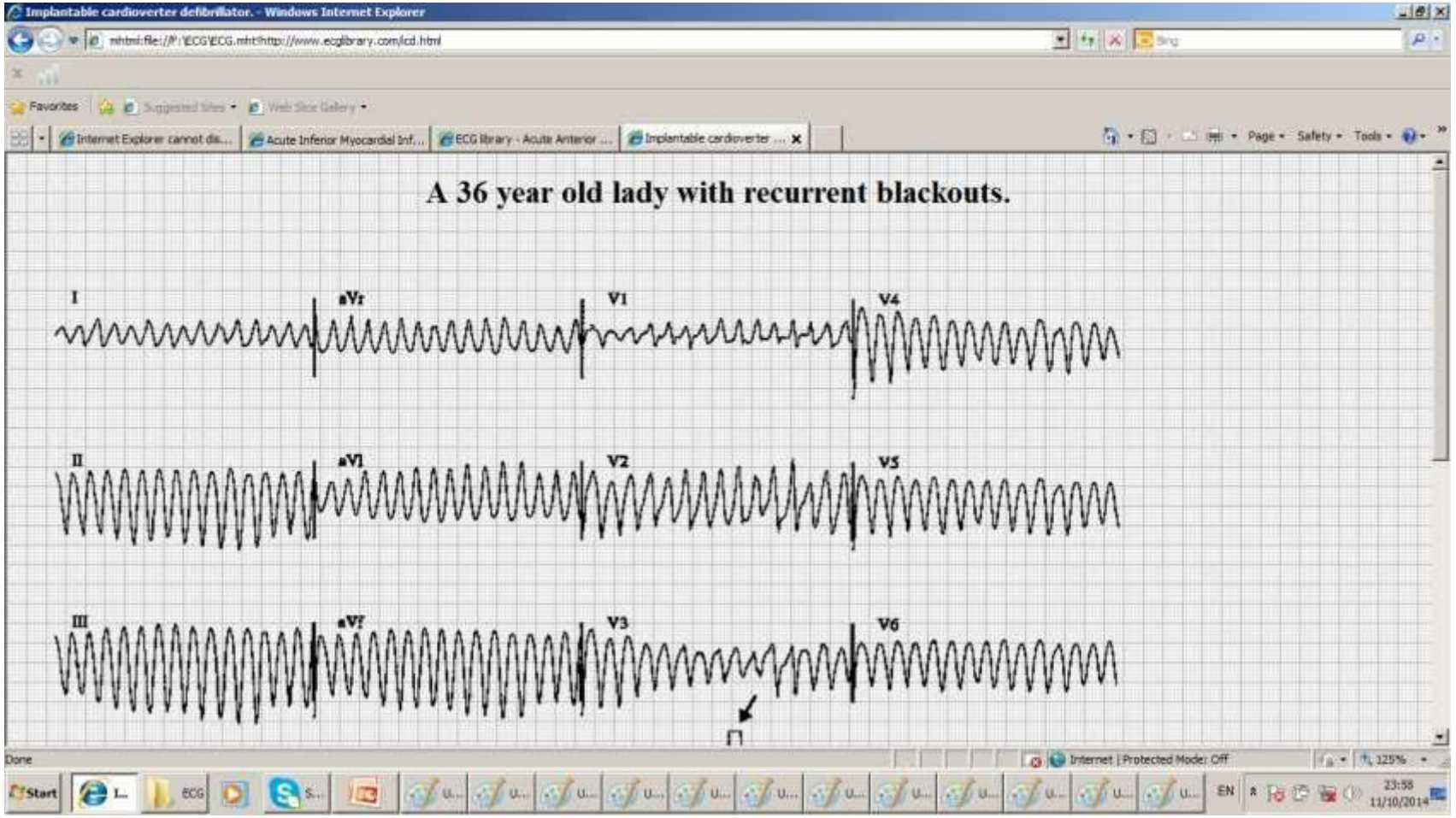
3if not give IV Amiodarone 5 mg /kg 20 min.- 2hrs bolus followed by 15mg/kg 24hrs infusion

4 Beta blockers can prevent VT

VF ; Ventricular Fibrilation



Ventricular Tachycardia



Atrial Fibrillation AF

1 common

2 frequently transient

3 require no emergency treatment

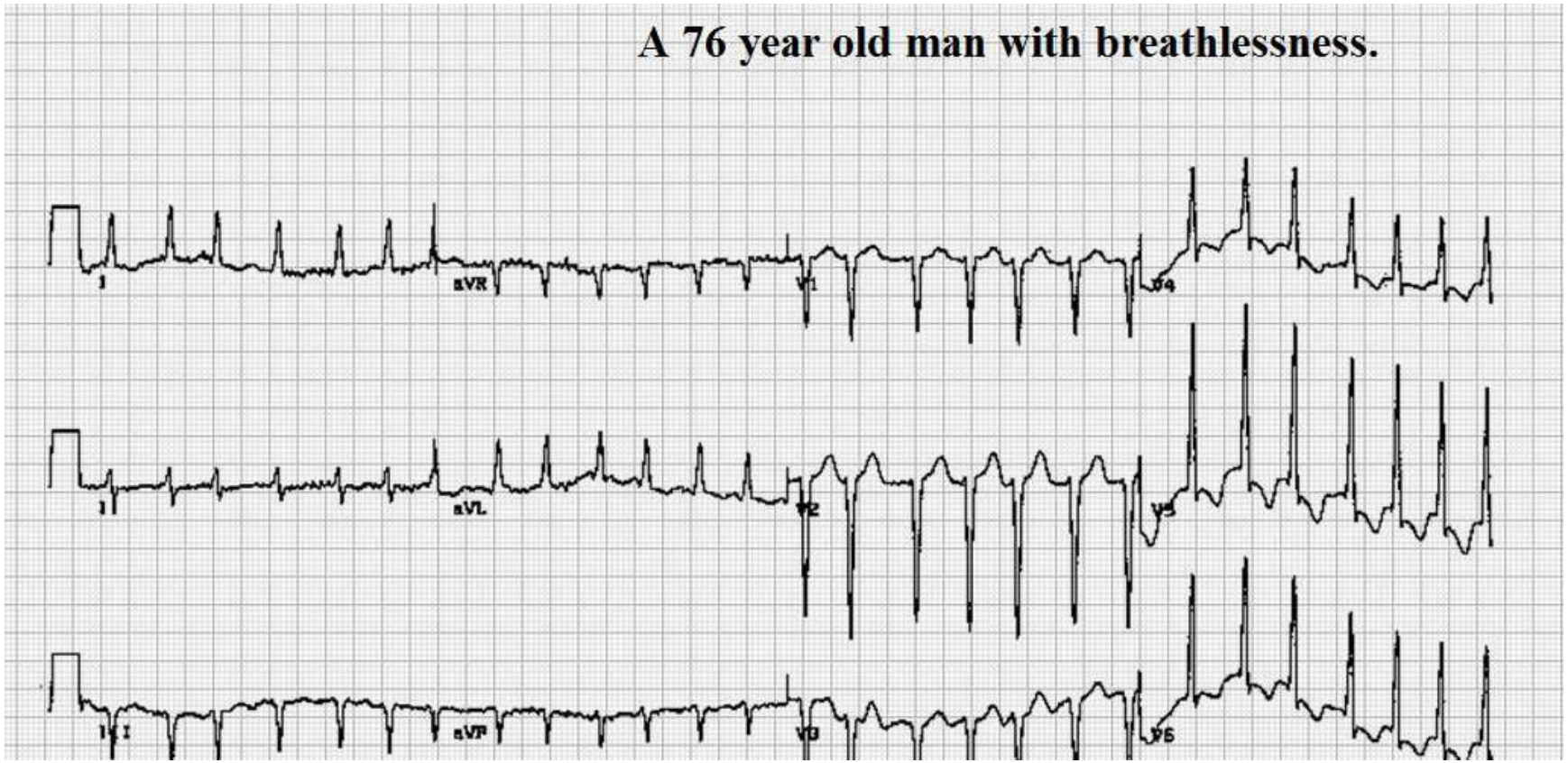
4 Rapid AF with Haemodynamic compromise

require urgent synchronized DC shock

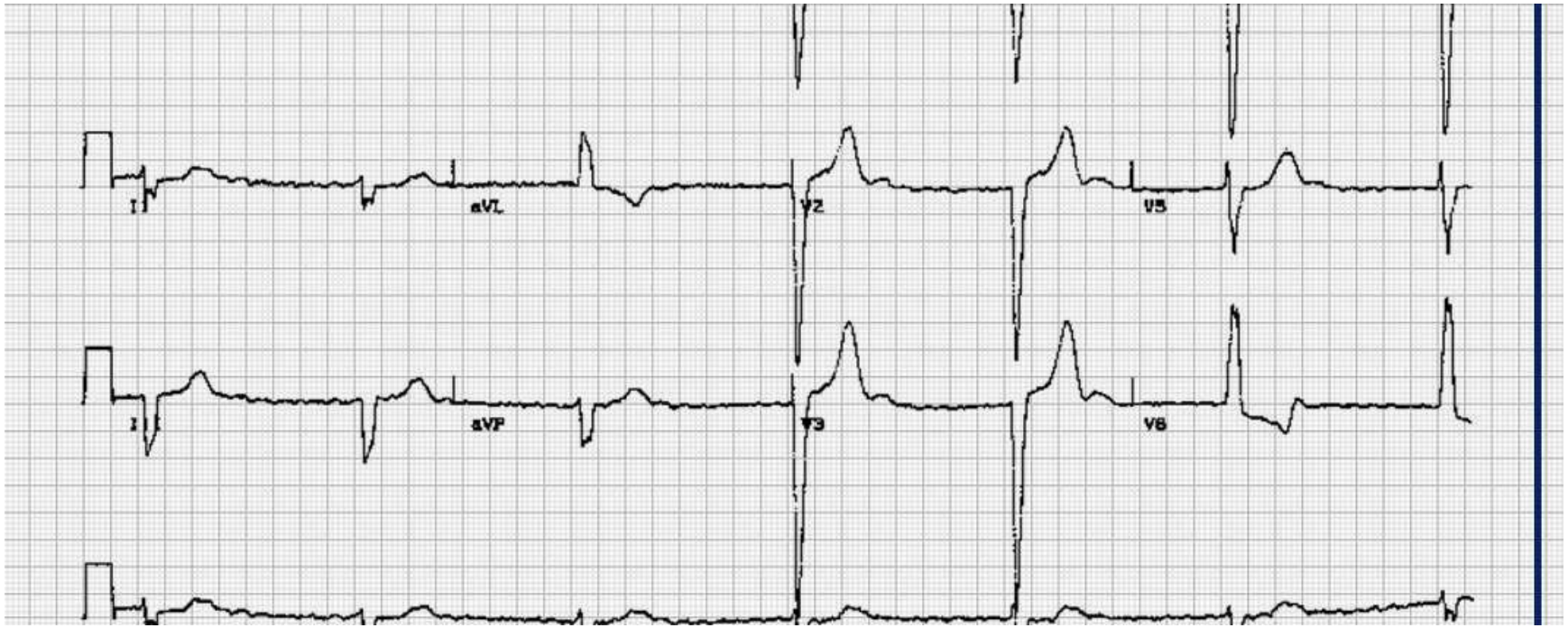
5AF due to stretch of atrial wall is often a feature of impending or overt LV failure and therapy are ineffective unless HF is treated appropriately eg IV diuretics

6Otherwise Digoxin 0. 25 m TID then 0.25 daily after or a betablocker

Fast AF


A 76 year old man with breathlessness.
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

?? Af and complete Heat Block



ACS complications; Arrhythmia

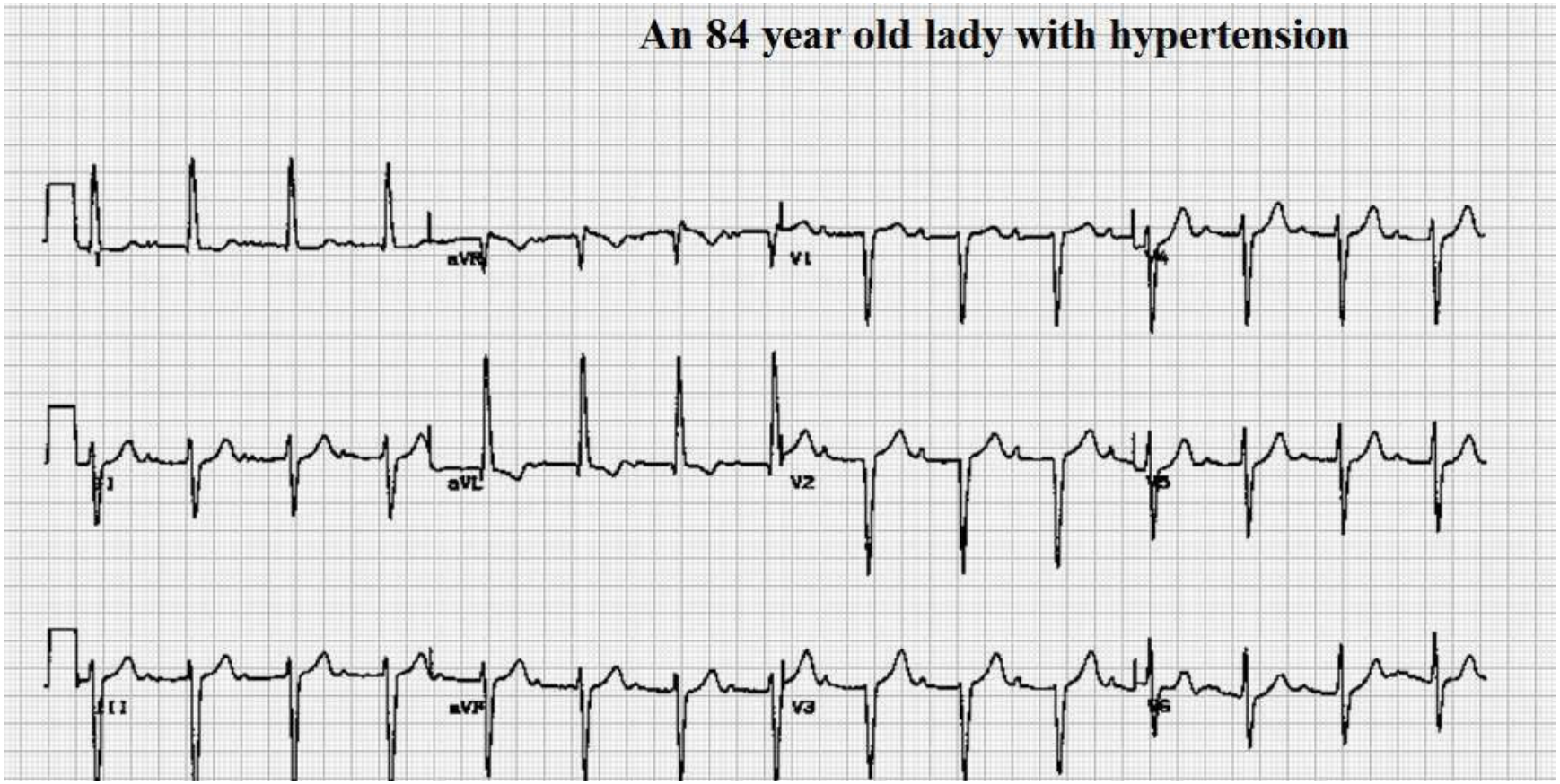
1- Sinus Bradycaridia and Atrio- ventricular block (2nd degree or complete AV Block) occur more frequently in pts with Inf. MI and both of them usually require no treatment unless ;They have led to haemodynamic deterioration then ;

a- Sinus Bradycardia ;- IV atropine 0.6- 1.2 mg

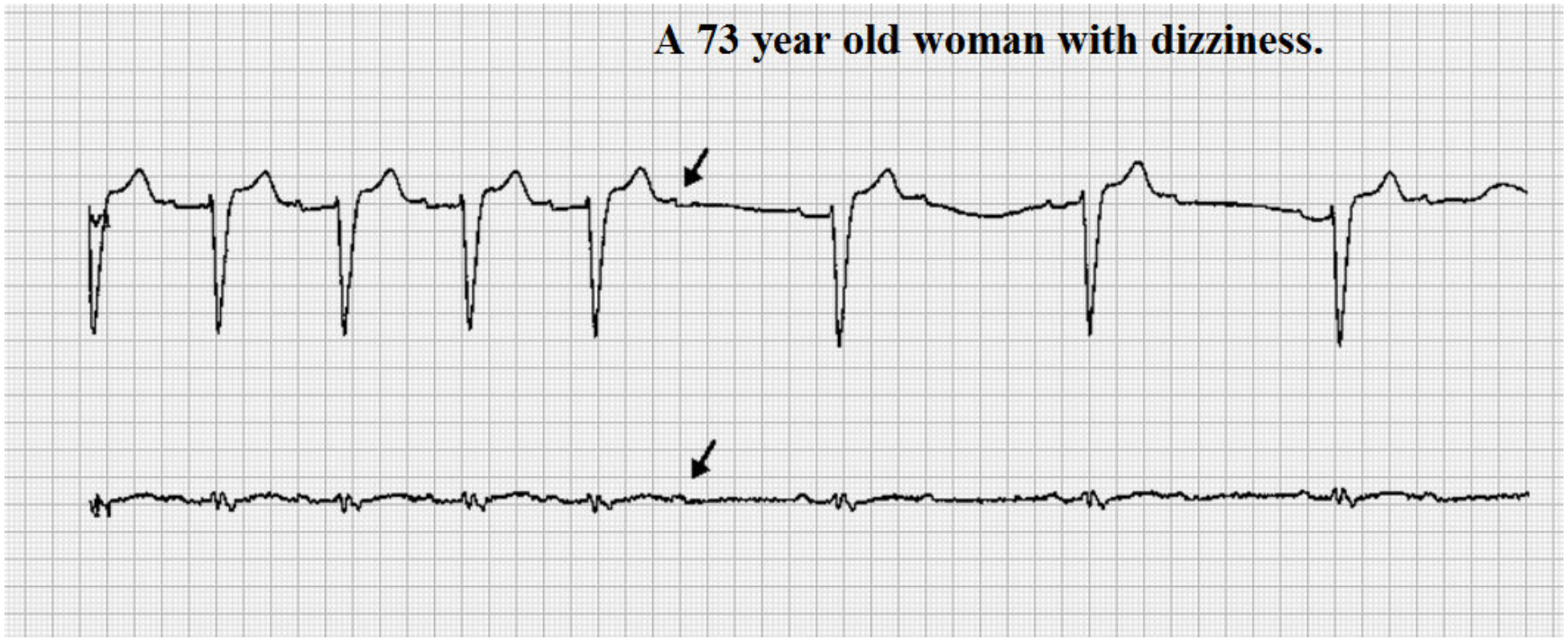
b-Complete AV block require temporary Pacemaker

3- A temporary Pacemaker is certainly indicated for complete heart block complicating Anterior MI because asystole may suddenly supervene

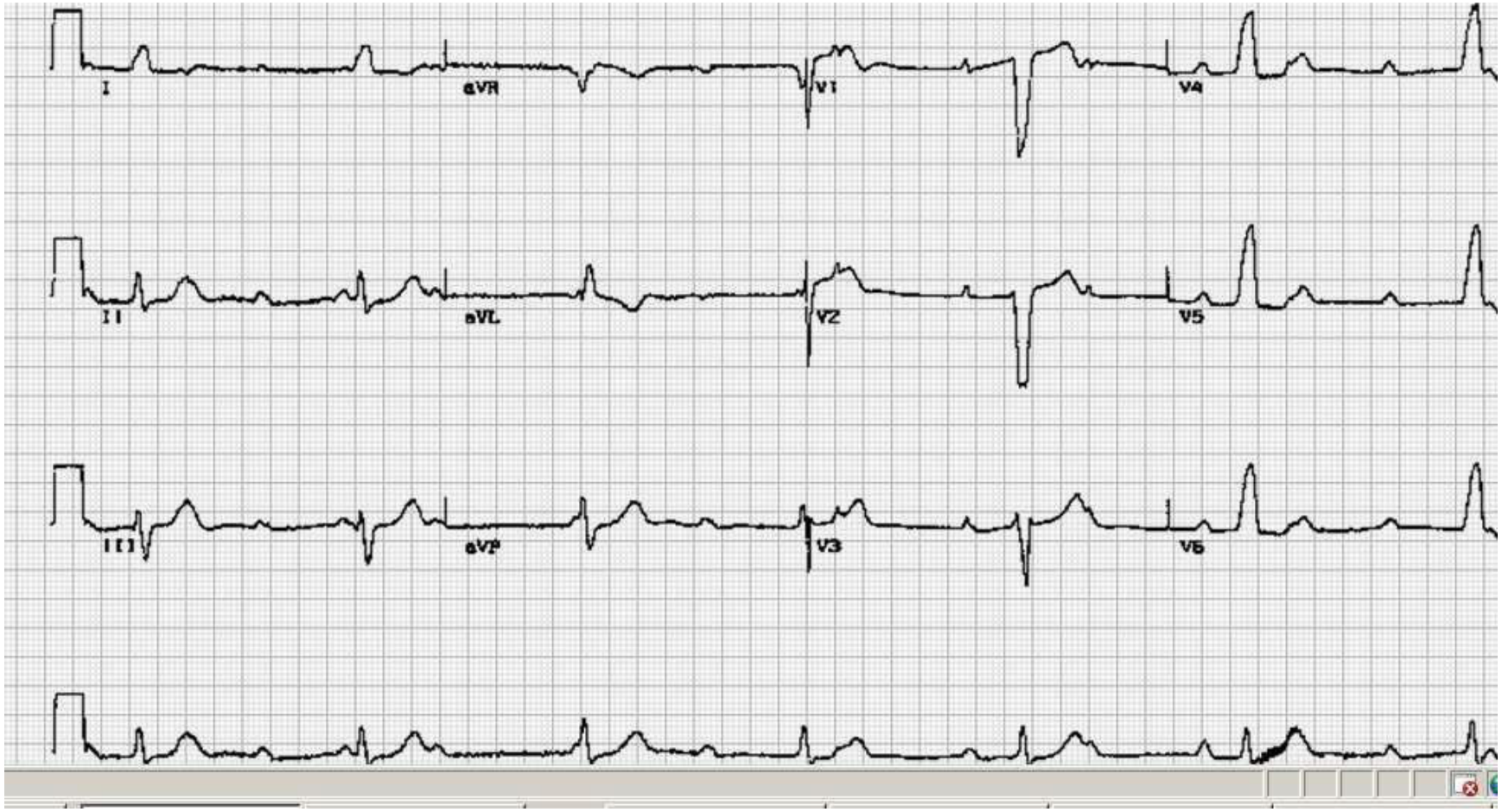
First degree heart block



2-1 Block



Complete AVblock



ACS **complications** Pericarditis:

Two types t

A- Early pericarditis

1 occur on the 2nd -3rd days after STEMI

2 Different pain ; little sharp, may be worse on lying down and inspiration

3- + Rub.

4- Use opiates. NoNonsteroidal Antiflamatory agents .

B. Late: Dressler's syndrome

- **In few weeks.- months**
- **Autoimmune.**
- **Fever, pericarditis and pleurisy.**
- **Aspirin, NSAID,…Steroid**

Post infarction Angina

1. **Occur in 50% of pts following thrombolysis due to residual stenosis**
2. **Pts must be on full scale RX ; nitroglycerine infusion , Betablockers . Heparin, aspirin and referred for urgent Angiography in the view of revascularization by PCI**
3. **Pts with dynamic ECG changes should receive IV GP 11b /11a receptors antagonist**
4. **Pts wih resistant pain or those who are haemodynamically unstable would needs Intraa-ortic Balloon counterpulsation**

Cardiogenic Shock

Caused by

1 -L.V dysfunction in 70 % of cases

2- RV MI

3- Mechanical complications due to rupture of part of myocardium including

a- RupturedIVS … → Acquired VSD

b Ruptured papillary muscle → Acute MR

c- Ruptured free wall → pericard. tamponade

Acute MI Haemodynamic subsets

- **Pts with Cadiogenic shock can be divided into into Four distinct groups depending upon their haemodynamic criteria they are**

G1 Normal CO and no P. Oedema ……No Rx

G2 Low CO and no P. Oedema. It is usually due to RV MI. Treatment :- Give IV fluids. Use Swanz Ganz catheter to monitor therapy. Consider PCI

G3 Normal CO and P Oedema .It is due moderate LV dysfunction Treatment:- Vasodilators and diuretics

G4 Low CO and P. Oedema due to extensive MI and poor prognosis ..Consider IAB, vasodilators, diuretics and inotrops and refer for PCI

Mechanical complications.....
Rupture of the papillary muscle

- **Sudden onset of Pulmonary Oedema and shock in pt who has apical pansystolic murmur and a third heart sound**
- **Very severe MR reduces the murmur intensity and increases the shock**
- **DX by Echo.**
- **Rx is urgent surgery**
- **Minor degree of MR is due to Papillary muscle dysfunction and can be transient**

Rupture of the interventricular septum Acquired VSD

- **Sudden haemdynamic deterioration**
- **New loud Lt.- sternal pansystolic murmur radiating to the Rt. sternal border**
- **Rt. sided heart failure rather than pul oedema**
- **Hence JVP is raised and the lungs are usually dry**
- **Without urgent operation it is usually fatal**

Free wall Rupture

- **Leads to sudden tamponade**
- **Usually fatal**
- **But in partial rupture it may be possible to support pt to undergo urgent surgery**

LV aneurysm

Occur in Transmural MI

Occur in 105 of Pts

More in pts with persistent IRA occlusion

Fibrosis leads to stretching, thinning,expansion of the infarct zone

Increased wall stress leads to progressive dilatation and hypertrophy of remaining muscle

LV dilation leads to reduction of vent. Efficiency

Heart Failure, vent arrhythmia, mural thrombi

ECG Persistent ST elevation

CXR Bulge. Echo is Diagnostic, Rx surgical Resection

Prinzmetal Angina

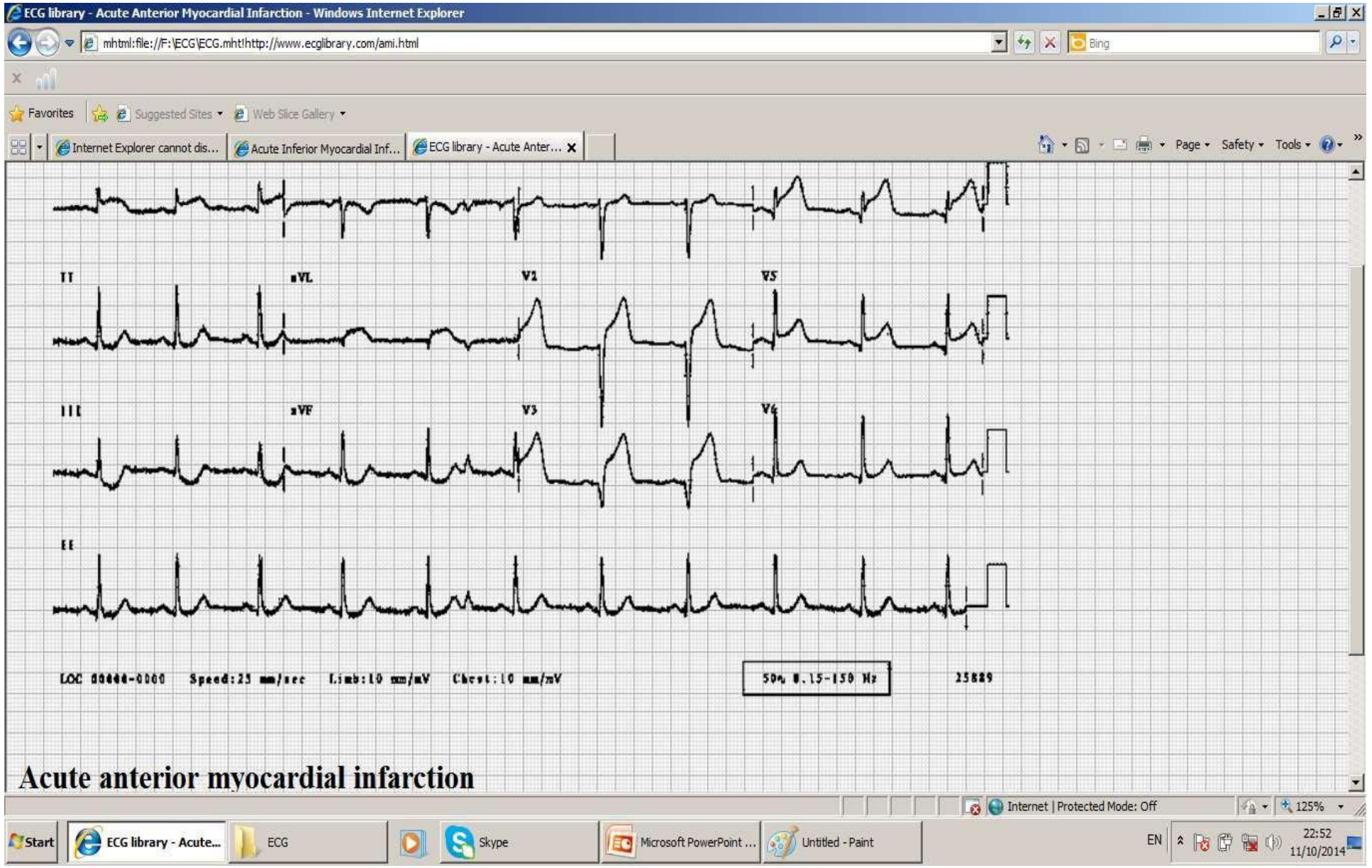
1. USUALLY WOMEN
2. DURING SLEEP
3. ST ↑ DRUING PAIN
4. DUE TO C.A. SPASM

IHD

SPECIAL ANGINAL PAINS

1. DECUBITUS ANGINA
   PAIN ON LYING DOWN
2. NOCTURNAL ANGINA
   PAIN THAT AWAKEN THE PT. FROM SLEEP
3. START - UP - ANGINA
   OCCUR AT START BUT WOULD NOT BE REPEATED LATER
4. PRINZMETAL ANGINA
   DUE TO COR. ART. SPASM.
5. CRESCENDO ANGINA; PRE-INFARCTION ANGINA

Anterolateral MI



ANGIOGRAPHY IN UNSTABLE ANGINA

1. IF PAIN DOESNOT SETTLE
2. IF ECG CHANGES ARE EXTENSIVE
3. IF HAS SEVERE PRE-EXISTING STABLE ANGIA
4. IF ET IS STRONGLY +VE
5. IF PT CHOOSE IT.

Investigations

- Serum urea, creatinine and electrolytes
- haemoglobin,
- thyroid function,
- ECG
- chest X-ray

May help to establish the nature and severity of the underlying heart disease and detect any complications.

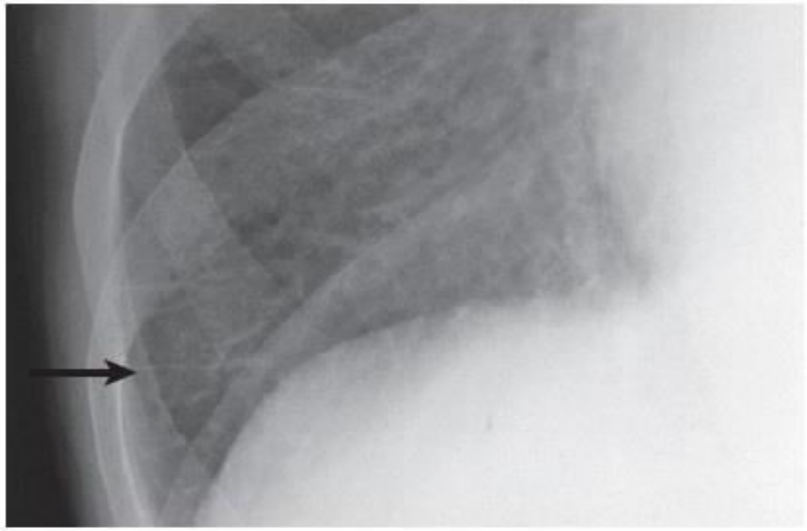
Brain natriuretic peptide (BNP) is elevated in heart failure and is a marker of risk; it is useful in the investigation of patients with breathlessness or peripheral oedema as a screeing test. .

Echocardiography

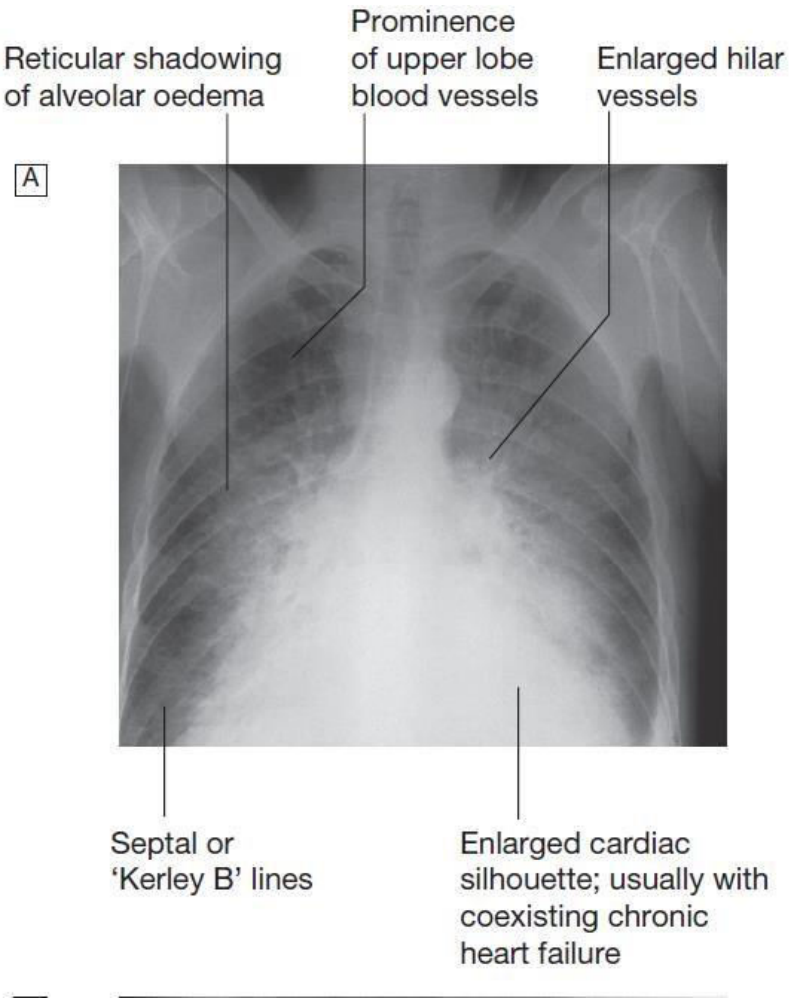
- is very useful and should be considered in all patients with heart failure in order to:

1. determine the aetiology
2. detect hitherto unsuspected valvular heart disease, such as occult mitral stenosis.
3. identify patients who will benefit from long-term drug therapy, e.g. ACE inhibitors.
4. Measurement of EF% .
5. For follow up .

Radiological features of heart failure



Chest X-ray of a patient with pulmonary edema.



Enlargement of lung base showing septal or 'Kerley B' lines (arrow).

Management of acute pulmonary oedema

This is an acute medical emergency:

- Sit the patient up to reduce pulmonary congestion.
- Give oxygen (high-flow, high-concentration).
- Non-invasive positive pressure ventilation (continuous positive airways pressure (CPAP) of 5–10 mmHg) by a tight-fitting facemask results in a more rapid clinical improvement.

- Administer nitrates, such as IV glyceryl trinitrate
- (10–200 µg/min or buccal glyceryl trinitrate 2–5 mg, titrated upwards every 10 minutes), until clinical improvement occurs or systolic BP falls to less than 110 mmHg.
- Administer a loop diuretic, such as furosemide (50–100 mg IV).

- The patient should initially be kept rested, with continuous cardiac monitoring of cardiac rhythm, BP and pulse oximetry.
- Intravenous opiates must be used sparingly in distressed patients, as they may cause respiratory depression and exacerbation of hypoxaemia and hypercapnia.

- If these measures prove ineffective, inotropic agents (dopamine , doputamine) may be required to augment cardiac output, particularly in hypotensive patients.
- Insertion of an intra-aortic balloon pump may be beneficial in patients with acute cardiogenic pulmonary oedema and shock

Management of chronic heart failure

- **General measures for the management of heart failure :**
- **Education**

Explanation of nature of disease, treatment and self-help strategies

- **Diet**

Good general nutrition and weight reduction for the obese , Avoidance of high-salt foods and added salt, especially for patients with severe congestive heart failure

- **Alcohol**

Moderation or elimination of alcohol consumption. Alcohol induced cardiomyopathy requires abstinence

- **Smoking**

  Cessation

- **Exercise**

  Regular moderate aerobic exercise within limits of symptoms

- **Vaccination**

  Consider influenza and pneumococcal vaccine .

Diuretic therapy

- Types : thiazide , loop and potassium sparing
- Site of action .
- Route of administration .
- Complication

Diuretic therapy

- In heart failure, diuretics produce an increase in urinary sodium and water excretion, leading to reduction in blood and plasma volume . Diuretic therapy reduces preload and improves pulmonary and systemic venous congestion. It may also reduce afterload and ventricular volume, leading to a fall in ventricular wall tension and increased cardiac efficiency.

- Although a fall in preload (ventricular filling pressure) tends to reduce cardiac output, the ‘Starling curve’ in heart failure is flat, so there may be a substantial and beneficial fall in filling pressure with little change in cardiac output

- Nevertheless, excessive diuretic therapy may cause an undesirable fall in cardiac output, especially in patients with a marked diastolic component to their heart failure, this leads to hypotension, lethargy and renal failure.

- In some patients with severe chronic heart failure, particularly if there is associated renal impairment, oedema may persist, despite oral loop diuretic therapy. In such patients, an intravenous infusion of furosemide (5–10 mg/hr) may initiate a diuresis.
- Combining a loop diuretic with a thiazide diuretic (e.g. bendroflumethiazide 5 mg daily) may prove effective, but this can cause an excessive diuresis.

- Mineralocorticoid receptor antagonists, such as spironolactone and eplerenone, are potassium-sparing diuretics that are of particular benefit in patients with heart failure with severe left ventricular systolic dysfunction.
- They may cause hyperkalaemia, particularly when used with an ACE inhibitor. They improve long term clinical outcome in patients with severe heart failure or heart failure following acute MI.

Angiotensin-converting enzyme (ACE) inhibition

- Interrupts the vicious circle of neurohumoral activation that is characteristic of moderate and severe heart failure by preventing the conversion of angiotensin I to angiotensin II, thereby preventing peripheral vasoconstriction, activation of the sympathetic nervous system , and salt and water retention due to aldosterone release.
- These drugs also prevent the undesirable activation of the renin–angiotensin system caused by diuretic therapy.

- In moderate and severe heart failure, ACE inhibitors can produce a substantial improvement in effort tolerance and in mortality.
- They can also improve outcome and prevent the onset of overt heart failure in patients with poor residual left ventricular function following MI

- ACE inhibitors can cause symptomatic hypotension and impairment of renal function, especially in patients with bilateral renal artery stenosis or those with preexisting renal disease.
- An increase in serum potassium concentration may occur that can offset hypokalaemia associated with loop diuretic therapy

- Short-acting ACE inhibitors can cause marked falls in BP, particularly in the elderly or when started in the presence of hypotension, hypovolaemia or hyponatraemia.

- In stable patients without hypotension (systolic BP over 100 mmHg), ACE inhibitors can usually be safely started in the community. However, in other patients, it is usually advisable to withhold diuretics for 24 hours before starting treatment with a small dose of a long-acting agent, preferably given at night.

- Renal function and serum potassium must be monitored and should be checked 1–2 weeks after starting therapy

Evidence based Medicine

- **ACE inhibitors and treatment of chronic heart failure**
- ACE inhibitors in chronic heart failure due to ventricular dysfunction reduce mortality and re-admission rates.

Angiotensin receptor blocker therapy (ARBs)

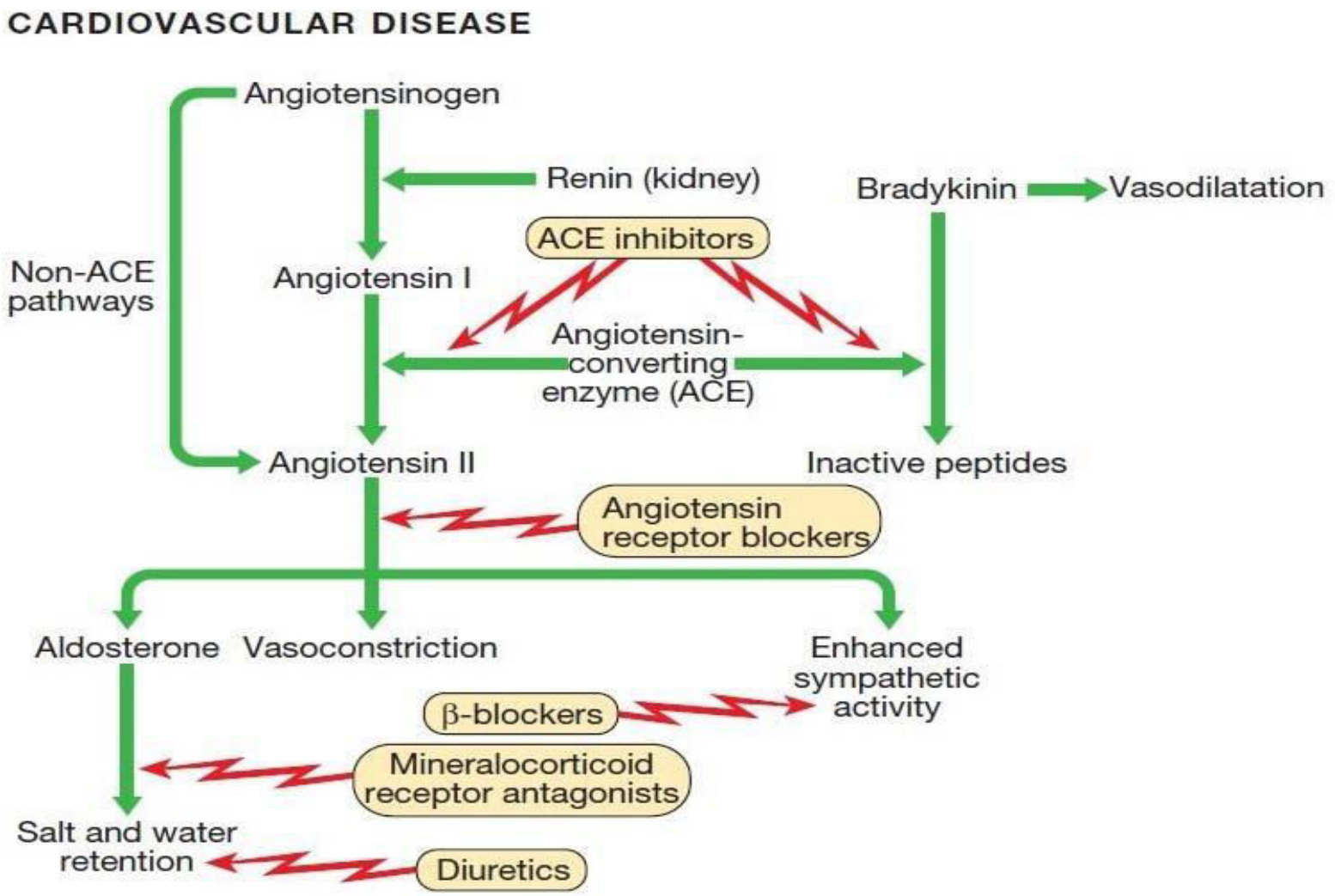
- Angiotensin receptor blockers (ARBs) act by blocking the action of angiotensin II on the heart, peripheral vasculature and kidney.
- In heart failure, they produce beneficial haemodynamic changes that are similar to the effects of ACE inhibitors but are generally better tolerated.
- They have comparable effects on mortality and are a useful alternative for patients who cannot tolerate ACE inhibitors .

- Unfortunately, they share all the more serious adverse effects of ACE inhibitors, including renal dysfunction and hyperkalaemia.
- ARBs are normally used as an alternative to ACE inhibitors, but the two can be combined in patients with resistant or recurrent heart failure.

Evidence Based medicine

- Angiotensin receptor blockers (ARBs) and chronic heart failure
- Compared with ACE inhibitors, ARBs are better tolerated and have similar efficacy in reducing cardiovascular events.
- ARBs reduce cardiovascular morbidity and mortality in patients with symptomatic heart failure who are intolerant of ACE inhibitors.

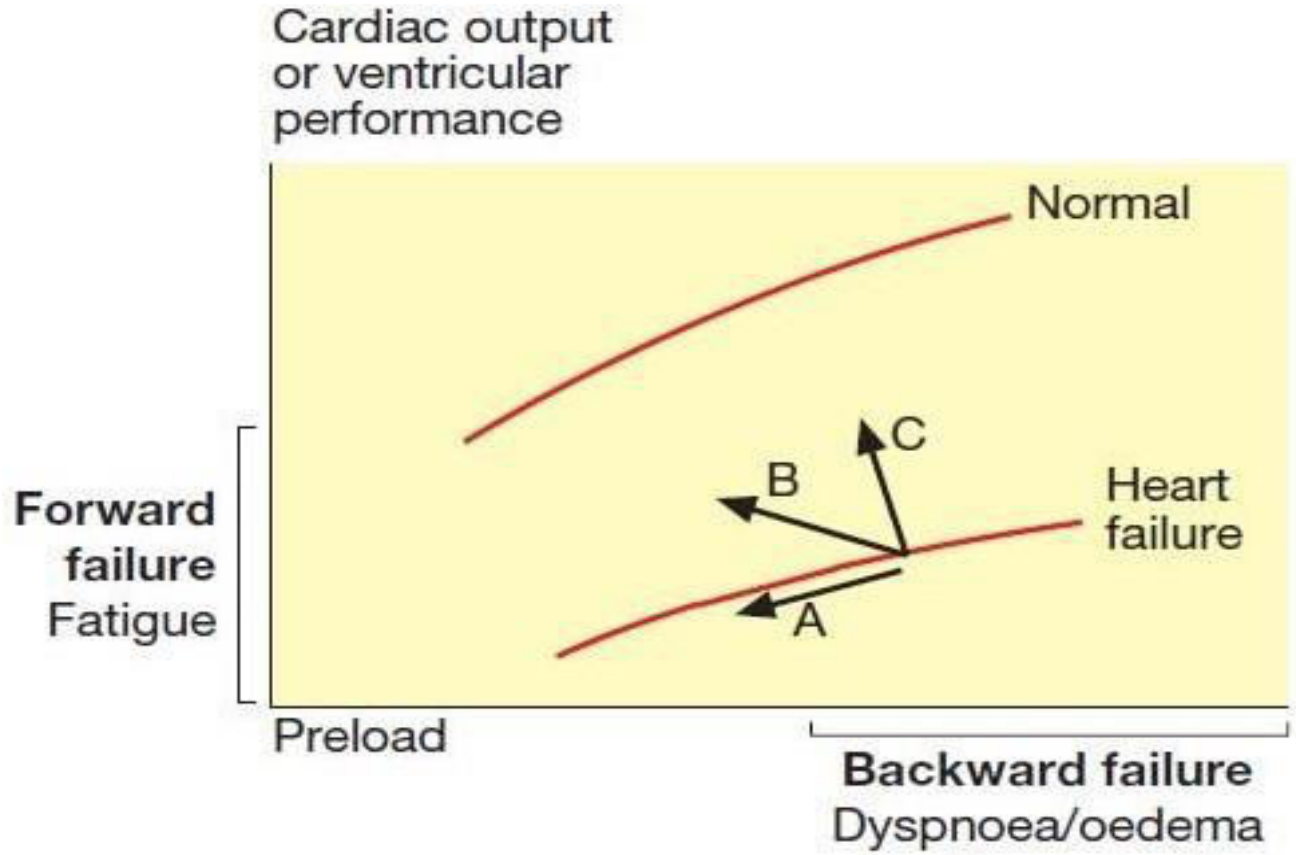
Neurohumoral activation and sites of action of drugs used in the treatment of heart failure



Beta adrenoseptor blocking therapy

- Beta-blockade helps to counteract the deleterious effects of enhanced sympathetic stimulation and reduces the risk of arrhythmias and sudden death.
- When initiated in standard doses, they may precipitate acute-on-chronic heart failure, but when given in small incremental doses (e.g. bisoprolol started at a dose of 1.25 mg daily, and increased gradually over a 12-week period to a target maintenance dose of 10 mg daily), they can increase ejection fraction, improve symptoms, reduce the frequency of hospitalisation and reduce mortality in patients with chronic heart failure .
-

- Beta blockers are more effective at reducing mortality than ACE inhibitors: relative risk reduction of 33% versus 20%, respectively.



The effect of treatment on ventricular performance
curves in heart failure. Diuretics and venodilators (A), angiotensinconverting enzyme (ACE) inhibitors and mixed vasodilators (B), and positive inotropic agents (C).

Vasodilator therapy

- These drugs are valuable in chronic heart failure, when ACE inhibitor or ARB drugs are contraindicated (e.g. in severe renal failure). Venodilators, such as nitrates, reduce preload, and arterial dilators, such as hydralazine, reduce afterload . Their use is limited by pharmacological tolerance and hypotension.

Ivabradine

- Ivabradine acts on the If inward current in the SA node, resulting in reduction of heart rate.
- It reduces hospital admission and mortality rates in patients with heart failure due to moderate or severe left ventricular systolic impairment.
- In trials, its effects were most marked in patients with a relatively high heart rate (over 77/min), so ivabradine is best suited to patients who cannot take β-blockers or in whom the heart rate remains high despite β-blockade.
- It is ineffective in patients in atrial fibrillation.

Digoxin

- can be used to provide rate control in patients with heart failure and atrial fibrillation. In patients with severe heart failure (NYHA class III–IV, digoxin reduces the likelihood of hospitalisation for heart failure, although it has no effect on long-term survival.

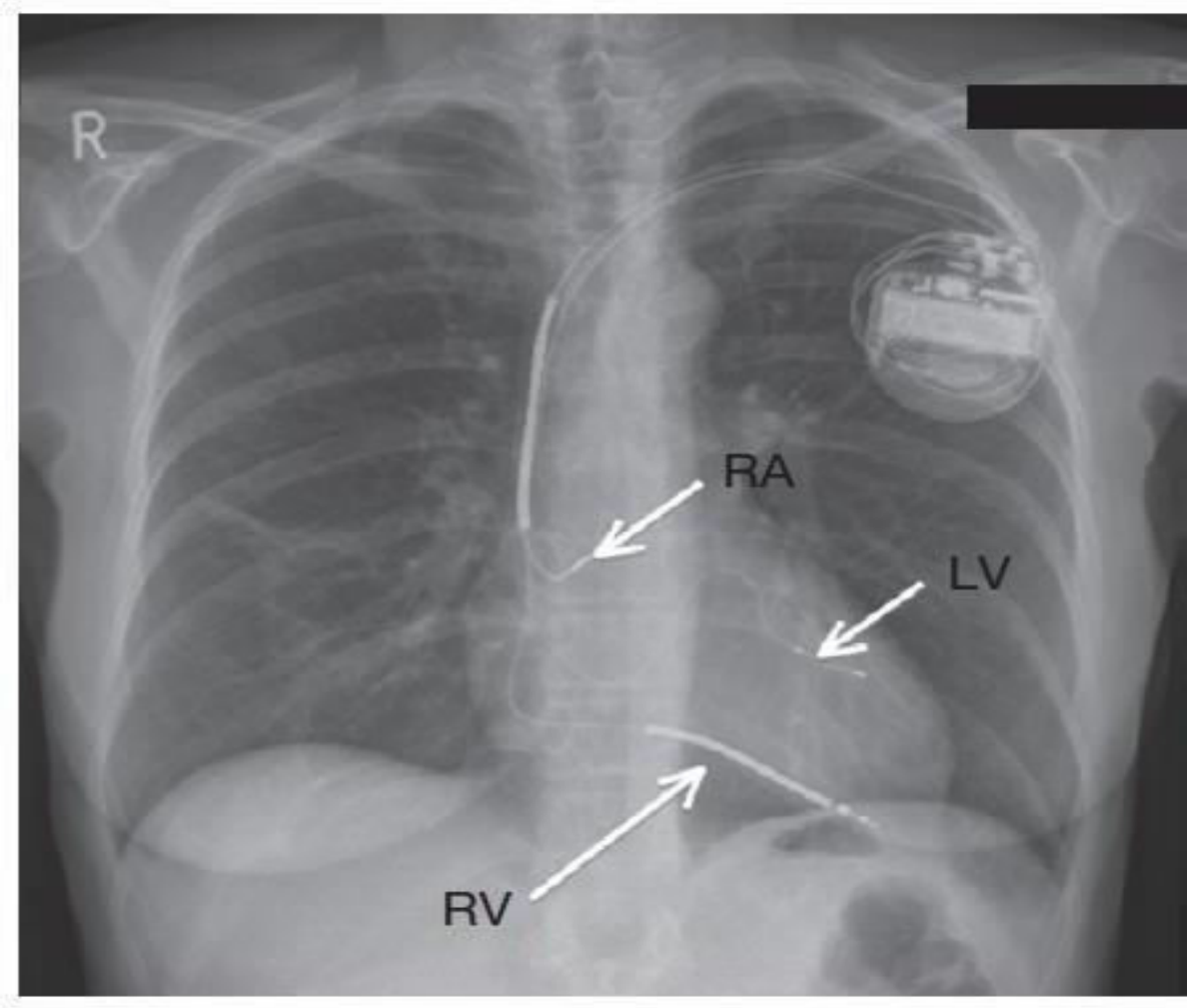
Amiodarone

- This is a potent anti-arrhythmic drug that has little negative inotropic effect and may be valuable in patients with poor left ventricular function.
- It is only effective in the treatment of symptomatic arrhythmias, and should not be used as a preventative agent in asymptomatic patients.

Implantable cardiac defibrillators and re synchronisation therapy

- Patients with symptomatic ventricular arrhythmias and heart failure have a very poor prognosis. Irrespective of their response to anti-arrhythmic drug therapy, all should be considered for implantation of a cardiac defibrillator because it improves survival .
- In patients with marked intraventricular conduction delay, prolonged depolarisation may lead to uncoordinated left ventricular contraction.
- When this is associated with severe symptomatic heart failure, cardiac resynchronisation therapy should be considered. Here, both the LV and RV are paced simultaneously to generate a more coordinated left ventricular contraction and improve cardiac output.
- This is associated with improved symptoms and survival.

Chest X-ray of a biventricular pacemaker and defibrillator (cardiac resynchronisation therapy)

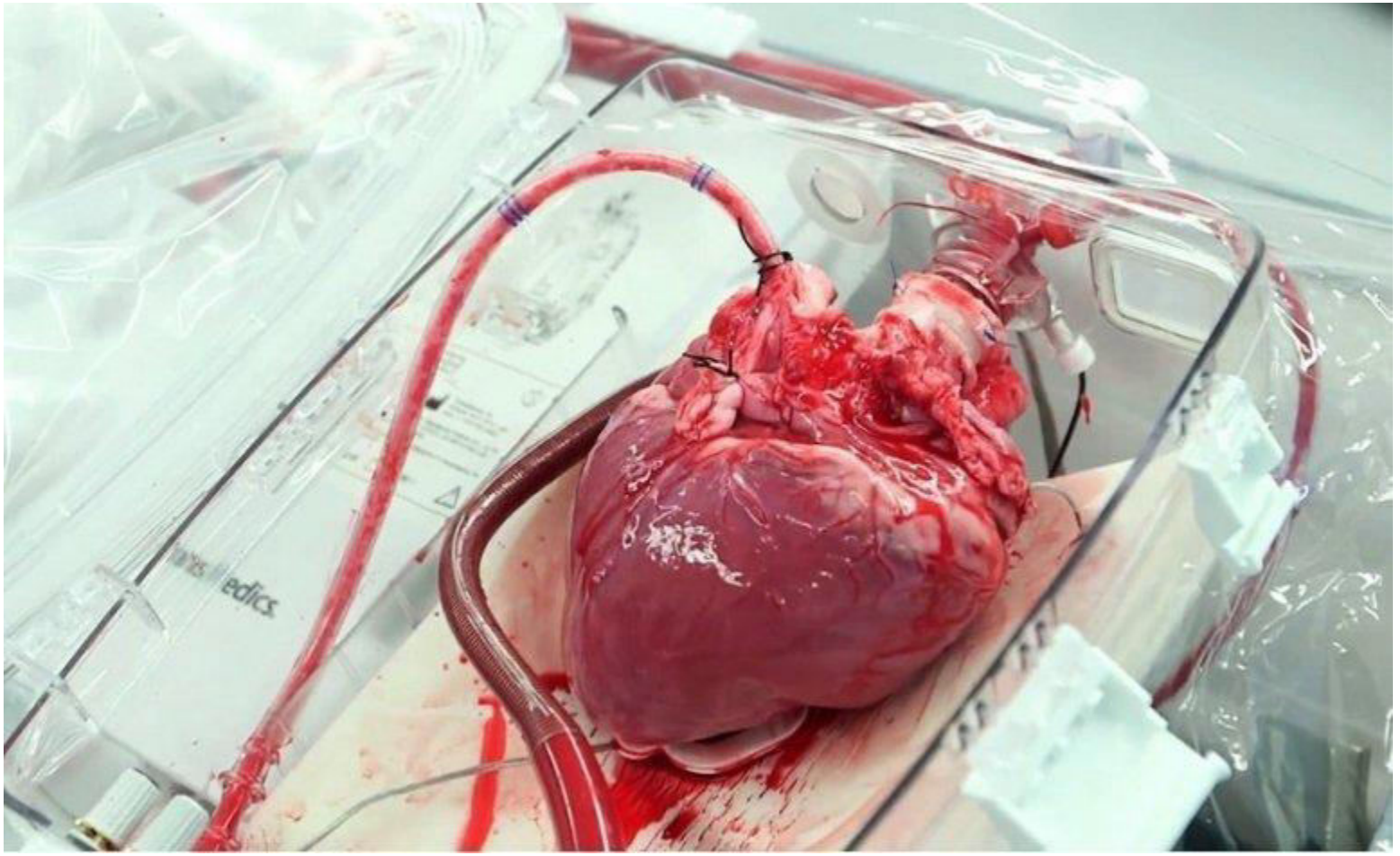


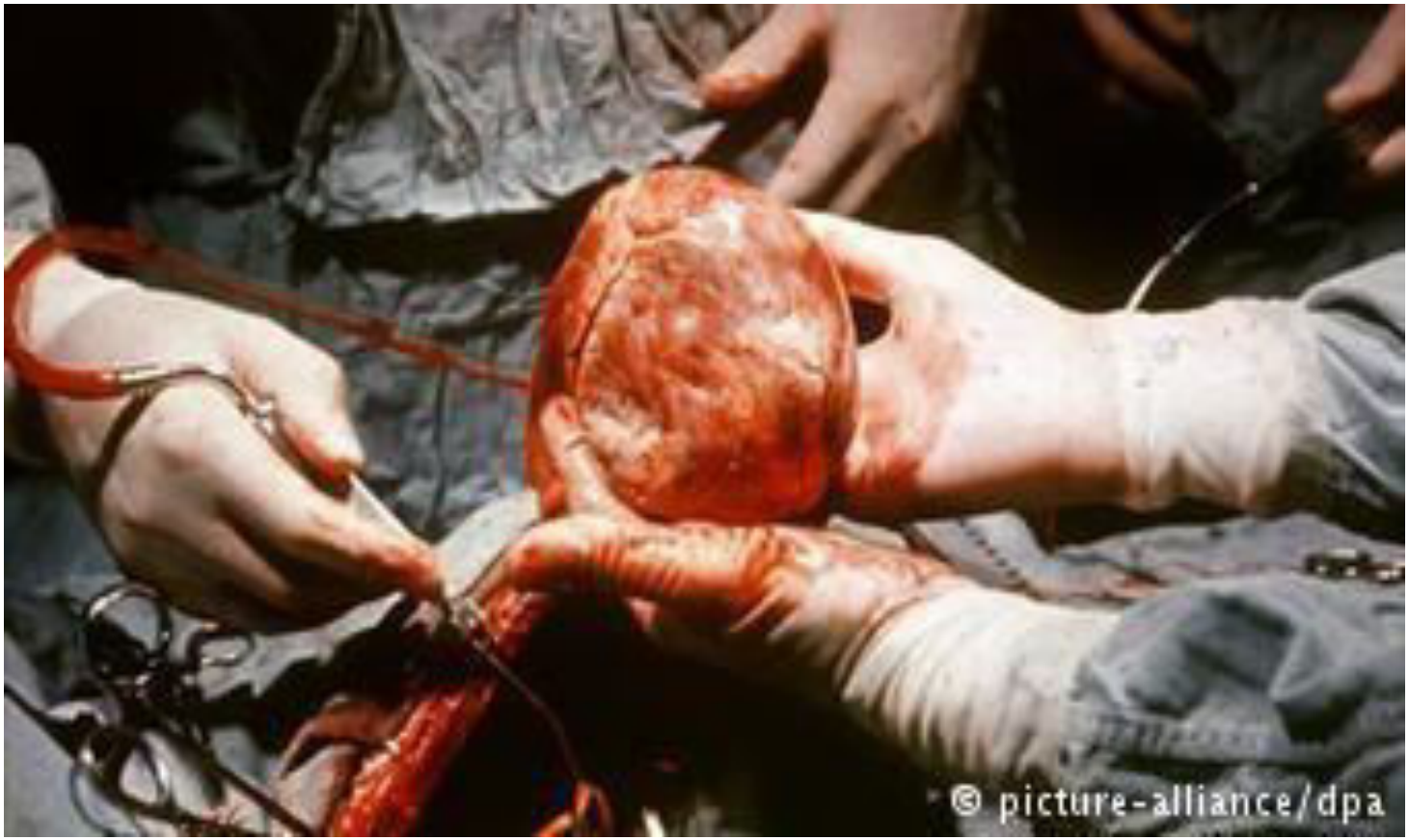
Coronary revascularisation

- Coronary artery bypass surgery or percutaneous coronary intervention may improve function in areas of the myocardium that are ‘hibernating’ because of inadequate blood supply, and can be used to treat carefully selected patients with heart failure and coronary artery disease. If necessary, ‘hibernating’ myocardium can be identified by stress echocardiography and specialised nuclear or MR imaging.

Heart transplantation

- Cardiac transplantation is an established and successful treatment for patients with intractable heart failure.
- Coronary artery disease and dilated cardiomyopathy are the most common indications. The introduction of ciclosporin for immunosuppression has improved survival, which is around 80% at 1 year.
- The use of transplantation is limited by the efficacy of modern drug and device therapies, as well as the availability of donor hearts, so it is generally reserved for young patients with severe symptoms despite optimal therapy.
- .




© picture-alliance/dpa

Ventricular assist devices

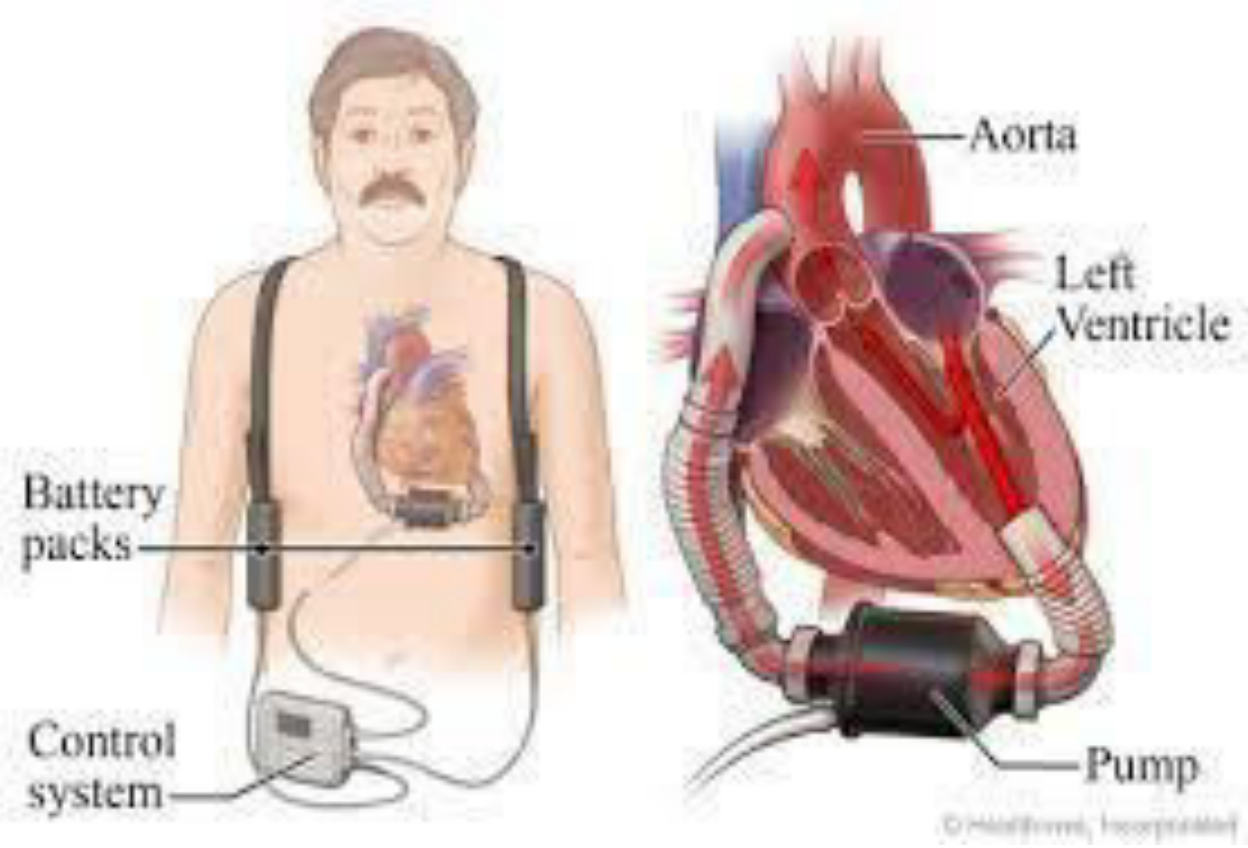
- Because of the limited supply of donor organs, ventricular assist devices (VADs) have been employed as:
- • a bridge to cardiac transplantation
- • potential long-term therapy
- • short-term restoration therapy following a potentially reversible insult, e.g. viral myocarditis.

- VADs assist cardiac output by using a roller, centrifugal or pulsatile pump that, in some cases, is implantable and portable.

- They withdraw blood through cannulae inserted in the atria or ventricular apex and pump it into the pulmonary artery or aorta. They are designed not only to unload the ventricles but also to provide support to the pulmonary and systemic circulations.

- Their more widespread application is limited by high complication

Ventricular assist device



Resources

- Davidson’s principles and practice of medicine 22nd edition.
- ACC/AHA heart failure guideline.

Infective endocarditis

Dr.ammar khalid

Infective endocarditis

Learning objectives

1. Define infective endocarditis and which patients may be susceptible.
2. Describe the typical clinical features.
3. Describe the morphological changes seen on an affected heart valve.
4. Describe the pathological complications of infective endocarditis including valve destruction with heart failure, embolic disease and Glomerulonephritis.
5. Outline important investigations including blood cultures, echocardiography, FBC, ESR and CRP, renal function tests
6. Outline the general principles of management of suspected and confirmed infective endocarditis.
7. Describe the indications for surgery.
8. Role fopophylaxis.

Definition

- This is caused by microbial infection of a heart valve (native or prosthetic), the lining of a cardiac chamber or blood vessel, or a congenital anomaly (e.g. septal defect.)
- The causative organism is usually a bacterium, but may be a rickettsia, chlamydia or fungus.

Infective endocarditis

- Typically occurs at sites of preexisting endocardial damage

- It can affect previously normal heart by infection with particularly virulent or aggressive organisms (e.g. *Staphylococcus aureus*;
- Staphylococcal endocarditis of the tricuspid valve is a common complication of intravenous drug misuse.
- High-pressure jet of blood may lead to areas of endocadial damage which is present in many acquired and congenital cardiac lesions such as ventricular septal defect, mitral regurgitation and aortic regurgitation, many of which are haemodynamically insignificant.
- In contrast, the risk of endocarditis at the site of haemodynamically important low-pressure lesions, such as a large atrial septal defect, is minimal.

Incidence

- The incidence of infective endocarditis in community based studies ranges from 5 to 15 cases per 100 000 per year. More than 50% of patients are over 60 years of age.
- Rheumatic heart disease in 24% of patients,
- congenital heart disease in ,19%
- Other cardiac abnormalities (e.g. calcified aortic valve, floppy mitral valve) in .25%
- The remaining 32% were not thought to have a pre-existing cardiac abnormality.

Pathogenesis

- Microbial adherence.
- Bacterial adherence to a platelet–fibrin nidus.
- S. aureus, viridans strept., enterococci, and Pseudomonas aeruginosa adhere more avidly to excised canine heart valves in vitro than species such as E. coli, which rarely causes endocarditis.

Microbiology

- %75of cases are caused by streptococci or staphylococci.
- The *viridans* group of streptococci (*Streptococcus mitis, Strep. sanguis*) are commensals in the upper respiratory tract that may enter the blood stream on chewing or teeth-brushing, or at the time of dental treatment, and are common causes of subacute endocarditis

- Other organisms, including *Enterococcus faecalis*, *E. faecium* and *Strep. bovis*, may enter the blood from the bowel or urinary tract. *Strep. milleri* and *Strep. bovis* endocarditis is associated with large-bowel neoplasms.

- *Staph. aureus* has now overtaken streptococci as the most common cause of acute endocarditis. It originates from skin infections, abscesses or vascular access sites (e.g. intravenous and central lines), or from intravenous drug use. It is highly virulent and invasive, usually producing

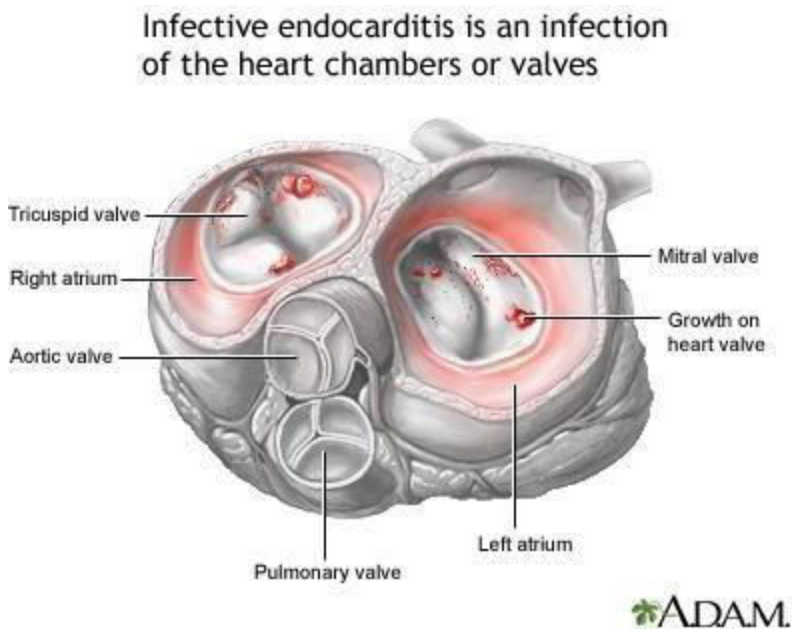
  florid vegetations, rapid valve destruction and abscess formation.

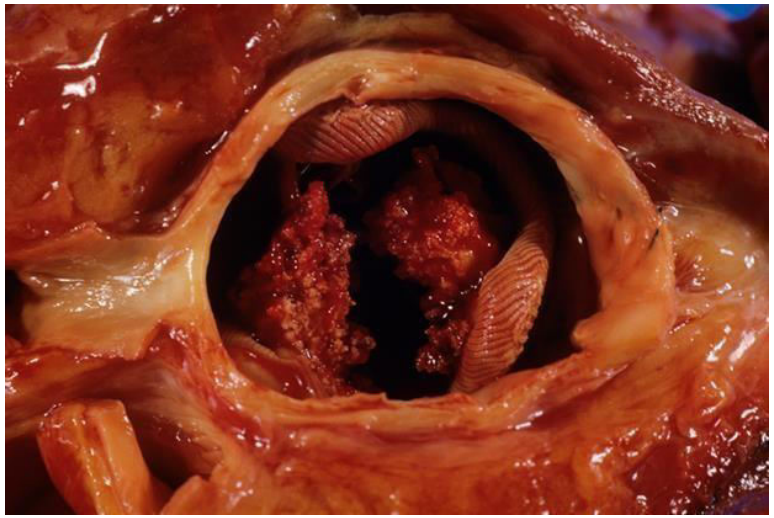
- Other causes of acute endocarditis include *Strep. pneumoniae* and *Strep. Pyogenes.*

The site of vegetation:

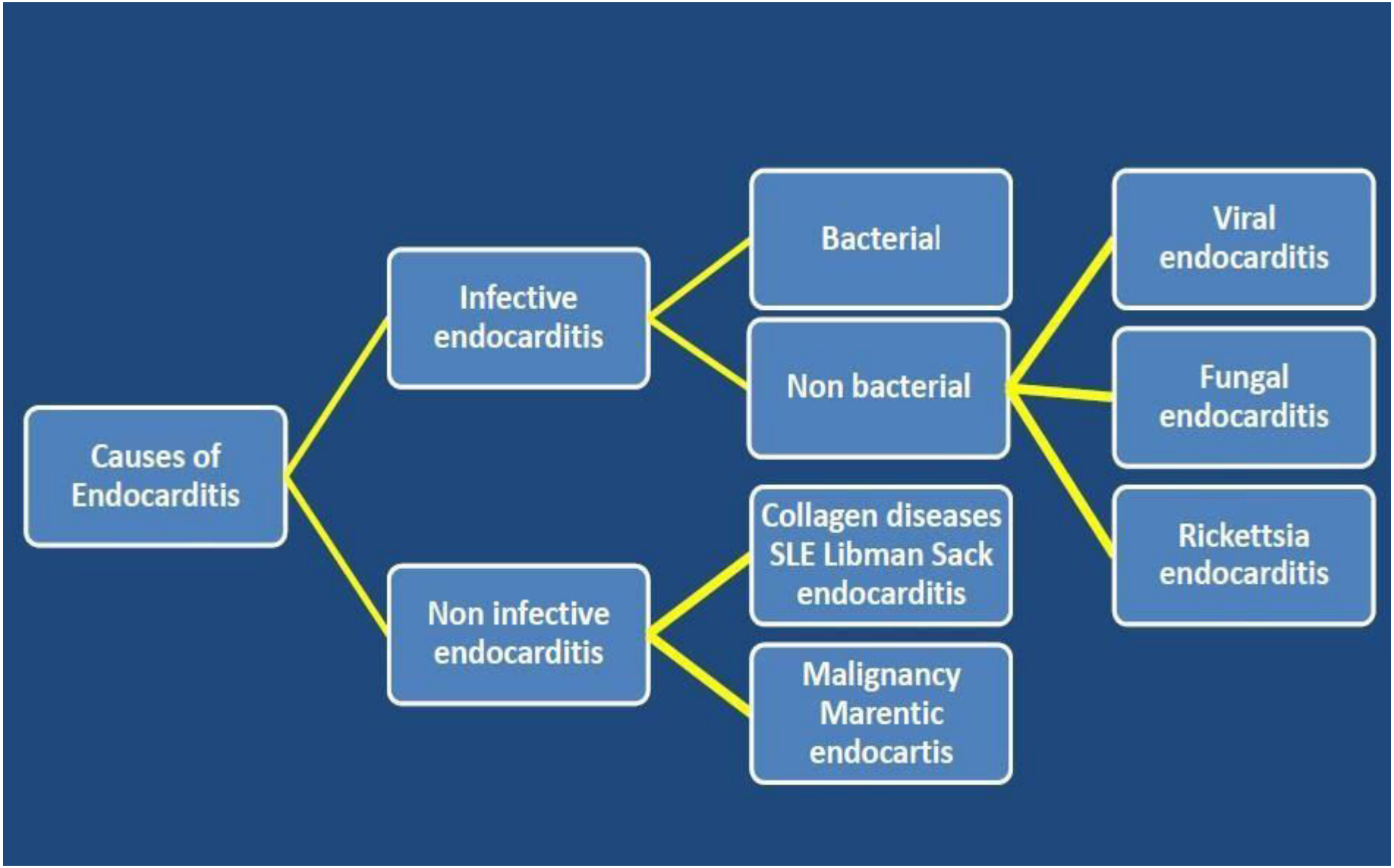
- The atrial surface of the A-V valves,
- The ventricular surface of the semilunar valves
- The jet lesion in a shunt, including the venous or pulmonary side of the A-V fistulae

Infective endocarditis , vegetation





Causes of infective endocarditis



Clinical features

- **Sub acute endocarditis***:*

- This should be suspected when a patient with congenital or valvular heart disease develops a persistent fever, complains of unusual tiredness, night sweats or weight loss, or develops new signs of valve dysfunction or heart failure.

- Less often, it presents as an embolic stroke or peripheral arterial embolism. Other features include purpura and petechial haemorrhages in the skin and mucous membranes, and splinter haemorrhages under the fingernails or toe nails.

- Osler's nodes are painful tender swellings at the fingertips that are probabl the product of vasculitis; they are rare. Digital clubbing is a late sign. The spleen is frequently palpable;
- in *Coxiella* infections, the spleen and the liver may be considerably enlarged. Microscopic haematuria is common.
- The finding of any of these features in a patient with persistent fever or malaise is an indication for re-examination to detect unrecognised heart disease.

Suspect Infective endocarditis:

In any patient with unexplained fever and murmur

Clinical classification

- Native IE (natural valve.)
- Prosthetic IE (surgical valve eplacement:)

    a. Early.

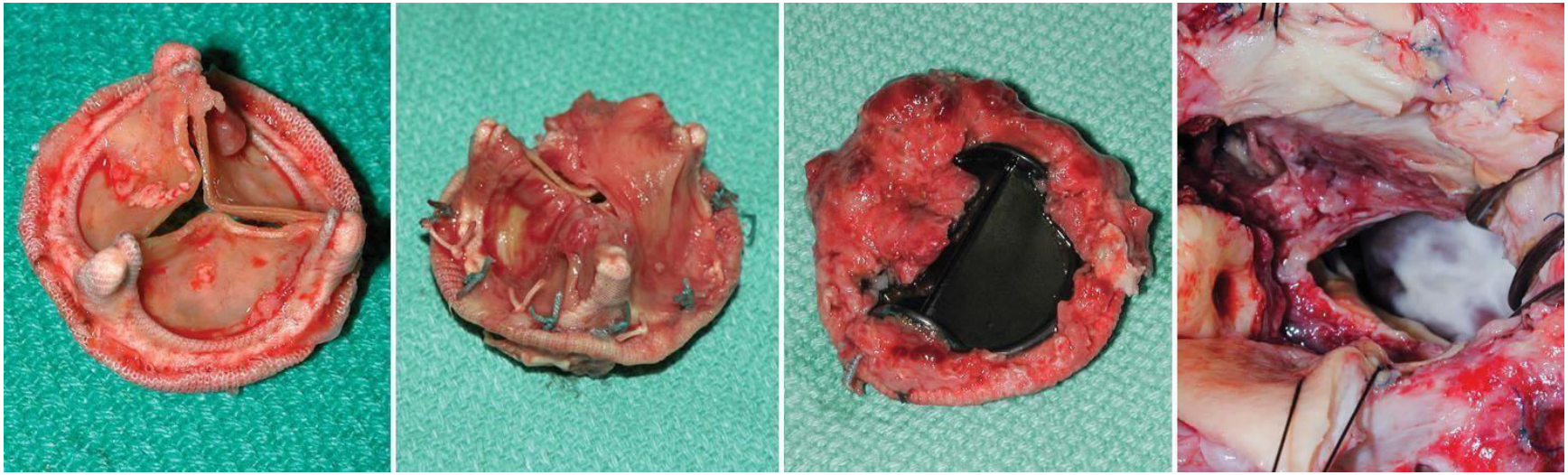
    b. Late.

The definition of early vs. Late, varies between 60 days, 6 months or the first year after the operation. The definition relates to ascribing the infection to the operation itself.

Incidence

- 6 - 0.6per 100,000 person-years.
- M:F ratio varies from 2:1 to .9:1
- PVE in the 1st post-op year is 1-4%
- PVE after the 1st post-op year is 1%/year

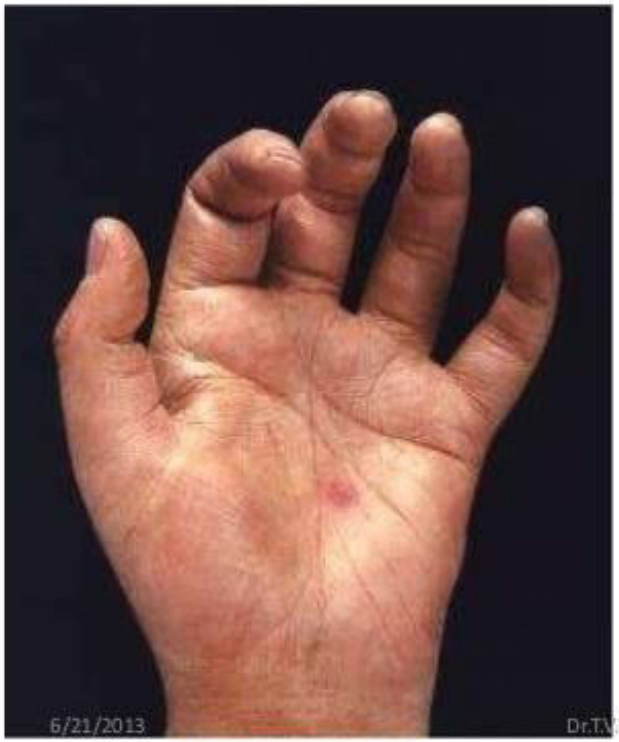
Prosthetic valve endocarditis

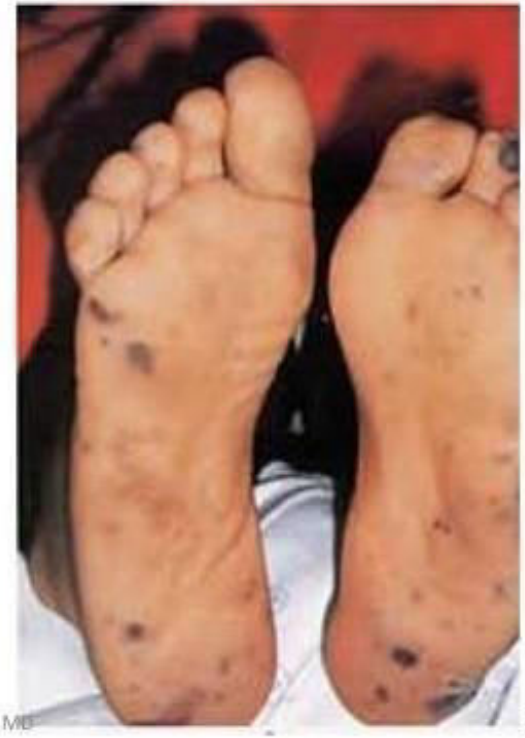


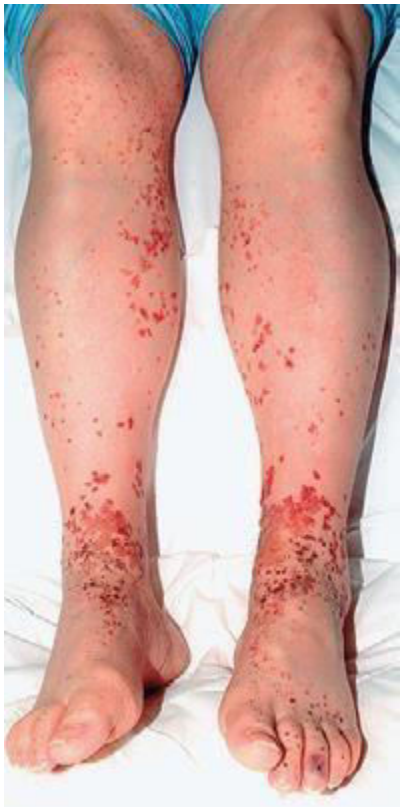
Acute endocarditis

- This presents as a severe febrile illness with prominent and changing heart murmurs and petechiae.
- Clinical stigmata of chronic endocarditis are usually absent.
- Embolic events are common, and cardiac or renal failure may develop rapidly. Abscesses may be detected on echocardiography. Partially treated acute endocarditis behaves like sub acute endocarditis.

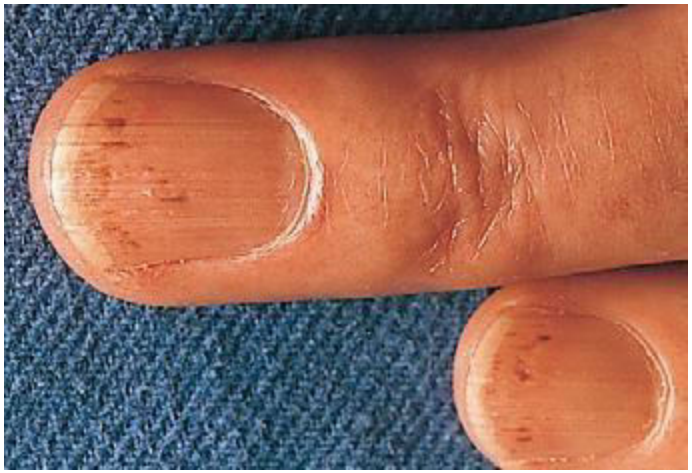
Janeway Lesions



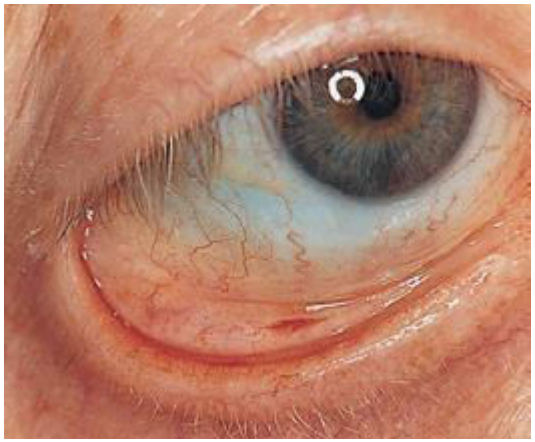




Petechial rash

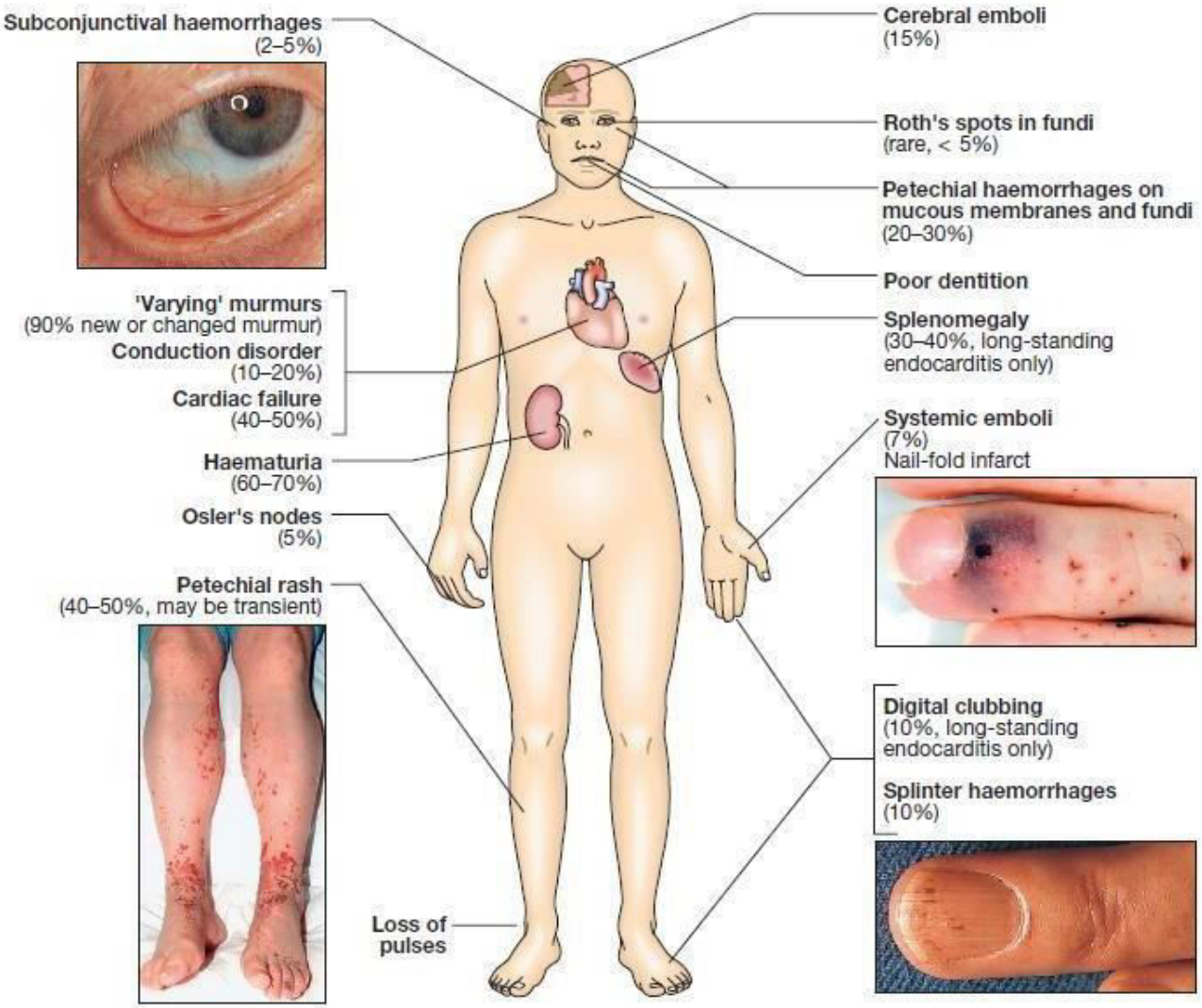


Splinter haemorrhages



Subconjunctival haemorrhages

Clinical features which may be present in Endocarditis



Peripheral stigmata

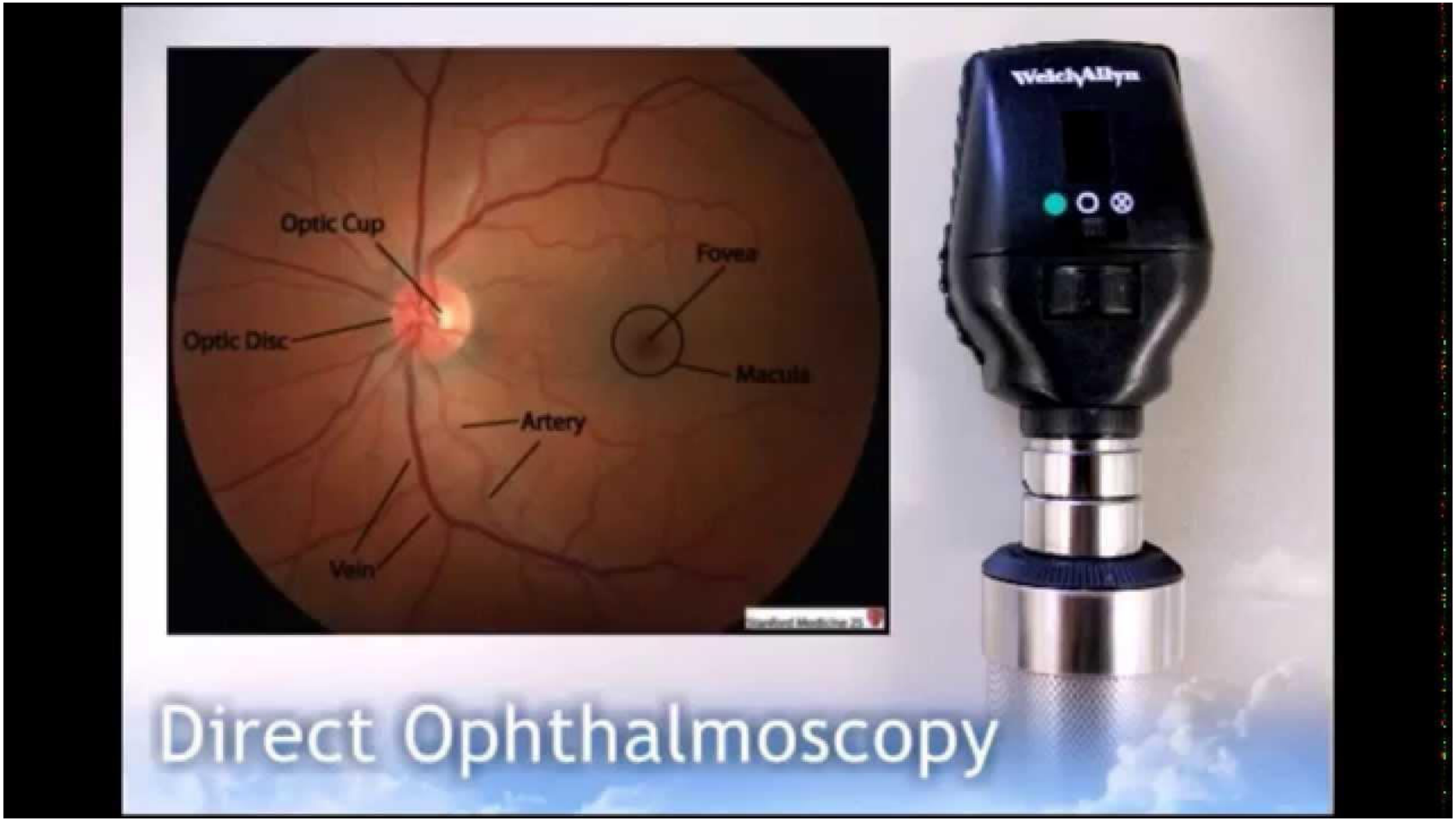
- Petechiae 10 to ,15%
- Splinter hemorrhages
- Osler's nodes (small, tender, purple, erythematous subcutaneous nodules are usually found on the pulp of the digits)
- Janeway lesions are erythematous, macular, nontender lesions on the fingers, palm, or sole
- Roth spots (fundoscopy.)

Clinical manifestations

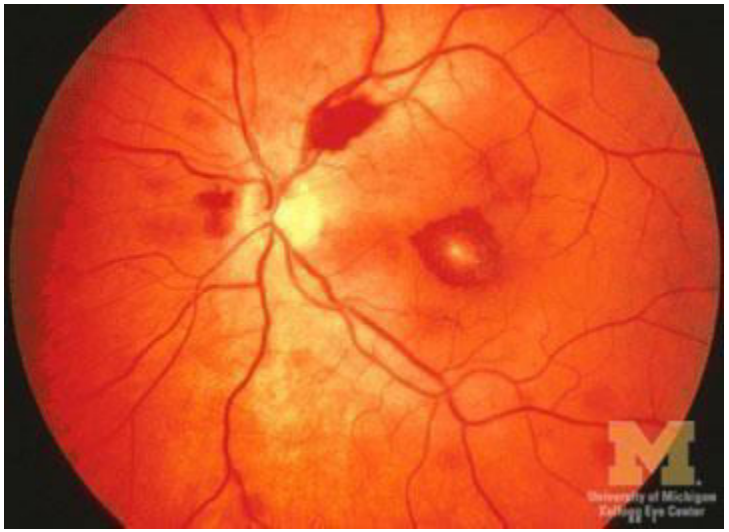
- Fever is the most common constitutional complaint.
- Fever may be absent in:

1. the elderly,
2. those with Heart Failure,
3. Chronic Renal Failure,
4. severe debility,
5. infection with coagulase -ve staphylococcus

- Chills, night sweats, and wt loss are also common.
- Non-Specific (30-40%), Musculoskeletal complaints are common too.


Optic Cup
Optic Disc
Fovea
Macula
Artery
Vein
WelchAllyn
Direct Ophthalmoscopy

Roth spots
Retinal hemorrhage with pale center



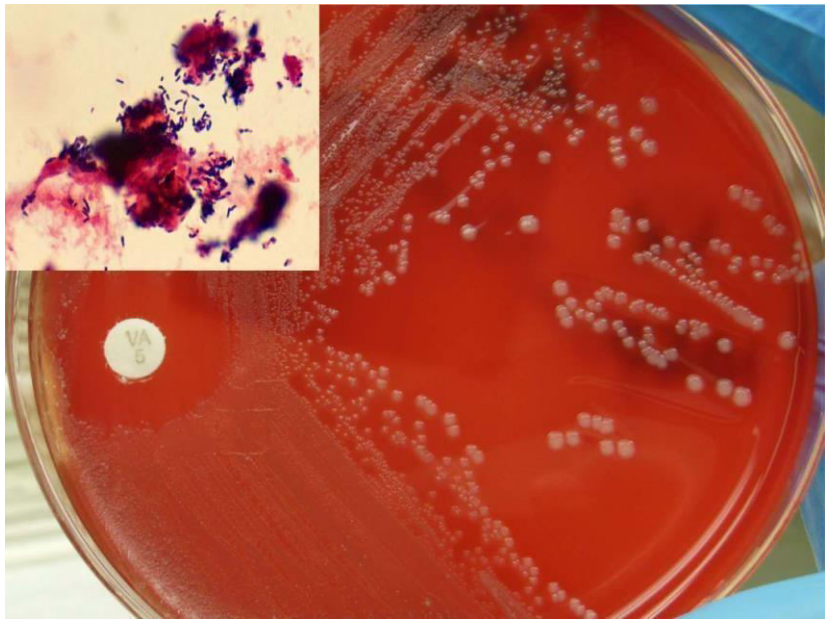
Investigations

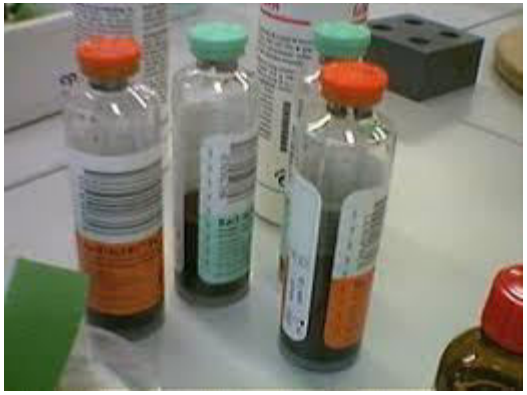
Blood culture:

- is the crucial investigation because it may identify the infection and guide antibiotic therapy.

- Three to six sets of blood cultures should be taken prior to commencing therapy and should not wait for episodes of pyrexia.
- The first two specimens will detect bacteremia in 90% of culture-positive cases.
- Aseptic technique is essential and the risk of contaminants should be minimized by sampling from different vene puncture sites.
- An in-dwelling line should not be used to take cultures.
- Aerobic and anaerobic cultures are required

Blood culture





Major criteria : Positive blood culture

- Typical organism from two cultures
- Persistent positive blood cultures taken > 12 hrs apart
- Three or more positive cultures taken over > 1 hr

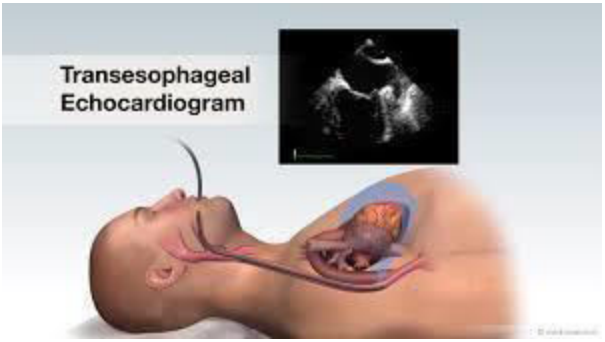
Echocardiography

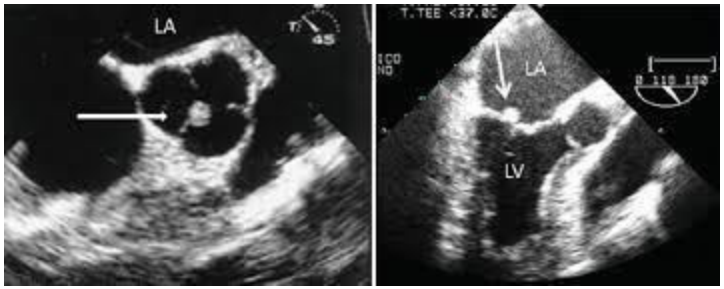
- Is key for :
- detecting and following the progress of vegetation,
- assessing valve damage and for detecting abscess formation.
- Vegetations as small as 2–4 mm can be detected by transthoracic echocardiography, and even smaller ones (–1 1.5mm) can be visualised by transoesophageal echocardiography (TOE), which is particularly valuable for identifying abscess formation and investigating patients with prosthetic heart valves.
- Vegetations may be difficult to distinguish in the presence of an abnormal valve; the sensitivity of transthoracic echo is approximately 65% but that of TOE is more than .90%

Endocardial involvement

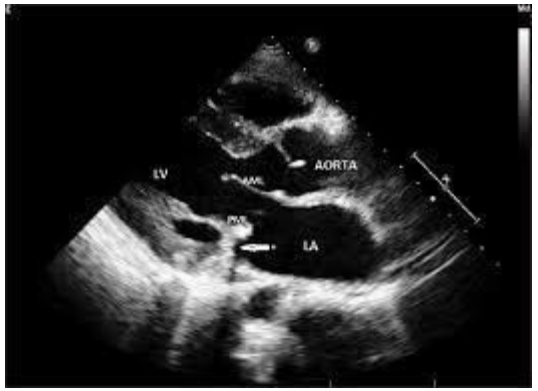
- Positive echocardiographic findings of vegetation
- New valvular regurgitation

Transthoracic Echocardiography or
Trans esophageal echocardiography





Aortic valve vegetation



Mitral valve vegetation

Important clinical point

Failure to detect vegetations does not exclude the diagnosis.

Diagnosis of infective endocarditis (modified Duke criteria)

Major criteria

Positive blood culture

- Typical organism from two cultures
- Persistent positive blood cultures taken > 12 hrs apart
- Three or more positive cultures taken over > 1 hr

Endocardial involvement

- Positive echocardiographic findings of vegetation
- New valvular regurgitation

Minor criteria

- Predisposing valvular or cardiac abnormality
- Intravenous drug misuse
- Pyrexia ≥ 38°C
- Embolic phenomenon
- Vasculitic phenomenon
- Blood cultures suggestive: organism grown but not achieving major criteria
- Suggestive echocardiographic findings

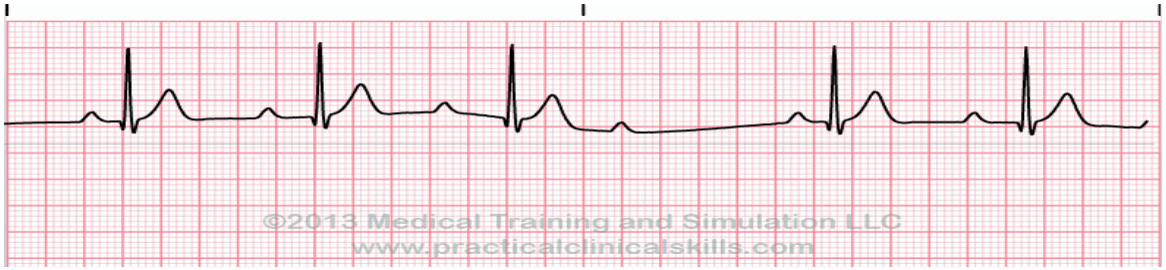
- Definite endocarditis = two major, or one major and three minor, or five minor
- Possible endocarditis = one major and one minor, or three minor.

Other lab investigations

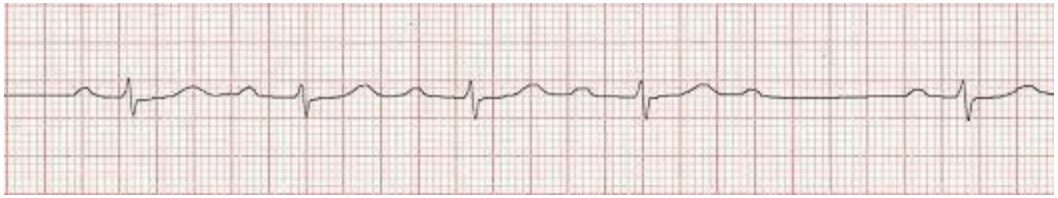
- Elevation of the ESR
- Normocytic normochromic anaemia
- leucocytosis are common but not invariable.
- Measurement of serum CRP is more reliable than the ESR in monitoring progress. Proteinuria may occur and microscopic hematuria is usually present

ECG

- The ECG may show the development of AV block (due to aortic root abscess formation) and occasionally infarction due to emboli.

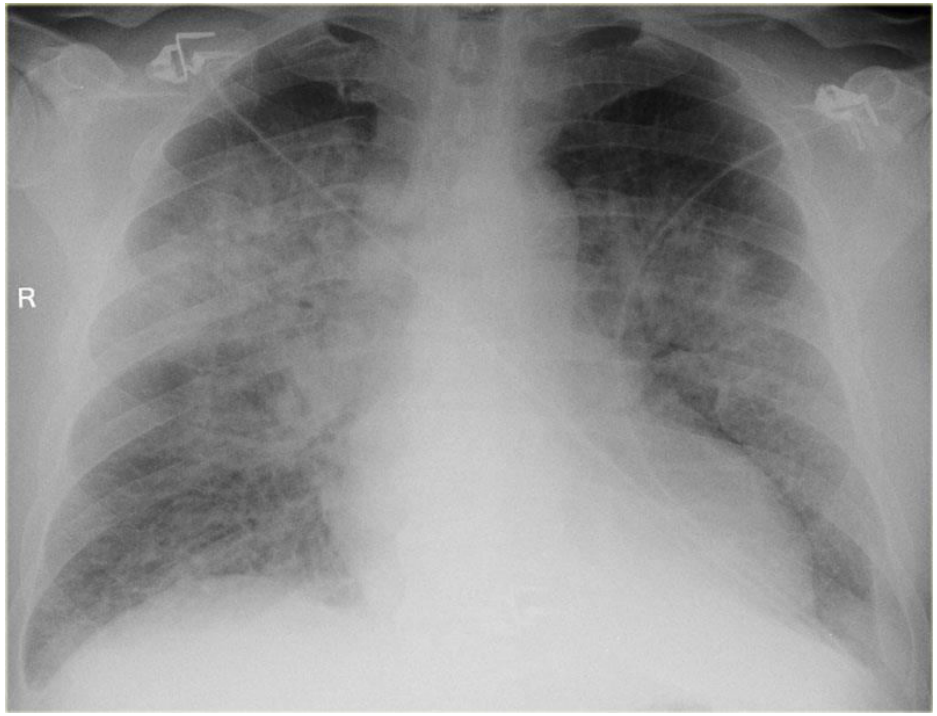


What is the abnormality?



CXR

- The chest X-ray may show evidence of cardiac failure and cardiomegaly.



Heat failure in patient with infective endocarditis. Cardiomegaly , pulmonary edema.

Management

- The case fatality of bacterial endocarditis is approximately 20% and even higher in those with prosthetic valve endocarditis and those infected with antibiotic resistant organisms.
- A multidisciplinary approach, with cooperation between the physician, surgeon and microbiologist, increases the chance of a successful outcome.
- Any source of infection should be removed as soon as possible; for example, a tooth with an apical abscess should be extracted.

Empirical treatment

Depends on:

1. The mode of presentation.
2. the suspected organism,
3. whether the patient has a prosthetic valve
4. Penicillin allergy.

- If the presentation is acute, flucloxacillin and gentamicin are recommended,
- For a subacute or indolent presentation, benzyl penicillin and gentamicin are preferred.

- In those with penicillin allergy, a prosthetic valve or suspected meticillin-resistant *Staph. aureus* (MRSA) infection, triple therapy with vancomycin, gentamicin and oral rifampicin should be considered.
- Following identification of the causal organism, determination of the minimum inhibitory concentration (MIC) for the organism is essential to guide antibiotic therapy.

- A 2-week treatment of parenteral regimen may be sufficient for fully sensitive strains of *Strep. viridans* and *Strep. bovis*. ,
- For the empirical treatment of bacterial endocarditis, penicillin plus gentamicin is the regimen of choice for most patients;
- when staphylococcal infection is suspected, however, vancomycin plus gentamicin is recommended..

Cardiac Surgery may be needed

- Cardiac surgery (debridement of infected material and valve replacement) is advisable in a substantial proportion of patients, particularly those with *Staph. Aureus* and fungal infections . Antimicrobial therapy must be started before surgery

Indications for cardiac surgery in infective endocarditis

- Heart failure due to valve damage
- Failure of antibiotic therapy (persistent/uncontrolled infection)
- Large vegetation on left-sided heart valves with evidence or high risk' of systemic emboli
- Abscess formation
- Patients with prosthetic valve endocarditis or fungal endocarditis often require cardiac surgery

Conditions for the short-course treatment of *Strep. viridans/bovis* endocarditis(2weeks)

- Native valve infection
- MIC ≤ 0.1 mg/L
- No adverse prognostic factors (e.g. heart failure, aortic regurgitation, conduction defect)
- No evidence of thromboembolic disease
- No vegetations > 5 mm diameter
- Clinical response within 7 days

Antimicrobial treatment of common causative organisms in infective endocarditis

- **Enterococci**
- **Staphylococci**
- **Usually treatment for 4-6 weeks.**

Prevention

- Until recently, antibiotic prophylaxis was routinely given to people at risk of infective endocarditis undergoing interventional procedures.
- However, as this has not been proven to be effective and the link between episodes of infective endocarditis and interventional procedures has not been demonstrated, antibiotic.
- prophylaxis is no longer offered routinely for defined interventional procedures.

Antibiotic prophylaxis may be indicated in moderate and high risk patients

AHA/ESC high risk

- Prior endocarditis
- Replacement heart valve
- Uncorrected cyanotic heart disease
- Any congenital disease in the first 6 months after repair with prosthetic material or a device
- Repaired congenital disease with a residual defect
- Congenital disease with a palliative shunt
- Heart transplantation with valve regurgitation

AHA/ESC moderate risk

- Bicuspid aortic valve
- Rheumatic valve disease
- Non rheumatic valve disease
- Mitral prolapse, mild MR
- Mitral prolapse, $moderate MR
- Mitral prolapse and flail leaflet

Resources

- Davidson's principles and practice of medicine 22nd edition.
- ACC/AHA 2008 guideline update on valvular heart disease: focused update on infective endocarditis: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

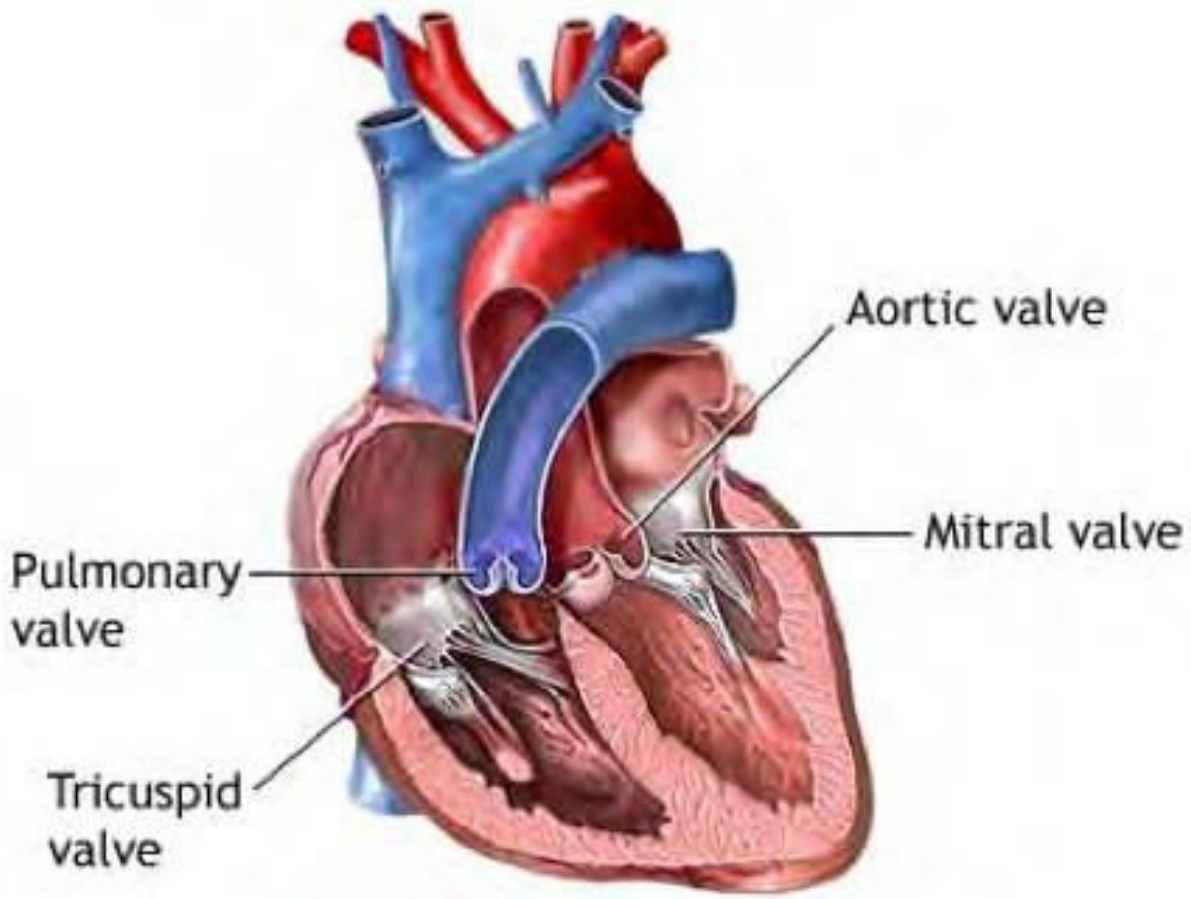
DISEASES OF THE HEART VALVES

Dr.ammar khalid

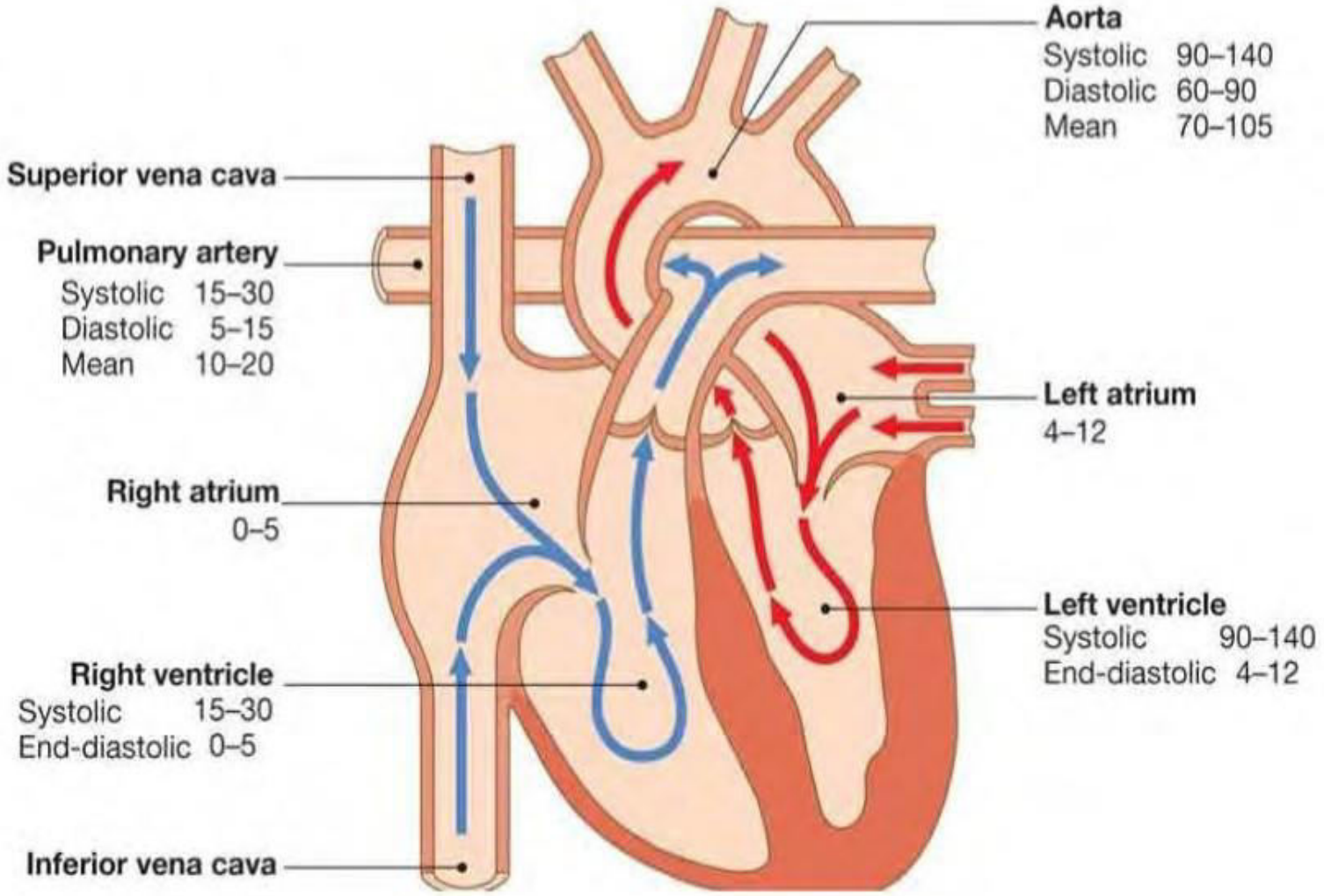
Cardiac valves

- 10% of heart failure is due to valvular pathology
- Valves act to stop retrograde flow
- Valve opening and closing dependent on pressure on either side
- Atrio ventricular valves (Mitral & Tricuspid)
- Semilunar valves (Pulmonary & Aortic)

Normal anatomy



Cardiac chambers , flow of blood

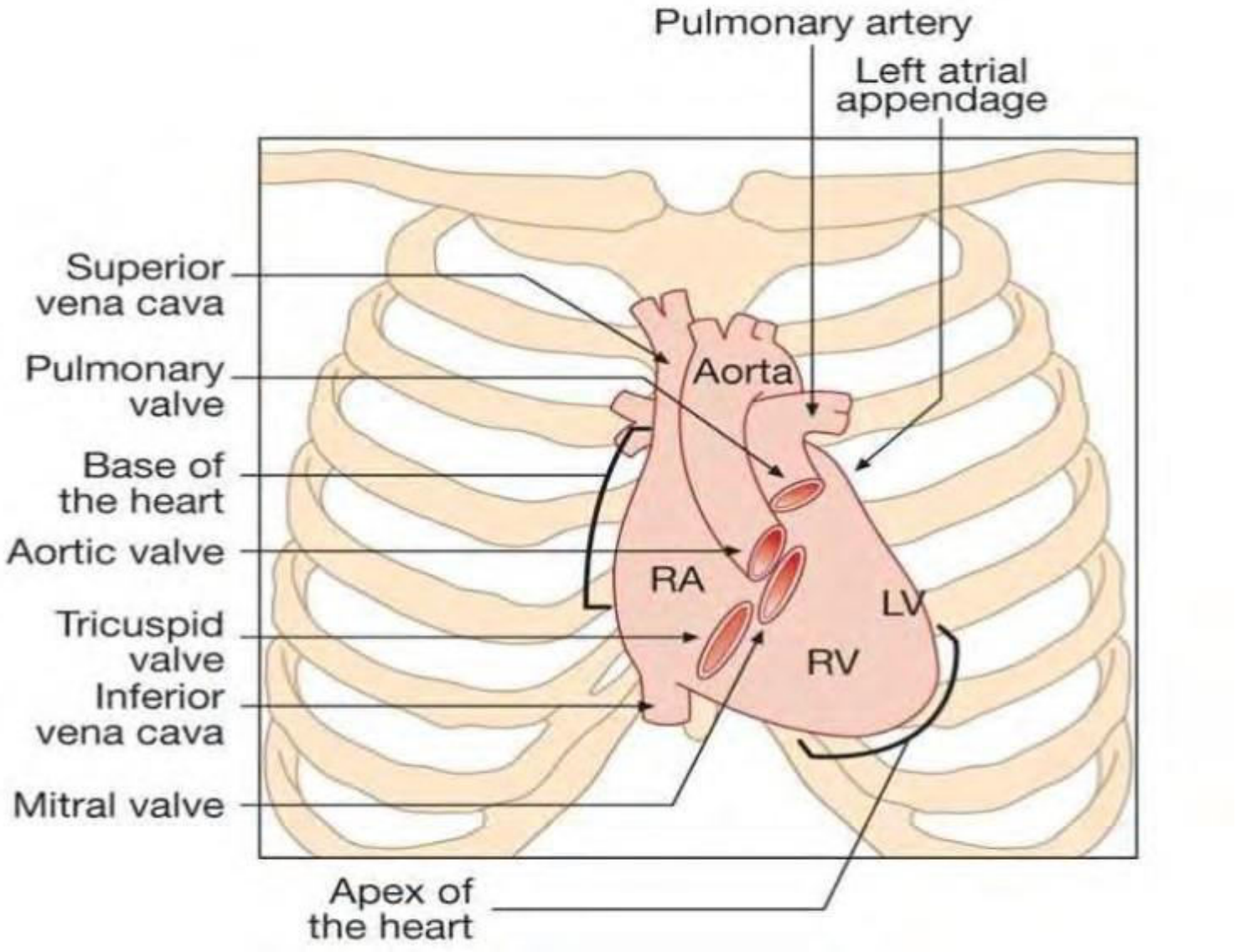


Normal valves

- Two inflow valves between atria and ventricle
  - Mitral (Left heart, systemic circulation)
  - Tricuspid (Right heart, pulmonary circulation)

- Two outflow valves between ventricle and great vessels
  - Aortic (Left heart, systemic circulation)
  - Pulmonary (Right heart, pulmonary circulation)

Surface area of cardiac valves



Murmurs

- Turbulent flow due to an abnormal valve or increased blood flow through normal valve (as in pregnancy and anemia)

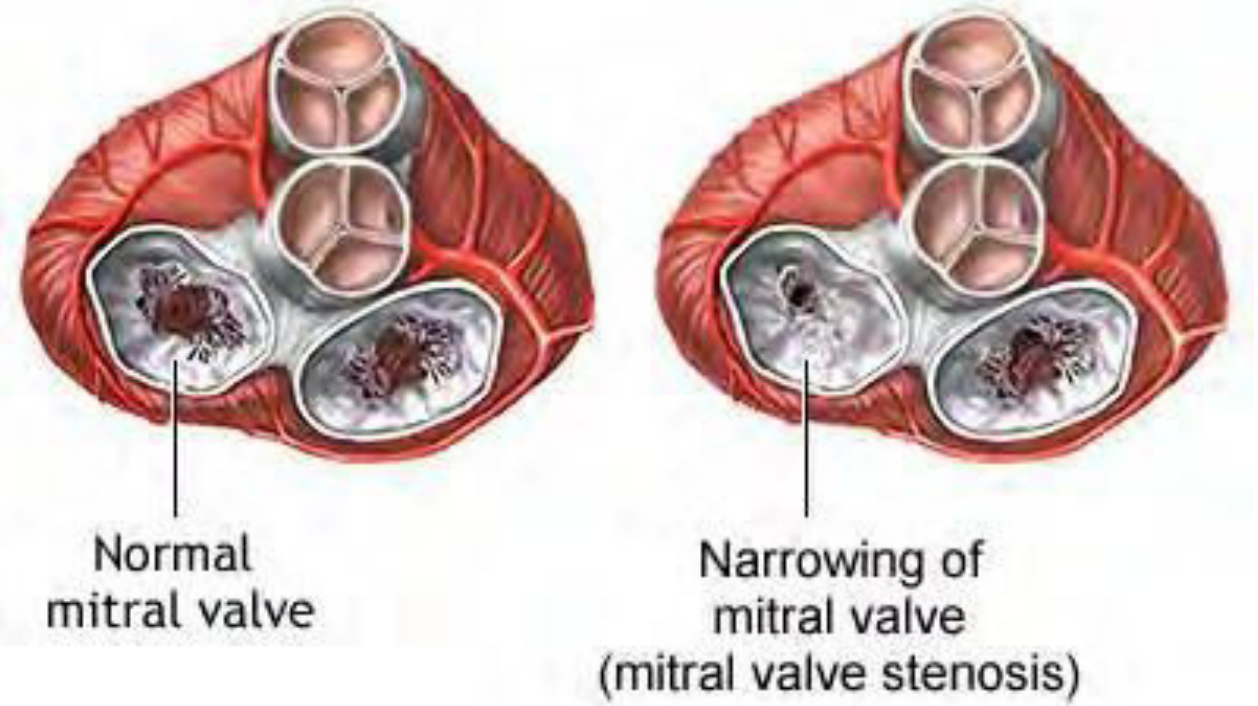
- If a valve is tight (stenosis) then it produces turbulence as the blood passes through it
- If a valve leaks (regurgitation) the turbulence is produced after the blood has passed through it

Mitral stenosis

- Almost always rheumatic in origin
- Heavy calcification of the mitral valve apparatus in older people
- Congenital mitral stenosis , rare

Mitral stenosis

- Physiological consequences
  - Volume overload LA
    - Left atrium fails to empty
    - Left Atrial dilatation and hypertrophy
    - Pulmonary venous congestion
    - Pulmonary arterial hypertension
    - RV hypertrophy
- Clinical consequence
  - Atrial fibrillation and systemic embolus


Normal
mitral valve
Narrowing of
mitral valve
(mitral valve stenosis)
A.D.A.M.

- Effort-related dyspnea and progressive exercise intolerance is usually the dominant symptoms .
- Palpitation (AF)
- Hemoptysis due to acute pulmonary edema o pulmonary hypertension.
- Systemic thromboembolism (due to atrial fibrillation AF).
- Right sided heart failure (ascites and pedal edema)

Mitral stenosis

- Mid diastolic murmur

- Turbulent flow occurs before ventricular systole as the ventricle fills

How do you link between hemodynamic changes and patient presentation ?

- The mitral valve orifice is normally about

5 cm2 in diastole and may be reduced to **1 cm2** in severe mitral stenosis.

Patients usually remain asymptomatic until the stenosis is less than **2 cm2** (50% stenosis) .

Reduced lung compliance, due to chronic pulmonary venous congestion, contributes to **breathlessness**, and a low cardiac output may cause fatigue.

Hemodynamic changes in Mitral valve stenosis

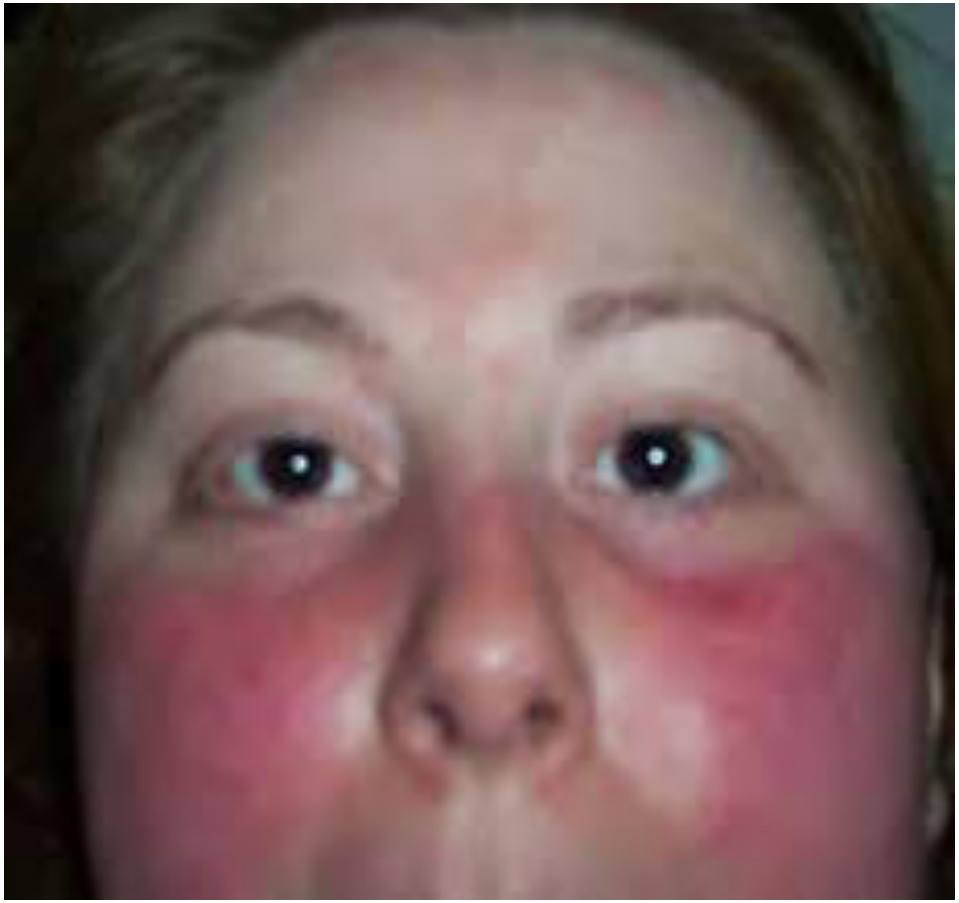
- The mitral valve orifice is normally about 5 cm2 In rheumatic mitral stenosis, the mitral valve orifice is slowly diminished by progressive fibrosis, calcification of the valve leaflets, and fusion of the cusps and subvalvular apparatus.
- The flow of blood from LA to LV is restricted and left atrial pressure rises, leading to pulmonary venous congestion and breathlessness.

- There is dilatation and hypertrophy of the LA, and left ventricular filling becomes more dependent on left atrial contraction.
- Any increase in heart rate shortens diastole when the mitral valve is open and produces a further rise in left atrial pressure.

- Situations that demand an increase in cardiac output also increase left atrial pressure, so exercise and pregnancy are poorly tolerated

- Pulmonary hypertension leads to right ventricular hypertrophy and dilatation, tricuspid regurgitation and right heart failure , ascites , leg edema
- Fewer than 20% of patients remain in sinus rhythm; many of these have a small fibrotic LA and severe pulmonary hypertension

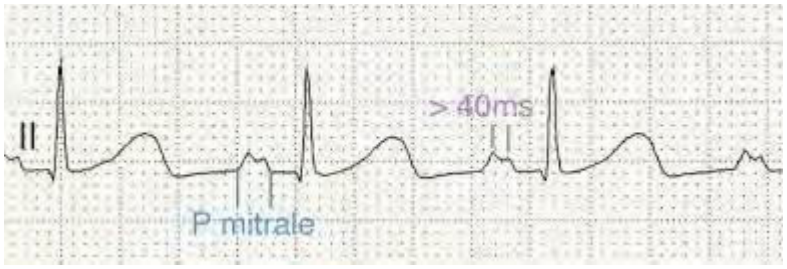
Mitral stenosis facies



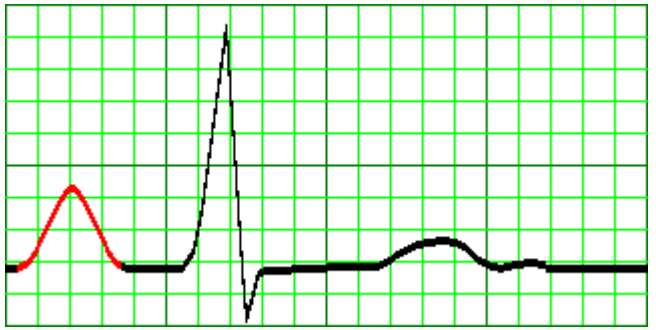
Investigations

ECG	
• Right ventricular hypertrophy: tall R waves in V_1–V_3	• P mitrale or atrial fibrillation
Chest X-ray	
• Enlarged LA and appendage	• Signs of pulmonary venous congestion
Echo	
• Thickened immobile cusps • Reduced valve area • Enlarged LA	• Reduced rate of diastolic filling of LV
Doppler	
• Pressure gradient across mitral valve	• Pulmonary artery pressure • Left ventricular function
Cardiac catheterisation	
• Coronary artery disease • Pulmonary artery pressure	• Mitral stenosis and regurgitation

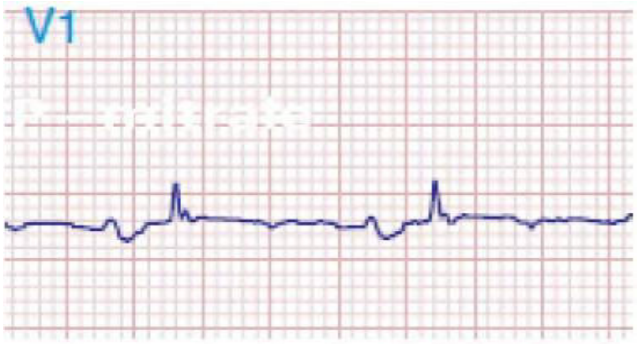
ECG



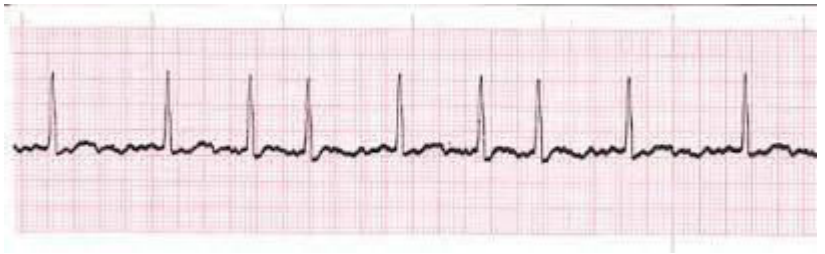
P wave Mitrale lead I



P wave Pulmonale

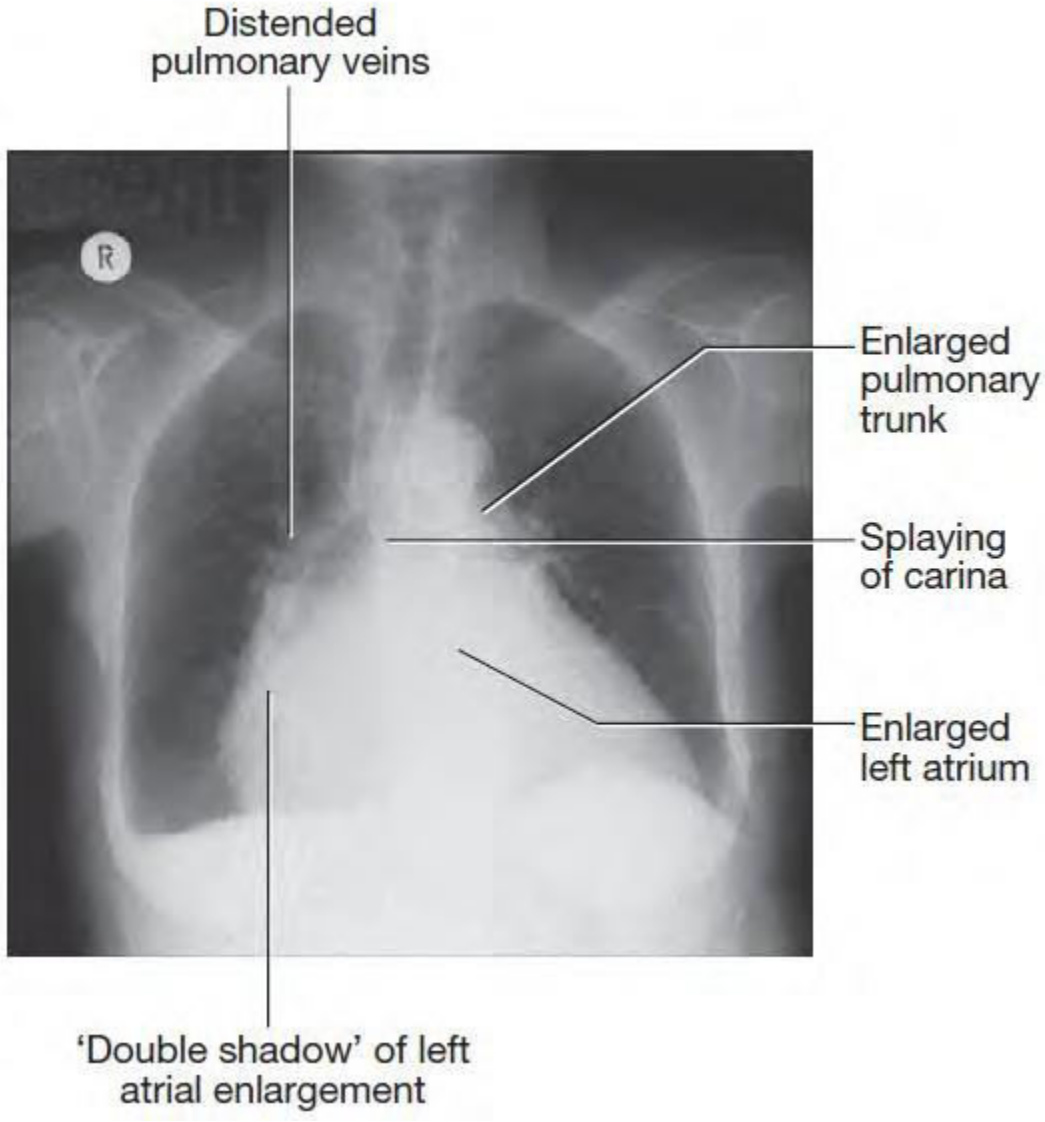


Biphasic P wave in lead V1

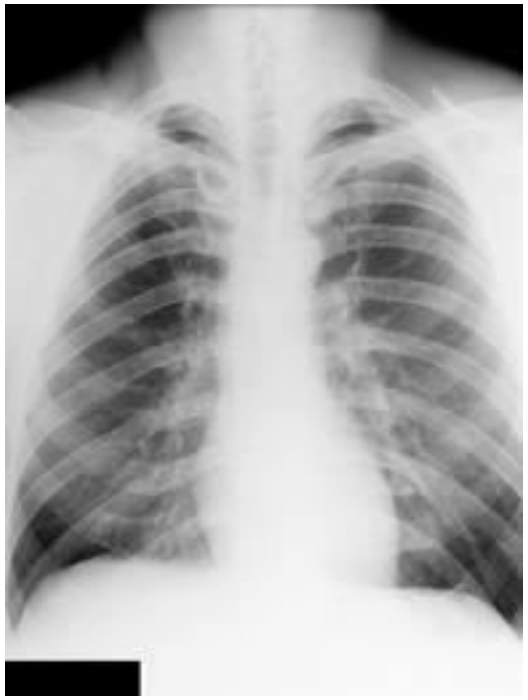


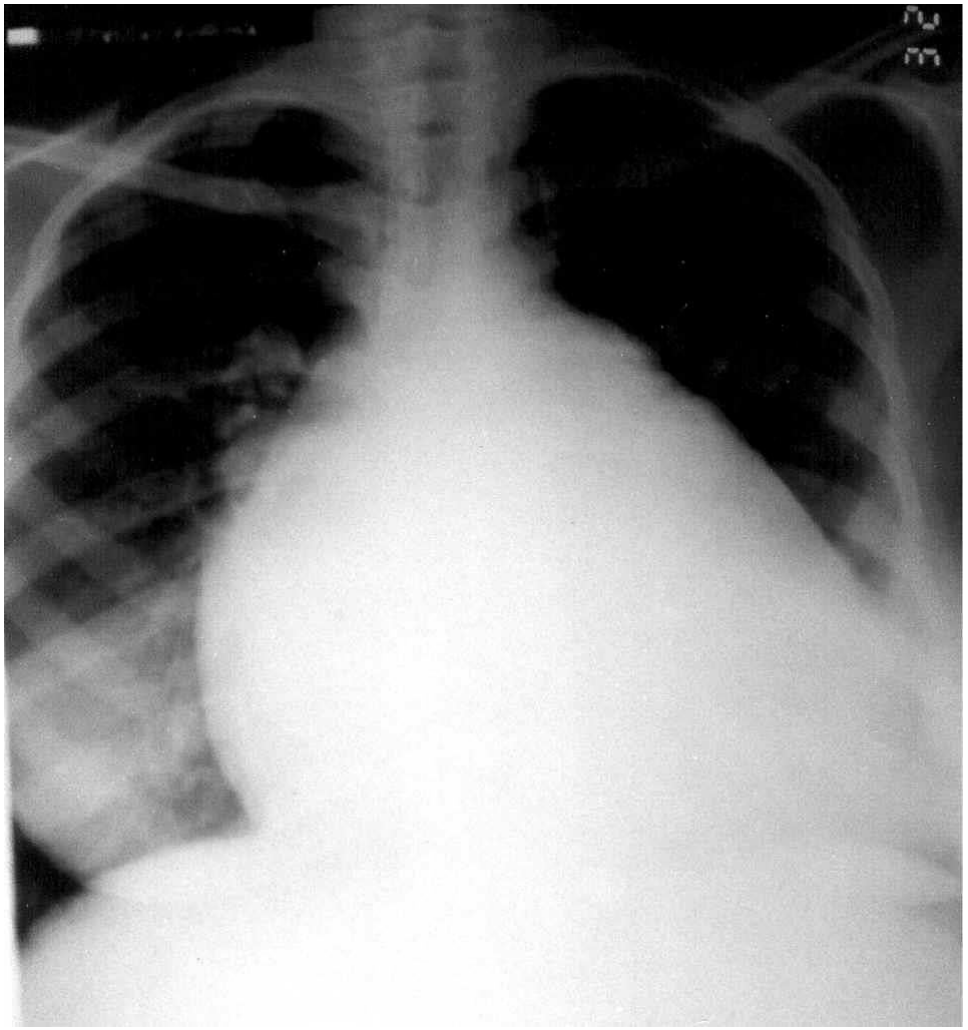
Atiral fibrillation

Chest X-ray of a patient with mitral stenosis and regurgitation indicating enlargement of the LA and prominence of the pulmonary artery trunk

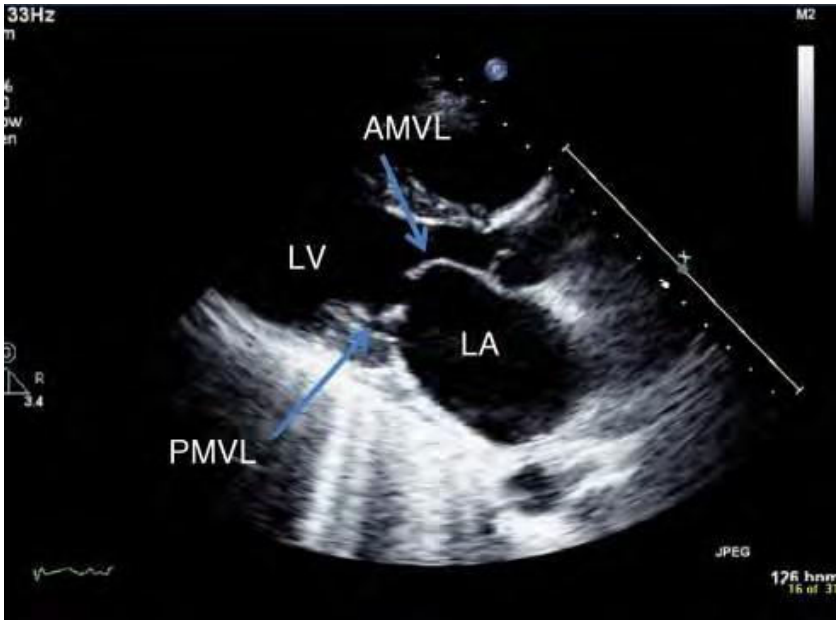


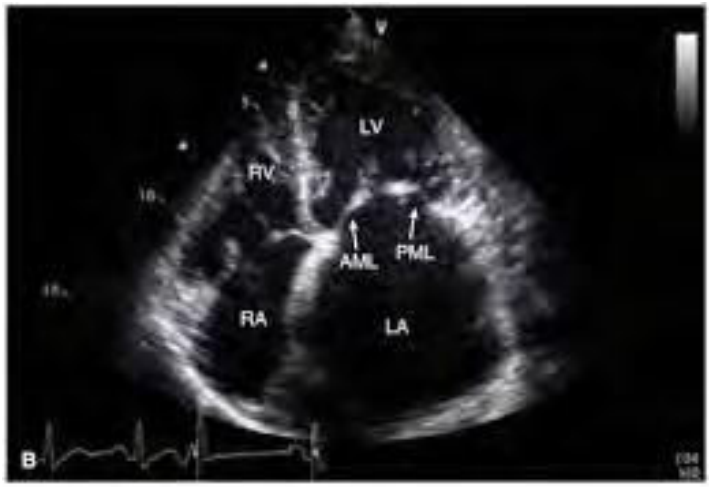
Consequences of Mitral stenosis



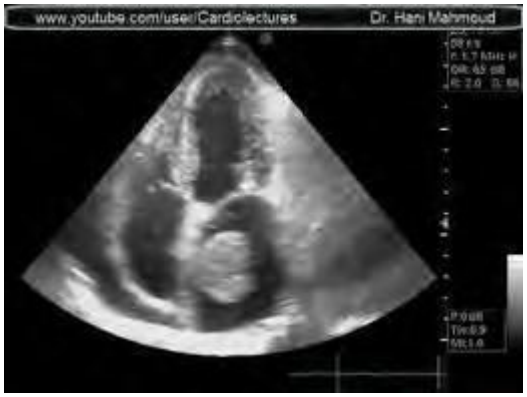


Mitral stenosis 2 Dimensional echocardiography





Thickened mitral leaflets ,
restricted motion , dilated LA ,
thickened sub valvular apparatus



LA thrombus

Management

Medical management consist of :

1. anticoagulation to reduce the risk of systemic embolism
2. ventricular rate control (digoxin, β-blockers or rate-limiting calcium antagonists) in atrial

Fibrillation.

3.diuretic therapy to control pulmonary and systemic congestion.

4. Antibiotic prophylaxis against infective endocarditis

Intervention and surgical

- Mitral balloon valvuloplasty
- Valve replacement

Mitral Valve Regurgitation

- It is a retrograde blood flow during systole from LV to LA due to mitral valve apparatus disorders and incomplete closure

Causes of mitral Regurgitation

Causes of cute MR :

- Endocarditis
- Papillary muscle rupture (post-MI) leading to flail MV leaflets
- Trauma
- Chordal rupture/Leaflet flail (MVP, IE)

Causes chronic MR :

- Myxomatous (MVP)
- Rheumatic fever
- Endocarditis (healed)
- Mitral annular calcification
- Congenital (cleft, AV canal)
- HOCM with SAM
- Ischemic (LV remodeling)
- Dilated cardiomyopathy

Other causes of mitral regurgitation

- Mitral valve function depends on the chordae tendineae and their papillary muscles;
- dilatation of the LV distorts the geometry of these and may cause mitral regurgitation
- Dilated cardiomyopathy and heart failure from coronary artery disease are common causes of so-called ‘functional’ mitral regurgitation.
- Endocarditis is an important cause of acute mitral
- regurgitation

Clinical features of MR

Depend on the onset and duration

Acute MR:

- Symptoms of acute pulmonary edema due to incompliance of LA to the sudden volume over load resulting in severe SOB and reduced cardiac output

Chronic MR:

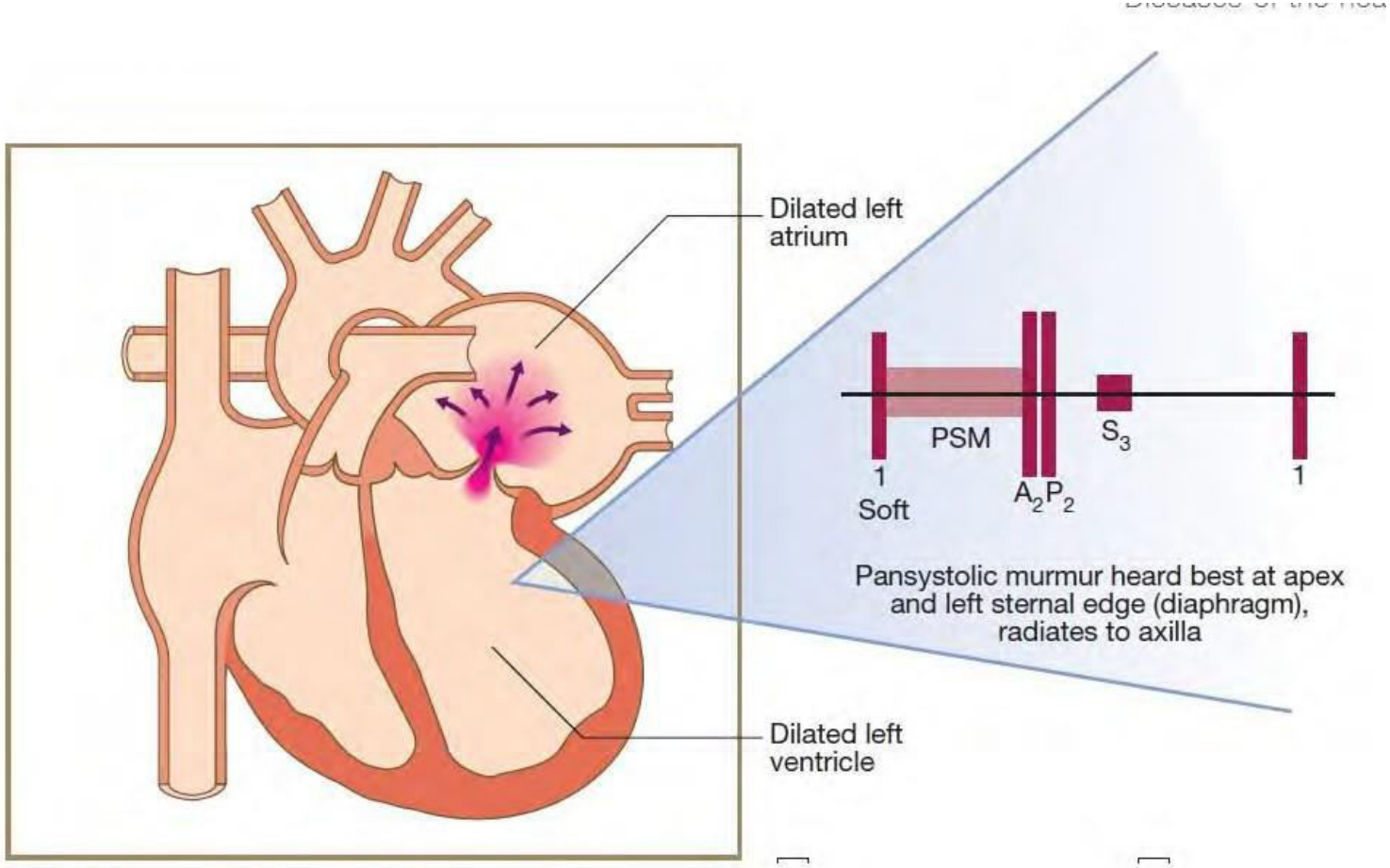
- Asymptomatic discover on routine examination
- Exertional dyspnoea
- Orthopnea
- Nocturnal dyspnoea
- Palpitation ?AF
- Symptoms of pulmonary edema build over time
- Symptoms of low cardiac output & fatigue
- Ankle edema
- Ascitis

Symptoms
• Dyspnoea (pulmonary venous congestion) • Fatigue (low cardiac output) • Palpitation (atrial fibrillation, increased stroke volume) • Oedema, ascites (right heart failure)
Signs
• Atrial fibrillation/flutter • Cardiomegaly: displaced hyperdynamic apex beat • Apical pansystolic murmur ± thrill • Soft S1, apical S3 • Signs of pulmonary venous congestion (crepitations, pulmonary oedema, effusions) • Signs of pulmonary hypertension and right heart failure

Physical signs of MR

- Large volume pulse regular or irregular pulse (atrial fibrillation /flutter)
- Raised JVP
- Displaced hyper dynamic apex beat ± thrill
- Left parasternal heave (Sign of PHT)
- Apical pan systolic murmur radiate to the axilla
- Soft S1 ,apical S3
- There might be signs of CHF
- Chest findings : crepitation indicate pulmonary edema with or without pleural effusions

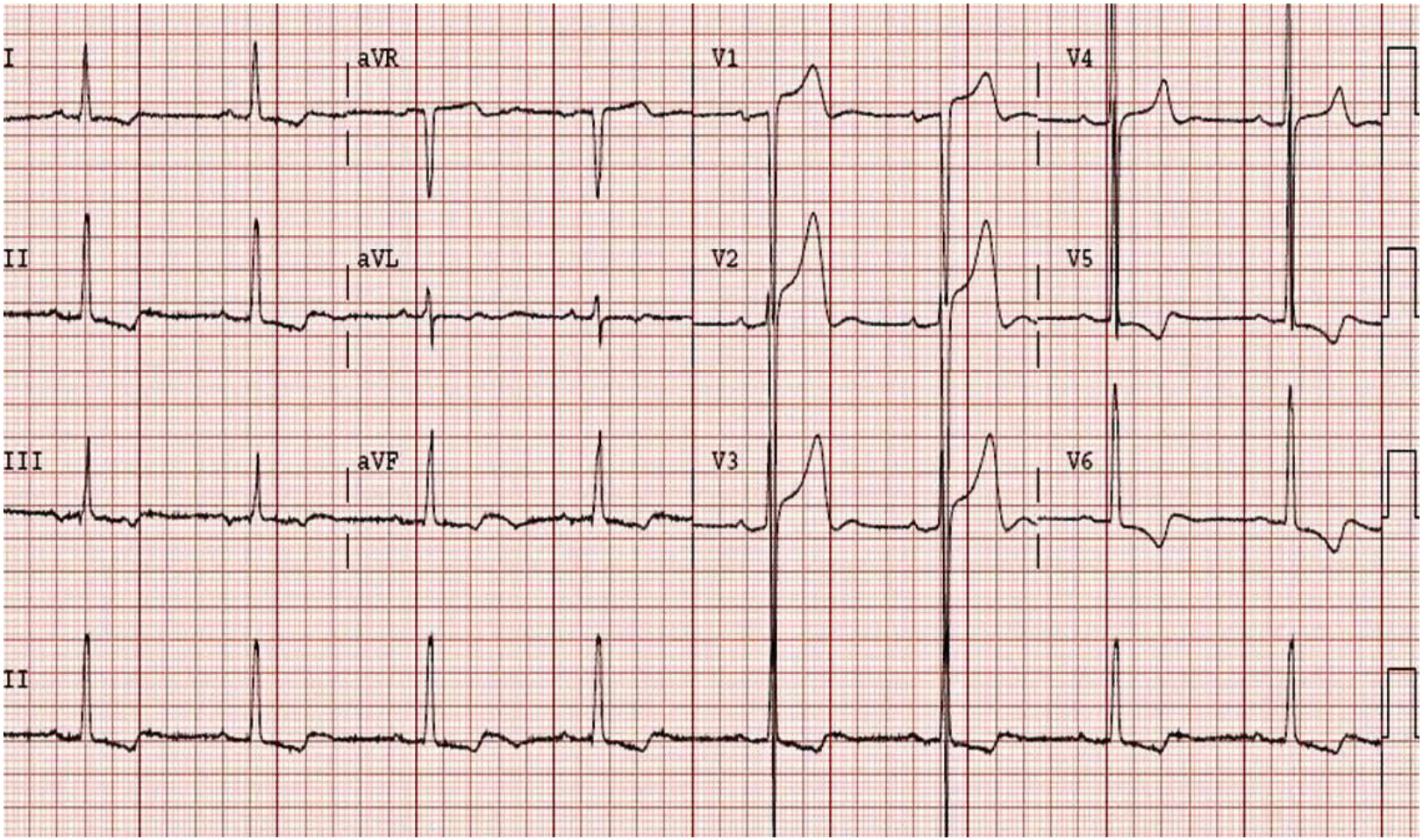
Auscultatory findings in MR



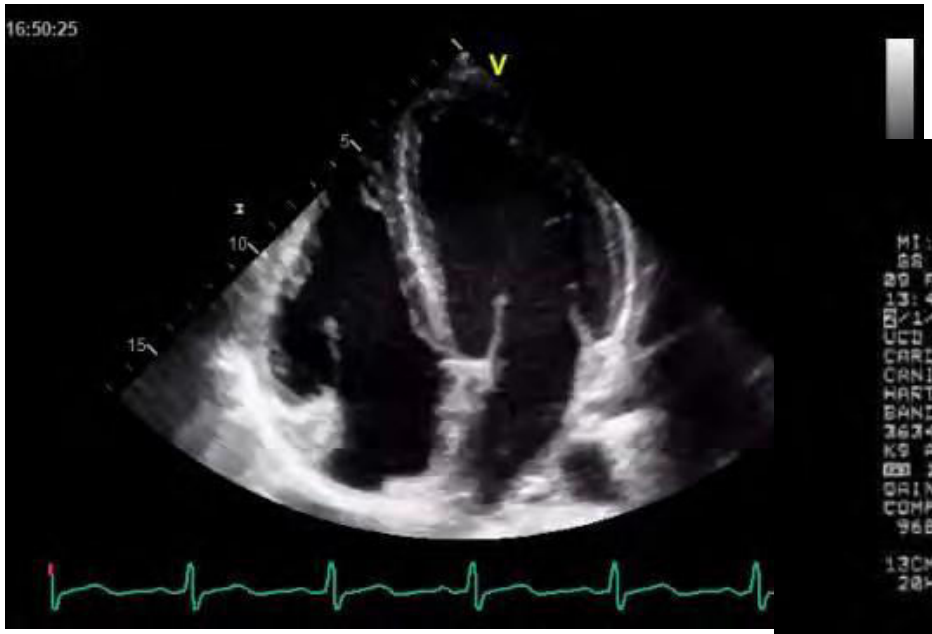
Investigations

ECG
• Left atrial hypertrophy (if not in atrial fibrillation) • Left ventricular hypertrophy
Chest X-ray
• Enlarged LA • Enlarged LV • Pulmonary venous congestion • Pulmonary oedema (if acute)
Echo
• Dilated LA, LV • Dynamic LV (unless myocardial dysfunction predominates) • Structural abnormalities of mitral valve (e.g. prolapse)
Doppler
• Detects and quantifies regurgitation
Cardiac catheterisation
• Dilated LA, dilated LV, mitral regurgitation • Pulmonary hypertension • Coexisting coronary artery disease

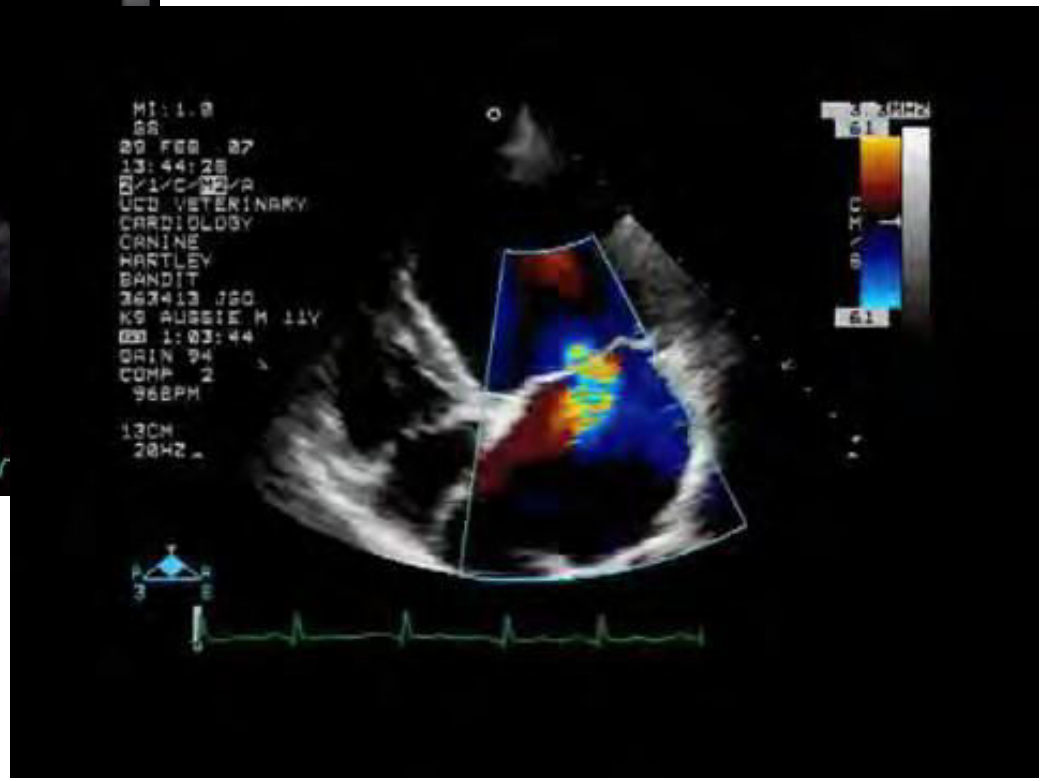
ECG , LVH



Mitral Regurgitation

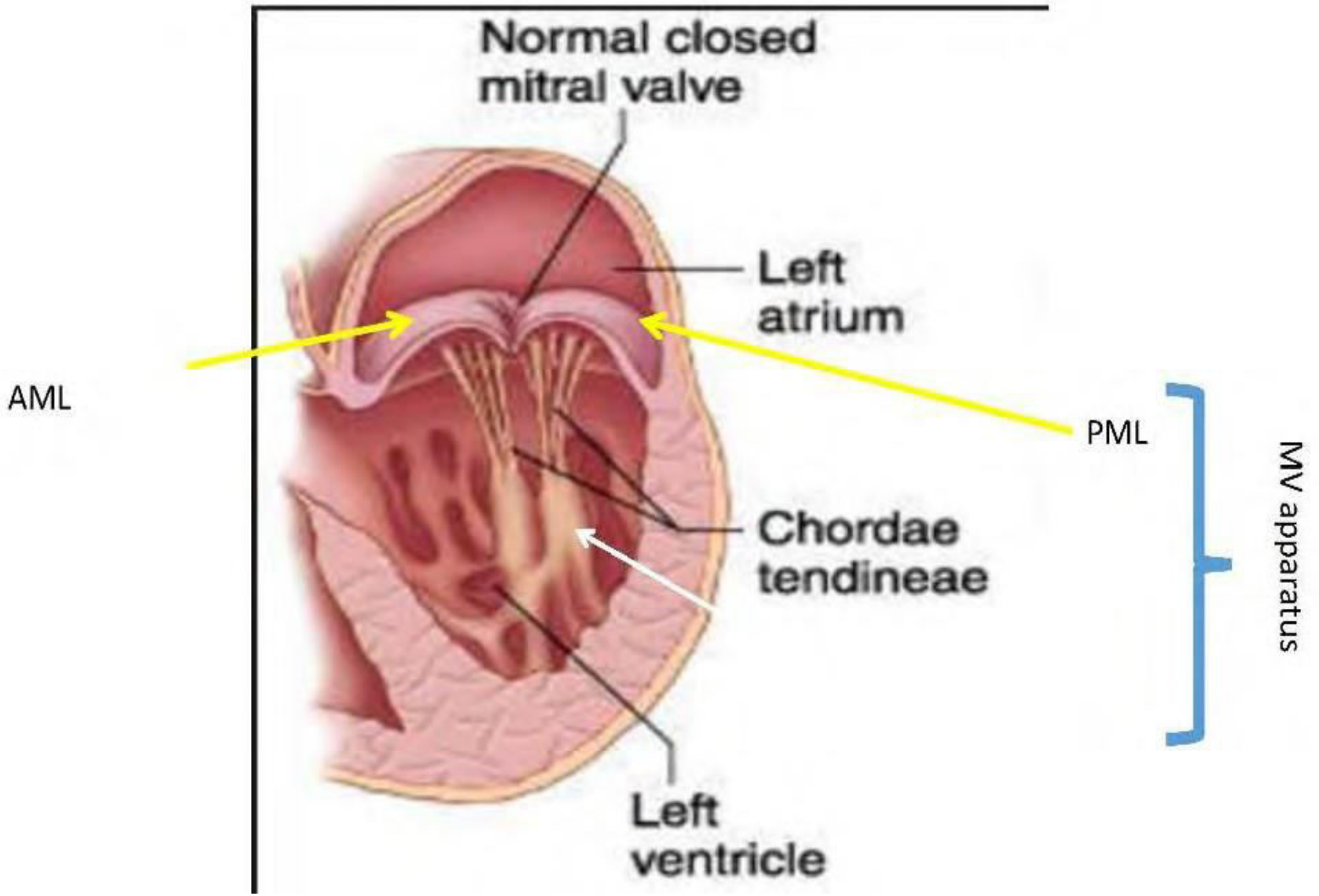


Dilated LV , LA



Improper closure of Mital leaflets
with regurgitant jet into LA

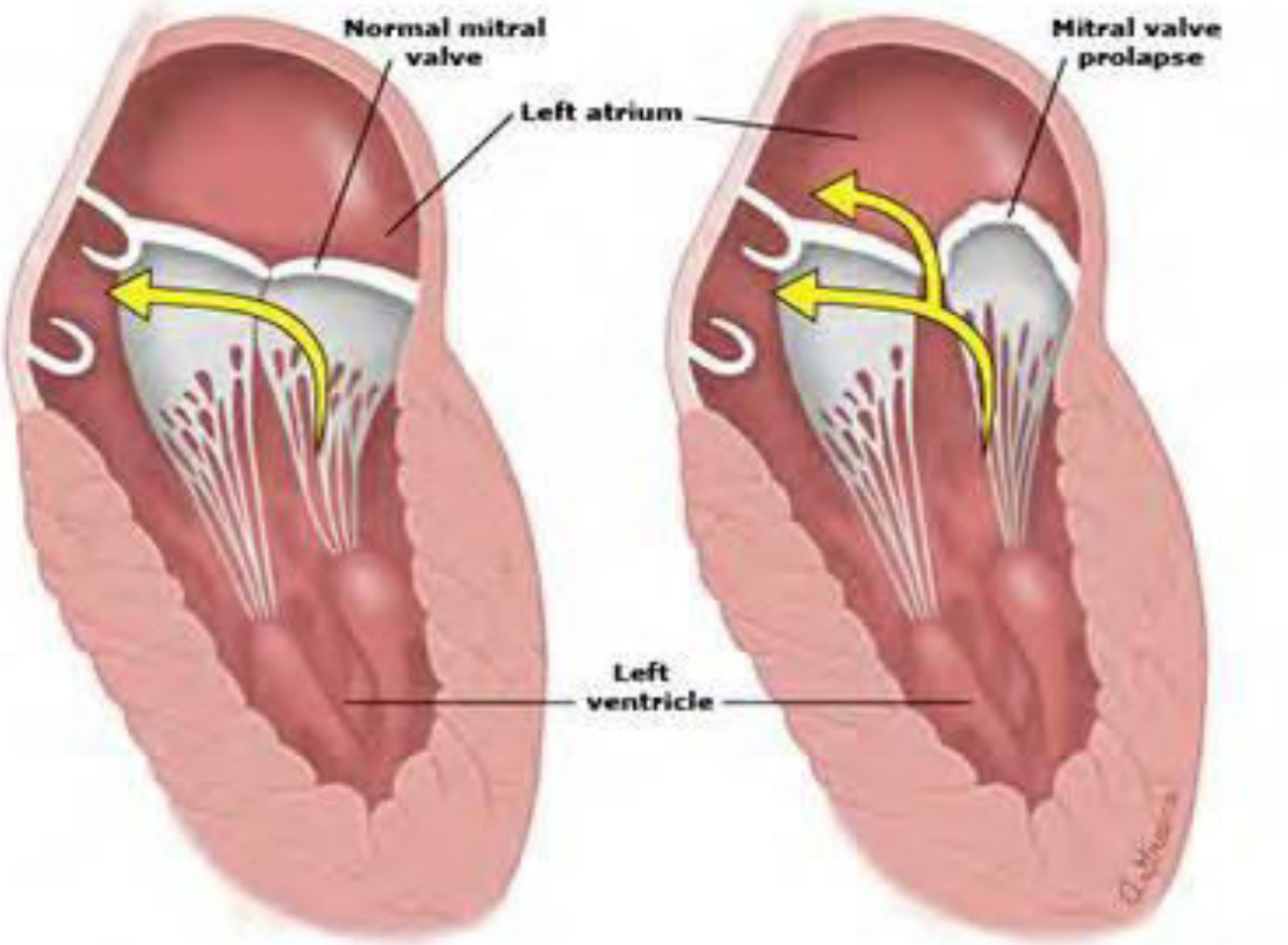
Mitral valve apparatus



Mitral valve prolapse
‘floppy’ mitral valve

- one of the more common causes of mild mitral regurgitation . It is caused by congenital anomalies or degenerative myxomatous changes, and is sometimes a feature of connective tissue disorders such as Marfan’s syndrome .
- In its mildest forms, the valve remains competent but bulges back into the atrium during systole, causing a mid-systolic click but no murmur. In the presence of a regurgitant valve, the click is followed by a late systolic murmur, which lengthens as the regurgitation becomes more severe.
-

Mitral Valve prolapse

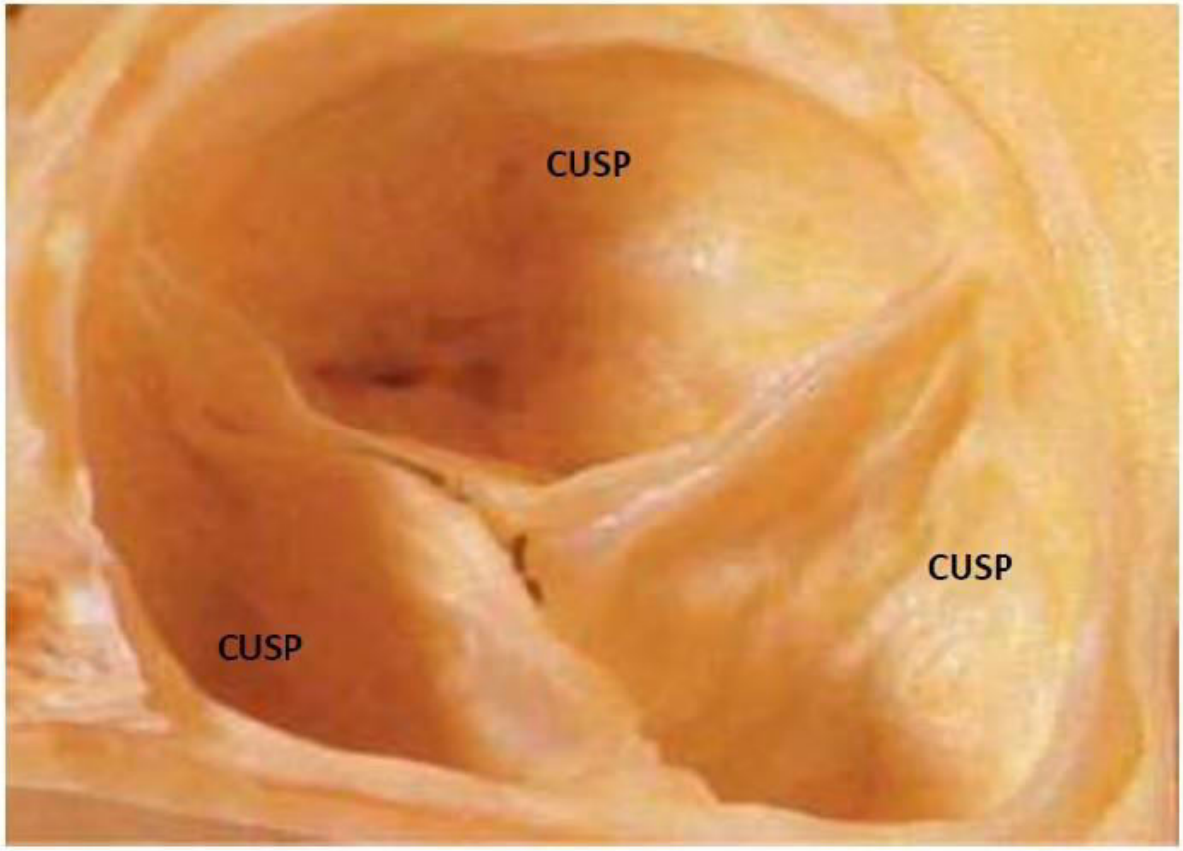


Management

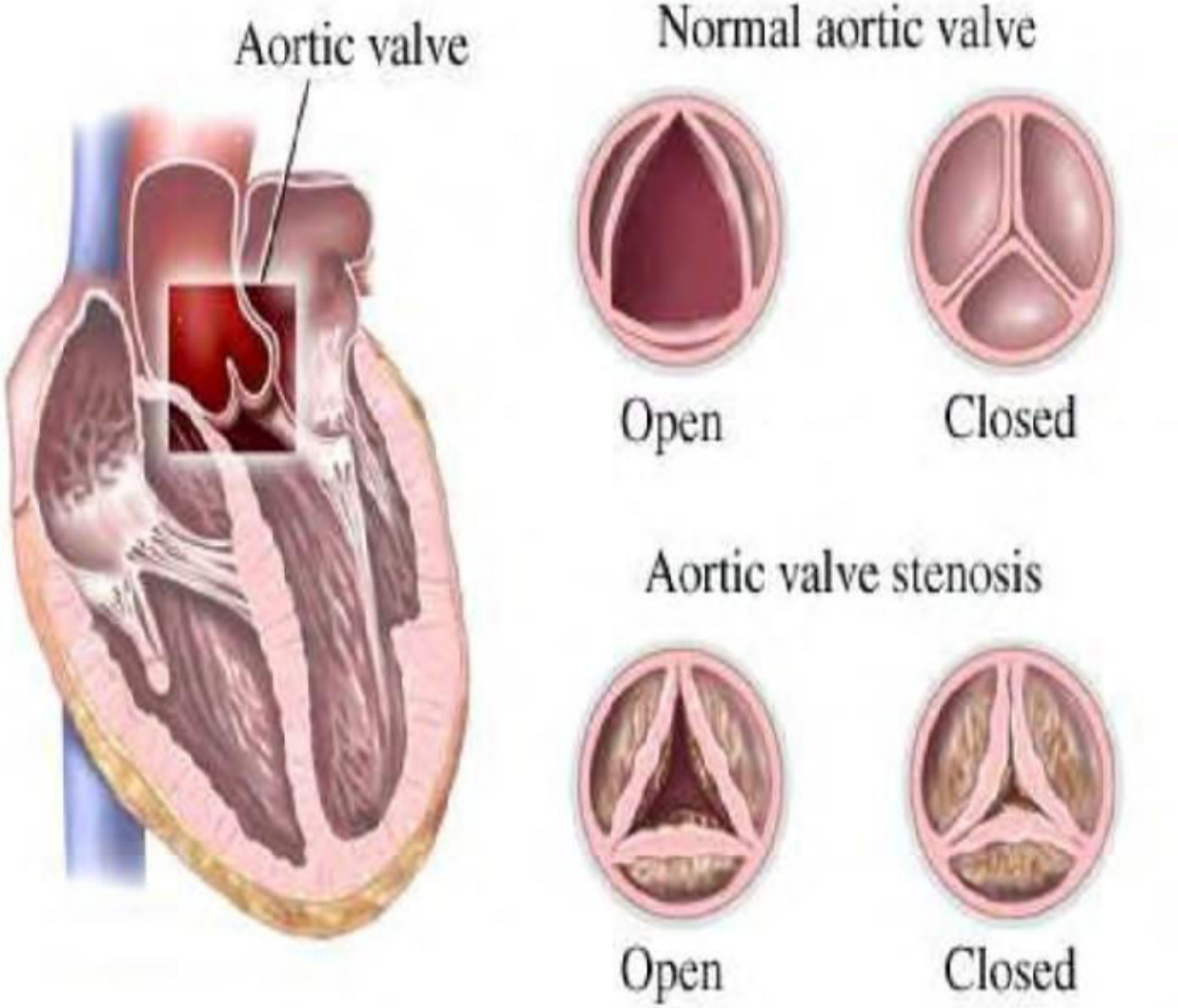
- Mitral regurgitation of mild -moderate severity can be treated medically .
- In all patients with mitral regurgitation, high afterload may worsen the degree of regurgitation, and hypertension should be treated with vasodilators, such as ACE inhibitors.
- Patients should be reviewed at regular intervals because worsening symptoms, progressive cardiomegaly or echocardiographic evidence of deteriorating left ventricular function are indications for mitral valve replacement or repair.

- Diuretics
- Vasodilators, e.g. ACE inhibitors
- Digoxin if atrial fibrillation is present
- Anticoagulants if atrial fibrillation is present

Aortic valve

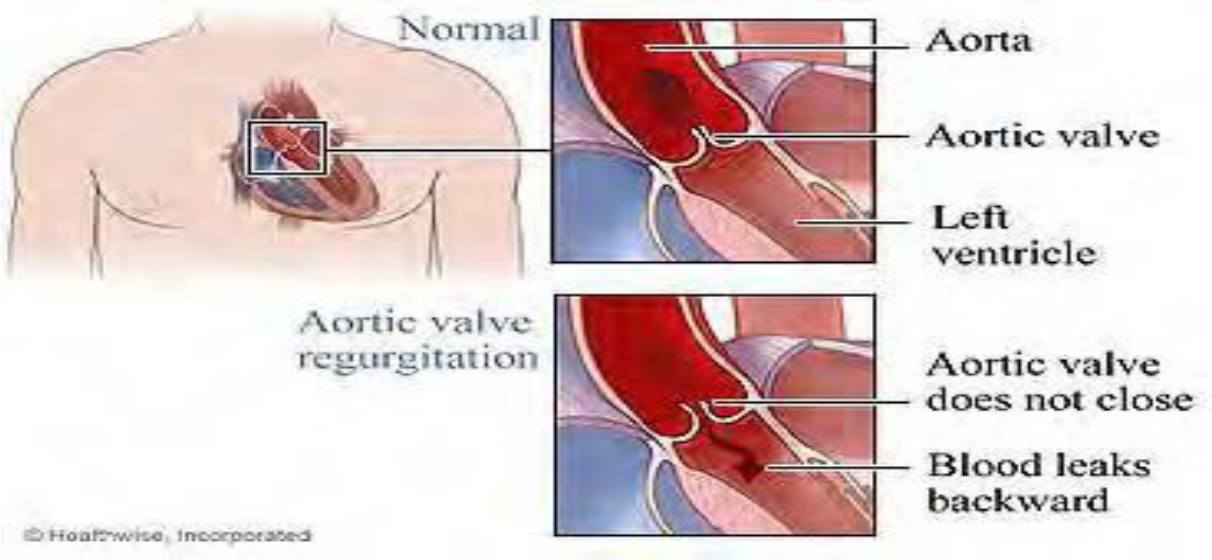


semilunar tricuspid valve allow blood flow from LV to the ascending aorta
The normal valve area is 3.0 to 4.0 cm2


Aortic valve
Normal aortic valve
Open
Closed
Aortic valve stenosis
Open
Closed

Aortic valve regurgitation

Incomplete closure of aortic valve cusps leading to regurgitation of blood back into left ventricle



Causes of aortic regurgitation

Valvular

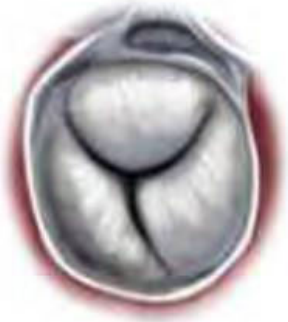
- Congenital (bicuspid aortic valve)
- Endocarditis
- Rheumatic fever
- Myxomatous (prolapse)
- Traumatic
- Syphilis
- Ankylosing spondylitis

Root disease

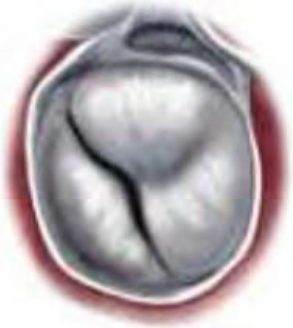
- Aortic dissection
- Cystic medial degeneration
- Marfan syndrome
- Familial aorticaneurysm
- Aortitis
- Hypertension

Congenital Bicuspid Aortic Valve

Normal tricuspid aortic valve



Bicuspid aortic valve



Clinical features od Aortic valve regurgitation

- May b asymptomatic , discover on routine exam .
- awareness of the heart beat particularly when lying on the left side, which results from the increased stroke volume
- Breathlessness.
- Paroxysmal nocturnal dyspnea is sometimes the first symptom
- peripheral edema or angina may occur.

Physical signs of AR

- **Bobbing or nodding of head with pulsation(de Musset sign)**
- **Systolic pulsations of the uvula(Müller sign)**
- **Capillary pulsations in nail (Quincke sign)**
- **Collapsing (water hamer pulse or Corrigan pulse)**
- **High Systolic BP and low diastolic BP**

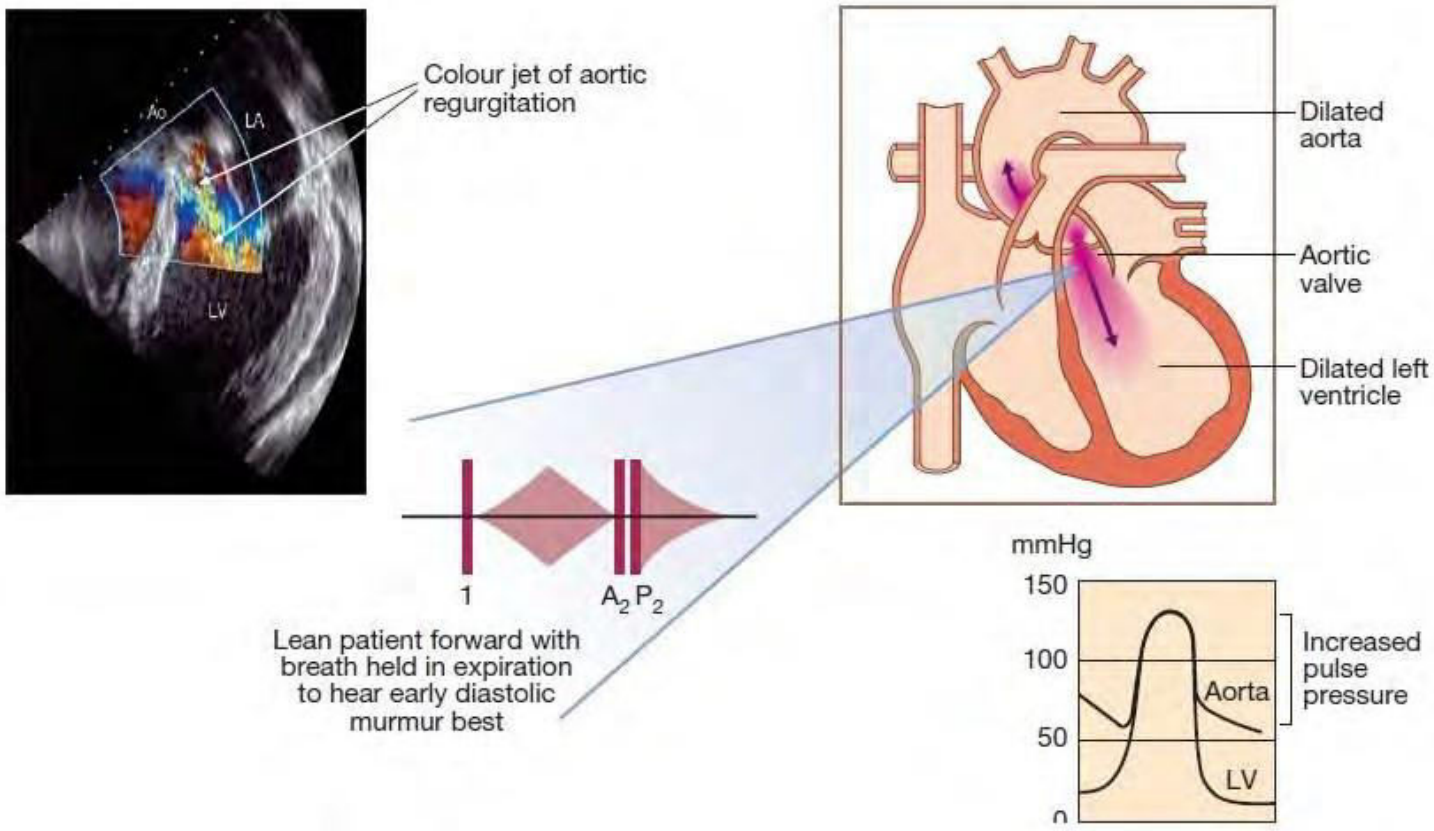
Palpation :

- **The apical impulse is diffuse and hyperdynamic and is displaced laterally and inferiorly**
- **Systolic thrill at the base of the heart or suprasternal notch and over the carotid arteries (Carotid shudder)**

Auscultation

- The characteristic **Early blowing decrescendo diastolic murmur** is best heard to the left of the sternum during held expiration a thrill is rare.
- A systolic murmur due to the increased stroke volume is common and does n necessarily indicate stenosis.
- The regurgitant jet causes fluttering of the mitral valve and, if severe, causes partial closure of the anterior mitral leaflet, leading to functional mitral stenosis and a soft mid-diastolic (Austin Flint) murmur.
- In acute severe regurgitation (e.g. perforation of aortic cusp in endocarditis), there may be no time for compensatory left ventricular hypertrophy and dilatation to develop and the features of heart failure may predominate.
- In this situation, the classical signs of aortic regurgitation may be masked by tachycardia and an abrupt rise in left ventricular end-diastolic pressure; thus, the pulse pressure may be near normal and the diastolic murmur may be short or even absent.

Auscultatory finding Aortic valve regurgitation



Symptoms

Mild to moderate aortic regurgitation

- Often asymptomatic
- Awareness of heart beat, 'palpitations'

Severe aortic regurgitation

- Breathlessness
- Angina

Signs

Pulses

- Large-volume or 'collapsing' pulse
- Low diastolic and increased pulse pressure
- Bounding peripheral pulses
- Capillary pulsation in nail beds: Quincke's sign
- Femoral bruit ('pistol shot'): Duroziez's sign
- Head nodding with pulse: de Musset's sign

Murmurs

- Early diastolic murmur
- Systolic murmur (increased stroke volume)
- Austin Flint murmur (soft mid-diastolic)

Other signs

- Displaced, heaving apex beat (volume overload)
- Pre-systolic impulse
- Fourth heart sound
- Crepitations (pulmonary venous congestion)

Investigations

- Regurgitation is detected by Doppler echocardiography
- In severe acute aortic regurgitation, the rapid rise in left ventricular diastolic pressure may cause premature mitral valve closure (leading to functional MS) .
- Cardiac catheterisation and aortography can help in assessing the severity of regurgitation, and dilatation of the aorta and the presence of coexisting coronary artery disease.
- MRI is useful in assessing the degree and extent of aortic dilatation

ECG

- Initially normal, later left ventricular hypertrophy and T-wave inversion

Chest X-ray

- Cardiac dilatation, maybe aortic dilatation
- Features of left heart failure

Echo

- Dilated LV
- Hyperdynamic LV
- Doppler detects reflux
- Fluttering anterior mitral leaflet

Cardiac catheterisation (may not be required)

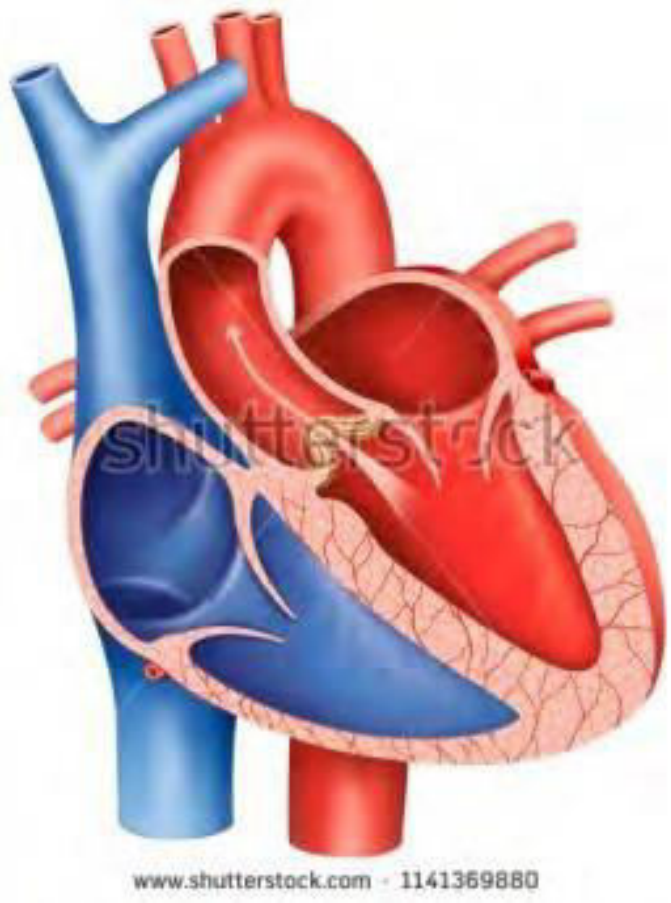
- Dilated LV
- Aortic regurgitation
- Dilated aortic root

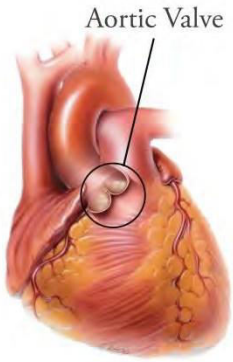
Management of AR

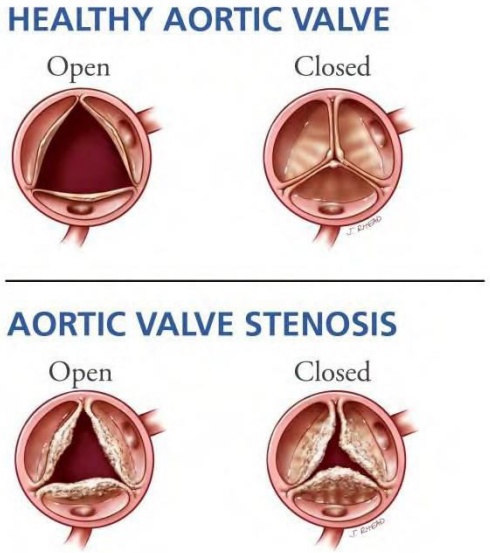
- Treatment may be required for underlying conditions, such as endocarditis or syphilis.
- Aortic valve replacement is indicated if aortic regurgitation causes symptoms, and this may need to be combined with aortic root replacement and coronary bypass surgery.
- Those with chronic aortic regurgitation can remain asymptomatic for many years because compensatory ventricular dilatation and hypertrophy occur, but should be advised to report the development of any symptoms of breathlessness or angina.
- Asymptomatic patients should also be followed up annually with echocardiography for evidence of increasing ventricular size. If this occurs or if the end-systolic dimension increases to 55 mm or more, then aortic valve replacement should be undertaken.
- Systolic BP should be controlled with vasodilating drugs, such as nifedipine or ACE inhibitors.
- When aortic root dilatation is the cause of aortic regurgitation (e.g. Marfan's syndrome), aortic root replacement is usually necessary

Aortic valve stenosis

- **When the valve area less than 3 cm 2 it indicate aortic valve stenosis associated with decreased flow across aortic valve .**
- **AS occurs in about 25% of all patients with chronic valvular heart disease; approximately 80% of adult patients with symptomatic valvular AS are male**


shutterstock
www.shutterstock.com · 1141369880


Aortic Valve


HEALTHY AORTIC VALVE
Open
Closed
AORTIC VALVE STENOSIS
Open
Closed

Causes of aortic stenosis

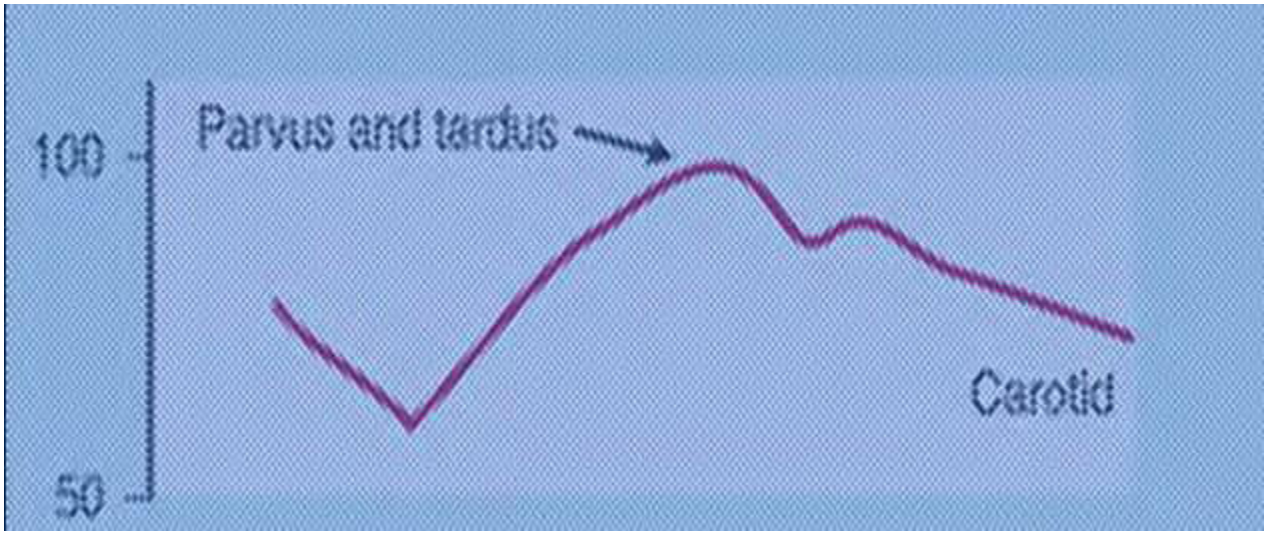
Infants, children, adolescents
• Congenital aortic stenosis • Congenital subvalvular aortic stenosis • Congenital supravalvular aortic stenosis
Young adults to middle-aged
• Calcification and fibrosis of congenitally bicuspid aortic valve • Rheumatic aortic stenosis
Middle-aged to elderly
• Senile degenerative aortic stenosis • Calcification of bicuspid valve • Rheumatic aortic stenosis

Clinical features of aortic stenosis

Symptoms	
• Mild or moderate stenosis: usually asymptomatic • Exertional dyspnoea • Angina	• Exertional syncope • Sudden death • Episodes of acute pulmonary oedema
Signs	
• Ejection systolic murmur • Slow-rising carotid pulse • Thrusting apex beat (LV pressure overload)	• Narrow pulse pressure • Signs of pulmonary venous congestion (e.g. crepitations)

Physical signs of AS

- **Carotid pulses are:**
- **slow-rising, late-peaking,**
- **low-amplitude carotid pulse, the “parvus and tardus” carotid impuls**



Clinical features

- Aortic stenosis is commonly picked up in asymptomatic patients at routine clinical examination but the three cardinal symptoms are :
- angina,
- Breathlessness
- syncope
- . Angina arises because of the increased demands of the hypertrophied LV working against the high-pressure outflow tract obstruction, leading to a mismatch between oxygen demand and supply, but may also be due to coexisting coronary artery disease, especially in old age, when it affects over 50% of patients.

- Exertional breathlessness suggests cardiac decompensation as a consequence of the excessive pressure overload placed on the LV.

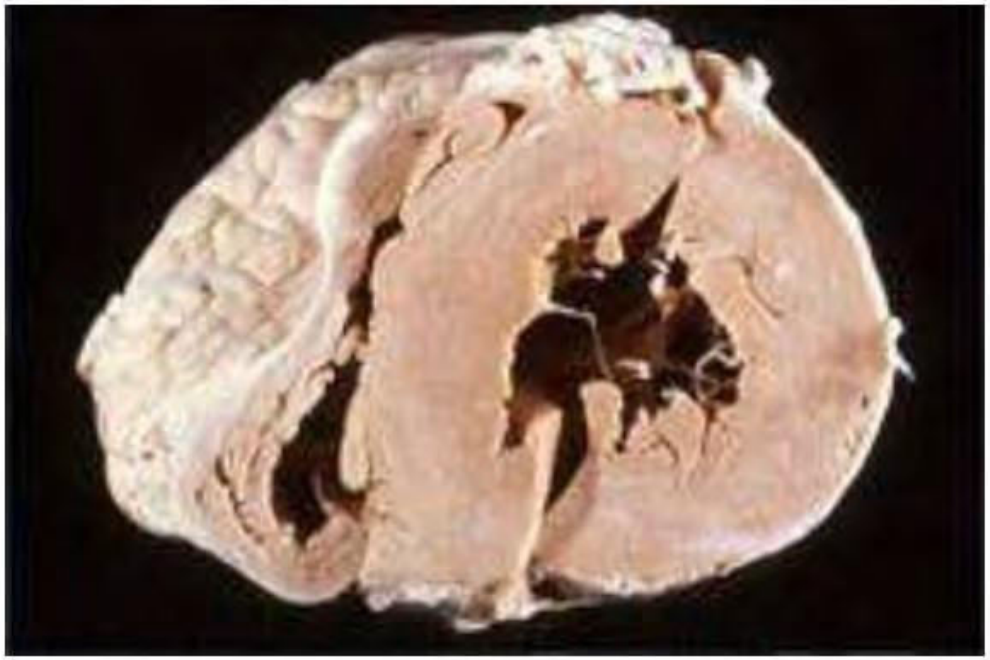
- Syncope usually occurs on exertion when cardiac output fails to rise to meet demand, leading to a fall in BP.
- A harsh ejection systolic murmur radiates to the neck, with a soft second heart sound, particularly in those with calcific valves.
- The murmur is often likened to a saw cutting wood and may (especially in older patients) have a musical quality like the ‘mew’ of a seagull .
- The severity of aortic stenosis may be difficult to gauge clinically, as older patients with a non-compliant ‘stiff’ arterial system may have an apparently normal carotid upstroke in the presence of severe aortic stenosis.
- Milder degrees of stenosis may be difficult to distinguish from aortic sclerosis, in which the valve is thickened or calcified but not

Have significant pressure gradient across it.

Investigations in aortic stenosis

ECG
• Left ventricular hypertrophy (usually) • Left bundle branch block
Chest X-ray
• May be normal; sometimes enlarged LV and dilated ascending aorta on PA view, calcified valve on lateral view
Echo
• Calcified valve with restricted opening, hypertrophied LV
Doppler
• Measurement of severity of stenosis • Detection of associated aortic regurgitation
Cardiac catheterisation
• Mainly to identify associated coronary artery disease • May be used to measure gradient between LV and aorta

Left Ventricular Hypertrophy



LVH Aortic Stenosis

Management

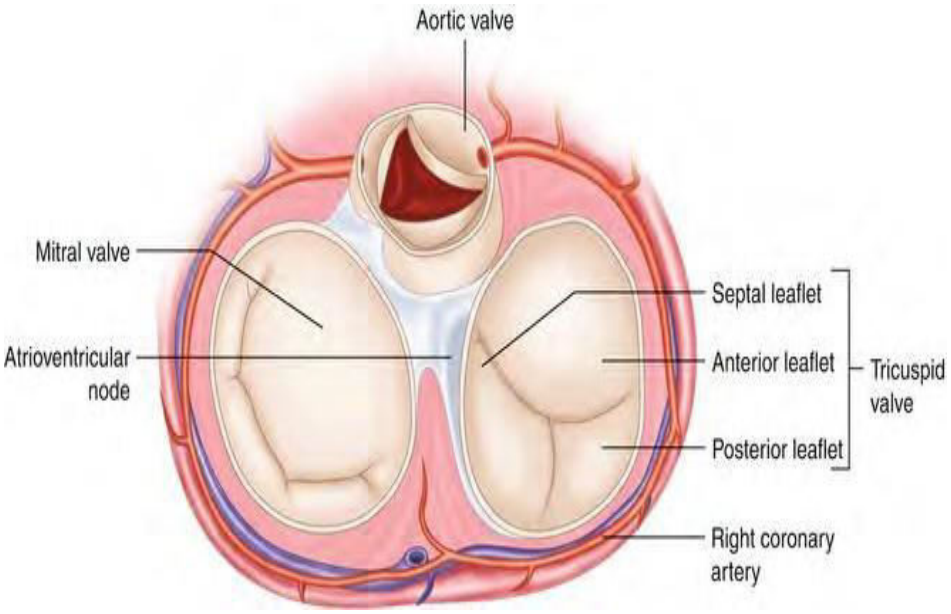
- Irrespective of the severity of valve stenosis, patients with asymptomatic aortic stenosis have a good immediate prognosis and conservative management is appropriate.
- Such patients should be kept under review, as the development of angina, syncope, symptoms of low cardiac output or heart failure has a poor prognosis and is an indication for prompt surgery.

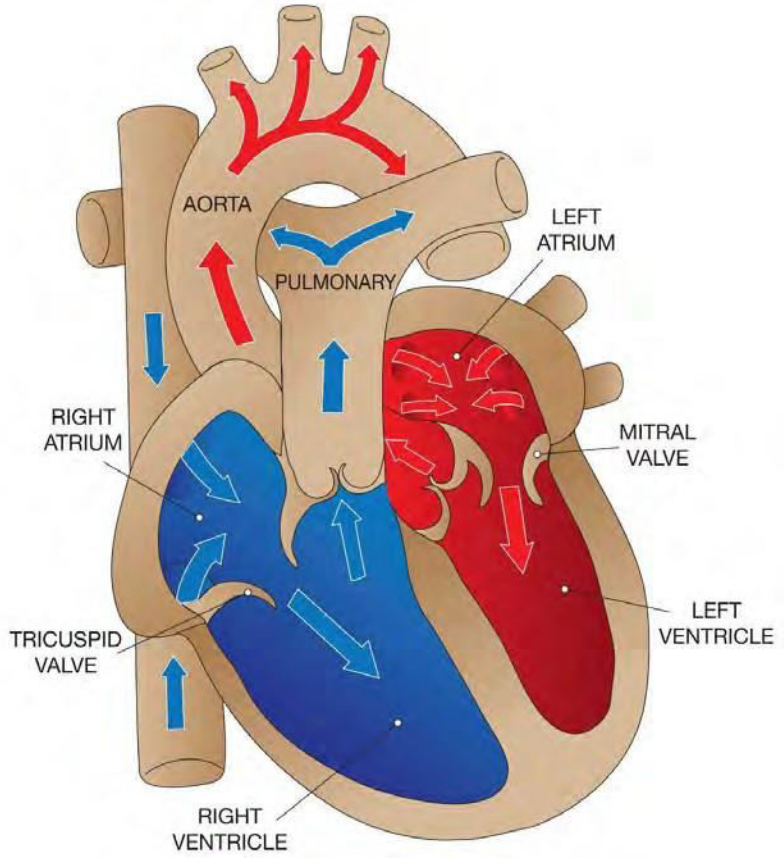
- In practice, patients with moderate or severe stenosis are evaluated every 1–2 years with Doppler echocardiography to detect progression in severity; this is more rapid in older patients with heavily calcified valves.
- Patients with symptomatic severe aortic stenosis should have prompt aortic valve replacement.

- Old age is not a contraindication to valve replacement and results are very good in experienced centers, even for those in their eighties .
- Delay exposes the patient to the risk of sudden death or irreversible deterioration in ventricular function.

Tricuspid valve

- It is a three leaflet atrio-ventricular valve between RA & RV allow the blood flow in one direction from RA to RV





Tricuspid valve disease

Tricuspid stenosis

Aetiology

- Tricuspid stenosis is usually rheumatic in origin and is rare in developed countries. Tricuspid disease occurs in fewer than 5% of patients with rheumatic heart disease and then nearly always in association with mitral and aortic valve disease.
- Carcinoid syndrome : Tricuspid stenosis and regurgitation

Clinical features and investigations

Although the symptoms of mitral and aortic valve disease predominate, tricuspid stenosis may cause symptoms of right heart failure including :

- hepatic discomfort
- peripheral edema.

The main clinical feature is a raised JVP with a prominent *a* wave, and a slow *y* descent due to the loss of normal rapid right ventricular filling .

There is also a mid-diastolic murmur, best heard at the lower left or right sternal edge.

This is generally higher-pitched than the murmur of mitral stenosis and is increased by inspiration.

Right heart failure causes hepatomegaly with pre-systolic pulsation (large *a* wave), ascites and peripheral edema. On Doppler echocardiography, the valve has similar appearances to those of rheumatic mitral stenosis

Management

- In patients who require surgery to other valves, either the tricuspid valve is replaced or valvotomy is performed at surgery.
- Balloon valvuloplasty can be used to treat rare cases of isolated tricuspid stenosis.

Tricuspid regurgitation

- Tricuspid regurgitation is common, and is most frequently ‘functional’ as a result of right ventricular dilatation Symptoms are usually non-specific, with tiredness related to reduced forward flow, and oedema and hepatic enlargement due to venous congestion.
- The most prominent sign is a ‘giant’ *v* wave in the jugular venous pulse (a *cv* wave replaces the normal *x* descent).

Causes of tricuspid regurgitation

Primary

- Rheumatic heart disease
- Endocarditis, particularly in injection drug-users
- Ebstein's congenital anomaly (see Box 18.123, p. 635)

Secondary

- Right ventricular dilatation due to chronic left heart failure ('functional tricuspid regurgitation')
- Right ventricular infarction
- Pulmonary hypertension (e.g. cor pulmonale)

- pan systolic murmur at the left Sternal border and a pulsatile liver.
- Echocardiography may reveal dilatation of the RV. If the valve has been affected by rheumatic disease, the leaflets will appear thickened and, in endocarditis, vegetation may be seen.
- Ebstein's anomaly is a congenital abnormality in which the tricuspid valve is displaced towards the right ventricular apex, with consequent enlargement of the RA. It is commonly associated with tricuspid regurgitation.

Management

- Tricuspid regurgitation due to right ventricular dilatation often improves when the cause of right ventricular overload is corrected, with diuretic and vasodilator
- Patients with a normal pulmonary artery pressure tolerate isolated tricuspid reflux well, and valves damaged by endocarditis do not usually need to be replaced.
- Patients undergoing mitral valve replacement, who have tricuspid regurgitation due to marked dilatation of the tricuspid annulus, benefit from valve repair with an annuloplasty ring to bring the leaflets closer together. Those with rheumatic damage may require tricuspid valve replacement.

Acute Coronary syndrome

ACS encompasses wide spectrum of Acute Ischaemic syndromes starting with Unstable Angina through Acute Non ST-elevation MI to Acute ST-Elevation MI.

It extends from Recurrent Angina at one end , to include sudden death due to extensive MI and Cardiogenic shock.

If the chest pain and the RFs are classical ACS can confidently diagnosis by history only. Investigations will confirm the diagnosis and will subclassify it and assess the severity of the case.

Clinical features of ACS

1 Anginal pain severe < 30 min in UA and longer MI. But can be painless in the elderly and in diabetic

2 SOB not severe unless developed Pul oedema

2 Sweating ; profuse in Acute MI

4- Nausea and Vomiting in acute MI

5- Tachycardia but may be bradycardia in Inf. MI

6- Anxiety and fear impending death

7- Collapse or syncope due hypotension or arrhythm.

7 Death from VF or asystole may occur in the first hour in 10-15% ie die intantly anywhere eg; at home or during sleep

ACS other symptoms

SOB depends on the amount of the LV dysfunction which becomes worse with pain reaching the feelong of suffocation. If the amount of Ischaemia is large it may lead to transient acute LV failure.

Palpitation and syncope can occur and are more frequent in extensive underlying disease.

Differential Diagnosis

- **A- central chst pain**
- **1--Aortic dissection**
- **3- Oesophageal spasm**
- **4- Pul Embolism**
- **B- Left sided Chest pain**
- **1 Pulmonary infarction**
- **2 Causes of atypical chest pain**

Unstable Angina Clinical Classification

UA is divided into four categories depending on the clinical Characteristics of the pain of

1- New onset Angina

2-Rapidly deteriorating Angina

3- Angina at rest

4- Long episode of angina Up to 30 min but without cardiac damage.

The pain can be recurrent or variable in intensity (wax and wane) and dictated by the coronary flow which is determined by stenosis severity, the underlying thrombus , and the possible spasm

Unstable Angina investigations

- **ECG and Echo**
- **Like CSA both ECG and Echo can show evidence of Ischaemia during pain.**
- **Cardiac enzymes and troponins as markers of myocardial damage are normal.**
- **Nowadays with advent of highly sensitive assays small minority of pts with UA a rise of troponins can be detected and is regarded as high risk group or they are regarded as Non St Elevation MI**

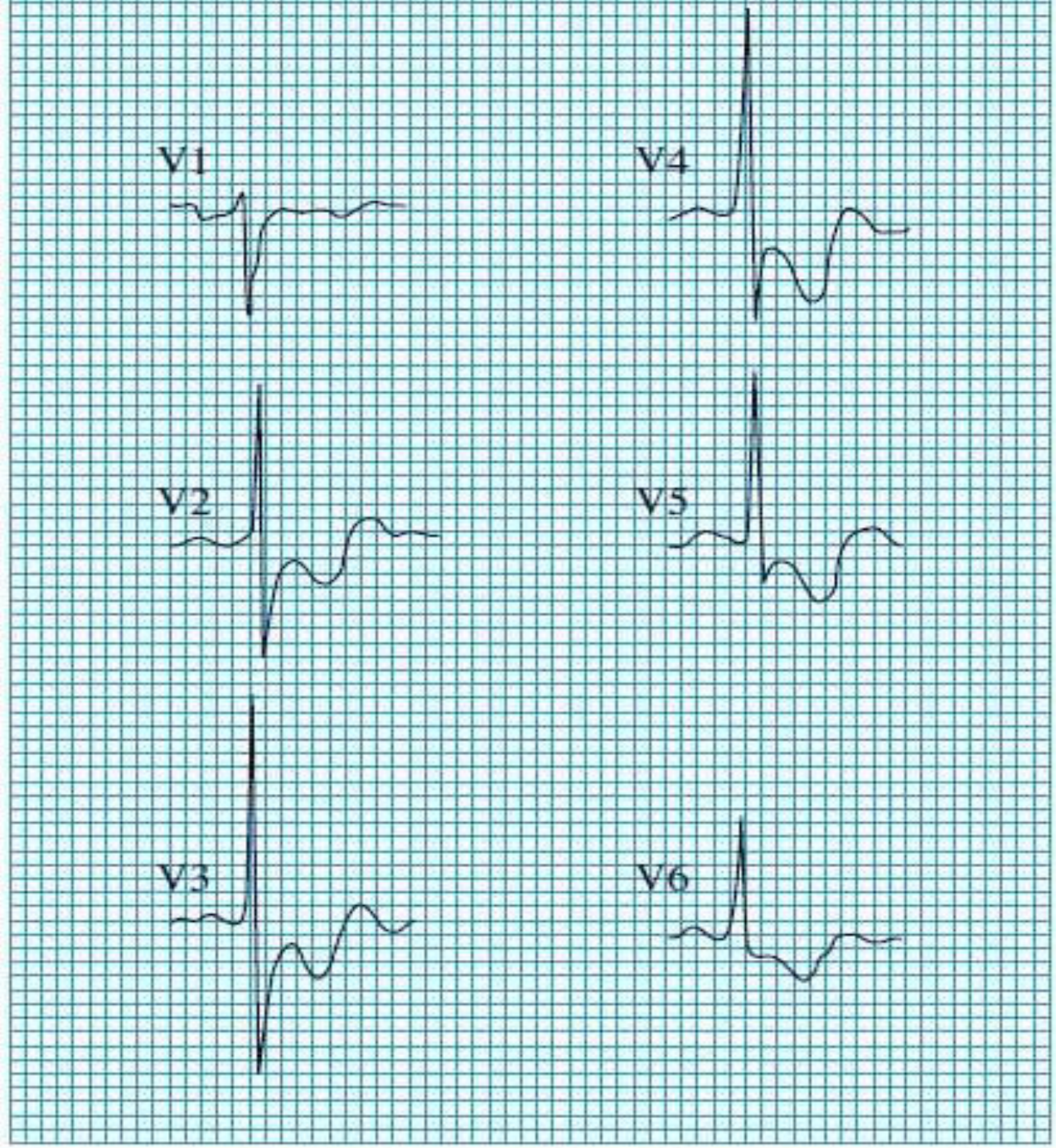
UA Diagnosis

1Classical pains in a susceptible pt is diagnostic

2Investigations may confirm or exclude the diagnosis

3if the case is doubtful the pt must be labeled as suspected UA and managed like a certain UA case until the diagnosis is clear.

downsloping. Whereas
ggests ischaemia,
as they are also found in
trophy and in patients
ment depression in any
R wave. Thus, ST segment
leads V4 to V6 of the 12
cause the height of the
gree of ST depression in
eat. ST segment
n the inferior leads
smaller. Substantial
ST depression is a grave
pread myocardial
rtery disease. ST segment
esolution with treatment is
s continuous ST segment
ctrocardiogram over a few
anges are associated with
elpful in confirming the
serial changes confer a
for increased drug



Widespread ST segment depression in patient with

UA assessing the Risk

Grace Risk score identifies pts at risk of death or MI based on admission clinical findings :-

1-Age HR, BP, RF, CCF, STE, C arrest , Troponins.

2-Medium score { 1-9}

3- High score (1-9),

4- Reccurent ischaemia

5-- Diabetics.

6 Haemodynamically unstable

7 Electerically Unstable

scors need invasive strarategy ie Angiography and Revascularization

ALSO the compromise

Low Risk pts (score <1)for Conservative Rx

Teachers story

He was put on ISMN 20 mg/d, Atenolol 50 mg /d Atorvastatin 20 mg /d, and Aspirin 100mg /d . He stopped smoking He became asymptomatic.

Then he was lost to follow up

- **Two years later He appeared in the casualty when he developed prolonged chest pain (for 20 min) with sweating. He admitted that his pains has recently become more frequent and occurring even at rest but with no nausea or vomiting. His wife said he was not complaint with medications and he was still smoking**

His Examinationn and his ECG and Echo were normal. His Trop- onins were negative He was admitted to the CCU and treated as a case of Unstable Angina

Common Management of UA

1- CCU admission 2- Serial ECG, 3- Biomarkers and 4- Haemodynamic moitoring 5- > 60% Oxygen

6 Aspirin 100 mg or Clopidogril 75 mg

7Nitroglycerine infusion 0.6-1.2 mg/hr or ISDN 1-2 mg/hr is given it can relive pain if maximal dose fail to relieve pain then use Narcotic analgesics

8 Heparin SC either Pentasaccharide Fondaparinux 2.5 mg s.c or OR LMW heparin Enoxaparin 1.0 mg/kg 12 hrly i

9- I.V. Betablocker Atenolol 5-10mg or Metoprolol 5-15m every 5.0 min followed by oral Atenolol 50mg daily or Metoprolol 50mg twice a day

10 – Statin eg Atorvastatin 20 m orally

Specific Treatment for the Invasive strategy

This group will be sent for intervention. They will be given in addition to the common RX

1- High dose Clopidogril 600mg then150 mg for one week,and the 75 mg afterwards

Or Ticagrelol 180 mg then 90 mg 12 hrly

2- GP 11b/111a Receptors Blockers such Tirofiban or Abciximab a powerful antithrombotic agent will be infused before and during the Intervention .

Acute Myocardial Infarction

- **Acute Ischaemic Myocardial necrosis due to sudden interuption of blood supply by an occlusive thrombus at the site of rupture or erosion of atheromatous plaque.**
- **Complete occlusion causesAcute Transmuural infarction ;- Acute ST-Elevation MI**
- **If the ensuing ischaemia is not involving the whole thickness off the wall then it causes Nontransmuural MI usually the subendocardial layer ie Non ST-Elevation MI**

The Teacher's story

- **Few weeks later he presented with severe retrosternal pain increasing in severity for an hr. The pain was constrictive associated with sweating and nausea but no vomiting .**
- **His ECG showed 2 mm ST depression and Symmetrical T wave inversion on V2-5**
- **BIOMARKERS were more than twice normal**
- **He was Treated as NSEMI in the causality and**

  improved he refused admission and decided to go home against advice.

Acute coronary Syndrome
Acute MI Sub-classification

- **It all depends on whether the patient has Evolutionary ST-Segment Elevation or NOT**

Hence we two type

1. **Acute ST Elevation MI (STEMI)**
2. **Acute Non-ST-Elevation (NSTEM)I**

Symptoms of Acute MI

- 1- Pain is the cardinal symptom.
- similar in characters CSA pain but it is usually
- A- Severe
- B – lasts longer >30 min
- C- Constricting ,Suffocating Chocking or Weight-like
- D- Retrosternal or across the chest and may be felt
- in the throat, epigastrium, arm, or in the back
- 2- **SOB is common**. This can be the only symptom
- 3- Palpitations , Syncope and Collapse may occur .
- They are due to Arrhythmia and Hypotension
- 4 -Can be Silent in the elderly or the diabetic

The Teacher's Story continued

- **As he was noncompliant with plan Few weeks later he developed severe continuous burning pain across his chest with profuse sweating , nausea and vomiting and arrested with VF on arrival there.**
- **He was promptly resuscitated and converted to sinus rhythm by DC cardio version**
- **his subsequent ECG showed ST segment Elevation by 5 mm on V3- V6 he was shifted to the CCU .**

Signs of ACUTE MI

1 Signs of Sympathetic stimulation :- Tachycardia ,Pallor, and Sweating

2 Signs of Parasympathetic stimulation :-Vomiting and bradycardia.

3 Signs of impaired function :- Hypotension Oliguria, cold peripheries Thredy pulse, queit 1st Ht sound, 3rd heart sound, diffuse apex, and basal crepitations.

4 Signs of tissue damage :- Fever

5 Signs of complications:- Mitral regurgitation, ETC

6 Sudden death VF can the first sign. The risk decrease as hours pass. LV .Failure comes after

&- No SIGNS ie Silent

Evolution (Sequence) of MI ECG changes

1- STEMI (ST-Elevation MI)

Total occlusion of a major CA proximally causes

- **ST Elevation**
- **R diminution**
- **Q appearance**
- **T- inversion that may persists** .

2- NSTEMI (Non ST elevation MI)

Partial occlusion of major CA or total occlusion of a minor vessel

1 **ST depression**

2 **R- diminution.**

3 **T- inversion, may be deep and symmetrical**

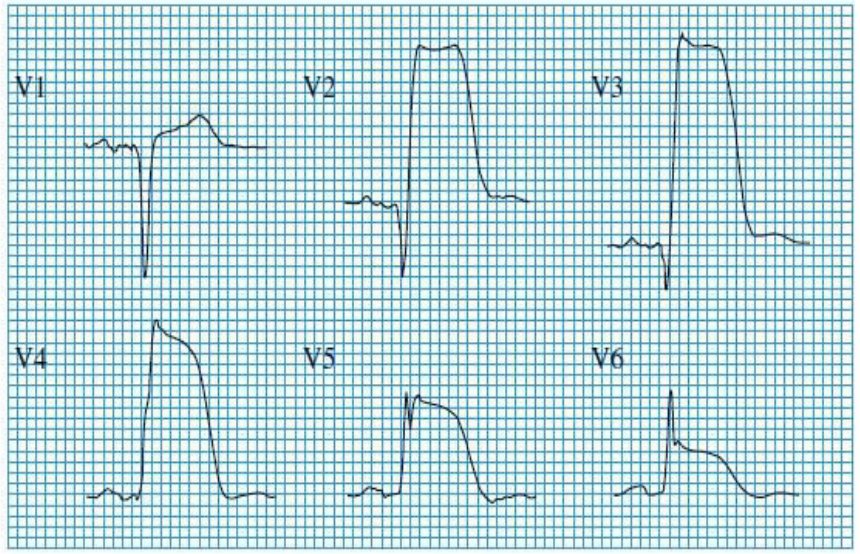
Localization of MI by ECG changes (needs two adjacent leads)

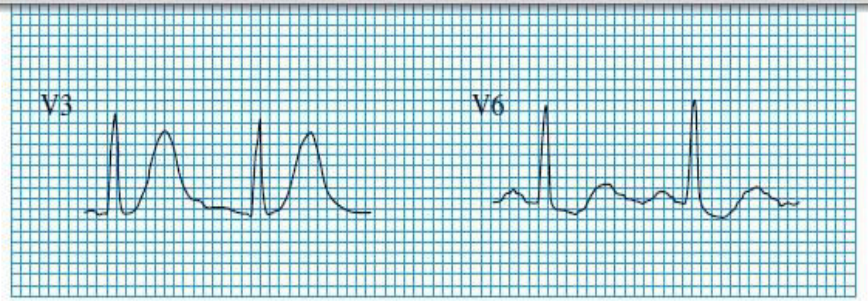
Anterior MI	**V2 –V6**
Inferior MI	**LII and / or LIII + AVF**
Lateral MI	**LI and AVL +- V5-6**

Antero-lateral	**V2 – V6 + LI and AVL**
Infero-lateral	**LII -LIII + AVF and L1 + AVL**
Antero-Septal	**V2 –V4**
True Posterior	**V1 – V4 (Tall R + ST↓)**
RV Infarction	**Inf. MI+ VR3-4**

Acute Anterior MI

varies between subtle changes of < 1 mm to gross elevation of > 10 mm.

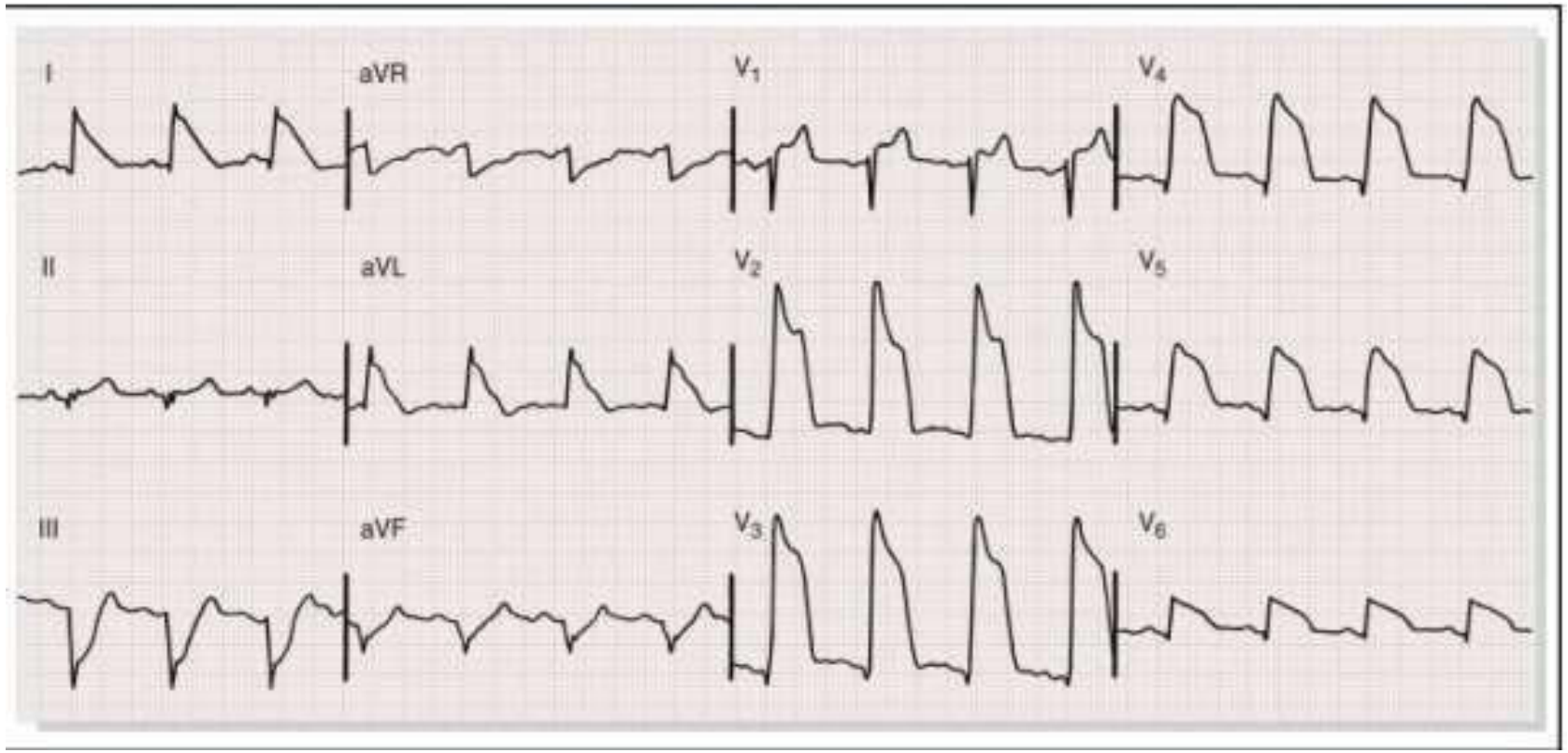




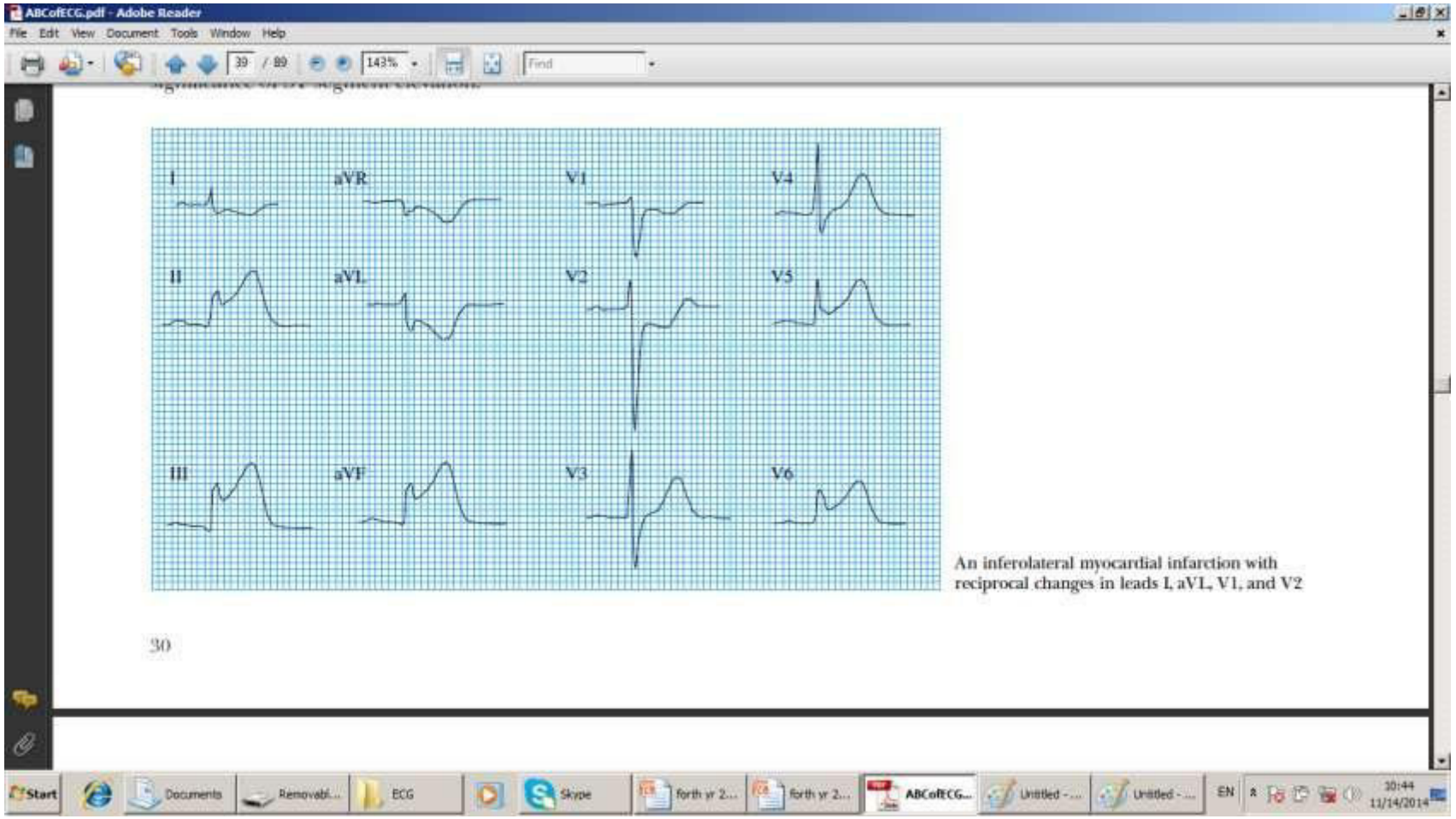
Hyperacute T waves

Sometimes the QRS complex, the ST segment, and the T wave fuse to form a single monophasic deflection, called a giant R wave or "tombstone"

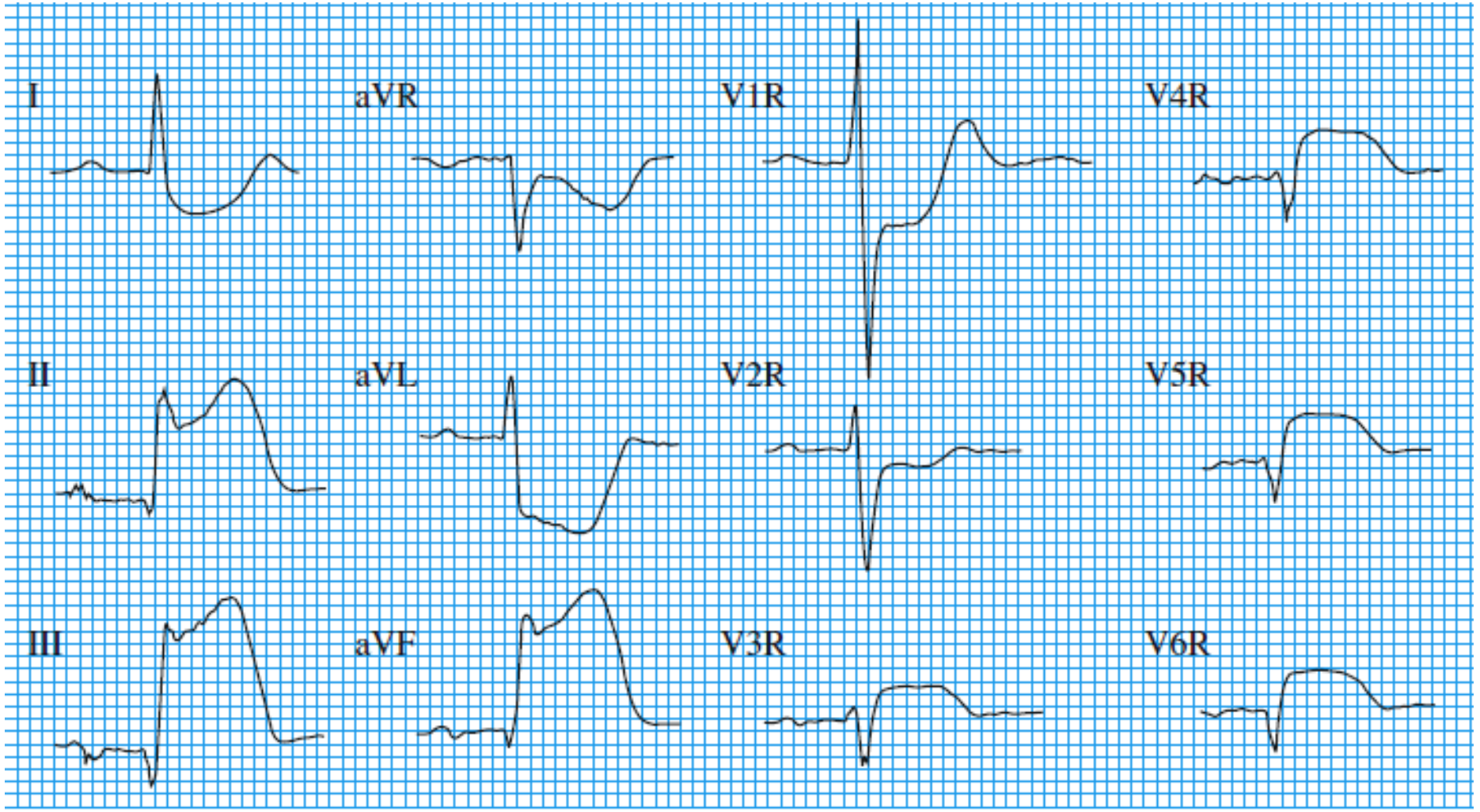
Anterior myocardial infarction with gross ST segment elevation (showing "tombstone" R waves)


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

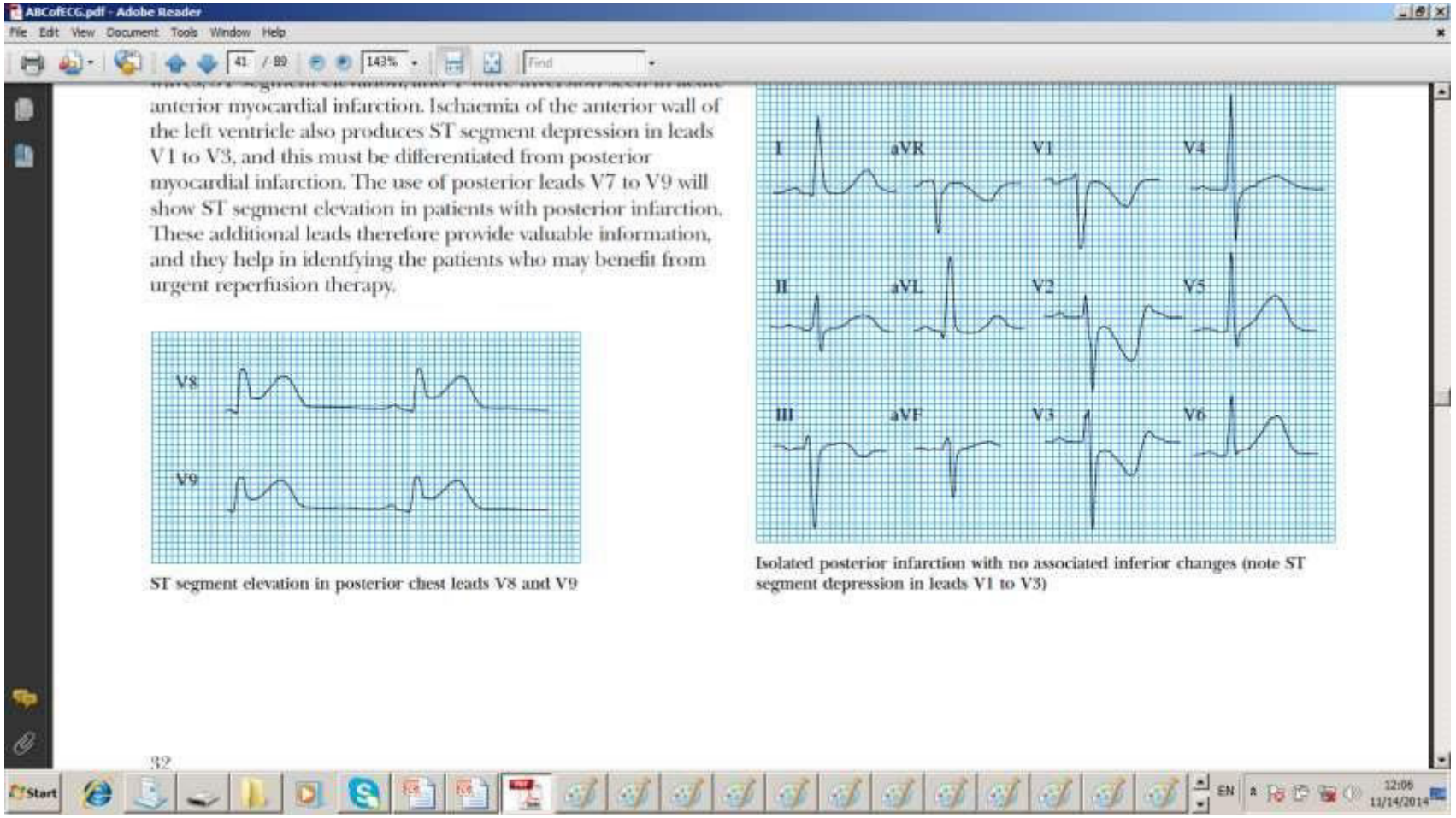
Acute Infero- lateral MI



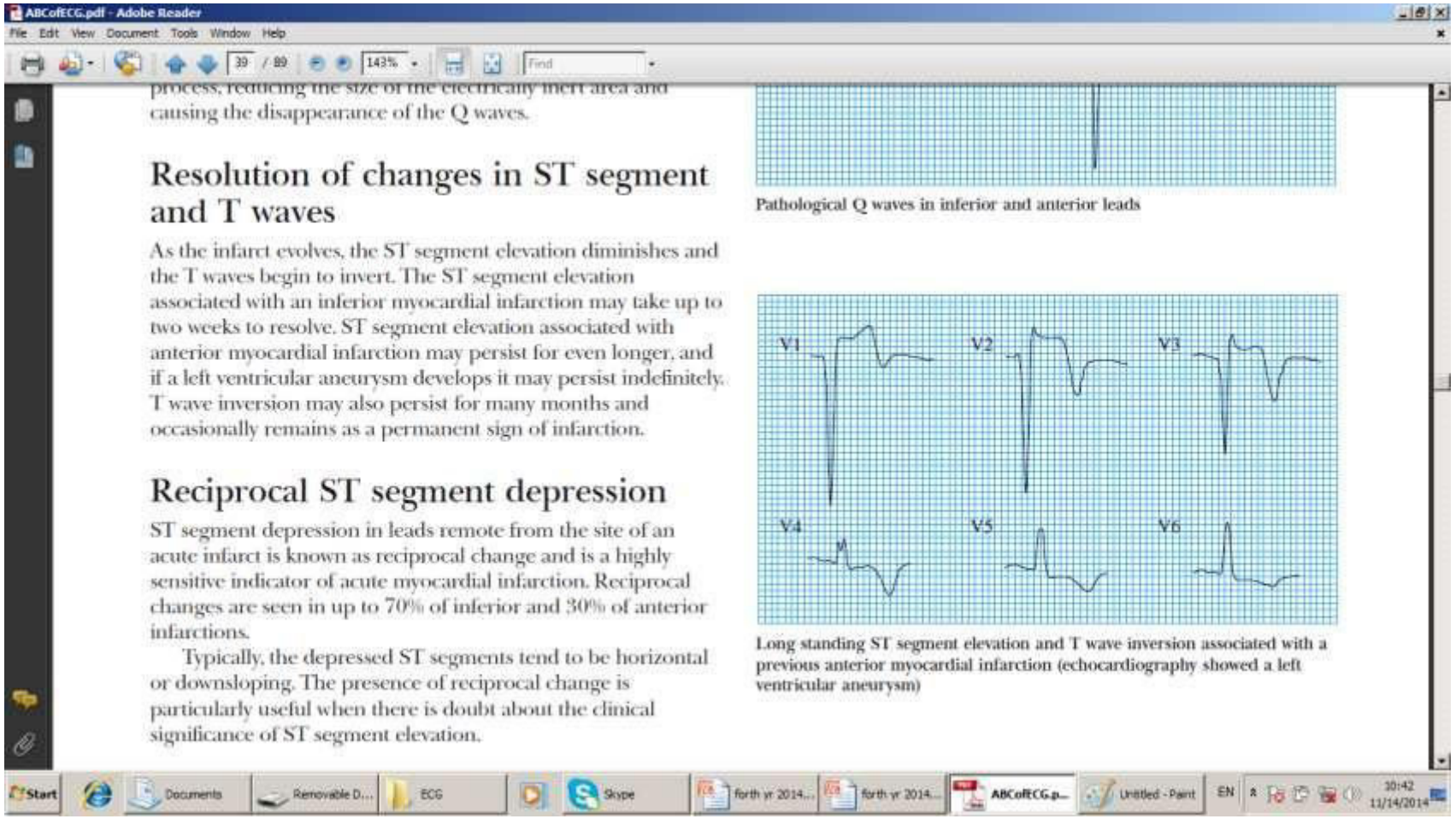
Acute inferior MI and RV infarction



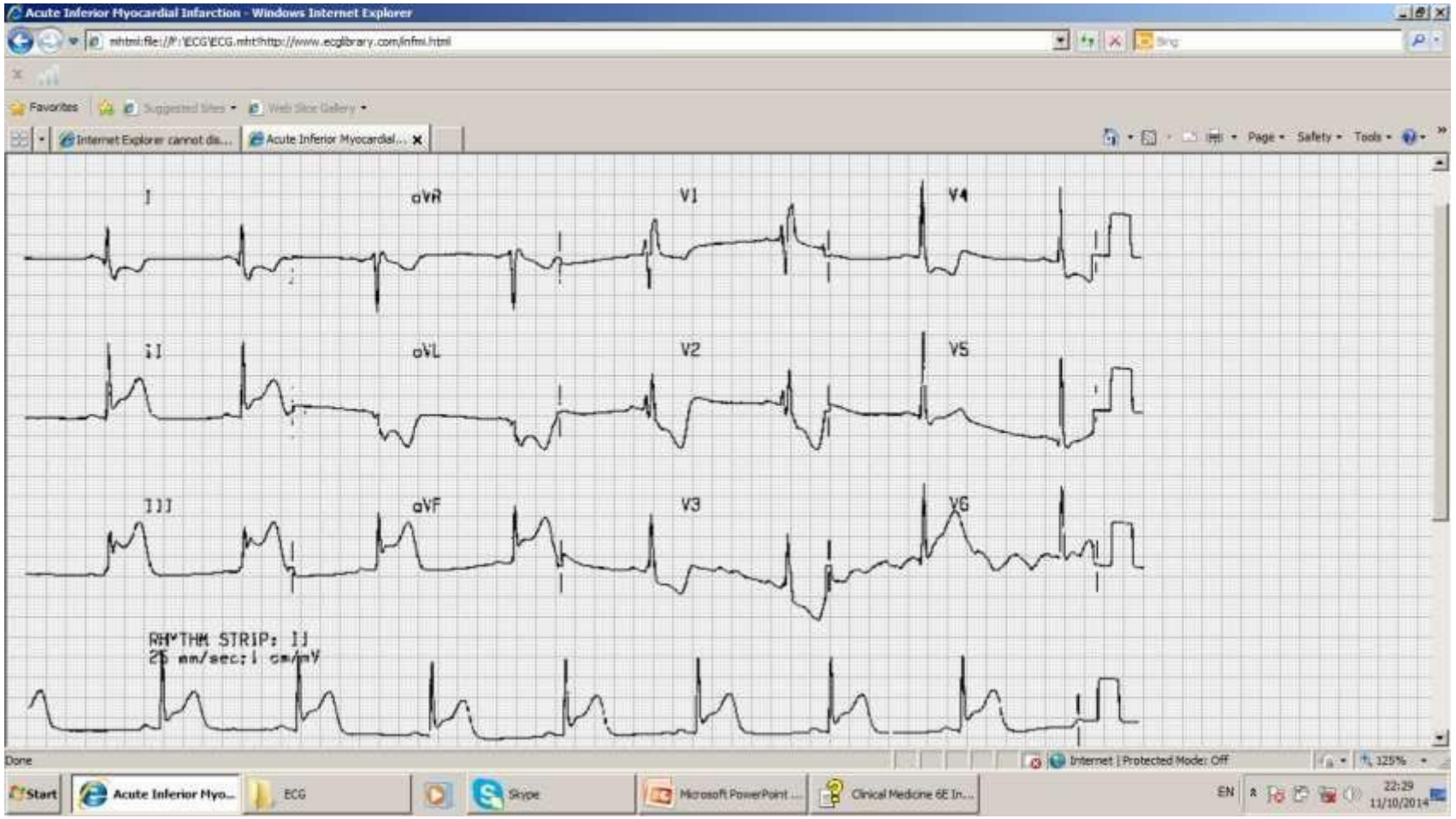
True Posterior MI



Persistent Q Wave indicates Old MI Persistent ST elevation May indicate Aneurysm



Acute Inferior MI and Partial RBBB



Normal Variance ST elevation

ABCofECG.pdf - Adobe Reader

File Edit View Document Tools Window Help

44 / 89 143% Find

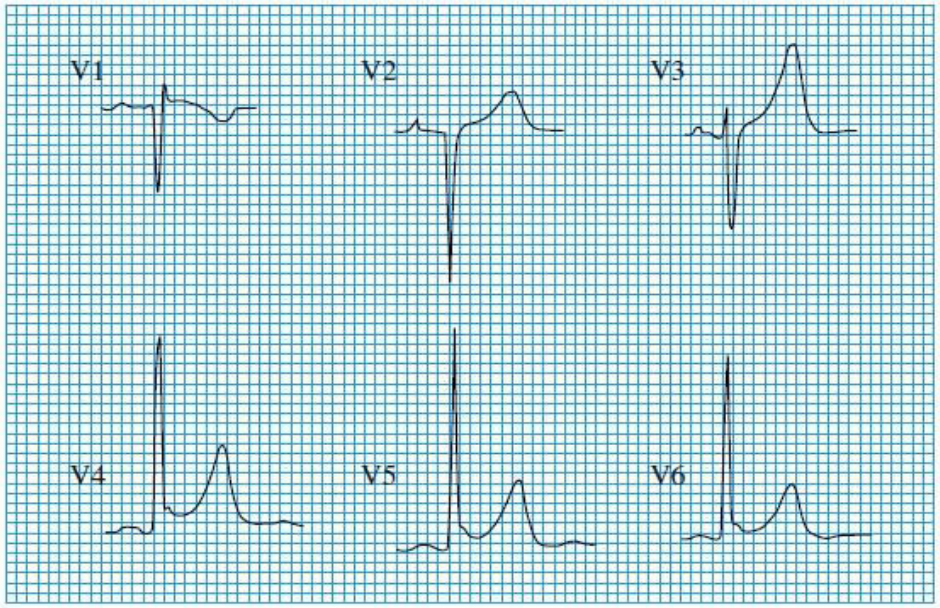
Serial electrocardiography or continuous ST segment monitoring is also useful as ischaemic ST segment elevation evolves over time. Old electrocardiograms are also useful for comparison.

"High take-off"

Care is required when interpreting ST segment elevation in right sided chest leads as the ST segments, particularly in leads V2 and V3, tend to be upsloping rather than flat. Isolated ST segment elevation in these leads should be interpreted with caution. (For more information on "high take-off" see the second article in this series.)

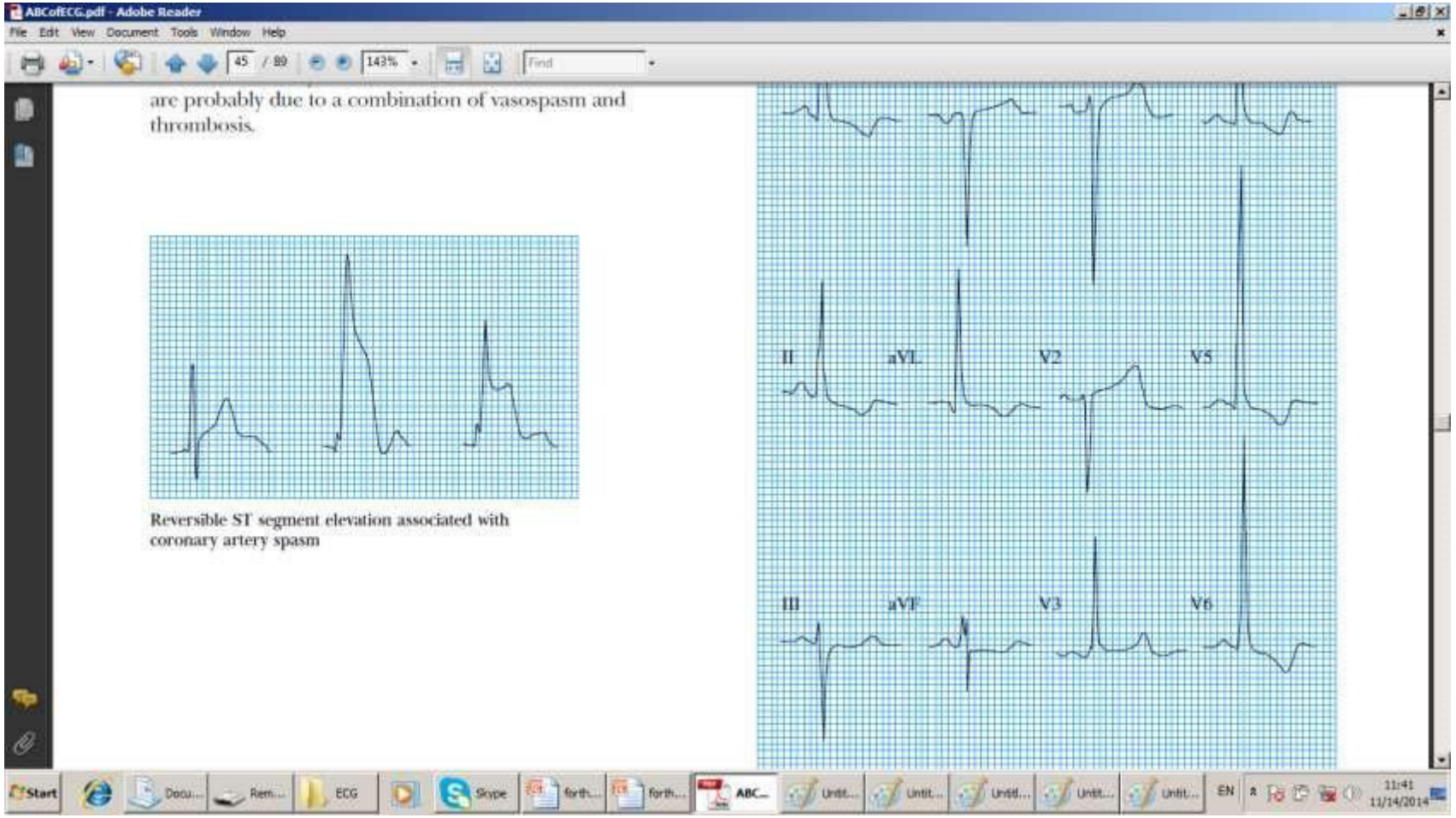
Benign early repolarisation

A degree of ST segment elevation is often present in healthy individuals, especially in young adults and in people of African descent. This ST segment elevation is most commonly seen in



Benign early repolarisation

CA spasm and LVH



Biomarkers and Cardiac Enzymes

- **Troponins I an T are very sensitive They rise early (in 4-6) and stay elevated up to 2 weeks days . Can rise in Pul embolism .and Acute Pul oedema but not in cardioversion**
- **CKMB Rises Early in(4-6) and drops in 48-72 hrs (not released from cardioversion)**
- **Myoglobin rises very early (2-3 hrs) and drops quickly. It can also be released from skeletal muscles**

Diagnosis of Acute MI

- **One of the following meet the diagnosis of MI :-**

1- > Twice normal rise and fall of Biomarkers or

Cardiac Enzymes with one of the followings

a. **Symptoms of Myocardial Ischaemia ie Chest Pain**

b. **ischaemic ST-T changes or new LBBB or new pathological Q-waves**

c - **Immaging evidence of loss of viable myocardium or new regional wall motion abnormality**

2- Cardiac arrest or sudden death with one of the above and / or evidence of fresh thrombus on angiography or autopsy

3-Pathological finding of Acute MI

Diagnosis of A MI

1- Troponins (T or I) **or** **Enzymes (rise and fall)**

PLUS either

2- Pain (Ischaemic) **OR** **ECG (Evolutionary)**

Other investigations

↑ WBC Peak

1st day

↑ ESR Peak in few days

CXR

Early: Normal Size heart

± LVF

Later: cardiomegaly in most cases

Echo + Doppler

1. Hypokinesia / Akinesia

LV or

RV dilatation

2.Detects complication

a. P. effusion

b. MR

c. VCD

d. Cardiac rupture

Thrombosis in ACUTE MI

- **Occur on the background of a plaque of any sizes but more frequent on a small plaque ; mild stenosis**
- **Plaque is usually cellular, soft, and sealed by a thin cap that will crack or ulcerate**
- **Thrombus formation is a dynamic process. It can dissolve and reform depending on the balance between endogenous thrombolysis and platelets disaggregation**
- **Usually spontaneous lysis will prevail . HENCE only**
- **20-30% of patients are left with total occlusion**
- **Obviously The underlying stenosis remains**

Adverse outcome of Acute MI

- **1- Recurrent Ischaemia**
- **2- Extensive ECG changes at rest**
- **3- release of Biomarkers ; Troponins or Enzymes**
- **4-Arrhythmias**
- **5- Haemdynamic compromize**

Estimated mortality of Acute MI which occur mainly in high risk patients.

_20% die during the fist six months. More than half of them (12%) die during the first month

--- 20% or more die at home

TOTAL MORTALITY Up to 50%

Management of ACS especially Acute MI

1-Ambulance + defibrillator +-A doctor (G.P)

2- Hospitalization CCU

3- Bed rest + Canula + Oxygen > 60%

4- **Serial ECG, Biomarkers. and close haemodynamic monitoring.**

5- **Antiplatelets :-**

a- ASPIRIN 300mg initally then 100 mg after

b-Clopidogrel 600mg , 150mg for aweek, then75 mg

c- OR Ticagrelol 180 mg the 90 mg afterwards

d- GP 11b/111a receptor antagonist Abciximabe or Tirofiban if PCI is needed

Mangement of ACS especially Aute MI

6- Narcotic Analgesics ;_

a- Morphine 5-10. mg or Diamorphine 2.5-5 mg.IV

b -Antiemetic :- Metoclopramide 10.0mg (I.V)

7 Anticagolants:-

a. The Pentasaccharide Fondaparinux 2.5 mg s.c

b. Or LMW heparin Enoxaparin 1.0 mg/kg 12 hrly 8

– Antianginal therapy A- Nitrates

a- GTN 500ug but it doesno relieve the pain

b- Nitroglycerine infusion 0.6-1.2 mg/hr or

ISDN 1-2 mg/hr is given it can relive pain ,

Mangement of ACS especially Acute MI

9 – Beta-blockers

a. I.V. Betablocker Atenolol 5-10mg or

b. Metoprolol 5-15m every 5.0 min followed by oral Atenolol 50mg daily or Metoprolol 50mg twice a day. Try to give smaller doses in LV Failure, hypotension and Bradycardia otherwise avoid it th

10- Calcium Antagonists

a- Nifedipine 19 mg 8 hrly or amlodipine 5-10 mg forpersistant pain

b- use Verapamil or ditaizem if Beta blocker are conraindiated eg Pul Oedema. And asthma

11 – Statin eg Atorvastatin 20 m orally

11- Reperfusion Therapy

1 -NSTEMI –

Emergency Reperfusion may be harmful however sellected Medium and High risk NSTEMI pts may benefit from emergency Reperfusion Therapy

2- STEMI

Immediate reperfusion if successful will

A- Restore coronary flow

B- Preserve left ventricular function

C- Improve Survival

D- Relieve pain

E- Resolve ST elevation

E- May induce transient idioventricular rhythm

Primary Percutanous Coronary Intervention

Primary PCI

1- **Primary PCI is the best treatment of acute STEMI**.

2- **Best with GP11b/111 a antagonist and stent**

3Better than Thrombolysis in reducing MACE ie

Major Adverse Cardiac Events ; death MI, stroke

4 Limited by a- It is not widely available

b-Must be done in 2 hrs from onset

5- Indicated within 12 hrs from onset of pain and within 24 hrs in high risk cases.

6 has to organized and performed quickly in a timely fashion ; the goal of Door to Balloon time of 90 min from presentation

Rescue PCI or delayed PCI

- **Rescue or delayed PCI is indicated**
- **1- if Thrombolysis had failed in achieving reperfusion as evidenced by ST Elevation fail to drop significantly**
- **2-Or symptoms continue**
- **3-Or pt has haemodynamic compromise**
- **4- 0r uncontrolled malignant arrhythmias**

Thrombolysis

1 Can reduce mortality by 25-30%

2 Survival benefits is maintained for 10 years

3 The earlier the better or minutes mean muscle.

If given to pts with

a- ST elevation . 1 mm in limb leads

b- OR ST elevation 2 mm in chest leads

c- OR LBBB

Then Short term (6 M) Survival will be ;

a- 1- 6 hrs from ONSET 50 more lives per 1000

b- 7- 12 hrs from onset 40 more lives per 1000

c- Otherwise no benefit if not harmful

Relative Contrandications to Thrombolysis

1) Recent surgery within one month
2) Uncontrolled hypertension
3) Previous subarachnoid and intracerebral bleed.
4) Recent Trauma including that of cardiac resuscitation.
5) Active internal bleeding.
6) High probability of active ulcer
7) pregnancy

tPA

4- tPA ; human tissue Plasminogen Activator;

15 mg IV bolus

< 50 mg Infusion over 30 min. (0.75 mg/kg)

<35 mg infusion over 60 min. (0.5 mg/kg)

Better Survival than Streptokinase

But slightly more Intracerebral bleed;

10 per 1000 more survivals BUT;

1 per 1000 more nonfatal intracerebral bleeds

Hazzards

Five extra non fatal stroks per 1000

0.5-1% other major bleeds . Hence

Thrombolysis ; tPA Analogues

5 tPA analogues

1 TNK Teneteplase and Alteplase

a. Same survival and cerebral bleeds

b. bolus IV ; hence easier and quicker

c.Can be given before hospitalization.

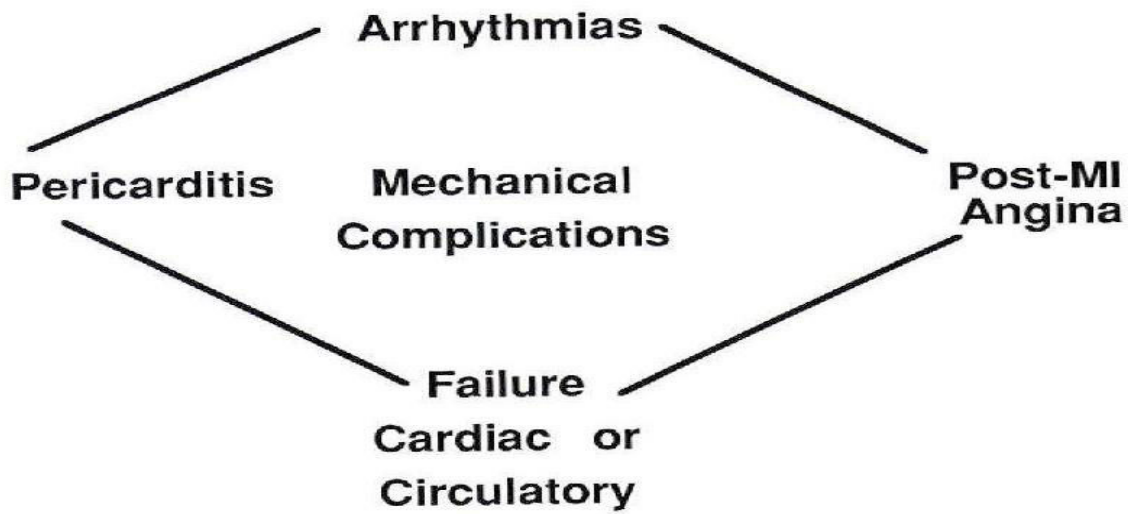
d -Less peripheral bleeds

11- rPA Retaplase

a- Same survival and cerebral bleeds

b - slightly more peripheral bleeds

ACUTE MI-COMPLICATIONS SUMMERY



Dr. Ammar khalid

Heat failure

Dr.ammr khalid

Heart failure
Learning objectives

1. Define " heart failure" syndrome , indicating its main types.
2. Be aware of the importance of " heart failure problem ' worldwide.
3. State the pathophysiology mechanisms of heart failure syndrome and link it to the clinical presentations.
4. Indicate the mode of presentations of patients with heart failure, correlates it with the symptoms and sings.
5. Differentiate acute form chronic heat failure and link it to the mode of treatment.

6.Draw a plan for workup in patients with heart failure , listing the main laboratory and radiology investigations.

7.State the mode of management in patients with heart failure , indication the those who affect survival .

8.Define “ acute pulmonary edema” , verity the mode of presentation and management

Heat failure : definition

- Heat failure is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.
- It happens when the heart cannot maintain adequate output, or can do so only at the expense of elevated ventricular filling pressure as a result thee will tissue under perfusion.

Why heat failure is important?

- Common medical problem : prevalence rises from 1% in those aged 50–59 years to over 10% in those aged 80–89 years.
- High morbidity and mortality : the commonest cause of hospital admission to UK hospitals , 50% will die with two years if left untreated.
- High cost.

Mode of presentation

- In mild to moderate forms of heart failure, cardiac output is normal at rest and only becomes impaired when the metabolic demand increases during exercise or some other form of stress.

- In practice, heart failure may be diagnosed when a patient develops the signs or symptoms of:

1. a low cardiac output : exercise intolerance and fatigue.

2.a pulmonary congestion : shortness of breath , orthopnea and paroxysmal nocturnal dyspnea.

3.Splanchnic or systemic venous congestion : abdominal distension (ascites) , pedal edema .

Presentations

- Some patients have exercise intolerance but little evidence of fluid retention, whereas others complain primarily of edema, dyspnea, or fatigue.

NYHA Functional Classification

NYHA classes focus on exercise capacity and the symptomatic status of the disease

Class I (Mild)	Patients with cardiac disease but without resulting in limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation (rapid or pounding heart beat), dyspnea (shortness of breath), or anginal pain (chest pain.)
Class II (Mild)	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain

Class III (Moderate)	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV (Severe)	Patients with cardiac disease resulting in the inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

The ACCF/AHA Heart Failure Stages

Emphasize the development and progression of disease and can be used to describe individuals and populations

- **Stage A:** Presence of heart failure risk factors but no heart disease and no symptoms
- **Stage B:** Heart disease is present but there are no symptoms (structural changes in heart before symptoms occur)
- **Stage C:** Structural heart disease is present AND symptoms have occurred
- **Stage D:** Presence of advanced heart disease with continued heart failure symptoms requiring aggressive medical therapy

Epidemiology

- The lifetime risk of developing HF is 20% for Americans 40 years of age . In the United States, 000, 650>new HF cases diagnosed annually.
- HF incidence increases with age, rising from approximately 20 per 1,000 individuals 65 to 69 years of age to >80 per 1,000 individuals among those 85 years of age.
- Approximately 5.1 million persons in the United States have clinically manifest HF, and the prevalence continues to rise.

- The most common etiology is coronary artery disease and myocardial infarction.
- Although the outlook depends, to some extent, on the underlying cause of the problem, untreated heart failure carries a poor prognosis; approximately 50% of patients with severe heart failure due to left ventricular dysfunction will die within 2 years, because of either pump failure or malignant ventricular arrhythmias

Mechanisms of heart failure

- Almost all forms of heart disease can lead to heart failure. An accurate etiological diagnosis important because treatment of the underlying cause may reverse heart failure or prevent its progression

.1Reduced ventricular contractility:

- Myocardial infarction (segmental dysfunction)
- Myocarditis/cardiomyopathy (global dysfunction)

.2Ventricular outflow obstruction (pressure overload:)

- Hypertension, aortic stenosis (left heart failure)
- Pulmonary hypertension, pulmonary valve stenosis (right heart failure)

.3Ventricular inflow obstruction:

- Mitral stenosis, tricuspid stenosis.

.4Ventricular volume overload:

- Ventricular septal defect Right ventricular volume overload (e.g. atrial septal defect)
- Increased metabolic demand (high output)

.5Arrhythmia:

- Atrial fibrillation
- Tachycardia cardiomyopathy.
- Complete heart block

Diastolic dysfunction:

- Constrictive pericarditis.
- Restrictive cardiomyopathy.
- Left ventricular hypertrophy and fibrosis
- Cardiac tamponade

Pathophysiology

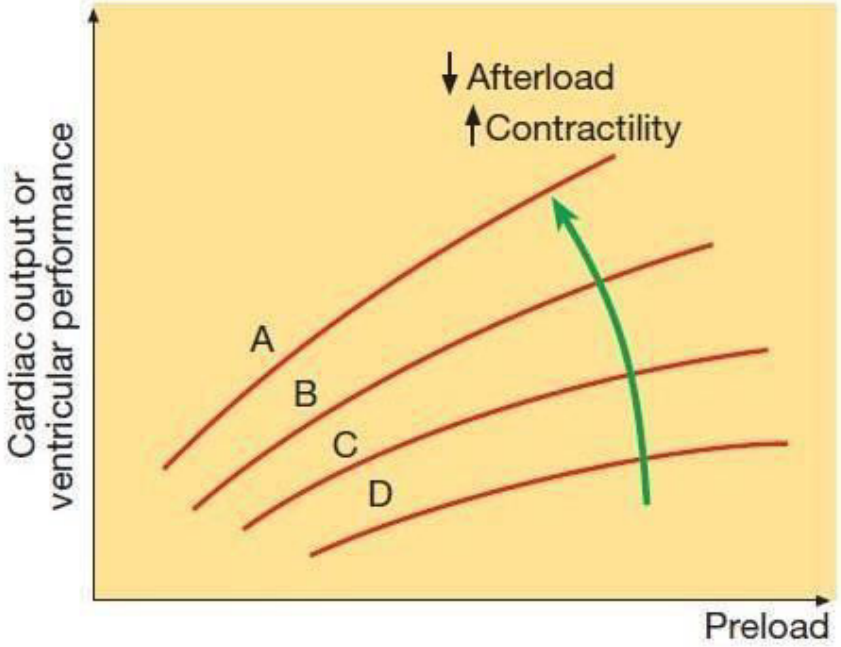
- Cardiac output is determined by:

1.preload (the volume and pressure of blood in the ventricles at the end of diastole.)

2.afterload (the volume and pressure of blood in the ventricles during systole.)

3. myocardial contractility.

Starling's Law



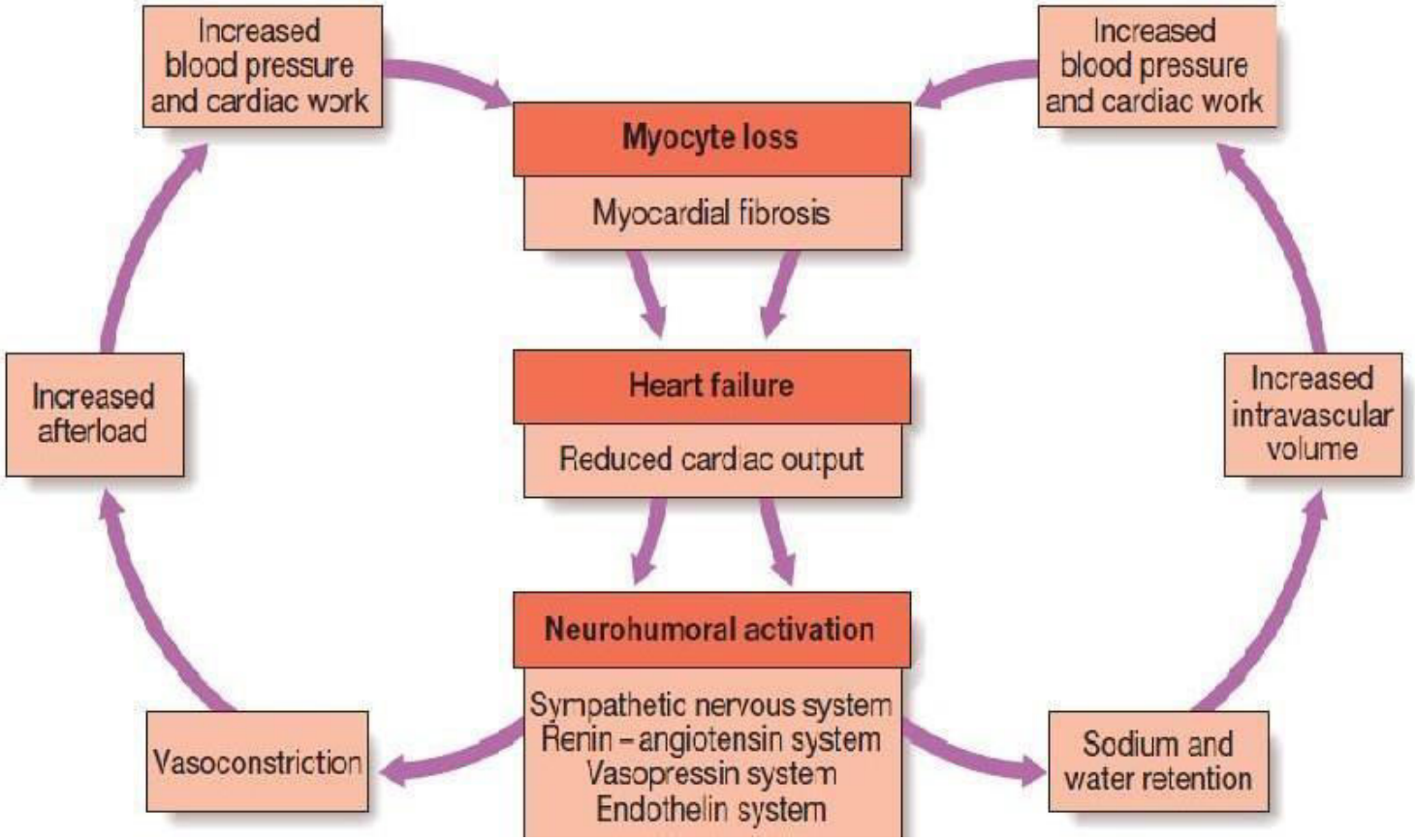
Normal (A), mild (B), moderate (C) and severe (D) heart failure.

Ventricular performance is related to the degree of myocardial stretching. An increase in preload (end-diastolic volume, end-diastolic pressure, filling pressure or atrial pressure) will therefore enhance function; however, overstretching causes marked deterioration. In heart failure, the curve moves to the right and becomes flatter.

An increase in myocardial contractility or a reduction in afterload will shift the curve upwards and to the left (green arrow.)

- impairment of ventricular myocardial ----- leading to a fall in cardiac output (because of impaired systolic contraction, impaired diastolic relaxation, or both ----- This activates counter regulatory neurohumoral mechanisms that can lead to a deleterious increase in both afterload and preload.
- A vicious circle may be established because any additional fall in cardiac output will cause further neurohumoral activation and increasing peripheral vascular resistance.

Neurohumoral activation and compensatory mechanisms in heart failure. There is a vicious circle in progressive heart failure



Types of heart failure

.1**Left-sided heart failure:.**

There is a reduction in left ventricular output and an increase in left atrial and pulmonary venous pressure.

- An acute increase in left atrial pressure causes pulmonary congestion or pulmonary oedema;
- A gradual increase in left atrial pressure, as occurs with mitral stenosis, leads to reflex pulmonary vasoconstriction, which protects the patient from pulmonary oedema.
- This increases pulmonary vascular resistance and causes pulmonary hypertension, which can, in turn, impair right ventricular function.

.2**Right-sided heart failure.** There is a reduction in right ventricular output and an increase in right atrial and systemic venous pressure.

- Causes of isolated right heart failure include chronic lung disease (cor pulmonale), pulmonary embolism and pulmonary valvular stenosis.

.3Biventricular heart failure.

- Failure of the left and right heart may develop because the disease process, such as dilated cardiomyopathy or ischaemic heart disease, affects both ventricles or because disease of the left heart leads to chronic elevation of the left atrial pressure, pulmonary hypertension and right heart failure

.4**High-output failure** A large arteriovenous shunt, beri-beri , severe anemia or thyrotoxicosis can occasionally cause heart failure due to an excessively high cardiac output

.5Acute and chronic heart failure

- Heart failure may develop suddenly, as in MI, or gradually, as in progressive valvular heart disease.
- When there is gradual impairment of cardiac function, several compensatory changes may take place.

.6compensated heart failure

- is sometimes used to describe the condition of those with impaired cardiac function, in whom adaptive changes have prevented the development of overt heart failure.

.7Decompensated heat failure

- A minor event, such as an intercurrent infection or development of atrial fibrillation, may precipitate overt or acute heart failure.

Factors that may precipitate or aggravate heart failure in pre-existing heart disease

- Myocardial ischaemia or infarction
- Intercurrent illness, e.g. infection
- Arrhythmia, e.g. atrial fibrillation
- Administration of a drug with negative inotropic (β-blocker) or fluid-retaining properties (NSAIDs, corticosteroids)
- Pulmonary embolism
- Conditions associated with increased metabolic demand, e.g. pregnancy, thyrotoxicosis, anaemia
- IV fluid overload, e.g. post-operative IV infusion

.8Diastolic and systolic dysfunction

- Heart failure may develop as a result of impaired myocardial contraction (systolic dysfunction.)
- Or poor ventricular filling and high filling pressures from abnormal ventricular relaxation (diastolic dysfunction.)
- The latter is caused by a stiff, noncompliant ventricle and is commonly found in patients with left ventricular hypertrophy.
- Systolic and diastolic dysfunction often coexist.

Left ventricular Ejection faction (EF)

- EF is considered important in classification of patients with HF because of differing patient demographics, comorbid conditions, prognosis, and response to therapies and because most clinical trials selected patients based on EF.

Heart failure with reduced Ejection (rEF) or Preserved ejection faction(pEF)

- Heart failure with reduced ejection fraction (HFrEF) EF<40% (systolic dysfunction)
- Heart failure with preserved ejection fraction (HFpEF) > 50% (diastolic dysfunction)
- HFpEF, borderline EF 41 to 49% (borderline)

Clinical assessment

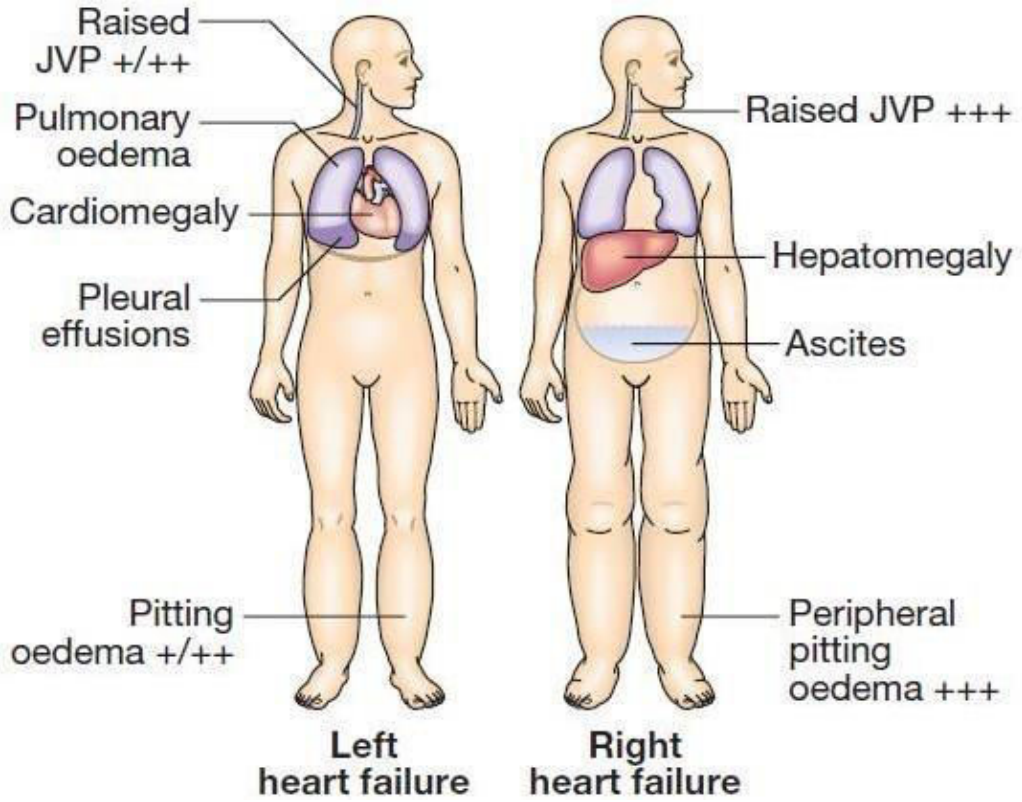
- Chronic heart failure*:*
- Patients with chronic heart failure commonly follow a relapsing and remitting course, with periods of stability and episodes of de compensation, leading to worsening
- symptoms that may necessitate hospitalization.
- The clinical picture depends on the nature of the underlying heart disease, the type of heart failure that it has evoked, and the neurohumoral changes that have developed.

- Low cardiac output : fatigue and a poor effort tolerance
- On clinical exam : the peripheries are cold and the BP is low.
- To maintain perfusion of vital organs, blood flow is diverted away from skeletal muscle and this may contribute to fatigue and weakness. Poor renal perfusion leads to oliguria and uremia.

- Pulmonary congestion due to left heart failure presents as above and with inspiratory crepitations over the lung bases.
- In contrast, right heart failure produces a high JVP with hepatic congestion and dependent peripheral oedema.
- In ambulant patients, the oedema affects the ankles, whereas, in bed-bound patients, it collects around the thighs and sacrum. Ascites or pleural effusion may occur .
- Consider other causes of perepheal odema.

- Chronic heart failure is sometimes associated with marked weight loss (cardiac cachexia), caused by a combination of anorexia and impaired absorption due to gastrointestinal congestion, poor tissue perfusion due to a low cardiac output, and skeletal muscle atrophy due to immobility.

Clinical features of left and right heart failure.



Complications

- *Renal failure* is caused by poor renal perfusion due to low cardiac output and may be exacerbated by diuretic therapy, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers.

- Electrolyte disturbance
- Hypokalaemia may be the result of treatment with potassium-losing diuretics or hyperaldosteronism caused by activation of the renin–angiotensin system and impaired aldosterone metabolism due to hepatic congestion.
- Most of the body's potassium is intracellular and there may be substantial depletion of potassium stores, even when the plasma concentration is in the reference range.

- Hyperkalaemia may be due to the effects of drugs which promote renal resorption of potassium, in particular the combination of ACE inhibitors (or angiotensin receptor blockers) and mineralocorticoid receptor antagonists. These effects are amplified if there is renal dysfunction due to low cardiac output or atherosclerotic renal vascular disease.
- Hyponatraemia is a feature of severe heart failure and is a poor prognostic sign. It may be caused by diuretic therapy, inappropriate water retention due to high ADH secretion, or failure of the cell membrane ion pump.

- Impaired liver function is caused by hepatic venous congestion and poor arterial perfusion, which frequently cause mild jaundice and abnormal liver function tests; reduced synthesis of clotting factors can make anticoagulant control difficult.

- Thromboembolism. Deep vein thrombosis and pulmonary embolism may occur due to the effects of a low cardiac output and enforced immobility.
- Systemic emboli occur in patients with atrial fibrillation or flutter, or with intracardiac thrombus complicating conditions such as mitral stenosis, MI or left ventricular aneurysm.

- Atrial and ventricular arrhythmias*:*

  are very common and may be related to electrolyte changes (e.g.
- hypokalaemia, hypomagnesaemia), the underlying cardiac disease, and the pro-arrhythmic effects of sympathetic activation.
- Atrial fibrillation occurs in approximately 20% of patients with heart failure and causes further impairment of cardiac function.
- Sudden death occurs in up to 50% of patients with heart failure and is often due to a ventricular arrhythmia.

- Frequent ventricular ectopic beats and runs of non-sustained ventricular tachycardia are common findings in patients with heart failure and are associated with an adverse prognosis.

- Acute left heart failure *Acute pulmonary edema* :
- a sudden onset of dyspnoea at rest progresses to acute respiratory distress, orthopnea and prostration. The precipitant, such as acute MI, is often apparent from the history.

- On clinical examination :
- The patient appears agitated, pale and clammy. The peripheries are cool , pulse is rapid. Inappropriate bradycardia or excessive tachycardia should be identified promptly.
- The BP is usually high because of sympathetic nervous system activation, but may be normal or low if the patient is in cardiogenic shock.

- The jugular venous pressure (JVP) is usually elevated, particularly with associated fluid overload or right heart failure. In acute de novo heart failure, there has been no time for ventricular dilatation and the apex is not displaced.
- A ‘gallop’ rhythm, with a third heart sound, is heard quite early in the development of acute left sided heart failure. A new systolic murmur may signify acute mitral regurgitation or ventricular septal rupture.
- Auscultatory findings in pulmonary edema are crepitations at the lung bases, or throughout the lungs if pulmonary oedema is severe. Expiratory wheeze often accompanies this.

rheumatic fever

Rheumatic Fever

Definition: **It is an immune complex disease affecting mainly connective tissue of heart, joint, brain and the skin**

Epidemiology

Rare in developed world.

Still common in developing countries.

Peak incidence ~5-15yr.

ARF is a major problem in the high-risk areas of the tropics, in countries with limited resources, and in communities with minority indigenous populations.

In those less developed nations, post ARF heart disease is the most commonly acquired heart disease in hospitalized children, adolescents, and young adults.

In some areas, the incidence of this entity exceeds that of congenital heart disease.

Rheumatic fever

- Causes chronic progressive damage to the heart and its valves.
- Until 1960, it was a leading cause of death in children and a common cause of structural heart disease.
- The disease has been known for many centuries.
- Baillou (1538-1616) first distinguished acute arthritis from gout.
- Sydenham (1624-1668) described chorea .
- In 1812, Charles Wells associated rheumatism with carditis and provided the first description of the subcutaneous nodules.
- The connection with scarlet fever was made in the early 1900s. In 1944,
- The Jones criteria were formulated to assist disease identification. These criteria, with some modification, remain in use today.
- The introduction of antibiotics in the late 1940s allowed for the development of treatment and preventive strategies.

Sex

No sex predilection exists, except that Sydenham chorea occur more often in females than in males.

Age

Although individuals of any age group may be affected, most cases are reported in persons aged 5-15 years.

Patterns of presentation of ARF.

The first pattern is sudden onset, begins as polyarthritis 2-6 weeks after streptococcal pharyngitis and is usually characterized by fever and toxicity.

The initial abnormality is mild carditis, ARF may be insidious or subclinical.

Causes

This auto immune disease follow throat infection with group A-Beta hemolytic streptococci (Rheumatogenic strain) by about 2-3weeks

ARF has been linked definitively with a preceding streptococcal infection, usually of the upper respiratory tract.

Predisposing factors

-Over crowding

-Poor housing

-Bad ventilation

-Low socioeconomic standard

Pathogenesis

2 mechanisms:

First:

Releasing toxins :

That causes damage to connective tissue --> release auto antigens in to circulation ---> stimulation of body to form and release auto antibodies against this connective tissue ---> causing rheumatic lesion.

Second

Cross reaction

These strains posses an antigen immunologicaly similar to that in heart connective tissue so produced antibodies against streptococci can react with the heart.

Pathophysiology

ARF is a sequela of a previous group A streptococcal infection, usually of the upper respiratory tract. One beta-streptococcal serotype (eg, M types 3, 5, 18, 19, 24) is linked directly to ARF.

Evidence is very strong that the M protein in certain streptococci subtypes is responsible for antigenicity.

Non–group A streptococci has never been shown to cause this disease.

The disease involves the heart, joints, central nervous system (CNS), skin, and subcutaneous tissues.

It is characterized by an exudative and proliferative inflammatory lesion of the connective tissue, especially that of the heart, joints, blood vessels, and subcutaneous tissue.

Pathology

- fibrinoid degeneration affecting connective tissue with inflammatory oedema

- Aschoff 's nodules paravascular nodules consists of at centre fibrinoid degeneration surrounded with aschoff's giant cells, lymphocytes and fibroplasts

Clinical picture

Patient has history of recent streptococcal infection 2-3 weeks ago as (tonsillitis-pharyngitis -scarlet fever)

Rheumatic manifestations are divided in to major and minor criteria

A-Major criteria

* Carditis.
* Arthritis.
* Chorea.
* Subcutaneous nodules.
* Erythema marginatum.

B- Minor criteria

Clinical

Fever, Arthralgia

Laboratry

***Acute phase reactants (leukocytosis – increased ESR , C reactive protein)**

***Prolonged PR interval at ECG.**

A- CARDITIS :

1- Rheumatic carditis (pan carditis)

Involves all layers of the heart

2- Endocarditis, affect valves mainly

Mitral valvitis 70%

A- Stenosis early due to inflammatory edema

Leading to mid diastolic rumbling murmur over apex and localized with accentuated S1A-

B- Incompetence :

Due to destruction and deformity of the valve.

Leading to pan systolic blowing murmur over apex and propagated to axilla with muffled S1

Aortic valvitis:

Incompetence

Due to destruction and deformity of the valve.
Leading to early diastolic soft murmur over aortic area and propagated to apex

3- Myocarditis :

*Tachychardia, not proportional to the fever and continous with sleep.

*Myocardial dilatation poor quality heart sounds

4- prolonged PR interval

5- Heart failure

6- Arrhythmia

B- Pericarditis

*Dry

-pain : stitchy and localized
-pericardial rub : superfacial ,scratchy, heared near to sternum and not related to respiration

*Effusion

-increase cardiac dullness

-distant heart sounds

-Rheumatic arthritis

-Affecting big joints (knee-ankle-elbow) 2 or more j

-Migratory with signs of inflammation(red-hot-swollen-limition of movement)

-Fleeting arthritis migrate from one to the other joint

-Dramatic response to salicylates.

Rheumatic chorea (sydenham's chorea)

Common in females(8-12y)
It is due to involvement of basal ganglia in rheumatic process

Its manifestations appear late .

3 MAIN MANIFESTATIONSS

Involuntary movment

hypotonia

Emotional instability

Involuntary movement

* Affecting face, limb, and tongue.

* Movement is involuntary, sudden, and jerky

* Patient complains from falling of objects from the hands

* Tongue movement interfere with speech

Hypotonia

* mainly proximal than distal

* associated with hyporeflexia

* if severe it leads to paralysis (chorea molis)

Emotional instability

* Sudden crying

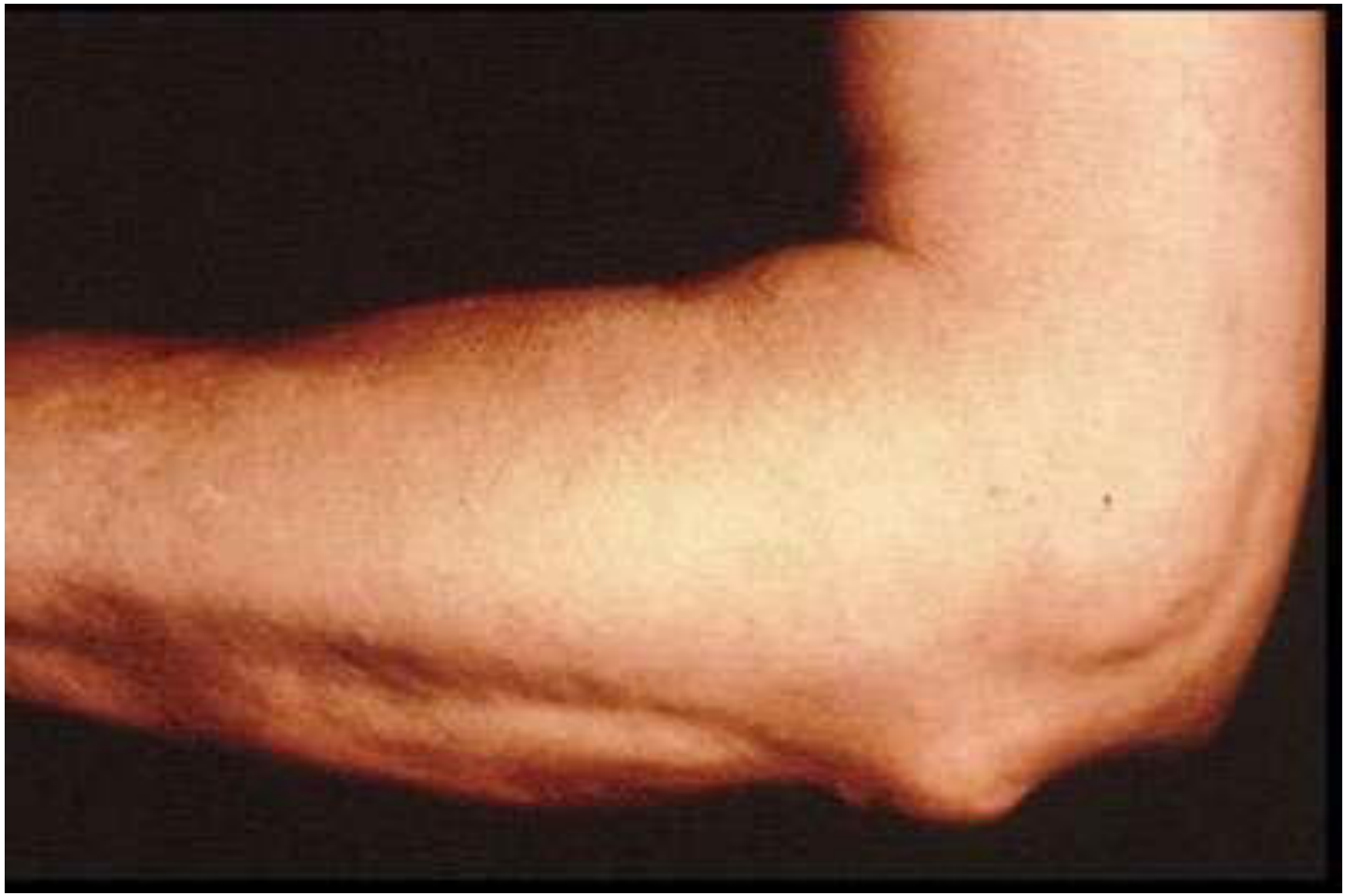
* Sudden laughing

Subcutaneous nodules

They are painless subcutaneous firm nodules freely mobile under the skin

Site : over extensor surfaces and bony prominences

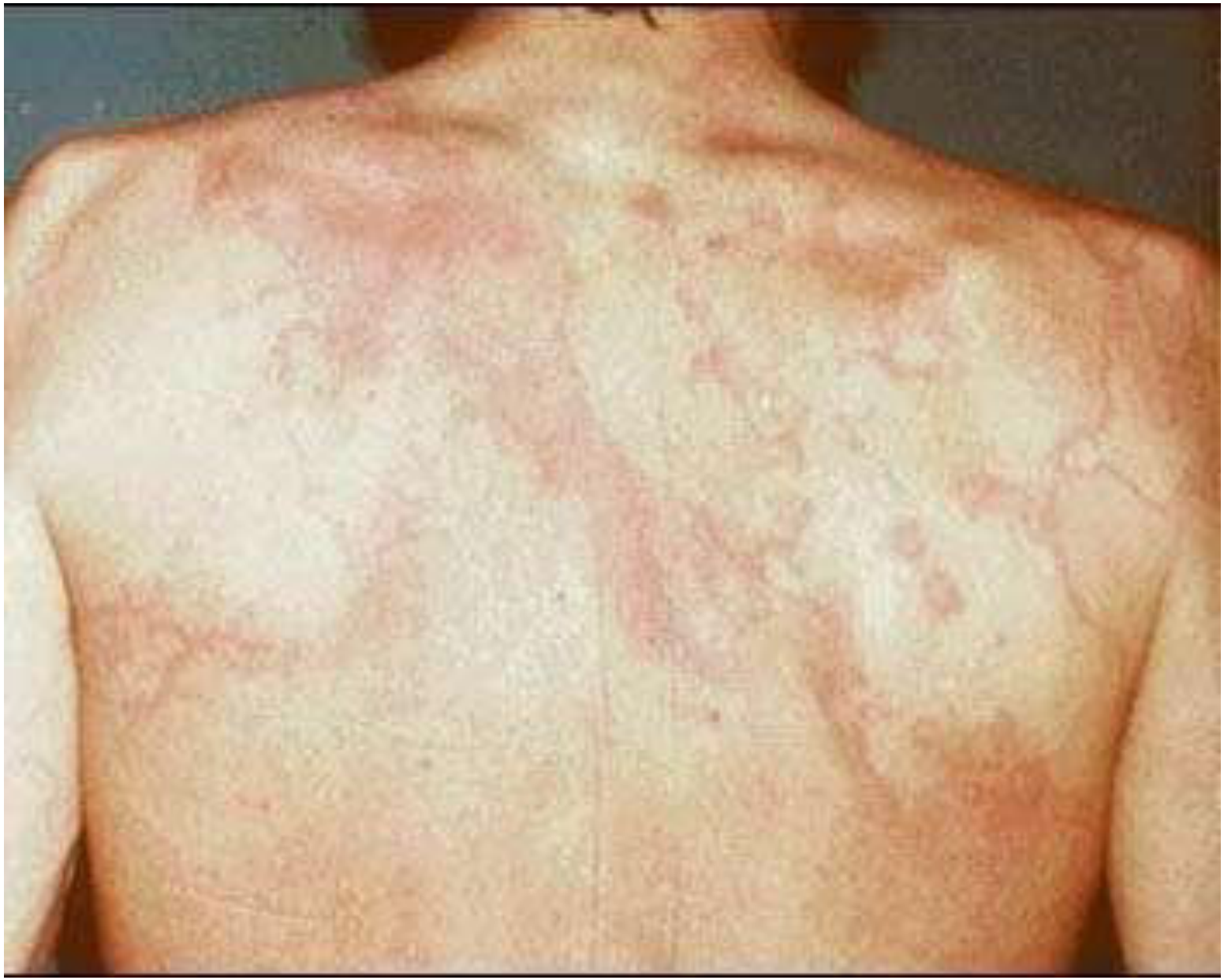
Indicate severe carditis



Erythema marginatum

They are rings of erythema with clear center not painful, not itchy

Site: over trunk and proximal parts of the extremities



Diagnosis of ARF:

Requires a high index of suspicion.

Guidelines of diagnosis used by the American Heart Association include:

Major and Minor criteria(Modified Jones criteria).

In addition to evidence of a previous streptococcal infection.

The diagnosis requires 2 major Jones criteria or 1 major plus 2 minor Jones criteria.

Diagnosis

HISTORY

-Recurrent tonsillitis ,pharyngitis or scarlet fever

-Abnormal movements.

EXAMINATION

According to modified jones criteria

2 MAJOR CRITERIA.
OR ONE MAJOR AND 2 MINOR CRITERIA

PLUS

EVIDENCE OF STREPT. INFECTION.

Some considerations and precautions during diagnosis

- If considered carditis as major criteria - should not consider prolonged PR interval as minor criteria

- If considered arthritis as major criteria should not consider arthralgia as minor criteria

- Can not depend on both subcutaneous nodules and erythema marginatum only as 2 major criteria as they are not Pathognomonic to RF and occur in other collagen diseases.

INVESTIGATIONS

Acute phase reactant (ESR- CRP- leucocytosis)
ASO TITRE

Throat culture for group A b-haemolytic strept.

ECG (prolonged PR)

Chest X RAY (cardiomegaly- pericardial effusion)

ECHO important and diagnostic(detect pericardial effusion and degree of valvular affection)

Treatment

Curative treatment

Bed rest for 3 weeks or till improvement of all sumptoms and signs

Diet salt restriction in heart failure

Eradication of streptococcal infection BY:

-longe acting penicillin 1.200.000 u deep im once OR
-penecilline procain 400.000 u only im twice daily for 10 days OR
-oral penicillin v 400.000 4 times daily for 10 days

Treatment

Prophylactic treatment

Long acting penicillin 1.200.000 u 2-4 weeks deep im.

Penicillin v orally 400.000 u twice daily

Or

Erythromycin 250 mg twice daily orally

Duration

-Rh fever without carditis:

5yrs or 21yr of age

-Rh fever with carditis but without residual heart disease: 10 yrs- adulthood

-Rh fever with carditis and residual heart disease: 10 yrs at least since last episode and at least 40 yr of age.

Prevention of sub acute bacterial endocarditis

Tonsillectomy if large with repeated infection

- ****Sensitivity test must be done before any long acting penicillin**
  If patient sensitive to penicillin we give erythromycin 50 mg /kg/day
  Orally for 10 days

Treatment

rheumatic symptoms as carditis and arthritis

Salicylates

*indication:

-Rh fever without carditis.

-Rh.with carditis but without cardiomegaly or congestive heart failure

Dose 100 mg/kg/day in 4 divided doses for 3-5 days.

followed by 75mg/kg/d in 4 divided doses for 4 weeks.

- **corticosteroids (prednisone)

  *Indications
  -Rh fever with carditis
  - No response to salicylates
  - Rh fever with heart failure

  Dose 2mg/kg/day with gradual withdrawal
  Duration for 2 -4 weeks

- **Treatment of rh chorea**

-phenobarbital
- Haloperidol 1-5 mg /day orally divided in doses

-Chlorpromazine

COMPLICATIONS

valvular lesion

infective endocarditis

heart failure

arrhythmias