CASE 1: CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) WITH OR WITHOUT COR PULMONALE

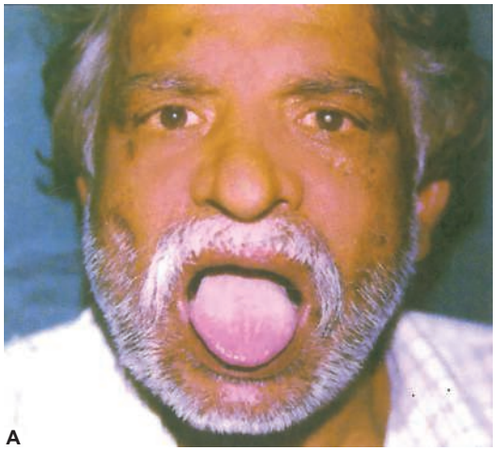
The patient (Fig. 1.1A) presented with cough with mucoid sputum for the last 8 years. These symptoms intermittently increased during windy or dusty weather. No history of hemoptysis, fever, pain chest. The sputum is white, small in amount with no postural relation.

Clinical Presentations

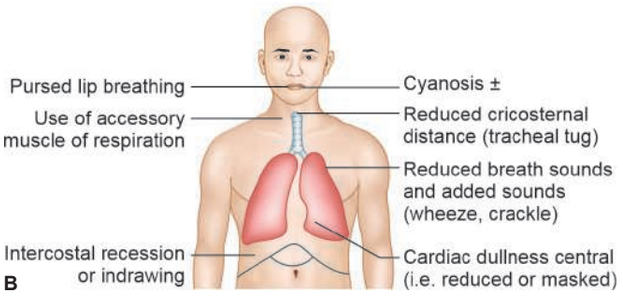
- Initially, the patients complain of repeated attacks of productive cough, usually after colds and especially during winter months which show a steady increase in severity and duration with successive years until cough is present throughout the year for more than 2 years.
- Later on with increase in severity of the disease, patient may complain of repeated chest infections, exertional breathlessness, regular morning cough, wheeze and occasionally chest tightness.
- Patient may present with acute exacerbations in which he/she develops fever, productive cough, thick mucopurulent or purulent sputum, often streaked with blood (hemoptysis) and increased or worsening breathlessness.
- Patient may present with complications, the commonest being ***cor pulmonale,*** characterised by right ventricular hypertrophy with or without failure. The symptoms of right ventricular failure include pain in right hypochondrium, ascites (swelling of abdomen) and swelling of legs (edema).

Points to be Noted in History

- **Cigarette smoking.** Exposure to smoke from cigarette or biomass and solid fuel fires, atmospheric smoke is important factor in pathogenesis as well as in acute exacerbation of COPD. The smoke has adverse effect on surfactants and lung defence.



A



B

Fig. 1.1A and B: Chronic obstructive pulmonary disease (COPD): **A.** Patient of COPD demonstrating central cyanosis; **B.** Clinical signs of COPD (Diag)

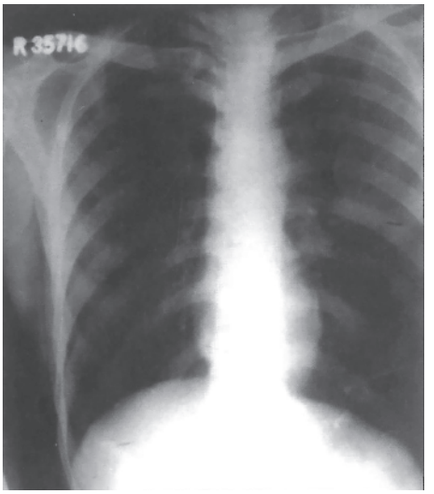


Fig. 1.1C: Chest-X-ray PA view showing hyperinflated (hyper-translucent) lungs and tubular heart

- **Precipitating factors,** e.g. dusty atmosphere, air pollution and repeated upper respiratory tract infections. They cause acute exacerbations of the disease.
- **Family history:** There is increased susceptibility to develop COPD in family of smokers than non-smokers.
- **Hereditary predisposition.** Alpha-1-antitrypsin deficiency can cause emphysema in non-smokers adult patients.

Physical Signs (See Table 1.1)

General Physical

- Flexed posture (leaning forward) with pursed lip breathing and arms supported on their knees or table.
- Central cyanosis, may be noticed in severe COPD.
- Bounding pulses (wide pulse pressure) and flapping tremors on outstretched hands may be present is severe COPD with type 2 respiratory failure. These signs suggest hypercapnia.
- Disturbed consciousness with apnoeic spells (CO_2 narcosis—type 2 respiratory failure).
- Raised JVP and pitting edema feet may be present if patient develops cor pulmonale with congestive heart failure.

> Edema feet without raised JVP indicate secondary renal amyloidosis due to pulmonary suppuration, e.g. bronchiectasis, bronchitis, chest infections.

- Respiratory rate is increased (hyperpnea). There may be tachycardia.

EXAMINATION

Inspection

Shape of the chest

- AP diameter is increased relative to transverse diameter.
- **Barrel-shaped chest:** The sternum becomes more arched, spines become unduly concave, the AP diameter is > transverse diameter, ribs are less oblique (more or less horizontal), subcostal angle is wide (may be obtuse), intercostal spaces are widened.

Movements of the chest wall

Bilaterally diminished

Respiratory rate and type of breathing

- Pursed lip breathing
- Intercostal recession (indrawing of the ribs)
- Excavation of suprasternal, supraclavicular and infraclavicular fossae during inspiration
- Widening of subcostal angle
- Respiratory rate is increased. It is mainly abdominal. The alae nasi and extra-respiratory muscles are in action.

> All these signs indicate hyperinflation of lung due to advanced airflow obstruction.

- Cardiac apex beat may or may not be visible.

Palpation

- Movements of the chest are diminished bilaterally and expansion of the chest is reduced.
- Trachea is central but there may be reduction in length of palpable trachea above the sternal notch and there may be tracheal descent during inspiration (tracheal tug).
- Intercostal spaces may be widened bilaterally.
- Occasionally, there may be palpable wheeze (rhonchi) during acute exacerbation.
- Cardiac apex beat may not be palpable due to superimposition by the hyperinflated lungs.

Percussion

- A hyperresonant note on both sides.
- Cardiac dullness is either reduced or totally masked
- Liver dullness is pushed down (below 5th intercostal space).
- There may be resonance over Kronig's isthmus and Traube's area (splenic dullness is masked).
- Diaphragmatic excursions are reduced on tidal percussion.
- Tactile vocal fremitus may be reduced bilaterally. It can be normal in early cases.

Auscultation

- Breath sounds may be diminished in intensity due to diminished air entry.
- Vesicular breathing with prolonged expiration is a characteristic sign of COPD.
- Vocal resonance may be normal or slightly diminished on both sides equally.
- Rhonchi or wheeze are common especially during forced expiration (expiratory wheeze/rhonchi). Sometimes crackles may be heard during acute exacerbation of chronic bronchitis.
- Check for forced expiratory time (FET). Ask the patient to exhale forcefully after full inspiration while you are listening over the trachea. If patient takes > 6 sec, airway obstruction is indicated.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your provisional diagnosis?

Ans. Chronic obstructive pulmonary disease (COPD).

Q 2. Summarise findings in your case. What are points in favor of your diagnosis?

Ans. A 45-year-old male presented with history of chronic cough and expectoration with exacerbation on exposure to dust and smoke with no positive history of such disease in the family.

Examination revealed **physical signs of *bronchitis***, i.e.

- Cyanosis
- Wheezing, rhonchi
- Vesicular breathing with prolonged expiration and **signs of *emphysema***, e.g.

1. Barrel-shaped chest.
2. Pursed lip breathing.
3. Excavation of suprasternal and supraclavicular fossae.
4. Diminished movement, and chest expansion.
5. Diminished vocal fremitus on both sides.
6. Hyperresonant note.
7. Obliteration of liver dullness.
8. Central apex indicates hyperinflated lungs.

Hence, my case has features of both chronic bronchitis and emphysema (COPD).

Table 1.1 Important differential physical signs in various respiratory disorders

	Sign	*Lobar consolidation*	*Lobar collapse*	*Fibrosis/ bronchiectasis*	*Cavity or lung abscess*	*Pleural effusion*	*Pneumo-thorax*	*Acute or chronic bronchitis*	*Bronchial asthma*	*Emphysema*
1.	Shape of the chest	N	Retraction on the side involved	Retraction on the side involved	N or slight retraction on the side involved	N	N	N	N	Hyperinflated or barrel-shaped
2.	Chest wall movement	Reduced on the side involved	Reduced on the side involved	Reduced on the side involved	Slightly reduced on the side involved	Reduced or absent on the side involved	Reduced or absent on the side involved	N	Bilateral diminished	Bilateral diminished
3.	Expansion of chest	Reduced on the side involved	Reduced on the side involved	Reduced on the side involved	Slightly reduced on the side involved	Reduced or absent on the side involved	Reduced or absent on the side involved	N	B/L reduced	B/L reduced
4.	Activity of extrarespira-tory muscles	A	A	A	A	A	A	P	P	P
5.	Position of trachea and mediastinum	N	Shifted to the side involved	Shifted to the side involved	Shifted to the side involved	Shifted to opposite side	Shifted to opposite side	N	N	N
6.	AP and trans-verse diameter	N	N	N	N	N	N	N or abnormal	N	Abnormal AP > T
7.	Vocal fremitus	Increased on the side involved	Reduced or absent on the side involved	Increased over the area involved	Increased over the area involved	Reduced or absent on the side involved	Reduced or absent on the side involved	N	N	N or reduced on both sides
8.	Percussion note	Dull on the side involved	Dull on the side involved	Impaired over the area involved	Impaired over the area involved	Stony dull on the side involved	N or hyper-resonant on the side involved	N	N or hyper-resonant during acute attack	Hyperresonant
9.	Breath sounds	High-pitched bronchial over the area involved	Diminished or absent over the area involved	Low-pitched bronchial over the area involved	Amphoric bronchial over the area involved	Absent or diminished over the area involved	Absent or diminished on the side involved	B/L vesicular with prolonged expiration	B/L vesicular with prolonged expiration	B/L vesicular with prolonged expiration
10.	Intensity of breath sounds (vocal resonance)	Increased over the area involved. Bronchophony and whispering pectoriloquy present	Decreased over the area involved	Increased over the area involved	Increased over the area involved whispering pectoriloquy present	Decreased over the area involved	Decreased on the side involved	N	N	N or diminished
11.	Added sounds	Fine crepitations, early coarse crepitations later on the area involved	None	Coarse crepitations on the area involved	Coarse crepitations on the area involved	Pleural rub in some cases over the area involved	None	Rhonchi with some coarse crepitations on both sides	Rhonchi, mainly expiratory and high-pitched	Expiratory rhonchi

Abbreviation: N: Normal; B/L: Bilateral; P: Present; A: Absent; AP: Aanteroposterior

Q 3. What is your differential diagnosis?

Ans. Based on the symptoms and signs, other two conditions that come into differential diagnosis are:

1. Bronchial asthma
2. Chronic asthmatic bronchitis

Note: For physical signs, read Table 1.1.

Q 4. What is COPD?

Ans. **Chronic obstructive pulmonary disease** is the internationally recognised term, includes chronic bronchitis and emphysema.

By definition, COPD is a chronic progressive disorder characterised by irreversible airflow obstruction (FEV1 <80% predicted and FEV_1/EVC ratio <70%) which does not change markedly over several months.

Q 5. What is tidal percussion?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 6. How do you define chronic bronchitis and chronic bronchitis with acute exacerbation?

Ans. **Chronic bronchitis** is a condition characterised by cough with or without expectoration on most of the days in a week for at least 3 months in a year for 2 consecutive years (WHO). Chronic bronchitis simply denotes mucoid sputum production. Chronic bronchitis with **acute exacerbation** means, fever, persistent or recurrent mucopurulent sputum in the absence of localised suppurative lung disease, e.g. bronchiectasis.

Q 7. Which clinical signs indicate airflow obstruction?

Ans. ***Measurement of forced expiratory time (FET).*** Ask the patient to exhale forcefully after full inspiration while you are listening over the trachea. Calculate the time taken by the patient (FET >6 sec indicates COPD).

Q 8. Name the accessory muscles of respiration.

Ans. *Alae nasi, sternomastoid, trapezius, serratus anterior, scalene, latissimus dorsi, pectoralis and abdominal muscles are accessory muscles* of respiration seen working in a patient with severe COPD.

Q 9. How COPD differs from bronchial asthma?

Ans. The differences between COPD and bronchial asthma are given in Table 1.2.

Q 10. How do you classify severity of COPD?

Ans. Severity of COPD is discussed in Table 1.3.

Q 11. How do you decide about which component of COPD is predominant, i.e. chronic bronchitis or emphysema?

Ans. Though COPD encompasses both chronic bronchitis and emphysema but one may predominate over the other. Clinically, patients with predominant bronchitis are cyanosed, have edema, hence are referred as *"blue-bloaters"*(blue refers to cyanosis, bloater—edema) and with predominant emphysema as *pink puffers* (pink refers to absence of cyanosis, puffers—pursed lip breathing). The difference between the two is enlisted in Table 1.4.

Q 12. What are the signs of advanced airflow obstruction?

Ans. Main signs are as follows:

- ***Dyspnea*** and even ***orthopnea*** with ***pursed lip breathing*** (a physiologic response to decreased air entry).

Table 1.2: Differentiating features between bronchial asthma and COPD

Bronchial asthma	*COPD (see Fig. 1.1B)*
Occurs in young age, seen in children and adults who are atopic	Occurs in middle or old aged persons
Allergo-inflammatory disorder, characterised by reversible airflow obstruction, airway inflammation and bronchial hypersensitivity	Inflammatory disorder characterised by progressive airway obstruction
Short duration of symptoms (weeks or months)	Long duration of symptoms, e.g. at least 2 years
Episodic disease with recurrent attacks	Nonepisodic usually but acute exacerbations may occur which worsen the symptoms and disease further
Variable nature of symptoms is a characteristic feature	Symptoms are fixed and persistent, may be progressive
Family history of asthma, hay fever or eczema may be positive	No positive family history
A broad dynamic syndrome rather than static disease	A chronic progressive disorder
Wheezing is more pronounced than cough	Cough is more pronounced and wheezing may/may not be present
Shape of the chest remains normal because of dynamic airway obstruction but AP diameter may increase with severe asthma	Barrel-shaped chest (AP diameter ≥ transverse) in patients with predominant emphysema
Pursed lip breathing is uncommon	Pursed lip breathing common
Respiratory movement may be normal or decreased, tracheal tug absent. Accessory muscles of respiration may be active and intercostal recession may be present.	Respiratory movements are usually decreased with: ▪ Reduced palpable length of trachea with tracheal tug ▪ Reduced expansion ▪ Excavation of suprasternal notch, supraclavicular and infraclavicular fossae ▪ Widening of subcostal angle ▪ Intercostal recession ▪ Accessory muscles of respiration hyperactive.

Table 1.3: Gold criteria for severity of COPD

GOLD stage	*Severity*	*Symptoms*	*Spirometry*
0	At risk	Chronic cough, sputum	Normal
I	Mild	With or without chronic cough or sputum production	$FEV_1/FVC < 70\%$ $FEV_1 = 80\%$ predicted
II	Moderate	With or without chronic cough or sputum production	$FEV_1/FVC < 70\%$ $FEV_1 = 50$ to 80% predicted
III	Severe	-do-	$FEV_1/FVC < 70\%$ $FEV_1 = 30–50\%$
IV	Very severe	-do-	$FEV_1/FVC < 70\%$ $FEV_1 < 30\%$ Or $FEV_1 < 50\%$ predicted with respiratory failure or signs of right heart failure

GOLD: Global Initiative for Obstructive Lung Disease

Table 1.4: Differences between chronic bronchitis and emphysema

Features	*Predominant chronic bronchitis (blue bloaters)*	*Predominant emphysema (pink puffers)*
Age at the time of diagnosis (years)	60 ±	50 ±
Major symptoms	Cough > dyspnea, cough starts before dyspnea	Dyspnea > cough; cough starts after dyspnea
Sputum	Copious, purulent	Scanty and mucoid
Cynosis	Common	Usually absent
Episodes of respiratory infection	Frequent	Infrequent
Episodes of respiratory insufficiency	Frequent	Occurs terminally
Hyperinflation of lungs	Absent	Present
Breath sounds	Vesicular beathing with prolonged expiration	Vesicular breathing with diminished intensity
Chest X-ray	Enlarged cardiac shadow with increased bronchovascular markings	Increased translucency of lungs (hyperinflation), central tubular heart, low flat diaphragm
Compliance of lung	Normal	Decreased
Airway resistance	High	Normal or slightly increased
Diffusing capacity	Normal to slight decrease	Decreased
Arterial blood gas	Abnormal in the beginning	Normal until late
Chronic cor pulmonale (raised JVP and edema)	Common	Rare except terminally
Cardiac failure	Common	Rare except terminally

- ***Excavation of the suprasternal notch, supraclavicular fossae*** during inspiration, together with ***indrawing (recession) of intercostal spaces***.
- ***Barrel-shaped chest*** (AP diameter > transverse diameter) with horizontality of the ribs.
- ***A reduction in the length of trachea palpable*** above the suprasternal notch.
- ***Contractions of extrarespiratory (accessory) muscles*** (sternomastoid and scalene muscles) on inspiration
- ***Central cyanosis***
- ***Expiratory filling of neck veins***
- ***Flapping tremors*** and bounding pulses (due to hypercapnia)
- ***Wheeze*** (rhonchi) especially on forced expiration.

Q 13. What do you understand by the term emphysema? What are its bedside diagnostic signs?

Ans. ***Emphysema*** is defined as hyperinflation or overdistension of air spaces (e.g. alveoli) distal to terminal bronchioles as well as destruction of the alveolar septae.

Bedside diagnostic signs are

- Pursed lip breathing
- Barrel-shaped chest
- Apex beat is not visible
- Diminished movements of chest with reduced expansion
- Diminished vocal fremitus and vocal resonance

- Hyperresonant percussion note on both sides
- Cardiac and liver dullness masked
- Heart sounds may get muffled
- Usually wheeze or crackles are absent
- Liver may become palpable due to descent of diaphragm.

Q 14. Why does a patient of COPD has pursed lip breathing?

Ans. Pursed lip breathing can occur both in COPD and bronchial asthma. A patient purses, her/his lips to maintain high intrabronchial pressure over and above that exists with surrounding alveoli so as to prevent the collapse of bronchial wall by these surrounding distended alveoli.

Q 15. What are complications of COPD?

Ans. Common complications are as follows:

- ***Pneumothorax*** due to rupture of bullae into pleural space
- ***Recurrent pulmonary infections***
- ***Cor pulmonale*** (right ventricular hypertrophy with pulmonary arterial hypertension)
- ***Congestive cardiac failure*** (raised JVP, hepatomegaly, cyanosis, ascites, peripheral edema with RVH).
- ***Type 2 respiratory failure*** (CO_2 narcosis) with flapping tremors, bounding pulses, worsening hypoxia and hypercapnia
- ***Secondary polycythemia*** due to hypoxia.

Clinical tips

1. A sudden worsening of dyspnea after prolonged coughing indicates pneumothorax due to rupture of bullae.
2. Edema of the legs in COPD indicates CHF or a secondary amyloidosis.
3. Flaps on outstretched hands indicate type 2 respiratory failure (carbon dioxide narcosis).

Q 16. How will you investigate the patient?

Ans. The following investigations are usually performed:

1. ***Hemoglobin,*** TLC, DLC and PCV for anemia or polycythemia (PCV is increased) and for evidence of infection.
2. ***Sputum examination***. It is unnecessary in case of COPD but during acute exacerbation, the organisms (*Strep. pneumoniae or H. influenzae*) may be cultured. Sensitivity to be done, if organisms cultured.
3. ***Chest X-ray*** (see Fig. 1.1C) will show:
   - Increased translucency with large voluminous lungs
   - Prominent bronchovascular markings at the hilum with sudden pruning/truncation in peripheral fields
   - Bullae formation
   - Low flat diaphragm. Sometimes, the diaphragm shows undulations due to irregular pressure of bullae
   - Heart is tubular and centrally located.

   Tip. An enlarged cardiac shadow with all of the above radiological findings suggests cor pulmonale.
4. ***Electrocardiogram (ECG).*** It may show:
   - Low voltage graph due to hyperinflated lungs
   - P-pulmonale may be present due to right atrial hypertrophy.
   - Clockwise rotation of heart.
   - Right ventricular hypertrophy (R>S in VI)
5. ***Pulmonary function tests.*** These show **obstructive ventilatory defect** (e.g. FEV_1, FEV_1/FVC and PEF—all are reduced, **lung volumes**—total lung capacity and residual volume increased and **transfer factor CO** is reduced). The differences between obstructive and restrictive lung defect are summarised in Table 1.5.
6. ***Arterial blood gas analysis*** may show reduced PaO_2 and increased $PaCO_2$ (hypercapnia).
7. ***Alpha-1 antitrypsin levels:*** Reduced level may occur in emphysema (normal range is 24 to 48 mmol/L).

Table 1.5: Pulmonary function tests in obstructive and restrictive lung defect

Test	*Obstructive defect (COPD)*	*Restrictive defect (interstitial lung disease)*
Forced expiratory volume during one second (FEV_1)	Markedly reduced	Slightly reduced
Vital capacity (VC)	Reduced or normal	Markedly reduced
FEV_1/VC	Reduced	Increased or normal
Functional residual capacity (FRC)	Increased	Reduced
Peak expiratory flow (PEF)	Reduced	Normal
Residual volume (RV)	Increased	Reduced
Total lung capacity	Increased	Reduced
Transfer or diffusion factor for CO (T_{CO} and D_{CO})	Normal	Low
PaO_2	Decreased	Decreased
$PaCO_2$	Increased	Low or normal

Q 17. What is the role of high resolution CT scan in the diagnosis of emphysema?

Ans. It is most sensitive technique for diagnosis of emphysema. It is useful in evaluating symptomatic patients with normal pulmonary function except for a low CO diffusing capacity.

Q 18. What do you understand by the term chronic cor pulmonale? What are its causes?

Ans. **Chronic cor pulmonale** is defined as right ventricular hypertrophy/dilatation secondary to chronic disease of the lung parenchyma, vasculature and/or bony cage (read case discussion on cor pulmonale).

Acute cor pulmonale refers to acute thromboembolism where pulmonary hypertension develops due to increased vascular resistance

leading to right ventricular dilatation with or without right ventricular failure.

Q 19. What do you understand by term obstructive sleep apnea syndrome?

Ans. ***Obstructive sleep apnea syndrome*** is characterised by spells of apnea with snoring due to occlusion of upper airway at the level of oropharynx during sleep. Apneas occur when airway at the back of throat is sucked closed during sleep. When awake, this tendency is overcome by the action of the muscles meant for opening the oropharynx which becomes hypotonic during sleep. Partial narrowing results in snoring, complete occlusion in apnea and critical narrowing in hyperventilation. The major features include:

1. Loud snoring
2. Daytime somnolence
3. Unfreshed or restless sleep
4. Morning headache
5. Nocturnal choking
6. Reduced libido and poor performance at work
7. Morning drunkenness and ankle edema.

The patient's family report the pattern of sleep as "snore-silence-snore" cycle. The diagnosis is made if there are more than 15 apneas/hyperpneas in any one hour of sleep with fall in arterial O_2 saturation on ear or finger oximetry.

Q 20. What is Pickwickian syndrome?

Ans. It is obesity-related alveolar hypoventilation syndrome in which obesity serves to reduce compliance of chest wall and functional residual capacity in the recumbent position.

In these patients obstructive sleep apnea is prominent feature and in some there may be sleep-induced hypoventilation.

These patients present with daytime somnolence, unrefreshing sleep, daytime fatigue, snoring, breathlessness, headache, poor concentration, systemic hypertension.

- They may develop pulmonary hypertension and right heart failure.
- Arterial blood gas analysis shows hypoxemia and hypercapnia.

Q 21. What is treatment of COPD?

Ans. Stable phase of COPD is treated by:

- **Cessation of smoking** and avoidance of precipitating factors.
- **Bronchodilators:** Inhaled route of bronchodilatation is preferred to oral and parenteral route due to low side effects. Beta-agonists are commonly used. Tremors and trachycardia are common side effects.
- **Anticholinergics,** e.g. ipratropium bromide is not useful in chronic stable phase, is used in acute exacerbation for symptomatic relief.
- **Corticosteroids:** They are not useful in chronic phase, to be used for short-term in tapering doses in acute exacerbations.
- **O_2 therapy:** Both the Medical Research Council Trial and Nocturnal O_2 therapy trial have documented the benefits of intermittent O_2 therapy for long hours in reducing the mortality in COPD.
- **Other agents**

i. N-Acetylcysteine is used as both mucolytic and antioxidant agent.
ii. Alpha-1-antitrypsin therapy is available for severe deficiency of alpha-1-trypsin. Hepatitis vaccination is must prior to this therapy.
iii. ***Lung transplantation*** is the last resort for end-stage lung disease, e.g. emphysema due to alpha-1-antitrypsin deficiency.

Q 22. What do you understand by the term acute exacerbation of COPD?

Ans. Acute exacerbation implies an episode of increased dyspnea and cough, and change in the amount and character of sputum. There may or may not be associated signs of illness such as fever, myalgia, sore throat.

Exacerbations are a prominent feature in the natural history of COPD.

Q 23. What are common precipitants of acute exacerbation?

Ans. Bacterial and viral respiratory infections.

Q 24. What are the organisms commonly associated with acute exacerbation?

Ans. *H. influenzae* and *S. pneumoniae* are the most common organisms

- *Moraxella catarrhalis, Chlamydia pneumoniae* and *Pseudomonas* are less common.

Q 25. What is role of molecular genetics in COPD?

Ans. α_1-antitrypsin deficiency, increased production of tumor necrosis factor-alpha (TNF-α), increased generation of microsomal epoxide hydrolase during smoking are associated with increased risk of COPD.

Q 26. What is treatment of acute exacerbation?

Ans. 1. **Antibiotics:** Repeated courses of antibiotics are better than rotating antibiotics. Choice of an antibiotic depends on sputum culture and sensitivity report. Most physicians treat acute exacerbation with an antibiotic on empirical basis without an evidence of infection, i.e. fever, leucocytosis.

2. **Bronchodilators and anticholinergics:** These patients are initially nebulised with beta-agonist and anticholinergic, followed by inhalation therapy. This therapy improves most of the patients. If response is not adequate, addition of theophylline IV may be considered.

3. **Glucocorticoids:** The GOLD guidelines recommend 30–40 mg oral predisolone or its equivalent in tapering doses for 10–14 days. Steroids have been demonstrated to reduce the hospital stay, hasten the recovery and reduce the chances of further exacerbations for a period of 6 months.
4. **Oxygen:** Supplemental O_2 therapy is given to keep arterial saturation above 90%.
5. **Noninvasive positive pressure ventilation (NIPPV):** It is considered if respiratory failure present.

Q 27. What do you know about noninvasive ventilation?

Ans. *Noninvasive ventilation* is an alternative approach to endotracheal intubation to treat hypercapnic ventilatory failure which occurs in COPD. Noninvasive positive pressure ventilation (NIPPV) delivered with a face mask and a piece of white foam placed in the face mask to reduce the amount of internal dead space. Recently it has been shown that NIPPV reduces the hospital stay, need for endotracheal intubation and in hospital mortality in patients with acute exacerbation of COPD.

Q 28. How will you treat acute respiratory failure?

Ans.
- If PaO_2 is <8 kPa, administer 24% O_2 through mask. There is no need of O_2 when PaO_2 >8 kPa.
- Monitor blood gases every one hourly.
- If PaO_2 continues to rise, administer doxapram;
- If in spite of this patient deteriorates, artificial respiration may be attempted.

Q 29. What are uses of long-term domiciliary O_2 therapy?

Ans. **1.** COPD with FEV <1.5 L and FVC <2 L with stable respiratory failure.
2. Terminal ill patients with hypoxia.

Q 30. What is unilateral emphysema? What are its causes?

Ans. Overdistension of one lung is called *unilateral emphysema.* It can be *congenital* or *acquired* (compensatory emphysema).
- Unilateral compensatory emphysema develops due to collapse or destruction of the whole lung or removal of one lung.
- ***Macleod's or Swyer-James syndrome*** is characterised by unilateral emphysema developing before the age of 8 years when the alveoli are increasing in number. This is an incidental radiological finding. In this condition, neither there is any obstruction nor there is destruction and overdistension of alveoli, hence, the term emphysema is not true to this condition. In this condition, the number of alveoli are reduced which appear as larger air spaces with increased translucency on X-ray.

Q 31. What do you understand by the term bullous emphysema?

Ans. Confluent air spaces with dimension >1 cm are called *bullae,* may occasionally be congenital but when occur in association with generalised emphysema or progressive fibrotic process, the condition is known as *bullous emphysema.* These bullae may further enlarge and rupture into pleural space leading to pneumothorax.

CASE 2: CONSOLIDATION OF THE LUNG

The patient (Fig. 1.2A) presented with fever, cough, hemoptysis with rusty sputum and pain chest increasing during respiration of 2 weeks duration.

Clinical Presentations of Patients with Consolidation

- Short history of fever with chills and rigors, cough, often pleuritic chest pain which is occasionally referred to shoulder or anterior abdominal wall is a classic presentation of a patient with pneumonic consolidation in young age. In children, there may be associated vomiting and febrile convulsions.
- A patient may present with symptoms of complications, of pneumonia consolidation, i.e. pleural effusion (dyspnea, intractable cough, heaviness of chest), meningitis (fever, neck pain, early confusion or disorientation, headache, violent behavior, convulsions, etc.)
- A patient with **malignant consolidation** presents with symptoms of cough, pain chest, dyspnea, hemoptysis, weight loss, etc. Associated symptoms may include hoarseness of voice, dysphagia, fever, weight loss, and loss of appetite. These patients are old and usually smokers.

Points to be Noted in History and Their Relevance

- Recent travel, local epidemics around point source suggest *Legionella* as the cause in middle to old age.
- Large scale epidemics, associated sinusitis, pharyngitis, laryngitis suggest *Chlamydia* infection.
- A patient with underlying lung disease (bronchiectasis, fibrosis) with purulent sputum suggests secondary pneumonia (bronchopneumonia).
- History of past epilepsy, recent surgery on throat suggest *aspiration pneumonia*.
- Co-existent debilitating illness, osteomyelitis or abscesses in other organs may lead to *staphylococcal consolidation*.
- Contact with sick birds, farm animals suggest *Chlamydia psittaci* and *Coxiella burnetii* pneumonia.
- History of smoking suggests *malignancy*
- Recurrent episodes suggests *secondary pneumonia*
- History of diabetes, intake of steroids or antimitotic drugs, AIDS suggests *pneumonia in immunocompromised host*.

Physical Signs

General Physical

- Toxic look *present* (patient appears apparently ill)
- Fever *present*
- Tachypnea *present*
- Tachycardia *present*
- Cyanosis *absent*
- Herpes labialis may be *present*
- Neck stiffness *absent*, if present suggests meningitis as a complication.

Systemic Examination

Inspection

- Shape of chest is normal
- Movements of the chest reduced on the side involved due to pain
- In this case (Fig. 1.2), movements of right side of the chest will be reduced.
- Trachea central
- Apex beat normal
- No indrawing of intercostal spaces; and accessory muscles of respiration are not working (active).

Palpation

- Restricted movement on the side involved **(right side in this case)**
- Reduced expansion of the chest **(right side in this case)**
- Trachea and apex beat normal in position
- Tactile vocal fremitus is *increased* on the side and over the part involved **(in this case, apparent in right axilla and front of central part of right chest)**.
- *Friction rub* may be palpable over the **part of the chest involved**.

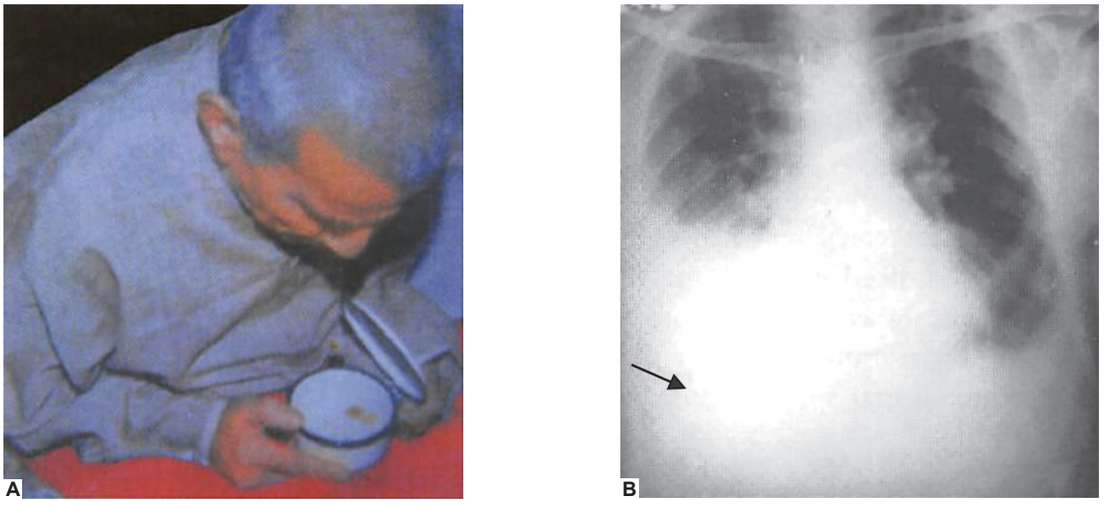


Fig. 1.2A and B: Pneumonic consolidation. **A.** A patient with pneumonia demonstrating hemoptysis; **B.** Chest X-ray showing right lower lobe consolidation (→)

Percussion

Dull percussion note on the side and over the part of the chest involved *(right axilla and right lower anterior chest in this case)*.

Auscultation

The following findings will be present **on the side and part involved (right axilla and right lower anterior chest in this case)**.

- Bronchial breath sounds
- Increased vocal resonance with *bronchophony* and *whispering pectoriloquy*.
- Aegophony
- Pleural rub.

> As the lung is solidified, no crackles or wheeze will be heard at present, but during resolution, crackles will appear due to liquefaction of the contents.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your provisional diagnosis and why?

Ans. The provisional clinical diagnosis in this case is *right pneumonic consolidation because of*

- Short duration of illness
- Classic triad of symptoms (fever, cough, pleuritic chest pain)
- All signs of consolidation on right side (read Table 1.1 for signs of consolidation).
- Tuberculosis can also be the cause, hence, to be ruled out.

Q 2. What is differential diagnosis?

Ans. All the conditions that produce consolidation come into differential diagnosis. Read causes of consolidation. Pleural effusion and collapse of lung also produce some signs that resemble consolidation, hence, come in differential diagnosis (Table 1.6).

Q 3. What is clinical triad of pneumonia?

Ans. **Cough** and **fever, chest pain and hemoptysis** is a clinical triad of pneumonia.

Q 4. What is the site of involvement in your case?

Ans. Because all the signs are present in the right axilla and right lower anterior chest, hence, it is likely due to involvement of right middle and lower lobe.

Q 5. What is the cause of chest pain in pneumonia?

Ans. Chest pain in pneumonia is acute, occurs due to involvement of overlying pleura leading to friction between two layers of pleura. The pain is pleuritic in origin, increases during respiration. A pleural rub may be heard.

Q 6. What is pleural rub? What are its causes? How would you differentiate it from crackles?

Ans. For all these questions, read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 7. What do you understand by the term consolidation? What are stages of pneumonia and their clinical characteristics?

Ans. **Consolidation** means solidification of the lung due to filling of the alveoli with inflammatory exudate. It represents second stage (red hepatization) and third stage (gray hepatization) of pneumonia (Table 1.7).

Q 8. Patient has consolidation on X-ray but is asymptomatic. How do you explain?

Table 1.6: Differential diagnosis of consolidation

I. **Bronchogenic carcinoma**
× Common in male, smokers, middle-aged persons
× Hemoptysis is common
× Cachexia/emaciation is present
× Patient is not toxic
× Clubbing may be present. There may be cervical lymphadenopathy
× No shift of trachea or mediastinum unless there is associated pleural effusion
× Crackles are heard over the mass
II. **Collapse of lung**
× There is depression of the chest on the side involved. Movements are diminished on the involved side
× Intercostal spaces are crowded. Trachea and mediastinum are shifted to same side
× Impaired percussion note and decreased intensity of breath sounds
× Patient is not toxic
× History may be suggestive, e.g. aspiration, foreign body, trauma, postoperative condition
III. **Pleural effusion**
× Gradual onset of cough and dyspnea
× Chest may be prominent on the side involved
× Trachea and mediastinum are shifted to opposite side
× Stony dull percussion note with rising dullness in axilla
× Vocal fremitus and vocal resonance are diminished over the area involved
× There may be a bronchial breathing (amphoric) or aegophony (increased vocal resonance) at the top of effusion posteriorly
IV. **Pulmonary infarct**
× Sudden onset of chest pain, fever, hemoptysis.
× DVT may be present in leg(s)
× Patient is not toxic
× Pleural rub may be present, P_2 may become loud
× ECG shows RVH or S I, Q III, T III syndrome

Ans. 1. Respiratory symptoms and signs in consolidation are often absent in elderly, alcoholics, immunocompromised and neutropenic patients.

2. *Note:* Children and young adults suffering from *Mycoplasma pneumoniae* may have consolidation with a few symptoms and signs in the chest, i.e. there is discrepancy between symptoms and signs with radiological appearance of consolidation.

Table 1.7: Stages of pneumonia

Stage	*Signs*
I. *Stage of congestion*	Diminished vesicular breath sounds with fine inspiratory crackles due to alveolitis
II. *Stage of red hepatization*	All signs of consolidation present as mentioned (Table 1.1)
III. *Stage of gray hepatization*	— do—
IV. *Stage of resolution*	× *Bronchial breathing* during consolidation is replaced either by bronchovesicular or vesicular breathing × *Mid-inspiratory and expiratory crackles* (coarse crepitations) appear × All other signs of consolidation disappear

Table 1.9: Differentiating features of pneumonia in younger and older persons

Pneumonia in young	*Pneumonia in old*
× Primary (occurs in previously healthy individuals)	× Secondary (previous lung disease or immunocompromised state)
× Common organisms are: *Pncumococci, Mycoplasma, Chlamydia, Coxiella*	× Common organisms are: *Pneumococci, H. influenzae, Legionella*
× Florid symptoms and signs	× Few or no symptoms and signs
× Systemic manifestations are less pronounced	× More pronounced systemic features
× Complications are less frequent	× Complications are frequent
× Resolution is early	× Resolution may be delayed
× Response to treatment is good and dramatic	× Response to treatment is slow

3. Deep seated consolidation or consolidation with non-patent bronchus may not produce physical signs on chest examination.

Q 9. What are the common sites of aspiration pneumonia?

Ans. The site of aspiration depends on the position of patient (Table 1.8).

Table 1.8: Aspiration during supine and upright position

Aspiration during supine position	*Aspiration in upright position*
Posterior segment of the upper lobe and superior segment of the lower lobe on the right side (right side is more involved than left side)	Basilar segments of both lower lobes

Q 10. What are the causes of consolidation?

Ans. Main causes of consolidation are as follows:

1. **Pneumonic** (lobar consolidation), may be bacterial, viral, fungal, allergic, chemical and radiation induced.
2. **Tuberculosis** causes apical consolidation.
3. **Malignant** (bronchogenic carcinoma).
4. Following **massive pulmonary infarct** (pulmonary embolism—may cause collapse consolidation).
5. **Collagen vascular disorders.**

Q 11. How pneumonia in young differs from pneumonia in old persons?

Ans. Pneumonia in young and old persons are compared in Table 1.9.

Q 12. How do you classify pneumonias?

Ans. Pneumonias can be classified in various ways:

I. **Depending on the immunity and host resistance**
- Primary (normal healthy individuals)
- Secondary (host defence is lowered). It further includes:
  - Acute bronchopneumonia (lobar, lobular, or hypostatic)
  - Aspiration pneumonia
  - Hospital-acquired pneumonia (nosocomial)
  - Pneumonias in immunocompromised host
  - Suppurative pneumonia including lung abscess.

II. **Anatomical classification**
- Lobar
- Lobular (bronchopneumonia, bilateral)
- Segmental (hypostatic pneumonia).

III. **Aetiological classification**
- Infective, e.g. bacterial, viral, *Mycoplasma*, fungi, protozoal, *Pneumocystis carinii*
- Chemical-induced (lipoid pneumonia, fumes, gases, aspiration of vomitus)
- Radiation
- Hypersensitivity/allergic reactions.

IV. **Empiricist's classification (commonly used)**
- *Community-acquired pneumonia (S. pneumoniae, Mycoplasma, Chlamydia, Legionella, H. influenzae,* virus, fungi, anaerobes, *Mycobacterium)*
- *Hospital-acquired pneumonia (Pseudomonas, Proteus, Klebsiella, Staphylococcus,* oral anaerobes)
- *Pneumonia in immunocompromised host (Pneumocystis carinii, Mycobacterium, S. pneumoniae, H. influenzae).*

Q 13. What are the characteristics of viral pneumonia?

Ans. Characteristics of viral pneumonia are as follows:
- **Marked constitutional symptoms,** e.g. headache, malaise, myalgia, anorexia are predominant (commonly due to *influenza, parainfluenza, measles* and *respiratory syncytial virus).*
- There may be **no respiratory symptoms or signs** and consolidation may just be discovered on chest X-ray.
- **Cough**, at times, with **mucoid expectoration**.
- **Hemoptysis, chest pain** (pleuritic) and **pleural effusion** are rare.

- Paucity of physical signs in the chest.
- **Chest X-ray** shows reticulonodular pattern instead of lobar consolidation.
- **Spontaneous resolution** with no response to antibiotics.
- **WBC count** is normal.

Q 14. What do you understand about *Mycoplasma pneumoniae*?

Ans. *Mycoplasma pneumoniae* is an important cause of community-acquired pneumonia and epidemics of this pneumonia are common. Its incubation period is 1–3 weeks and it affects usually children and young adults. It is also common in winter months.

Q 15. What are the extrapulmonary manifestations of *Mycoplasma pneumoniae*?

Ans.
i. **Articular,** e.g. arthritis, arthralgia
ii. **Cardiac,** e.g. pericarditis, myocarditis
iii. **Blood,** e.g. autoimmune hemolytic anemia, DIC
iv. **Skin,** e.g. erythema multiforme, Stevens-Johnson syndrome
v. **Hepatitis and glomerulonephritis.**

Q 16. What are the characteristics of various bacterial pneumonias?

Ans. Characteristics of bacterial pneumonias are enlisted in Table 1.10.

Q 17. What are the complications of pneumonia?

Ans. Common complications of pneumonia are:
- Pleural effusion and empyema thoracis
- Lung abscess
- Adult respiratory distress syndrome
- Meningitis, brain abscess
- Circulatory failure (Waterhouse-Friderichsen's syndrome)
- Septic arthritis, septicemia
- Pericarditis, congestive heart failure (myocarditis)
- Multiorgan failure, renal failure
- Peripheral thrombophlebitis
- Herpes labialis (secondary infection).

Q 18. What are the causes of recurrent pneumonias?

Ans. **Recurrent pneumonias** mean two or more attacks within a few weeks. It is due to either reduced/lowered resistance or there is a local predisposing factor, i.e.
- *Chronic bronchitis*
- Hypogammaglobulinemia
- Pharyngeal pouch
- Bronchial tumor.

Q 19. What is normal resolution? What is delayed resolution and nonresolution? What are the causes of delayed or nonresolution of pneumonia?

Ans. **Normal resolution** in a patient, with pneumonia means disappearance of symptoms and signs within two weeks of onset and radiological clearance within four weeks. **Delayed resolution** means when physical signs persist for more than two weeks and radiological findings persist beyond four weeks after proper antibiotic therapy. **Causes** are:
- *Inappropriate antibiotic therapy*
- *Presence of a complication* (pleural effusion, empyema)

Table 1.10: Clinical and radiological features of bacterial pneumonias

Pathogens	*Clinical features*	*Radiological features*
Common organisms		
Pneumococcal pneumonia	× Young to middle aged, rapid onset, high fever, chills, and rigors, pleuritic chest pain, herpes simplex labialis, *rusty* sputum. Toxic look, tachypnea and tachycardia. All signs of consolidation present	× Lobar consolidation (dense uniform opacity), one or more lobes
Mycoplasma pneumoniae	× Children and young adults (5–15 years), insidious onset, headache, systemic features, often few signs in the chest. IgM cold agglutinins detected by ELISA × Arthralgia or arthritis erythema nodosum, myocarditis, pericarditis, hepatitis, glomerulonephritis, rash, meningoencephalitis, hemolytic anemia, DIC are extrapulmonary manifestations	× Patchy or lobar consolidation. Hilar lymphadenopathy present
Legionella	× Middle to old age, history of recent travel, local epidemics around point source, e.g. cooling tower, air conditioner × Headache, malaise, myalgia, high fever, dry cough, GI symptoms × Confusion, hepatitis, hyponatremia, hypoalbuminemia	× Shadowing continues to spread despite antibiotics and often slow to resolve
Uncommon organisms		
H. influenzae	× Old age, often underlying lung disease bronchopneumonia (COPD), purulent sputum, pleural effusion. Signs of underlying disease present and common are more pronounced	
Staphylococcal pneumonia	× Occurs at extremes of ages, coexisting debilitating illness, often complicates viral infection × Can arise from, or cause abscesses in other organs, e.g. osteomyelitis × Presents as bilateral pneumonia, cavitation is frequent	× Lobar or segmental thin walled abscesses formation (pneumatoceles)
Klebsiella	× Systemic disturbances marked, widespread consolidation often in upper lobes × Red-currant jelly sputum, lung abscess and cavitation frequent	× Consolidation with expansion of effected lobes, bulging of interlobar fissure

- *Depressed immunity*, e.g. diabetes, alcoholism, steroids therapy, neutropenia, AIDS, hypogammaglobulinemia
- *Partial obstruction of a bronchus by a foreign body* like denture or malignant tumor
- *Fungal or atypical pneumonia*
- *Pneumonia due to SLE* and *pulmonary infarction* or due to recurrent aspirations in GERD or cardia achalasia.

Nonresolution means radiological findings persisting beyond eight weeks after proper antibiotic therapy. **Causes** are:

- Neoplasm
- Underlying lung disease, e.g . bronchiectasis
- Virulent organisms, e.g. *Staphylococcus*, *Klebsiella*
- Underlying diabetes
- Old age.

Q 20. How will you investigate a patient with community acquired pneumonia (CAP)?

Ans. 1. **Radiology:** Chest X-ray is most useful investigation, detects consolidation in most of the cases (see Fig. 1.2B). If pneumonia is suspected on clinical grounds and no opacity is seen on initial chest X-ray, it is useful to repeat either X-ray after 24–48 hours or perform CT scan. High resolution CT scan detects opacities in patients with symptoms and signs suggestive of pneumonia but chest X-ray is normal.

2. **Blood culture:** All patients who are admitted to the hospital should have two seconds of blood culrures done before initiation of antibiotic therapy. The most common isolates, in ascending order, are *S. pneumoniae*, *S. aureus* and *E. coli*.

3. **Sputum stains and culture:** Gram's staining of sputum is used for persumptive etiologic diagnosis. Other types of sputum stainings are also useful for determining the cause of CAP. A variety of stains for acid-fast bacilli are used to diagnose tuberculosis. *Pneumocystis pneumonia* common in HIV patients can be diagnosed with monoclonal antibody staining. Special stains are also available for fungi, etc.

   Sputum should be sent for culture and sensitivity. Bronchoscopy and bronchoalveolar lavage may be attempted in case there is no sputum.

4. **Detection of antigens in urine:** Urine antigen test by ELISA is used to diagnose *Legionnaires disease*. Similarly, *S. pneumoniae* urinary antigen detection by ELISA is also useful.

5. **Serology:** The detection of lgM antibody or demonstration of 4-fold rise in titre of antibody in blood to a particular agent between acute and convalescent phase is considered a good evidence that this agent is the cause of pneumonia. The various serological tests used include complement fixation, indirect immunofluorescence and ELISA. The following etiological agents are often diagnosed serologically, i.e. *Mycoplasma*, *C. pneumoniae*, *Chlamydia*, *Legionella* spp. *C. burnetii*, viruses (adeno, influenza, parainfluenza).

6. **Polymerase chain reaction (PCR):** A multiplex PCR allows detection of DNA of *Legionella* spp., *M. pneumoniae* and *C. pneumoniae*.

7. **Blood counts:** Leukocytosis with polymorphonuclear response indicates bacterial infection.

Q 21. How would you treat CAP?

Ans.
- First of all, assess pneumonia severity and pay attention to vital signs.
- Ensure adequate O_2 therapy and support to circulation.
- Perform etiological work-up as described above. Never forget tuberculosis as etiological agent .
- **Antibiotic therapy:** Institute empirical antibiotic therapy followed by antibiotics based on the isolation of organism. The duration of antibiotics therapy is 10–14 days.
- **Monitor and treat comorbid illnesses:** Consider measures such as counselling for cessation of smoking and prevention of *pneumococcal* and *influenza infection by vaccination*.
- Follow-up chest X-rays.

Q 22. What are the causes of failure of improvement of CAP?

Ans. **Causes** are:
- **Incorrect diagnosis:** Reconsider the diagnosis as there may be some illness such as collagen vascular disease presenting as pneumonia.
- **Incorrect choice of antibiotic.**
- **Virulent pathogens or antibiotics** are being used for wrong etiology, e.g. for tubercular or viral or fungal pneumonia.
- **Mechanical reasons** such as underlying lung cancer or sequestrated lung segment.
- **Immunocompromised** state or hypogammaglobulinemia.

Q 23. What do you know about bronchopulmonary sequestration?

Ans. It is a congenital condition in which a portion of nonfunctioning lung tissue is detached from the normal lung and is supplied by an anomalous system artery which arises from the aorta or one of its branches; the segment/tissue has no bronchopulmonary connection/communication. The sequestration may be extralobar (sequestrated segment has separate pleural lining which separates it from the lung) or intralobar (portion or segment shares its pleura with the adjacent normal lung). The patients with lung sequestration present with cough, recurrent pneumonia and occasional hemoptysis.

Q 24. What are poor prognostic indicators in CAP?

Ans.
- Old age (>65 years).
- Coexisting conditions such as heart failure, renal failure, COPD, malignancy, lung abscess.
- Immunocompromised state, e.g. diabetes, alcoholism, HIV, immunosuppression, etc.
- Severe pneumonia, i.e. respiratory rate >30/minute hypotension, high fever, impaired mental status, septicemia.
- Multilobar pneumonia
- Hypoxemia, Pa_2 <60 mmHg while breathing room air or O_2 saturation <90%.
- Virulent organism and presence of pleural effusion.

Q 25. How would you investigate a patient with suspected malignant consolidation?

Ans.
- **Sputum cytology:** It provides high yield for endobronchial tumors such as squamous cell and small cell carcinoma
- **Chest X-ray**
- **Pleural fluid** for biochemistry and cytology
- **Bronchoscopy** gives a higher yield when tumor is accessible endobronchially.
- **CT scan** of the chest and upper abdomen for liver metastases
- **Bone scan** for metastases
- **PET scanning** is highly sensitive and specific for mediastinal staging
- **Pulmonary function tests** so as to evaluate the patient for treatment.

Q 26. What is the aim of staging bronchogenic carcinoma?

Ans. The main aim of staging is to identify candidates for surgery, since this approach offers highest porential cure for lung cancer. The staging assessment covers 3 major issues; distant metastases, state of the chest and mediastinum and the condition of the patient.

Q 27. What is role of surgery in lung cancer?

Ans. Surgery is beneficial in peripheral non-small cell carcinoma. Its role is limited in small cell carcinoma.

Q 28. Which tumors respond to chemotherapy?

Ans. Small cell carcinoma. The drugs used include cyclophosphamide, doxorubicin, cisplatin, etoposide and vincristine. The combination of etoposide and cisplatin appears to have the best therapeutic index of any regimen.

Q 29. What are indications of radiotherapy in bronchogenic carcinoma?

Ans.
- Pain either local or metastatic
- Breathlessness due to bronchial obstruction
- Dysphagia
- Hemoptysis
- Pancoast tumor
- Mediastinal compression/superior vena cava obstruction
- Before and after surgery.

Q 30. How do you diagnose pleural effusion in a patient with consolidation?

Ans. The clues to the diagnosis are:
- **History suggestive of pneumnoia** (fever, pain chest, hemoptysis, cough) and persistence of these symptoms beyond 2–4 weeks.
- **Signs of pleural effusion,** e.g. stony dull percussion note, shifting of trachea and mediastinum.
- **The obliteration of costophrenic angle** in presence of consolidation on chest X-ray.

Q 31. What is the mechanism of trachea being shifted to same side in consolidation?

Ans. Usually, trachea remains central in a case of consolidation but may be shifted to the same side if:
1. **Consolidation is associated with collapse** on the same side (collapse consolidation due to malignancy)
2. **Consolidation is associated with underlying old fibrosis** on the same side.

Q 32. What is typical or atypical pneumonia syndrome?

Ans. **The typical pneumonia syndrome** is characterised by sudden onset of fever, productive cough, pleuritic chest pain, signs of consolidation in the area of radiological abnormality. This is caused by *S. pneumoniae*, *H. influenzae*, *oral anaerobes* and *aerboes* (mixed flora).

The atypical pneumonia syndrome is characterised by insidious onset, a dry cough, predominant extrapulmonary symptoms, such as headache, myalgia, malaise, fatigue, sore throat, nausea, vomiting and diarrhea, and abnormalities on the chest X-ray despite minimal or no physical signs of pulmonary involvement. It is produced by *M. pneumoniae*, *L. pneumophila*, *P. carinii*, *S. pneumoniae*, *C. psittaci*, *Coxiella burnetii* and some fungi *(H. capsulatum)*.

Q 33. What will be the features in malignant consolidation?

Ans. Common features in malignant consolidation are:
1. Patient will be **old** and usually **smoker.**
2. History of **dry persistent hacking cough**, **dyspnea**, **hemoptysis**, **pleuritic chest pain**.
3. There will be **weight loss**, **emaciation** due to malignant cachexia.
4. **Cervical lymphadenopathy** may be present.
5. **Trachea will be central**, i.e. but is shifted to same side if there is associated collapse or to the opposite if associated with pleural effusion.
6. **All signs of consolidation**, i.e. diminished movements, reduced expansion, dull percussion note, bronchial breathing may be present if bronchus is occluded. The bronchial breathing is from the adjoining patent bronchi. The bronchial breathing will, however, be absent if there is partial bronchial obstruction.

7. **Signs and symptoms of local spread,** i.e. pleura (pleural effusion), to hilar lymph nodes (dysphagia due to esophageal compression, dysphonia due to recurrent laryngeal nerve involvement, diaphragmatic paralysis due to phrenic nerve involvement, superior vena cava compression), brachial plexus involvement (i.e. pancoast tumor producing monoplegia), cervical lymphadenopathy (Horner's syndrome—cervical sympathetic compression) may be evident.
8. **Sometimes, signs of distant metastases**, e.g. hepatomegaly, spinal deformities, fracture of rib(s) are present.

Q 34. What are the pulmonary manifestations of bronchogenic carcinoma?

Ans. It may present as:

- **Localised collapse of the lung** due to partial bronchial obstruction.
- **Consolidation**—a solid mass lesion.
- **Cavitation** Secondary degeneration and necrosis in a malignant tumor leads to a cavity formation.
- **Mediastinal syndrome** will present with features of compression of structures present in various compartments of mediastinum (superior, anterior, middle and posterior). These include:
  - Superior vena cava obstruction with edema of face, suffused eyes with chemosis, distended nonpulsatile neck veins, and prominent veins over the upper part of the chest as well as forehead. (Read case discussion on Superior Mediastinal Compression.)
  - Dysphonia and bovine cough due to compression of recurrent laryngeal nerve, stridor due to tracheal obstruction.
  - Dysphagia due to esophageal compression.
  - Diaphragmatic paralysis—phrenic nerve compression.
  - Intercostal neuralgia due to infiltration of intercostal nerves
  - Pericardial effusion due to infiltration of pericardium, myocarditis (arrhythmias, heart failure).
  - Thoracic duct compression leading to chylous pleural effusion.
  - Brachial plexus compression (pancoast tumor) producing monoplegia.

Q 35. What are the extrapulmonary nonmetastatic manifestations of carcinoma lung?

Ans. The paraneoplastic/nonmetastatic extrapulmonary manifestations occur in patients with oat cell carcinoma and are not due to local or distant metastatic spread. These are:

a. **Endocrinal** (hormones produced by the tumor)
   ACTH—Cushing's syndrome
   PTH—hypercalcemia
   ADH—hyponatremia
   Insulin-like peptide—hypoglycemia
   Serotonin—carcinoid syndrome
   Erythropoietin—polycythemia
   Sex hormone—gynecomastia
b. **Skeletal:** Digital clubbing
c. **Skin,** e.g. acanthosis nigricans, pruritus
d. **Neurological**
   - Encephalopathy
   - Myelopathy
   - Myopathy
   - Amyotrophy
   - Neuropathy
e. **Muscular**
   - Polymyositis, dermatomyositis
   - Myasthenia—myopathic syndrome *(Lambert-Eaton syndrome)*
f. **Vascular**
   Migratory thrombophlebitis
g. **Hematological**
   - Hemolytic anemia
   - Thrombocytopenia.

Q 36. Where do the distant metastases occur in bronchogenic carcinoma?

Ans. It spreads to distant organs in **three ways**:

1. ***Lymphatic spread*** involves mediastinal, cervical and axillary lymph nodes
2. ***Hematogenous spread*** involves liver, brain, skin, bone and subcutaneous tissue
3. ***Transbronchial spread*** leads to involvement of other side.

CASE 3: PLEURAL EFFUSION AND EMPYEMA THORACIS

The patient (Fig. 1.3A) presented with fever, pain chest, dyspnea for the last 6 months. No associated cough or hemoptysis.

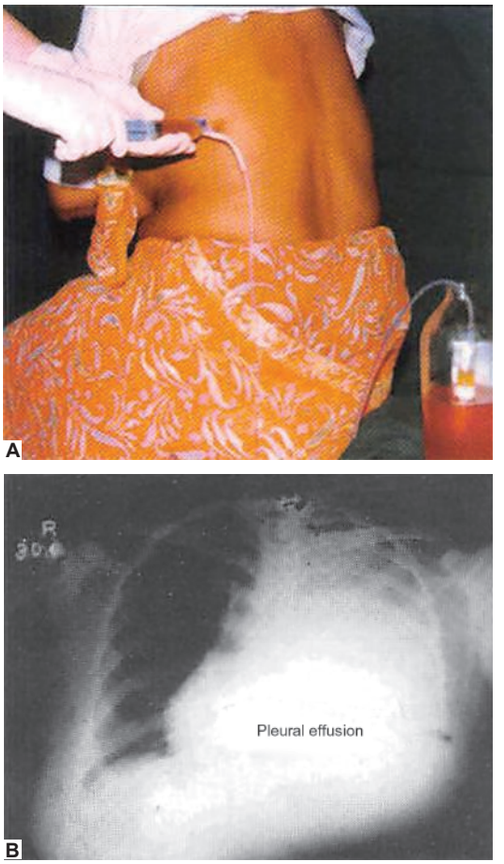


Fig. 1.3A and B: Pleural effusion left side: **A.** Fluid drainage; **B.** Chest X-ray

Clinical Presentations

- Fever, nonproductive cough and pleuritic chest pain
- Heaviness/tightness of chest in massive effusion
- Dyspnea due to compression collapse of the lung by large amount of fluid and shift of the mediastinum to opposite side leading to reduction of vital capacity
- Presence of signs and symptoms of toxemia in case of empyema thoracis.

History

Points to be Noted in History

- History of breathlessness and pleural pain.
- History of fever, cough, rigors, removal of fluid in the past
- History of trauma
- Past/present history of tuberculosis, malignancy
- Occupational history (exposure to asbestos)
- Any skin rash, swelling of joints, lymphadenopathy
- Any history of dysentery in the past
- Hemoptysis
- Is there history of edema, pain abdomen, distension of abdomen (ascites), edema legs?
- Any menstrual irregularity in female

Treatment History—drug taken or being taken.

Examination

Proceed as follows:

I. General Physical Examination (GPE)

- Any puffiness of face or malar flush or rash
- Fever
- Tachypnea
- Tachycardia
- Patient prefers to lie in lateral position on uninvolved side
- Emaciation, clubbing of fingers tar stain
- Cervical lymph nodes may be palpable if effusion is tubercular
- Neck veins may be full due to kinking of superior vena cava or raised JVP
- Signs of underlying cause, e.g. rheumatoid hands or butterfly rash.
- Edema may be present if pleural effusion is due to a systemic disorder
- Look for any rash, arthritis/arthralgia
- Note the vitals, pulse, BP, temperature and respiration.
- Comment on aspiration mark, mastectomy scar or radiation mark.

II. Systemic Examination

Inspection

- Increased respiratory rate
- *Restricted respiratory movement* on affected side (left side in this case)
- *Intercostal spaces* are full and appear widened on the affected side (left side in this case).

Palpation

- *Diminished movement* on the side involved (left side in this case)
- *Chest expansion* on measurement is reduced
- Trachea and apex beat (mediastinum) shifted to opposite side (right side in this case)
- *Vocal fremitus* reduced or absent on affected side (left side in this case)
- No tenderness
- Occasionally, in early effusion, pleural rub may be palpable.

Percussion

- *Stony dull note* over the area of effusion on the affected side (left side in this case)
- *Rising dullness* in axilla (S-shaped Ellis' curve) due to capillary action
- *Skodiac band of resonance* at the upper level of effusion because of compensatory emphysema
- *Traube's area* is dull on percussion
- *No shifting dullness*
- No tenderness.

Auscultation

- Breath sounds are absent over the fluid (left side in this case)
- Vocal resonance is reduced over the area of effusion (left side in this case)
- Sometimes, bronchial breathing (tubular—high-pitched, bronchophony and whispering pectoriloquy) and egophony present at the upper border (apex) of pleural effusion (left interscapular region in this case)
- Pleural rub can be heard in some cases.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. The **diagnosis** is pleural effusion left side probably due to tuberculosis. The positive features in support of **diagnosis** are:

i. Diminished movements on the involved side.
ii. Trachea and mediastinum shifted to opposite side
iii. Stony dull percussion note with rising dullness in left axilla
iv. Vocal fremitus reduced on the side involved
v. Breath sound absent over the effusion but there is bronchial breath sound with egophony at the top of effusion on the back.

Q 2. What are the causes of dullness at lung base?

Ans.
- Pleural effusion
- Thickened pleura
- Collapse of lung
- Raised hemidiaphragm due to amebic liver abscess or ascites.

Q 3. What do you understand by pleural effusion?

Ans. Normal pleural space on each side contains 50–150 ml of fluid but excessive collection of fluid above the normal value is called *pleural effusion* which may or may not be detected clinically.
- Fluid between 150 and 300 ml can be detected radiologically by chest X-ray (obliteration of costophrenic angle).
- More than 500 ml fluid can be detected clinically.

Note: USG of the chest is the earliest means of detecting the small amount of fluid.

Q 4. What are the causes of pleural effusion? What is transudative or exudative fluid?

Ans. Pleural fluid may be ***clear*** (***hydrothorax***) or ***turbid*** (***pyothorax***), may be ***bloodstained*** (***hemorrhagic***) or milky white (***chylous***).

Biochemically, the fluid may be ***transudate*** or ***exudate***; the differences between the two are summarised in Table 1.11.

The **diagnosis of various types of fluids** is given in Table 1.12.

Various types of effusions and their causes are given in Table 1.13.

Q 5. What does raised fluid ADA level indicate?

Ans. 1. Tubercular effusion
2. Effusion due to rheumatoid arthritis.

Q 6. Name the drugs causing pleural effusion.

Ans. Read Table 1.12.

Q 7. What are causes of unilateral, bilateral and recurrent pleural effusion?

Ans. I. **Bilateral pleural effusion.** The causes are:
- Congestive heart failure
- Collagen vascular diseases, e.g. SLE, rheumatoid arthritis

Table 1.11: Characteristics of pleural fluid

Fluid	*Transudate (SFAG >1.1)*	*Exudate (SFAG <1.1)*
1. Appearance	Clear, light yellow	Straw-coloured, turbid or purulent, milky or hemorrhagic
2. Protein	<3 g% or <50% of serum proteins	>3 g% or >50% of serum proteins
3. Serum/fluid albumin gradient	>1.1	<1.1
4. Glucose	Normal	Low
5. pH	>7.3	<7.3
6. Cells (WBCs)	<1000/mm^3	Usually >1000/mm^3
7. Fluid LDH	<2/3rds of serum LDH	>2/3rds of serum LDH
8. Fluid/serum LDH ratio	<0.6	>0.6
9. Fluid adenosine deaminase (ADA) levels	Low	High
10. Fluid cholesterol	Low (<60 mg/dl)	High (>60 mg/dl)
11. Culture	Sterile	May yield organisms

SFAG: Serum fluid albumin gradient.

Table 1.12: Causes of pleural effusion depending on the fluid characteristic

Common	*Uncommon*
I. Transudate (SFAG >1.1)	
× Congestive heart failure	× Superior vena cava obstruction
× Cirrhosis of liver	× Myxedema
× Nephrotic syndrome	× Peritoneal dialysis
× Hypoproteinemia due to any cause	
× Pericardial effusion	
II. Exudate (SFAG <1.1)	
× *Infections*, e.g. tubercular, bacterial (pneumonia), viral	× Chylothorax
× *Malignancy*, e.g. bronchogenic (common), mesothelioma (rare), lymphoma rare	× Pancreatitis
× *Collagen vascular disorders*, e.g. SLE, rheumatoid arthritis, Wegener's granulomatosis	× Esophageal perforation
× *Pulmonary emboli*	× Subphrenic abscess
× *Meig's syndrome*	× Postcardiac injury syndrome
× *Sarcoidosis*	× Uremia
× *Asbestosis*	× Radiation injury
× *Ruptured liver abscess* into pleural space	× Iatrogenic
	Drug-induced effusion, e.g.
	× Nitrofurantoin
	× Dantrolene
	× Methysergide
	× Bromocriptine
	× Procarbazine
	× Amiodarone

Table 1.13: Various types of fluids and their causes

1. *Chylous (milky) effusion* (triglyceride >1000 mg% with many large fat globules)
   - Nephrotic syndrome
   - Tubercular
   - Malignancy
   - Lymphoma
   - Filariasis
   - Myxedema
   - Trauma to chest wall

Ether extraction dissolves fat and leads to clearing; confirms true chylous nature of fluid

2. *Chyliform* (fat present is not derived from thoracic duct but from degenerated leukocytes and tumor cells). The fat globules are small. Causes are:
   - Tubercular
   - Carcinoma of lung and pleura
3. *Pseudochylous*. Milky appearance is not due to fat but due to albumin, calcium, phosphate and lecithin. Causes are:
   - Tuberculosis
   - Nephrosis
   - Heart disease
   - Malignancy

Alkalinisation dissolves cellular protein and clears the fluid thus differentiates it from true chylous

4. *Cholesterol effusion* (glistening opalescent appearances of fluid due to cholesterol crystals). Causes are:
   Long-standing effusion, e.g. tuberculosis, carcinoma, nephrotic syndrome, myxedema and postmyocardial infarction
5. *Hemorrhagic effusion* (hemothorax, e.g. bloodstained fluid or fluid containing RBCs)
   - Neoplasm, e.g. primary or secondary pleural mesothelioma
   - Chest trauma (during paracentesis)
   - Tubercular effusion
   - Leukemias and lymphoma
   - Pulmonary infarction
   - Bleeding diathesis
     - Anticoagulant therapy
     - Acute hemorrhagic pancreatitis

- Lymphoma and leukemias
- Bilateral tubercular effusion (rare)
- Pulmonary infarction.

II. **Unilateral pleural effusion.** The causes are:
Right-sided effusion
- Rupture of acute amebic liver abscess into pleura
- Cirrhosis of the liver
- Congestive cardiac failure
- Meig's syndrome—fibroma of ovary with pleural effusion and ascites.

III. **Causes of recurrent pleural effusion**
- Malignancy lung (e.g. bronchogenic, mesothelioma)
- Pulmonary tuberculosis
- Congestive heart failure
- Collagen vascular disorder.

Q 8. What is empyema thoracis? What are its causes?

Ans. Collection of pus or purulent material in the pleural cavity is called *empyema thoracis*.

The causes are

1. **Diseases of the lung** (infection travels from the lung to the pleura either by contiguity or by rupture)
   - Lung abscess
   - Pneumonia
   - Tuberculosis
   - Infection
   - Bronchiectasis
   - Bronchopleural fistula.
2. **Diseases of the abdominal viscera** (spread of infection from abdominal viscera to pleura)
   - Liver abscess (ruptured or unruptured)
   - Subphrenic abscess
   - Perforated peptic ulcer.
3. **Diseases of the mediastinum:** There may be infective focus in the mediastinum from which it spreads to the pleura.
   - Cold abscess
   - Esophageal perforation
   - Osteomyelitis.
4. **Trauma with superadded infection**
   - Chest wall injuries (gunshot wound, stab wound)
   - Postoperative
5. **Iatrogenic:** Infection introduced during procedure.
   - Chest aspiration
   - Liver biopsy.
6. **Bloodborne infection,** e.g. septicemia.

Q 9. What are physical signs of empyema thoracis?

Ans. Patient has a toxic look and prostration:
- **Signs of toxemia** (fever, tachypnea and tachycardia). There is hectic rise of temperature with chills and rigors.
- **Digital clubbing** may be evident.
- **Intercostal spaces** are full and may be **tender.**
- **All signs of pleural effusion** will be present except rising dullness in axilla. This is due to collection of thick pus rather than clear fluid which does not obey the law of capillary action.
- **The skin is red, edematous and glossy overlying empyema** of recent onset. There may be a scar mark of an intercostal drainage (tube aspiration).
- Rarely, a **subcutaneous swelling on the chest** wall may be seen called *empyema necessitans*. The swelling increases with coughing.

Tip: The presence of signs of toxemia (toxic look, fever, tachypnea, tachycardia, sweating) in a patient with pleural effusion indicates *empyema thoracis.*

Q 10. What is massive pleural effusion?

Ans. It refers to a large collection of fluid causing gross shirring of the mediastinum to the opposite side with stony dull note extending up to 2nd intercostal space or above on front of the chest.

Q 11. What is Meig's syndrome?

Ans. It comprises right-sided transudative pleural effusion associated with an ovarian tumor usually benign (e.g. fibroma).

Q 12. What is phantom tumor (pseudotumor)?

Ans. This is nothing but an interlobar effusion (effusion in interlobar fissure) producing a rounded homogenous opacity on chest X-ray. This mimics a tumor due to its dense opacity but disappears with resolution of effusion, hence, called *phantom tumor*. This is occasionally seen in patients with congestive heart failure and disappears with diuretic therapy.

Q 13. What is subpulmonic effusion? When would you suspect it?

Ans. A collection of fluid below the lung and above the diaphragm is called *subpulmonic effusion*.

This is suspected when diaphragm is unduly elevated on one side on chest X-ray. Chest X-ray taken in lateral decubitus position shows pleural effusion (layering out of the opacity along the lateral chest wall) which confirms the diagnosis.

Q 14. How do you explain the position of trachea either as central or to the same side in a case with pleural effusion?

Ans. Remember that negative intrapleural pressure on both sides keeps the trachea central, but, it is shifted to opposite side when a positive pressure develops in one of the interpleural spaces, therefore, midline trachea despite pleural effusion on one side could be due to:

- **Mild pleural effusion** (insignificant positive pressure develops).
- **Loculated or encysted pleural effusion** (positive pressure develops but not transmitted to opposite side—no pushing effect).
- **Bilateral pleural effusion** (both pleural cavities have positive pressure that neutralise each other's effect).
- **Pleural effusion associated with apical fibrosis** (fibrosis pulls the trachea to same side and neutralises die pushing effect of pleural effusion on the same side).
- **Malignant pleural effusion with absorption collapse** due to endobronchial obstruction. Due to collapse, trachea toes to shift towards the same side but pushing effect of effusion keeps it central in position.
- **Collapse consolidation due to any cause** (isolated collapse and isolated consolidation has opposing effects).

Remember: Trachea can be shifted to same side in a case of effusion, if an underlying lung disease (e.g. collapse or fibrosis on the same side) exerts a pulling effect on the trachea and overcomes the pushing effect of effusion.

Q 15. What are signs at the apex (upper level) of pleural effusion?

Ans. The following signs develops only and occasionally in moderate (500–1000 ml) pleural effusion.

- **Rising dullness;** S-shaped Ellis curve in axilla
- **Skodiac resonance**—a band of hyper-resonance due to compensatory emphysema
- **Bronchial breathing**—high-pitched tubular with bronchophony, whispering pectoriloquy and aegophony
- **Pleural rub**—rarely.

Q 16. What are the causes of recurrent filling of pleural effusion after paracentesis?

Ans. Recurrent filling of the pleural effusion means appearance of the fluid to same level or above it on X-ray chest within few days (rapid filling) to weeks (slow filling) after removal of die fluid. That is the reason, a chest X-ray is taken before and after removal of the fluid to know the result of the procedure, its complications and later on its refilling. **The causes** are:

1. ***Rapid refilling of pleural effusion***
   - Malignancy
   - Acute tuberculosis.
2. ***Slow refilling***
   - Tubercular effusion on treatment
   - Congestive cardiac failure—slow response or no response to conventional diuretics
   - Collagen vascular disorders
   - Meig's syndrome.

Q 17. What are the pathogenic mechanisms of pleural effusion?

1. ***Involvement of pleura by malignant infiltration,*** primary tumor or inflammatory process resulting in increased permeability.
2. ***Disruption of fluid containing structure in pleural cavity*** such as thoracic duct, esophagus, blood vessels with leakage of contents into pleural space.
3. ***Rupture of subpleural lung abscess*** or ***amoebic liver abscess*** into pleura.
4. ***Abnormal hydrostatic or lower osmotic pressure*** on an otherwise healthy pleura leading to transudation into pleural cavity.

Q 18. What are the complications of pleural effusion?

Ans. Common complications of pleural effusion are:

- **Thickened pleura** (indicates healed pleural effusion).
- **Empyema thoracis**—spontaneous or iatrogenic (during tapping of effusion with introduction of infection with improperly sterilised needle).
- **Nonexpansion of the lung.** Usually, after removal of pleural fluid, there is re-expansion of the compressed lung immediately, but sometimes in long-standing cases, it may not occur due to underlying fibrosis.
- **Acute pulmonary edema** is a procedural complication, develops with sudden withdrawal of a large amount of fluid. It is uncommon.
- **Hydropneumothorax** is again iatrogenic (procedural complication) due to lung injury and leakage of air into pleural space during

pleural aspiration. To know this complication, a repeat X-ray chest is necessary after aspiration.

- **Cachexia** may develop in long-standing and malignant pleural effusion.

Q 19. What are clinical differences between thickened pleura and pleural effusion.

Ans. The differences are:

Thickened pleura	*Pleural effusion*
Chest is normal or retracted on the side involved	Chest is normal or prominent on side involved
Movements are diminished	Movements of chest are markedly diminished
No shift of trachea or mediastinum	Trachea or mediastinum is shifted to opposite side
Percussion note is impaired with no rising dullness	Percussion note is stony dull and there is rising dullness
Breath sounds are just diminished over the site involved	Breath sounds are absent over the area of effusion

Q 20. What are causes of lymphadenopathy with pleural effusion?

Ans. **Common causes** are:

1. **Tubercular lymphadenitis** with pleural effusion (lymph node in cervical, axillary, mediastinal regions may be enlarged)
2. **Lymphomas** (effusion with generalised lymphadenopathy and splenomegaly)
3. **Acute lymphoblastic leukemia** (cervical and axillary lymph nodes enlargement)
4. **Malignancy lung** (scalene node, Virchow's gland, mediastinal lymph node)
5. **Collagen vascular disorder** (generalised lymphadenopathy)
6. **Sarcoidosis** (cervical, bilateral hilar lymphadenopathy).

Q 21. What are differences between tubercular and malignant pleural effusions?

Ans. Tubercular and malignant pleural effusions are differentiated in Table 1.14.

Table 1.14: Differentiating features between tubercular and malignant pleural effusions

Tubercular	*Malignant*
A. Clinical characteristics	
Commonest cause of effusion in all age groups	Common cause in old age
Slow, insidious onset, can be acute or sudden	Acute sudden onset
Slow filling	Rapid filling
Cough, fever (evening rise), hemoptysis, night sweats are common complaints	Cough, hemoptysis, dyspnea, tightness of chest, hoarseness of voice are presenting symptoms
Cervical, axillary lymph nodes may be enlarged	Scalene nodes or Virchow's gland enlarged
Weakness, loss of weight present	Marked cachexia and prostration
Clubbing uncommon	Clubbing common
No signs of local compression	Signs of local compression, e.g. superior vena cava (prominent neck veins and chest veins), trachea (dysphonia), esophagus (dysphagia), and phrenic nerve (diaphragmatic paralysis) may be accompanying symptoms
Localised crackles or rhonchi may be present depending on the site and type of lung involvement	Localised wheeze or rhonchi common than crackles
B. Fluid characteristics	
Straw-coloured exudate	Hemorrhagic, exudate
Lymphocytes present	Malignant cells may be present along with RBCs
Cob-web coagulum on standing	RBCs may settle down on standing if hemorrhagic

Q 22. What do you know about pleural involvement in rheumatoid arthritis (RA)?

Ans. Pleural involvement in RA is associated with male gender, positive rheumatoid factor in serum (seropositive disease), presence of nodules and other systemic manifestations. The effusion is usually left-sided, may be bilateral, develops as an inflammatory response to the presence of multiple subpleural nodules. The pleural fluid is an exudate with low glucose concentration. Low glucose content is due to consumption of glucose by the inflammatory cells.

Q 23. How will you investigate a case of pleural effusion?

Ans. A pleural effusion being of varied etiology, needs investigations for confirmation of the diagnosis as well as to find out the cause.

1. ***Routine blood tests*** (TLC, DLC and ESR). High ESR and lymphocytosis go in favour of tubercular effusion.
2. ***Blood biochemistry***
   - Serum amylase for pancreatitis
   - Autoantibodies for collagen vascular disorders
   - Rheumatoid factor for rheumatoid arthritis.
3. ***Chest X-ray*** (PA view, Fig. 1.3B) shows:
   - A lower homogenous opacity with a curved upper border which is concave medially but rising laterally towards the axilla.
   - Obliteration of costophrenic angle. It is the earliest sign hence, present in all cases of pleural effusion irrespective of its cause except loculated or encysted effusion.
   - Shift of trachea and mediastinum to opposite side.
   - Lateral view is done to differentiate it from lobar consolidation.
   - Lateral decubitus view is taken in case of subpulmonic effusion.
   - Repeat X-ray chest after therapeutic aspiration of fluid.
4. ***Sputum examination***
   For AFB and malignant cells

5. ***Mantoux test.*** It is not much of diagnostic value, may be positive in tuberculosis, negative in sarcoidosis, lymphoma and disseminated (miliary) tuberculosis or tubercular effusion in patients with AIDS.
6. ***FNAC of lymph node,*** if found enlarged.
7. ***Ultrasonography*** is done to confirm the diagnosis and to mark the site for aspiration, and to find out the cause.
8. ***CT scan and MRI*** are usually not required for diagnosis, but can be carried out to find out the cause wherever appropriate, and to differentiate localised effusion from pleural tumor.
9. ***Aspiration of pleural fluid for***
   Confirmation of diagnosis. At least 50 ml of fluid is to be removed and subjected to:
   - Biochemistry (transudate/exudate), LDH, ADA, cholesterol and pH of fluid if empyema is suspected
   - Cytology (for malignant cells, RBCs, WBCs and pus cells)
   - Smear examination (e.g. Gram' stain, Ziehl-Neelsen stain, special stains for malignant cells)
   - Culture for AFB. Recently introduced BACTEC system gives result within 7 days. Amylase level when malignancy or pancreatitis is suspected.

Note: For indications of pleural aspiration, read bedside procedures and instruments used.

10. ***Bronchoscopy*** in a suspected case of bronchogenic carcinoma.
11. ***Pleural biopsy*** for histopathological examination and mycobacterial culture or to find out the cause.
12. ***Thoracoscopy*** to inspect the pleura so as to find out the cause. It is done rarely.

Q 24. What are the uses of ultrasonography in pleural effusion?

Ans. Uses other than the confirmation and exclusion:
1. For diagnosis of loculated effusions
2. For guided thoracocentesis, closed pleural biopsy or insertion of a chest drain.
3. To differentiate pleural fluid from pleural thickening.

Q 25. What investigations would you carry out to find out the cause?

Ans.
- Pleural biopsy
- CT chest
- MRI chest.

Q 26. Name the conditions in which fluid pH and glucose concentration are low?

Ans.
- Empyema thoracis
- Malignancy lungs
- Tuberculosis of lung
- Rheumatoid pleural effusion
- SLE with effusion.

Q 27. What is the role of pleural fluid cytology in diagnosis of pleural effusion?

Ans.
- **Pleural fluid cell count.** Pleural fluid contains 1500 cells/HPF (predominantly mononuclear cells). Counts >50,000 are seen in parapneumonic effusion or empyema, whereas low count <1000 cells/HPF indicates transudate.
- **Pleural fluid lymphocytosis** indicates tuberculosis, malignancy, collagen vascular disease, lymphoma and sarcoidosis.
- **Computerised interactive morphometry** (analyses the size and nuclei of cells in a centrifuged specimen of fluid) differentiates between malignant cells and reactive lymphocytosis.

Q 28. What does a pleural fluid total neutral fat levels >400 mg/dl and triglyceride levels >1000 mg/dl indicate?

Ans. It indicates chylous pleural effusion. Read the causes in Table 1.13.
The patient whose X-ray is depicted in Fig. 1.4A presented with acute severe dyspnea, tachypnea and tachycardia of few days duration. The patient was cyanosed and was admitted as an emergency.

CASE 4: PNEUMOTHORAX

The patient whose X-ray is depicted in Fig. 1.4A presented with acute severe dyspnea, tachypnea and tachycardia of a few days duration. The patient was cyanosed and was admitted as an emergency.

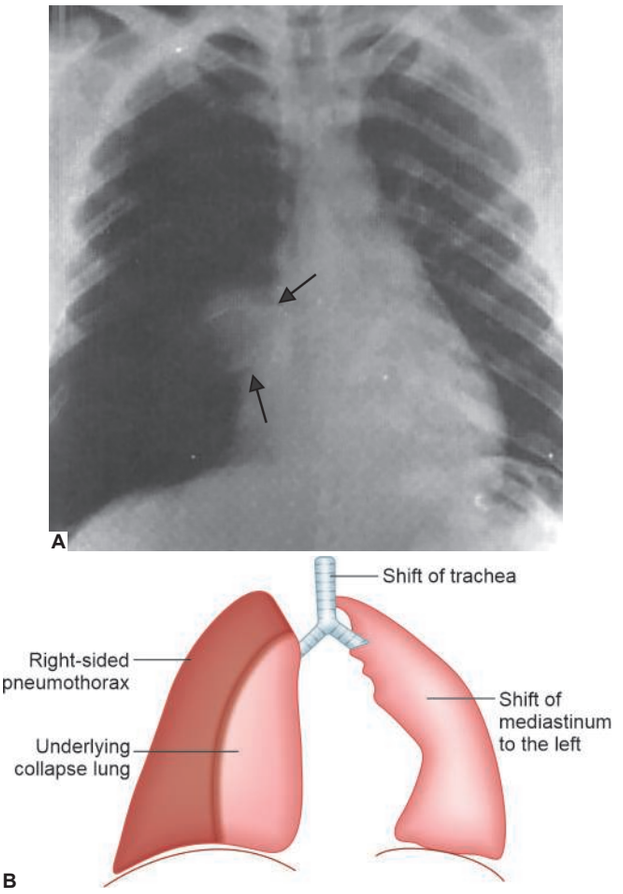


Fig. 1.4A and B: Pneumothorax: **A.** Chest X-ray of a patient showing right-sided pneumothorax. The collapsed lung is indicated by arrows; **B.** Diagrammatic illustration of pneumothorax

Clinical Presentations

- Acute onset of dyspnea at rest
- Associated pain chest or tightness of chest
- Symptoms nonprogressive
- Palpitation and tachypnea common
- Increasing breathlessness, cyanosis, tachycardia, tachypnea, and hypotension suggest spontaneous tension pneumothorax
- Patient may have wheezing or other symptoms of COPD if it is the cause
- Cough aggravates breathlessness which is not relieved by any means except sitting posture.

History

Points to be Noted in History

- Ipsilateral acute pleuritic pain
- Past/present history of COPD, asthma, tuberculosis, hemoptysis or trauma
- History of similar episodes in the past
- History of recent pleural aspiration or insertion of subclavian line or recent surgery on head and neck
- History of Marfan's syndrome
- History of HIV (sexual contact)
- History of positive pressure ventilation
- Any history of IHD (chest pain in the present or past)
- Any history of prolonged immobilisation or calf pain (pulmonary thromboembolism).

Examination

Proceed as follows:

I. General Physical Examination

- Posture: Patients prefer to lie on the uninvolved side in lateral decubitus position or propped up position.
- Restlessness.
- Tachypnea (respiratory rate is increased), dyspnea at rest
- Tachycardia
- Central cyanosis indicates tension pneumothorax
- Lymph nodes may or may not be palpable
- Trachea may be shifted to opposite side (sternomastoid sign or Trail's sign may be positive)
- Accessory muscles of respiration may be actively working
- Ear, nose, throat may be examined
- Note the vitals, i.e. pulse, BP, temperature and respiration. Presence of hypotension or shock indicates tension pneumothorax, creates an emergency situation and warrants removal of the air.
- Look for clues regarding etiology, e.g.
  - Pleural aspiration site
  - Infraclavicular region for a bruise from the central line.
  - Marfanoid features
  - Inhalor or peak flowmeter by bedside to ascertain asthma or COPD.

II. Systemic Examination

Inspection

- Diminished movements on the side involved (right side in this case)
- Intercostal spaces widened and full on the side involved (right side in this case)
- Apex beat displaced to opposite side (left side in this case)
- Accessory muscles of respiration are hyperactive and stand out prominently in tension pneumothorax.

Palpation

- Shift of trachea and apex beat (mediastinum) to the opposite side (e.g. left side in this case)
- Diminished movements on the side involved (e.g. right side)
- Expansion of chest decreased (on manual or tape measurement)

- Tactile vocal fremitus is reduced on the side involved (right side).

Percussion

- Hyperresonant percussion note on the side involved (right side). It is a diagnostic sign and differentiates it from pleural effusion.
- Obliteration of liver dullness if right side is involved (obliterated in this case), splenic dullness if left side is involved (not applicable in this case).

Auscultation

- Diminished vesicular breathing or absent breath sounds on the side involved (right side in this case). Bronchial breathing indicates bronchopleural fistula (open pneumothorax)
- Vocal resonance diminished over the area involved (right side)
- No adventitious sound.

Tip: Silent hyperresonant chest is characteristic of pneumothorax.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your diagnosis and why?

Ans. Sir, my provisional diagnosis is right-sided pneumothorax. The points in favour of diagnosis are:

i. Patient is slightly dyspneic.
ii. **Prominent chest on the side involved** with diminished movements.
iii. **Shifting of trachea and mediastinum** to opposite side (left side in this case).
iv. **Reduced vocal fremitus and vocal resonance** on the side involved (right side).
v. **Hyperresonant percussion note** with diminished/ absent breath sounds on the side involved (right side in this case).

Q 2. What is pneumothorax?

Ans. Presence of air in the pleural cavity is called *pneumothorax*.

Q 3. What is your differential diagnosis?

Ans. It has to be differentiated from large air cyst or a large bulla.

Table 1.15 differentiates between a large bulla and pneumothorax.

Table 1.15: Differentiating features of bulla from pneumothorax

Large air cyst or bulla	*Pneumothorax*
× May be congenital or acquired	× Acquired usually
× Mediastinum not shifted (trachea central)	× Mediastinum shifted to opposite side (trachea shifted to opposite side)
× No underlying collapse of the lung on chest X-ray	× Collapse of the lung is demarcated from the pneumothorax by a thin line on chest X-ray

Q 4. What type of pneumothorax does your patient has?

Ans. Table 1.16 discusses various types of pneumothorax and their clinical features. My patient has closed pneumothorax.

Q 5. Does the patient has tension pneumothorax?

Ans. No, patient does not have signs of cardiorespiratory embarrassment, i.e. *tachypnea*, *tachycardia*, *hypotension*, *pulsus paradoxus* and *cyanosis*.

Q 6. What emergency measure would you adopt on bedside if it develops?

Ans. I will put a large bore needle in second intercostal space in sitting position on the side involved to relieve tension pneumothorax followed by appropriate drainage.

Q 7. How do you classify pneumothorax?

Ans. The pneumothorax is divided into two categories; *spontaneous* and *traumatic*.

I. The spontaneous pneumothorax may be **primary** (underlying lung is healthy) or **secondary** (occurs as a complication of some lung disease).
II. The traumatic pneumothorax results from trauma (e.g. chest injury or procedural trauma). The causes of pneumothorax are given in Table 1.17.

Q 8. What is recurrent spontaneous pneumothorax?

Ans. This refers to occurrence of second episode of pneumothorax within few weeks following the first episode. It occurs due to rupture of subpleural blebs or bullae in patients suffering from COPD. It is serious condition, needs chemical pleurodesis (instillation of kaolin, talcom, minocycline or 10% glucose into pleural space) or by surgical pleurodesis (achieved by pleural abrasions or parietal pleurectomy at thoracotomy or thoracoscopy). The causes of recurrent pneumothorax are given in Table 1.18.

Caution: Patients, who are at increased risk of developing recurrent pneumothorax after the first episode (e.g. flying or diving personnel) should undergo preventive treatment (respiratory exercises) after first episode. The respiratory exercises include to inflate air pillows, balloons or football bladder. It will also help to achieve expansion of the collapsed lung.

Q 9. What are the complications of pneumothorax?

Ans. Common complications of pneumothorax are:

1. Hydropneumothorax
2. Empyema thoracis, pyopneumothorax
3. Hemopneumothorax
4. Thickened pleura
5. Acute circulatory failure—cardiac tamponade in tension pneumothorax
6. Atelectasis of the lung

Table 1.16: Types of pneumothorax and their clinical features

Feature	*Closed (Fig. 1.4A)*	*Open*	*Tension (valvular)*
Pathogenesis	The rupture sidte (opening) gets closed and underlying lung is collapsed (deflated). There is no communication between bronchus and the pleural space	The opening between the bronchus and pleural space does not close, remains patent, hence, called *bronchopleural fistula*	The communication between bronchus and pleural space persists and acts as a check valve (air can get in but cannot get out)
Mean pleural pressure	Negative (less than atmospheric pressure) hence, air can get absorbed and lung re-expands	Mean pleural pressure is atmospheric, hence, lung cannot reexpand. Secondly, due to patent communication, pneumothorax is likely to be infected leading to *pyopneumothorax*—a common complication	Mean pleural pressure is positive, hence, there is compression collapse of the underlying lung. It is an emergency situation because mean pleural pressure goes on building due to constant air entry during inspiration resulting in mediastinal shift and impaired venous return leading to cardiac tamponade requiring urgent drainage
Causes	× Rupture of subpleural bleb or emphysematous bullae × COPD × Spontaneous due to congenital bleb rupture × Rupture of pulmonary end of pleural adhesion × Secondary to lung disease × Chest injury	× Tubercular cavity × Lung abscess × Necrotizing pneumonia × Chest trauma × Barotrauma × Empyema thoracis × Lung resection	× It can occur due to any cause × Catamenial pneumothorax (endometriosis in female)
Symptoms	× Mild cases may be asymptomatic and only chest X-ray may show pneumothorax × Some patients may present with breathlessness, pain chest/tightness of chest × Onset of dyspnea may be acute or subacute	× Majority of patients with bronchopleural fistula present with cough, fever, mucopurulent or purulent expectoration. Dyspnea is minimal. × Some complain of sensation of splash of fluid in the chest during jumping (e.g. hydropneumothorax)	× The presenting symptoms include acute onset of dyspnea, cough, tachypnea, tachycardia × Cough worsens dyspnea. No relieving factor known except sitting position × Hypotension or shock and central cyanosis may be present due to cardiac tamponade
Signs on the side involved	× Reduced chest movement × Shift of trachea and mediastinum to opposite side × Hyperresonant note × Markedly diminished or absent breath sounds × Vocal fremitus and resonance are also reduced × *Coin test* is positive	× All signs of closed pneumothorax present ***plus*** × Crack-pot sounds on percussion × Amphoric breath sounds with increased vocal resonance × Succussion splash indicates hydropneumothorax × Shifting dullness present if hydropneumothorax develops × *Coin test* may be positive	× All signs of closed pneumothorax present ***plus*** × Dyspnea, tachypnea, tachycardia, cyanosis × Pulsus paradoxus × Neck veins full, markedly raised JVP × Hypotension × Obtainded consciousness × Progressive mediastinal shift to opposite side with laboured respiration
Plan of treatment	× Observation till air is automatically absorbed × Water-seal drainage, if necessary	× Water seal drainage × Treat hydro- or pyopneumothorax with proper antibiotic × Thoracic surgeon consultation should be sought	× Immediate relief can be given by putting a wide bore needle (No. 20) in second intercostal space in sitting position in midclavicular line on side involved followed by water-seal drainage system. × Antitubercular drugs/antibiotic therapy as considered appropriate × O_2 inhalation and propped up position × Resuscitation of shock × Morphine 5–10 mg subcutaneous

7. Surgical emphysema and pneumomediastinum.

Q 10. How would you grade the degree of collapse in pneumothorax?

Ans. **British thoracic society grading** is:

- **Small;** where there is small rim of air (translucent area) around the lung.
- **Moderate;** when the lung is compressed towards the hilum (*see* Fig. 1.4A) by a large translucent area containing air.
- **Complete;** Airless lung, separate from diaphragm (aspiration is necessary)
- **Tension;** Any pneumothorax with signs of cardiorespiratory distress.

Q 11. When would you suspect tension pneumothorax?

Ans. Tension pneumothorax should be suspected in patients with signs of pneumothorax with any of the following:

- *Severe progressive dyspnea*
- *Tachypnea* (RR >30 min) tachycardia (HR >130/min), cyanosis
- *Hypotension, pulsus paradoxus*
- *Marked mediastinal shift.*

Q 12. What do you understand by the term subcutaneous emphysema? What are its causes?

Ans. *Subcutaneous emphysema* (or surgical emphysema—an older term) refers to presence of

Table 1.17: Causes of pneumothorax

I. **Spontaneous**

A. *Primary*
- Rupture of apical subpleural bleb or bulla in young patients
- Subpleural emphysematous bullae in old patients
- Rupture of the pulmonary end of pleuropulmonary adhesion. The risk factors for it include:
  - Tall body habitus
  - Smoking
  - Marfan's syndrome
  - Mitral valve prolapse
  - Going to high altitude
  - Bronchial anatomical abnormalities

B. *Secondary*
- COPD
- Pulmonary tuberculosis (subpleural focus) usually results in hydropneumothorax
- Infections, e.g. necrotising pneumonia, staphylococcal lung abscess, usually result in hydropneumothorax or pyopneumothorax
- Occupational lung disease, e.g. silicosis, coal-worker's pneumoconiosis
- Malignancy lung
- Interstitial lung disease
- Catamenial (endometriosis in females)
- Miscellaneous, e.g. esophageal rupture, cystic fibrosis, Caisson's disease, asthma, pulmonary infarct, postradiation, etc.

II. **Traumatic**

Injury	*Iatrogenic (procedural)*
Blunt injury to the chest or abdomen	Pleural tap
Penetrating chest injury	Pleural biopsy, lung biopsy
	Bronchoscopy, endoscopy and sclerotherapy

III. **Induced (artificial)**

It was induced in the past to obliterate a tubercular cavity but is now obsolete term

Table 1.18: Causes of recurrent pneumothorax
- Rupture of apical subpleural bleb or emphysematous bullae
- Cystic fibrosis
- Rupture of lung cysts
- Rupture of bronchogenic carcinoma or esophageal carcinoma
- Catamenial pneumothorax
- AIDS
- Interstitial lung disease

air in the subcutaneous space either formed by necrotizing inflammation of the tissue by gas-forming organisms (gas gangrene) or by leakage of air from the lungs or neighbouring hollow structures. The **causes** are:
- Pneumothorax
- Rib fracture or flail chest with leakage of air
- Fractures of paranasal sinuses
- Perforation of a hollow viscus, e.g. esophagus or larynx (spontaneous or procedural)
- Gas gangrene.

Always look for subcutaneous emphysema in a case of pneumothorax by palpation with pressure of fingers over the side involved. There will be palpable crepitus on finger pressure.

Q 13. How will you investigate a patient with pneumothorax?

Ans. Investigations are done for sake of diagnosis and to find out the cause.

1. ***Chest X-ray (PA view,*** Fig. 1.4A***)*** should be done first of all before any other investigation in case of suspected pneumothorax. It is done in erect position, sometimes expiratory film is taken especially in small pneumothorax. The radiological features are:
   - Increased translucency of the lung on die side involved with absence of peripheral lung markings.
   - The underlying lung is collapsed which is separated from airless peripheral translucent shadow (pneumothorax) by a pencil—sharp border.
   - Mediastinum is shifted to opposite side.
   - Costophrenic angle is clear.
   - Underlying lung disease may be apparent such as a tubercular cavity.
2. ***Routine blood tests,*** e.g. TLC, DLC, ESR (raised ESR with relative mononuclear leukocytosis suggest tubercular etiology).
3. ***Mantoux test*** may be positive in tuberculosis.
4. ***Sputum for AFB*** (3 consecutive specimens).
5. ***Pulmonary function tests*** (FEV_1, FEV_1/VC ratio, PFR, etc. for COPD).

Q 14. What are similarities and dissimilarities between pleural effusion and pneumothorax?

Ans. Similarities and dissimilarities are as follows:
- Some clinical features on chest examination whether there is air or fluid in the pleural space are similar due to shift of the mediastinum to opposite side and collapse of the underlying lung as a result of positive intrapleural pressure (normally there is negative pressure in the pleural space on both sides which keeps the mediastinum in the center). The similarity of signs include diminished movements and expansion, fullness of intercostal spaces on the side involved, shift of mediastinum to opposite side, hyperactivity of extrarespiratory muscles, diminished or bronchial breath sounds and decreased or increased vocal resonance with no added sounds.
- The dissimilarities include hyperresonant note on percussion in pneumothorax with obliteration or masking of liver dullness in right-sided pneumothorax and splenic dullness on left side pneumothorax. In pleural effusion, the percussion note is stony-dull on the side and over the part involved. The dullness is continuous with liver dullness on right side and cardiac dullness on left side with obliteration of resonance of Traube's area.

Tip: Absolute similarity is silent chest, i.e. no added sounds in both the conditions.

Absolute dissimilarity is hyperresonant note in pneumothorax and stony dull in pleural effusion.

Note: Bronchial breath sounds with increased vocal resonance can occur both in pleural effusion (at the upper level or apex) and bronchopleural fistula (open pneumothorax).

N.B.: Questions regarding water-seal intercostal tube drainage, its indications, complications and reasons for nonexpansion of the lungs after drainage have been discussed in instruments and procedures (Chapter 2).

Q 15. How would you manage this patient?

Ans. As this patient has a large pneumothorax, hence aspiration is needed. Large pneumothorax with normal lungs is managed by simple aspiration rather than an intercostal tube drainage, aspiration is less painful than intercostal drainage, leads to shorter admission and reduces the need for pleurectomy with no increase in recurrence rate.

When there is rapid re-expansion following simple aspiration an intercostal tube with underwater seal drainage is used. The tube should be left for 24 hours. When the lung re-expands, clamp the tube for 24 hours. If repeat chest X-ray shows that lung remains expanded, the tube can be removed. If not, suction should be applied to the tube.

If fails to resolve within one week, surgical pleurodesis should be considered.

Small pneumothorax (<20% in size) spontaneously resolve within weeks.

Q 16. How would you perform a pleurodesis?

Ans. By injecting talc into pleural cavity via intercostal tube.

Q 17. In which patient, pleurodesis is not performed?

Ans. In patients with fibrosis, pleurodesis is not attempted as they need lung transplantation in future and pleurodesis would make it technically not feasible.

Q 18. What are indications of open thoracotomy?

Ans. It is considered when one of the following is present:

- A third episode of spontaneous pneumothorax
- An occurrence of bilateral pneumothorax
- Failure of the lung to expand after tube thoracotomy.

CASE 5: HYDROPNEUMOTHORAX

The patient whose X-ray is depicted as Fig. 1.5A presented with fever, cough with expectoration, mucopurulent foul smelling without hemoptysis. The patient gave history of some abnormal sounds (crack-pots) on running or walking.

Clinical Presentation

- Dyspnea at rest, cough with mucopurulent foul smelling sputum
- Pain chest or heaviness in chest
- Splashing sound during jumping
- Fever, high grade with chills and rigors if pyopneumothorax.

Points to be Noted in the History

- History of fever or injury in the past
- History of tuberculosis in the past
- Any history of pain chest, hemoptysis or a cardiac disorder
- Any history of drainage of fluid in the past.

EXAMINATION

General Physical Examination

- Patient is orthopneic, sitting in the bed
- Fever
- Tachypnea, tachycardia
- Cyanosis
- Clubbing of fingers present in pyopneumothorax
- Accessory muscles of respiration may be active
- Shift of trachea and mediastinum to opposite side—*Sternomastoid sign or Trail sign* may be positive.

Systemic Examination

Inspection

Signs similar to open pneumothorax.

Palpation

Signs similar to open pneumothorax.

Percussion

- A horizontal fluid level, above which percussion note is hyperresonant and below which it is stony dull hence, there is a clear cut transition between a hyperresonant to stony dull note
- Shifting dullness present because fluid has space (occupied by air) to shift
- Coin test may be positive.

Auscultation

- Succussion splash present
- Amphoric bronchial breathing present in bronchopleural fistula—a common cause of hydropneumothorax
- Tingling sounds heard.

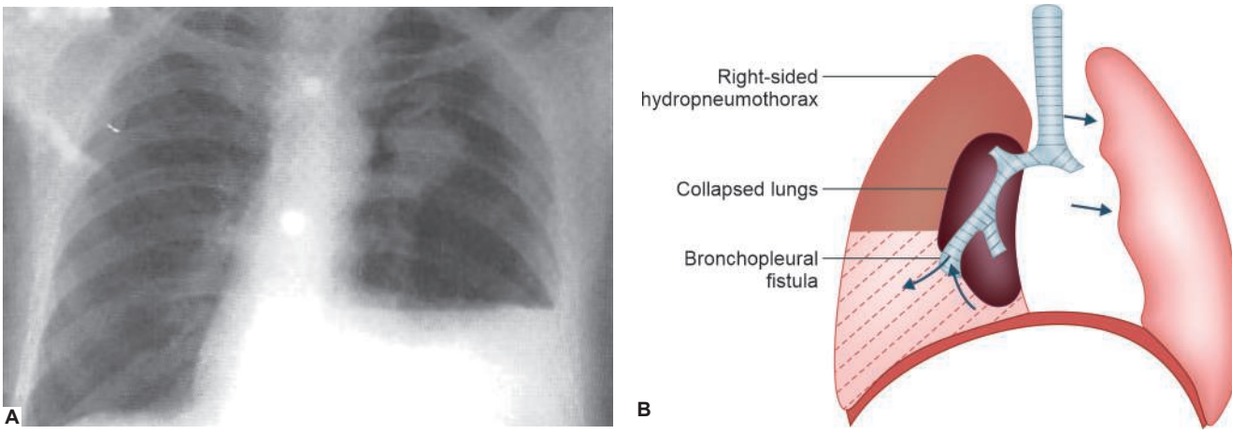


Fig. 1.5A and B: Hydropneumothorax: **A.** Chest X-ray (PA view) shows hydropneumothorax (left side); **B.** Diagrammatic illustration of bronchopleural fistula with hydropneumothorax (right side)

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your provisional diagnosis and why?

Ans. Patient has left-sided hydropneumothorax (bronchopleural fistula). The presence of clear cut horizontal fluid level defined on percussion with hyperresonant note above it and presence of shirting dullness, succussion splash and amphoric bronchial sounds support my diagnosis.

Q 2. What is hydropneumothorax?

Ans. The presence of both **air** (above) and **fluid** (below) in pleural cavity is called *hydropneumothorax.* If instead of fluid, pus collects along with air, then it is called *pyopneumothorax.* Similarly, collection of air and blood is called *hemopneumothorax.*

Q 3. What is your differential diagnosis?

Ans. Following conditions may mimic hydropneumothorax:

1. **Pyopneumothorax** (there will be fever, signs of toxemia in addition to hydropneumothorax).
2. **Pleural effusion** (shifting dullness, succussion splash and classical horizontal fluid level will be absent).
3. **Eventration of diaphragm** with herniation of stomach into chest (this will produce succussion splash with resonant percussion note. Borborgymi sounds may be heard over the chest).
4. **A large lung abscess** partially filled with exudate will produce signs of cavity and coarse crackles are characteristics.

Q 4. What are causes of succussion splash?

Ans. Read *Clinical Mediods in Medicine* by Prof SN Chugh.

Q 5. What is bronchopleural fistula?

Ans. Actually, it is a communication between outside atmosphere and pleura via the bronchus. It is open type of pneumothorax in which repeated infections are common and result in hydro- or pyopneumothorax. All signs of hydropneumothorax are present. **Amphoric bronchial sounds** indicate a patent communication and confirm the diagnosis.

Q 6. What are the differences between hydropneumothorax and pleural effusion?

Ans. Table 1.19 differentiates between hydropneumothorax and pleural effusion.

Table 1.19: Differentiating features of hydropneumothorax and pleural effusion

Hydropneumothorax (Fig. 1.5B)	*Pleural effusion*
× Shifting dullness on percussion present	× Shifting dullness absent (the rising dullness—Ellis S-shaped curve is nowadays obsolete term)
× Horizontal fluid level, i.e. there is transition between hyperresonant note (above) and stony dull note (below)	× No such level
× Succussion splash present	× No succussion splash
× Tingling sounds especially after cough may be audible	× No such sound
× Coin test sound in upper part of hydropneumothorax may occasionally be positive	× Coin test negative
× Diminished breath sounds and vocal resonance except in bronchopleural fistula where amphoric breath sounds may be heard	× Sometimes, a tubular bronchial breathing with increased vocal resonance (bronchophony, whispering pectoriloquy and egophony) present over the top of effusion

Q 7. What are the causes of hydropneumothorax?

Ans. Common causes of hydropneumothorax are:

1. Rupture of subpleural tubercular cavity (the most common cause)
2. Rupture of lung abscess—actually, it causes pyopneumothorax
3. Penetrating chest injury with infection—again a cause of hemopneumothorax
4. Acute pulmonary infarction (embolism)
5. Following cardiac surgery
6. ***Iatrogenic***, i.e. introduction of the air during aspiration of pleural effusion
7. ***Pneumothorax***. Actually bronchopleural fistula (open pneumothorax) of tubercular etiology is the most common cause, but sympathetic collection of fluid in closed and tension pneumothorax may also lead to hydropneumothorax.

Q 8. What are the causes of bronchopleural fistula?

Ans. Common causes include:

1. Rupture of tubercular cavity into pleural space
2. Rupture of lung abscess into pleura with patent bronchus
3. Trauma to chest or barotrauma
4. Necrotizing pneumonia leading to empyema thoracis
5. Following lung resection.

Q 9. How would you explain absent shifting dullness in a case of hydropneumothorax?

Ans. *Hydropneumothorax* contains air above (occupying a large space) and fluid below (occupying smaller space), both in moderate amount and are separated by a horizontal level (a line seen in peripheral lung held on chest X-ray, Fig. 1.5A). Shifting dullness is present because fluid has space to shift by displacing air. Therefore, *shifting dullness in hydropneumothorax will be absent* if above-mentioned conditions are not fulfilled.

The causes of absent shifting dullness in hydropneumothorax are

- Loculated or encysted hydropneumothorax (both air and fluid are tightly packed)
- Too little air in hydropneumothorax
- Too much fluid in hydropneumothorax
- Thick viscid pus (sometime in pyopneumothorax).

Q 10. What are the characteristic features of pyopnemothorax?

Ans. The patient will have all the clinical features of hydropneumothorax ***plus:***

- Presence of toxic look and prostration
- Hectic fever with chills and rigors
- Tachycardia, tachypnea and clubbing of fingers
- Intercostal tenderness and tenderness during percussion (patient winces during percussion).

Q 11. What are the differences between empyema thoracis and pyopneumothorax?

Ans. Clinical features of both empyema thoracis and pyopneumothorax are similar (*hectic fever*, *signs of toxemia*, *intercostal tenderness*, *diminished movements* and *diminished* or *absent breath sounds*). The differentiating features between the two are same as in case of pleural effusion versus hydropneumothorax such as:

i. presence of a horizontal level (transition between hyperresonant and stony-dull percussion note)
ii. Shifting dullness
iii. Succussion splash in pyopneumothorax but not in case of empyema thoracis
iv. However, it will be difficult to differentiate a loculated pyopneumothorax from empyema thoracis because of absence of above-mentioned features.

Q 12. How will you differentiate between a lung abscess and pyopneumothorax?

Ans. Table 1.20 differentiates between lung abscess and pyopneumothorax.

Table 1.20: Differentiating features of pyopneumothorax and lung abscess

Pyopneumothorax	*Lung abscess*
× Cough and expectoration minimal	× Copious purulent expectoration is a predominant feature
× Shift of the mediastinum and trachea to opposite side	× No shift of trachea or mediastinum
× Added sounds are absent	× Added sounds such as crackles will be present
× Chest X-ray will show horizontal level starting from the periphery	× A horizontal fluid level does not touch the periphery of the lung
× Vocal fremitus, breath sounds and vocal resonance diminished or absent	× Vocal fremitus and vocal resonance may be decreased (cavity full of pus) or increased if lung abscess is empty and superficially placed. There can be a bronchial breathing as heard over a cavity

Q 13. How will you investigate a patient with pyopneumothorax?

Ans. Investigations are as follows:

1. ***Routine blood tests,*** such as TLC, DLC and ESR for leukocytosis as an evidence of infection
2. ***Sputum examination*** for culture and sensitivity
3. ***Chest X-ray (PA view)*** will show:
   - A horizontal fluid level
   - Increased radiolucency above the horizontal level without lung markings with a homogeneous opacity below the horizontal level (Fig. 1.5A)
   - Shifting of trachea and mediastinum to the opposite side.

N.B.: X-ray should be taken in upright position to show a fluid level.

   - The collapsed lung due to compression from outside is usually hidden within homogeneous opacity of fluid and may not be visible on X-ray.
4. ***Aspiration of fluid*** or the thick exudate (pus) will be done which is sent for culture and sensitivity.

Q 14. Name the diagnostic signs of hydropneumothorax/pyopneumothorax. How will you elicit them?

Ans. Diagnostic signs are as follows:

1. ***A horizontal level,*** i.e. upper part of hydropneumothorax is hyperresonant due to presence of air and lower part is dull due to presence of fluid/pus
2. ***Shifting dullness***
3. ***Succussion splash***
4. ***Tingling sounds on auscultation***
5. ***Coin test*** may sometimes be present.

Q 15. What is coin test and how would you elicit it?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 16. How will you treat a patient with hydropneumothorax/bronchopleural fistula?

Ans.

1. ***Water-seal intercostal tube drainage*** by putting a Foley's catheter in pleural space and connecting it with water-seal. The fluid will be drained and the air is also expelled with it while remaining air will get absorbed automatically.
2. ***Antibiotics*** depending on the cause. If cause is tubercular, institute ATT.
3. ***Surgery*** is done in resistant cases especially with pyo- or hemopneumothorax.

CASE 6: COLLAPSE OF THE LUNG

The patient whose X-ray (Fig. 1.6A) is depicted and presented with cough, dry hacking without hemoptysis and acute breathlessness.

Clinical Presentations

- Chest deformity
- Pain on the affected side
- Breathlessness
- Dry cough and fever.

Presence of Symptoms

Depends on:

- Rapidity with which they develop
- Amount of the lung involved
- Presence or absence of infection.

Points to be Noted in the History

- Past history of tuberculosis or malignancy or asthma
- Any history of swelling in the neck, axilla or groin
- Past history of mumps, measles and whooping cough during childhood
- Past history of rheumatic heart disease or pericardial disease (fever, chest pain).

EXAMINATION

General Physical Examination

Look for the following:

- Patient may dyspneic, orthopneic if major bronchus is involved
- Central cyanosis
- Tachypnea, tachycardia
- Fever (develops in fibrosing alveolitis or in bronchogenic carcinoma).

Systemic Examination

Inspection

- Flattening or depression of die chest on affected side
- Crowding of the ribs and narrowing of intercostal spaces
- Diminished movements on the side involved
- Shifting of trachea, apex beat towards the side involved (pulling effect)—Trail's sign
- Kyphoscoliosis may result in long-standing collapsed lung with fibrosis
- Drooping of shoulder if apex of the lung is collapsed.

Palpation

- *Shifting of trachea and mediastinum to the same side*
- Reduced movements of the chest on involved side
- Reduced expansion of the chest on side involved
- Vocal fremitus on the affected side may be:
  - Diminished or absent if bronchus is totally occluded
  - Increased if bronchus is patent.

Percussion

Impaired or dull note on the side affected.

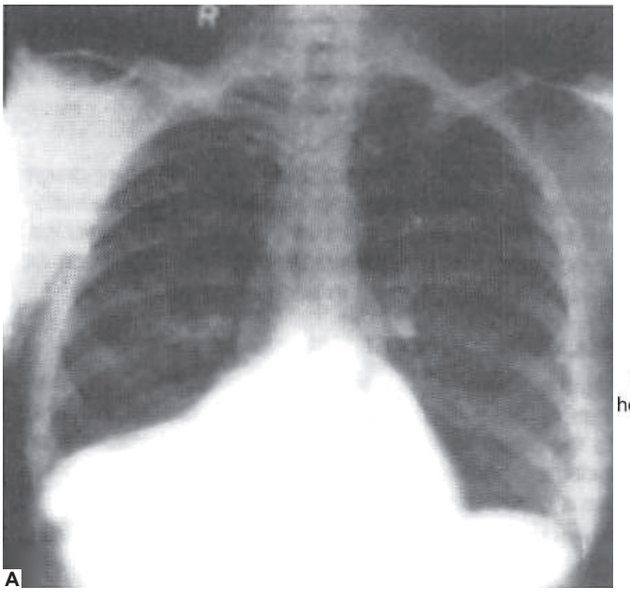
Auscultation

Collapse with obstructed bronchus

- Diminished or absent breath sounds
- Diminished/absent vocal resonance
- No added sounds.

Collapse with patent bronchus

- Tubular bronchial breath sounds
- Increased vocal resonance with bronchophony and whispering pectoriloquy
- Coarse crackles may be heard occasionally.



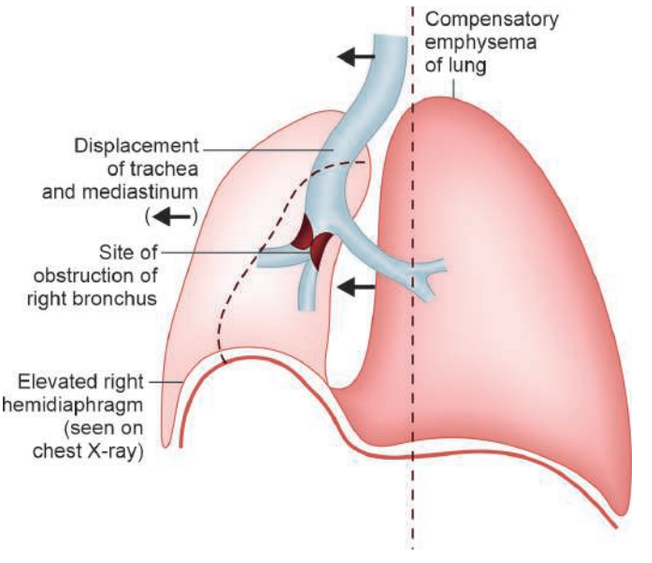


Fig. 1.6A and B: **A.** Chest X-ray showing collapse of right upper lobe; **B.** Diagrammatic illustration of collapse lung

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your diagnosis and why?

Ans. The *provisional diagnosis is collapse of right upper lobe*. *Points in favour of diagnosis are:*

- Depressed chest and decreased movements on the side involved (right side in this case).
- Shift of trachea and mediastinum to the side involved (right side)
- Dull percussion note on the site involved (right side)
- Breath sounds are diminished on the affected part of lung (right side).

Q 2. What is the probable cause?

Ans. ***Could be tubercular*** due to following reasons:

- Cradual onset of weight loss, anorexia, fever with evening rise and night sweats
- Physical signs are localised to apical region of upper lobe
- No signs of toxemia or cachexia.

Q 3. What is your alternate diagnosis?

Ans. The only condition from which collapse is to be differentiated is ***pulmonary fibrosis***. Table 1.21 differentiates between collapse and fibrosis.

Table 1.21: Differentiating features of lung collapse and fibrosis

Feature	*Collapse*	*Fibrosis*
Onset	Acute	Chronic
Chest wall	Flattened	Retracted
Breath sounds	Absent	Feeble but never absent

Q 4. What do you understand by the term collapse of the lung?

Ans. ***Pulmonary collapse or atelectasis*** is defined as *'airlessness with shrinkage'* of a part or the whole lung. ***Atelectasis*** may be present since birth *(atelectasis neonatorum)* due to failure of the lung to expand, or may occur anytime during life (*acquired atelectasis*) due to absorption of air secondary to obstruction, compression, contraction or surfactant loss.

Q 5. What are various types of collapse?

Ans. *Localised/hemithoracic loss of lung volume (collapse of the lung)* can occur with patent bronchus or with occluded bronchus (obstructive collapse) or there is compression of the lung from outside (intrapleural positive pressure), hence, it is of two main types:

I. ***Obstructive collapse (absorption or resorption collapse,*** Fig. 1.6B***).*** It occurs due to absorption of air distal to obstruction in the alveoli. The site of obstruction can be central or peripheral.

i. Central obstructive collapse is with obstructed major bronchus.

ii. Peripheral obstructive (absorption) collapse is always with patent surrounding bronchus.

II. ***Compression collapse (relaxation collapse).*** It occurs from relaxation of the lung due to pleural disease (e.g. pleural effusion, pneumothorax and hydropneumothorax).

Q 6. What are the causes of collapse of the lung?

Ans. I. ***Obstructive (absorption collapse)***

A. *Central (major bronchus):* The causes are:

Common	*Rare*
× Bronchial adenoma or carcinoma	× Aortic aneurysm
× Enlarged tracheobronchial lymph nodes (malignant, tubercular)	× Congenital bronchial atresia
× Inhaled foreign body, misplaced endotracheal tube	× Giant left atrium
× Mucus plugging	× Stricture/stenosis
	× Pericardial effusion

B. *Peripheral (divisions of bronchus/bronchi)*

- Pneumonias
- Mucus plugging (sputum retention)
- Asthma
- Pulmonary eosinophilia.

II. ***Compression collapse (relaxation collapse)***

- Pleural effusion
- Pneumothorax
- Hydropneumothorax, pyopneumothorax, hemopneumothorax.

Q 7. What are the clinical differences between central obstructive and peripheral obstructive collapse?

Ans. Remember that *peripheral collapse* does not involve the major bronchus, involves divisions of bronchus or bronchi with the result the collapse occurs with patent bronchus (i.e. surrounding bronchi are patent) while, *central obstruction of a major bronchus* leads to collapse of all its divisions, hence, the whole lobe is airless with no patent bronchus.

The differentiating features are summarised in Table 1.22.

The causes of both types of obstructive bronchus are given above. *Signs of compression collapse* means signs of pleural effusion/pneumothorax.

- The underlying collapsed lung is silent (relaxed hence called relaxation collapse).
- In this type of collapse, trachea and mediastinum is shifted to the opposite side due to pushing effect of fluid/air.

Q 8. What are the clinical pulmonary presentations of bronchogenic carcinoma?

Ans. Clinical pulmonary presentations of bronchogenic carcinoma are:

- *Collapse*
- *Collapse consolidation*
- *Cavitation*
- *Mediastinal compression/obstruction—superior vena cava syndrome*

Table 1.22: Differentiative features of central obstructive and peripheral obstructive collapse of lung

Feature	*Central obstructive collapse (occluded bronchus)*	*Peripheral obstructive collapse (patent bronchus)*
Shift of trachea and mediastinum	To the same side	To the same side
Elevated dome of the diaphragm	On the same side	On the same side
Breath sounds	Absent on the side involved	Tubular (bronchial) breath sounds
Vocal resonance	Decreased/absent on the side involved	Increased vocal resonance with whispering pectoriloquy
Common cause	Tumor or lymph node or a foreign body	Mucus plugging, ipsilateral bronchial cast or clot
CT scan or chest X-ray	Collapse with loss of open bronchus sign—Golden's "S" sign	Collapse with open bronchus
Signs on the other side	Signs of compensatory emphysema, i.e. hyperresonant note, vesicular breathing with prolonged expiration	No signs of compensatory emphysema on the other side

- *Pancoast's tumor*—apical carcinoma may involve brachial plexus producing monoplegia
- *Consolidation*—a solid tumor
- *Pleural effusion*—rapid filling, hemorrhagic.

Q 9. How will you investigate a patient with lobar collapse?

Ans. Investigations of lobar collapse are:

1. ***Routine blood examination***
2. ***Sputum examination***—cytology, microbiology and culture
3. ***Chest X-ray*** (PA and lateral view). It will show:
   - Homogeneous opacity of the collapsed lung
   - Displacement of trachea and cardiac shadow (mediastinum) to the diseased (involved) side
   - Crowding of the ribs with reduction of intercostal spaces due to loss of volume of the lung on the side involved
   - Elevation of hemidiaphragm on the side involved
   - Pleural effusion on the side involved if collapse is due to malignancy of lung
   - Sometimes, the radiological features of underlying cause (hilar lymphadenopathy), foreign body may be evident
4. CT scan to find out the cause
5. Bronchoscopy to find out the cause and to take biopsy
6. Scalene node biopsy, if lymph node enlarged or malignancy lung suspected
7. Pleural fluid examination if pleural effusion present.

Note: Investigations of compression collapse are same as that of pleural effusion.

Q 10. What are the complications of collapse?

Ans. Common complications of collapse are:

- Secondary infection
- Spontaneous pneumothorax from ruptured bullae of compensatory emphysema on the uninvolved side of the lung.

CASE 7: DIFFUSE FIBROSING ALVEOLITIS

The patient (i.e. a coal-mine worker) whose CT scan is depicted in Fig. 1.7A presented with progressive dyspnea and cough for the last 2 years. The dyspnea was exertional in the beginning, increased to occur now at rest. There was history of associated fever, weight loss, malaise and fatigue.

Clinical Presentations

- Progressive exertional dyspnea
- Persistent dry cough
- Fever, weight loss, fatigue
- At the late stages, patient may complain of symptoms of *cor pulmonale* (abdominal pain due to hepatomegaly, ascites, swelling legs).

Points to be Noted in the History

- Past history of tuberculosis or lung suppuration
- Any history of radiation exposure
- Any history of joint pain, arthralgia, rash
- Drug history
- Occupational history, e.g. coal-miner, stone cutter, farmer or industrial worker
- Past history of rheumatic heart disease or any other cardiac disorders.

EXAMINATION

General Physical Examination

- Dyspnea, orthopnea
- Tachypnea
- Central cyanosis (if severe)
- Clubbing of the fingers
- Signs of occupation
- Raised JVP and ankle edema if severe disease
- Examine hands for rheumatoid arthritis, systemic sclerosis.
- *Face:* Look for heliotropic rash for dermatomyositis, typical rash of SLE, pinched faces of systemic sclerosis and lupus pernio of sarcoidosis.
- *Mouth:* Look for aphthous ulcers of Crohn's disease, dry mouth of Sjögren's syndrome.

Systemic Examination

Inspection

- Increased respiratory rate
- Bilateral symmetrical reduction in chest movements
- Accessory muscles of respiration may be hyperactive.

Palpation

- Reduced bilateral chest movements
- Reduced expansion of the chest
- Bilateral reduction of vocal fremitus.

Percussion

Dullness on percussion at lung bases on both sides.

Auscultation

- Bilateral crackles (end-inspiratory) at both the bases (lower zones) of the lungs which may disappear or become quieter on leaning forward but do not disappear on coughing unlike those of pulmonary edema
- Vesicular breathing diminished in intensity
- Vocal resonance bilaterally diminished.

Other System Examination

- *Signs of right heart failure* (raised JVP, loud P2, hepatomegaly, central cyanosis and pitting edema) may or may not be present, if present indicates chronic cor pulmonale.

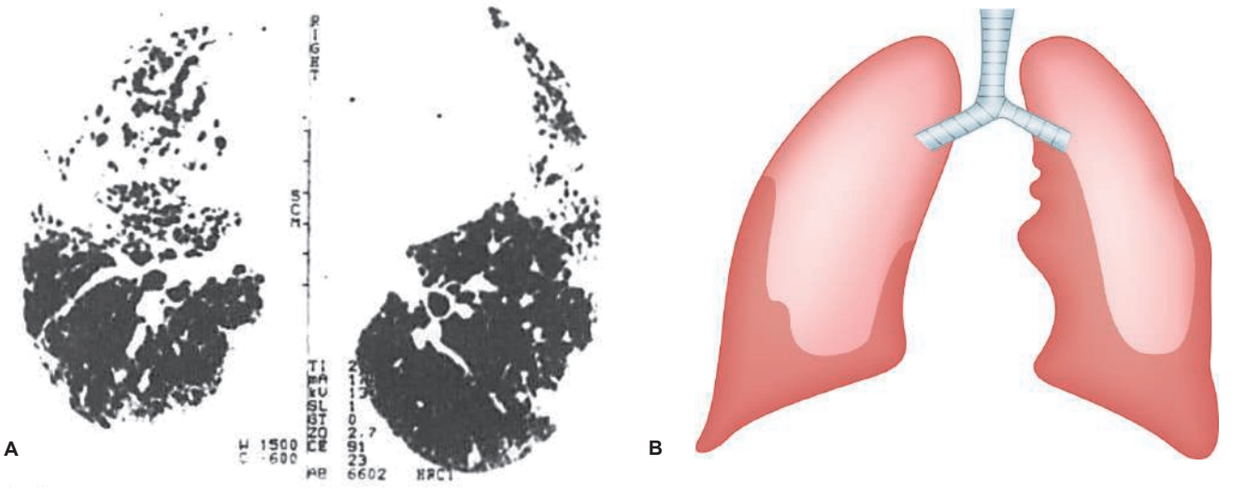


Fig. 1.7A and B: A. CT scan chest showing honeycomb appearance in a patient with diffuse fibrosing alveolitis; **B.** Diagrammatic illustration

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. The patient being an occupational workers (coal-miner), developed symptoms of progressive dyspnea, cough, fever and weight loss, the probable diagnosis will be *occupational lung disease*, e.g. *coal-miner pneumoconiosis*.

Q 2. Summarise your findings in favour of your diagnosis.

Ans.
1. A middle-aged coal-miner presented with progressive dyspnea, cough, fever, malaise and weight loss.
2. There is tachypnea, tachycardia, central cyanosis and clubbing of fingers.
3. *Chest* shows reduced bilateral chest movements, expansion and vocal fremitus.
4. The lung bases are dull on percussion.
5. On auscultation, there is vesicular breathing with fine, basal end-inspiratory crackles.

Q 3. What is your differential diagnosis?

Ans. **Differential diagnosis** lies between the causes of bilateral interstitial fibrosis. (Read the cause of fibrosis.) The common conditions to be differentiated are:
- Idiopathic interstitial fibrosis
- Farmer's lung
- Respiratory bronchiolitis
- Silicosis
- Asbestosis.

Q 4. What are the causes of crackles at the lung bases with clubbing?

Ans. All the following conditions constitute the differential diagnosis:
1. Bronchogenic carcinoma
2. Bronchiectasis
3. Asbestosis
4. Pulmonary edema.

Q 5. What do you understand by fibrosis of the lung? What are its causes?

Ans. Fibrosis of the lung means replacement of lung parenchyma by fibrous tissue. It occurs usually as a reactive process or a healing/reparative process.

Causes

1. ***Focal fibrosis:*** Pneumoconiosis
2. ***Reparative fibrosis/replacement fibrosis***
   - Tuberculosis
   - Following bronchiectasis, lung abscess, pulmonary infarction
   - Following radiation.
3. ***Interstitial fibrosis (it is bilateral fibrosis of alveolar walls and septa)***

   A. *Pulmonary origin*
   - *Hypersensitivity*
     - Diffuse fibrosing alveolitis (Fig. 1.7A)
     - Farmer's lung
   - *Collagen vascular disorders*
     - SLE
     - Systemic sclerosis
     - Rheumatoid arthritis (rheumatoid lung)
   - Lymphangitis carcinomatosis
   - Drug-induced, e.g. busulphan, bleomycin, nitrofurantoin, methysergide, hydralazine, hexamethonium, amiodarone
   - *Miscellaneous*
     - Sarcoidosis
     - Aspiration pneumonitis
     - Histiocytosis
     - Tuberous sclerosis
     - Xanthomatosis.

   B. *Cardiac origin*
   - Multiple pulmonary infarcts
   - Mitral stenosis

   C. *Idiopathic:* Hamman-Rich disease.

Q 6. What is Hamman-Rich syndrome? What are its clinical features?

Ans. *Diffuse interstitial fibrosis or fibrosing alveolitis* of acute onset, progressive course of unknown etiology is called *Hamman-Rich syndrome.*
- It is characterised by progressive dyspnea, dry cough, fever, weight loss and signs of bilateral fibrosis of the lung.

The clinical characteristics (physical signs) have already been described in the beginning.

Q 7. What are causes of end-inspiratory crackles?

Ans. Read *Respiratory System in Clinical Methods in Medicine* by Prof SN Chugh.

Q 8. How will you investigate a patient with cryptogenic fibrosing alveolitis?

Ans. The common investigations are as follows:
1. ***Routine blood tests.*** ESR in high.
2. ***Blood for rheumatoid factor and antinuclear antibodies.*** Immunoglubulins are raised.
3. ***Chest X-ray (PA view) shows:***
   - Diffuse pulmonary opacities in the lower zones peripherally
   - The hemidiaphragm are high and the lungs appear small
   - In advanced disease, there may be 'honeycomb' appearance of the lungs in which diffuse pulmonary shadowing is interspersed with small cystic translucencies.
4. ***High resolution CT scan*** may show honeycombing (Fig. 1.7A) and scarring, most marked peripherally in both the lungs or there may be ground glass appearance. CT scan is useful in early diagnosis when chest X-ray may not show the radiological changes. MRI is useful to determine disease activity.
5. ***Pulmonary function tests.*** There is restrictive ventilatory defect with reduction in FEV_1 and

vital capacity (VC). The carbon monoxide transfer factor is low and lung volumes are reduced. (Read pulmonary function tests in the beginning of this chapter, Table 1.5.)

6. ***Bronchoalveolar lavage*** may show a large number of lymphocytes and *transbronchial biopsy* may sometimes be helpful.
7. ***Open lung biopsy*** for histological patterns of idiopathic cases of interstitial lung disease. In early stages, there is mononuclear cell infiltration in alveolar wall with interstitial fibrosis; in late stages, honeycombing, bronchial dilatation and cysts are seen.

Q 9. What is respiratory bronchiolitis?

Ans. *Respiratory bronchiolitis* is an interstitial lung disease of smokers in which there is accumulation of pigment-laden macrophages in the respiratory bronchioles and adjacent alveoli leading to mononuclear cell infiltration and fibrosis. It may reverse on cessation of smoking.

N.B. Clinical picture is similar to cryptogenic fibrosing alveolitis.

Q 10. What is farmer's lung?

Ans. It is an occupational lung disease caused by an inhalation of organic dust (mouldy hay, straw, grain)

- It is characterised by features of extrinsic allergic alveolitis (e.g. *headache*, *muscle pains*, *malaise*, *pyrexia*, *dry cough* and *breathlessness without wheeze*) which may progress to irreversible pulmonary fibrosis.

The pathogenic mechanism is local immune response to fungal antigen, e.g. *Micropolyspora faenae or Aspergillus fumigatus*.

The **diagnosis** is based on; (i) clinical features, (ii) characteristic radiological features as described above, (iii) high-resolution CT scan and (iv) identification of potential antigen by ELISA or precipitin antibody test.

The **treatment** is removal of the source of antigen wherever possible and a course of 3–4 week of prednisolone (40 mg/day) may arrest the process.

Q 11. What is coal-worker's pneumoconiosis?

Ans. The disease follows prolonged inhalation of coal dust hence, is an occupational lung disease seen in coal-workers. The condition is subdivided into *simple pneumoconiosis* and *progressive massive fibrosis* for both clinical purposes and certification. The simple coal miner's pneumoconiosis is reversible (it does not progress if miner leaves the industry), non-progressive and radiologically characterised by nodulation without cavitation. On the other hand, progressive massive fibrosis—a variety of coal miner's pneumoconiosis is irreversible, progressive and radiologically characterised by large dense masses, single or multiple, occur mainly in upper lobes associated with cavitation. Tuberculosis may be a complication. It carries poor prognosis.

Q 12. What is Caplan's syndrome?

Ans. It consists of association of rheumatoid arthritis (positive rheumatoid factor) in patients with coal-worker's pneumoconiosis with rounded fibrotic nodules (nodular shadowing) 0.5 to 5 cm in diameter distributed mainly in the periphery of the lung field.

Q 13. What is silicosis?

Ans. This disease is caused by inhalation of silica dust or quartz particles, characterised by progressive development of hard nodules which coalesce as the disease progresses followed by fibrosis. The clinical and radiological features are similar to coal worker's pneumoconiosis though changes tend to be more marked in the upper lobe. The hilar shadow may be enlarged; *egg-shell* calcification in the hilar lymph node is a distinct feature. Tuberculosis may be a complication and may modify the silicotic process with ensuring caseation and calcification. The disease progresses even when the exposure to dust ceases.

Q 14. What is asbestosis? What are its possible effects on respiratory tract?

Ans. Table 1.23 explains features of asbestosis and its effects on respiratory tract presented diagrammatically.

Table 1.23: Features of asbestosis

Asbestosis is an occupational lung disorder, occurs due to exposure to fibrous mineral asbestos in certain occupations such as in the mining and milling of the mineral. The main types of mineral asbestos involved in asbestosis are:

- *Chrysolite* (white asbestos—a common factor)
- *Crocidolite* (blue asbestos—uncommon factor)
- *A mosite* (brown asbestos—a rare factor)

The possible effects of asbestosis are depicted in Fig. 1.7C.

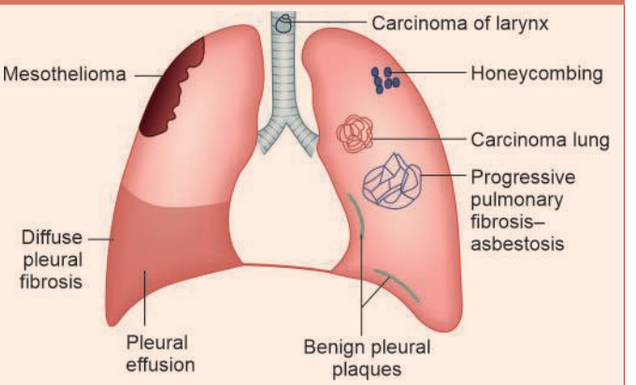


Fig. 1.7C: Effects of asbestosis

CASE 8: CAVITY WITH FIBROSIS

The young patient whose X-ray is depicted in Fig. 1.8A presented with cough, fever, hemoptysis and weight loss for the last 6 months. There was history of weakness and decreased appetite and night sweats.

Clinical Presentations

- Cough, fever and night sweats, weakness may be initial manifestations of *tubercular cavity*
- Cough, massive expectoration, fever, purulent sputum with postural and diurnal variation suggest lung *abscess* or *bronchiectasis*
- Cough, hemoptysis, breathlessness, fever, weight loss, anorexia suggest *malignancy* as the cause of cavity.

Points to be Noted in the History

- Onset and progression of the symptoms
- Past history of tuberculosis or malignancy, ankylosing spondylitis
- Past history of pneumonia (e.g. fever, cough, hemoptysis and pain chest) or lung suppuration (cough with mucopurulent or purulent sputum)
- Any history of headache, vomiting, visual disturbance or neurological deficit
- Any history of radiation.

EXAMINATION

General Physical Examination

- Patient may be ill-looking, emaciated
- Repeated coughing and bringing out a large amount of sputum
- Tachypnea and tachycardia
- Fever
- Clubbing of fingers and toes
- Weight loss
- Edema feet if secondary amyloidosis develops and involves the kidneys.

Systemic Examination

Inspection

Diminished movement on the side involved (right side in this case).

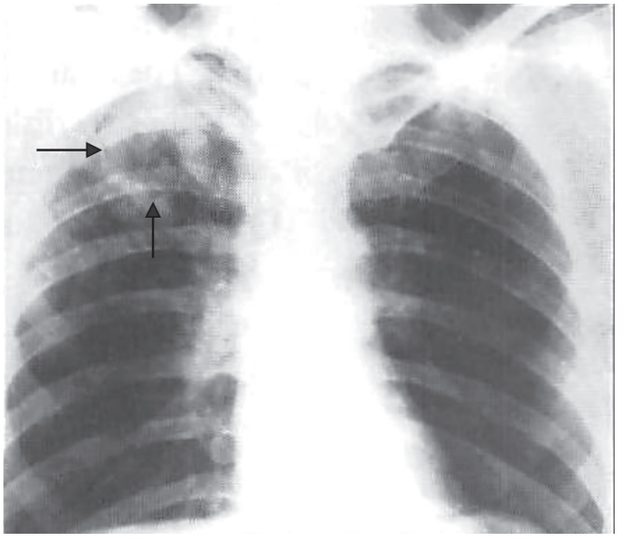


Fig. 1.8A: Chest X-ray (PA view) showing a cavity with fibrosis

Palpation

- Movements of the chest reduced on the side involved (right side in this case)
- Expansion of the chest is reduced if cavity is large
- Shift of trachea and mediastinum to the same side if there is a large cavity with fibrosis (right side in this case).

Percussion

Dull percussion note over the cavity. Rest of the lung is normally resonant.

Auscultation

- Amphoric or cavernous bronchial breathing over the cavity
- Increased vocal resonance over the area of **cavity** with bronchophony
- Mid-inspiratory and expiratory crackles
- Post-tussive crackles
- Crackpot sounds.

All the above-mentioned signs will be present only if the cavity is large, superficial and communicates with bronchus. Deep seated cavity may not produce any physical sign.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. In view of history of cough, fever, hemoptysis of 6 months duration and presence of signs of cavitation in this patient suggest either a tubercular or a malignant cavity in the right lung.

Q 2. What is your differential diagnosis?

Ans. 1. **Bronchiectasis (could be tubercular). Read clinical case discussion on bronchiectasis**
2. **Resolving consolidation** will produce massive expectoration and bronchial breath sounds.
3. **Lung abscess.** Read symptoms and signs of lung abscess in this case discussion.
4. **Malignancy lung.** Cough, hemoptysis, weakness, weight loss, cachexia along with signs of a cavity and hilar lymphadenopathy are pointers to its diagnosis.

Q 3. What do you understand by the term 'cavity'?

Ans. *Pulmonary cavity* is an area of liquefaction necrosis within the lung parenchyma in communication with a patent bronchus. The cavity may be empty

or may be filled with secretions and infected material. *Pseudocavity* means appearance of a cavity on chest X-ray which may be obtained with summation of shadows of vessels, ribs and calcification.

Q 4. What are causes of cavitation in the lung?

Ans. Common causes are:

1. ***Infection***
   - Tuberculosis
   - Lung abscess
   - Bronchiectasis
   - Fungal infection
   - Ruptured hydatid cyst with infection
2. ***Congenital***
   - Infected bronchogenic cyst
   - Sequestration
   - Polycystic lungs
3. ***Neoplasm***
   - Bronchogenic carcinoma
   - Metastasis
   - Lymphoma
4. ***Trauma***
   Resolving hematoma
5. ***Immunological***
   - Rheumatoid arthritis
   - Wegener's granulomatosis
6. ***Vascular***
   Pulmonary infarction
7. ***Infected emphysematous bullae.***

Five common causes of cavity in the lung:

1. Tubercular cavity
2. Lung abscess, bronchiectasis
3. Malignancy lung
4. Pulmonary infarction
5. Wegener's granulomatosis.

Q 5. What are the various types of cavity seen in the lung?

Ans. Types of cavities are as follows:

I. **Thin-walled:** A cavity is surrounded by a thin-walled margin of lung tissue. The margin may be irregular, shaggy in lung abscess (staphylococcal) and bronchogenic carcinoma while it is smooth and regular in tuberculosis, lung cyst, emphysematous bullae, hydatid cyst and fungal infection.

II. **Thicked walled:** A thick wall is formed by thick exudative material or heaps of cells such as in lung abscess, tuberculosis and bronchogenic carcinoma.

Q 6. What are the physical signs of a cavity?

Ans. Typically, a superficial large cavity communicating with the bronchus produces signs which depend on whether the cavity is empty or filled with fluid at the time of examination. The signs of cavity are given in Table 1.24.

Q 7. What are post-tussive crackles?

Ans. These are crackles which are heard after coughing due to dislodgement of secretions in a cavity. They are characterstic of a tubercular cavity.

Table 1.24: Physical signs over a cavity

Signs	*Empty cavity*	*Filled cavity*
Movement of chest on the side and area involved	Diminished	Diminished
Retraction/flattening of chest	Present	Present
Tactile vocal fremitus and vocal resonance	Increased	Decreased
Percussion note	Crackpot sound	Diminished
Breath sounds	Amphoric/cavernous	Diminished
Whispering pectoriloquy	Present	Absent
Post-tussive crackles/rales	Absent	Present

Q 8. What is amphoric breath sounds? What are its causes?

Ans. Read *Clinical Methods* by Prof SN Chugh.

Q 9. Which type of breathing occurs over a cavity?

Ans.
- *Thin-walled cavity with narrow bronchus* produces **amphoric bronchial breathing**
- *Thick-walled cavity with patent* (narrow or wide) bronchus produces **cavernous breathing**.

Q 10. What are complications of a tubercular cavity?

Ans.
- A source of intercurrent infections
- Meningitis (tubercular) or miliary tuberculosis
- Secondary amyloidosis in case of long-standing cavity
- Hydropneumothorax
- Chronic cavity may lead to malnutrition or hypeproteinemia

Q 11. What do you understand by the term lung abscess? What are its causes?

Ans. ***Definition:*** It is defined as collection of purulent material in a localised necrotic area of the lung parenchyma. It is a suppurative lung disease.
Causes: Most of the lung abscesses are pyogenic in origin, but, sometimes it may be nonpyogenic such as necrosis in a tumor followed by cavitation and collection of material. This is called *malignant lung abscess*. The causes of the abscesses are given in Table 1.25.

Q 12. What are clinical features of lung abscess?

Ans. Clinical presentations and examinations of lung abscess are given in Table 1.26.

Q 13. How will you investigate a case with lung abscess?

Ans. The tests done are:
- **Blood examination** for anemia and leukocytosis. Raised ESR that suggests infection especially tuberculosis (markedly elevated).
- **Sputum examination** for isolation of the organisms (Gram's staining, Ziehl-Neelsen stain), for cytology including malignant cell; and culture and sensitivity.
- **Blood culture** to isolate the organism. It is mostly sterile.
- **Urine examination** for proteinuria, pus cells and casts. Albuminuria indicates secondary renal amyloidosis.

Table 1.25: Causes of lung abscess

1. **Necrotising infection**
   a. Pyogenic, e.g. *Staph aureus*, Klebsiella, group A streptococci, Bacteroides, anaerobes, Nocardia
   b. Tubercular—a tubercular cavity with collection of purulent material
   c. Fungi, e.g. Aspergillus, Histoplasma
   d. Amebic lung abscess secondary to liver abscess
2. **Embolic infarction with cavity formation**
   - Thromboembolism of the lung
   - Metastatic lung abscess
3. **Malignancy of the lung with cavitation**
   - Bronchogenic carcinoma with secondary degeneration and cavitation
   - Metastatic lung abscess
4. **Miscellaneous**
   - Infected congenital cysts
   - Coal-miner's pneumoconiosis

- **Chest X-ray** (PA view—Fig. 1.8B and lateral view) will show:
  - An area of consolidation with breakdown and translucency. The walls of the abscess may be outlined
  - The presence of a fluid level inside the translucent area confirms the diagnosis
  - Empyema, if develops, will be detected by radiological appearance of a pleural effusion. (Read radiological appearance of pleural effusion.)

Lateral film will show the site of an abscess depending on the position of patient at the time of abscess formation (Table 1.27).

Table 1.27: Localisation of lung on lateral chest X-ray

1. **Patient in lying down position**
   - Right lung (commonest site)
   - Posterior segment of upper and superior segment of lower lobe
2. **Patient in upright position**
   - Basal segments of both the lobes

   Note: The lung abscess is more common on right side due to less obliquity of right bronchus

- **Bronchoscopic aspiration** for diagnosis. The aspirate is subjected to cytology, microbiology and culture
- **Aspiration of empyema**—if develops.
- **MRI** of upper lobe.

Q 14. What is common site for lung abscess?

Ans. Right middle lobe.

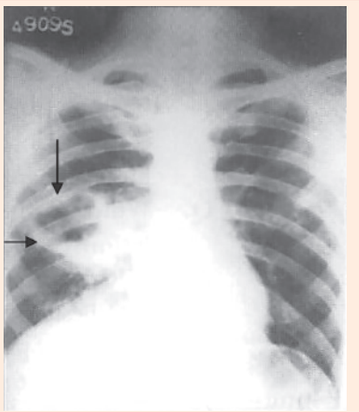
Q 15. What are pathogens of lung abscess?

Ans. Read causes of lung abscess.

Q 16. What are the complications of a lung abscess?

Ans. Common complications are:
1. Involvement of other lung (transbronchial spread)
2. Septicemia, toxemia

Table 1.26: Physical and systemic examinations of lung abscess

General physical examination		*Systemic presentations*
• Toxic look • Fever, sweating, tachycardia, tachypnea • Poor nutrition • ± Cyanosis • Clubbing of the fingers present • Edema of legs if secondary renal amyloidosis or hypoproteinemia due to massive expectoration develops • Foul smelling (fetid) sputum and breath (halitosis) • Source of infection in upper respiratory tract, e.g. tonsillar or parapharyngeal abscess or throat sepsis may be evident • Cervical lymphadenopathy may be present	 **Fig. 1.8B:** Chest X-ray PA view showing lung abscess on right side (↑) *Clinical presentations* • Fever, sweating, palpitations, tachypnea • Copious purulent or mucopurulent sputum with diurnal (more in the morning) and postural (more in lying down than sitting position) relation • Hemoptysis • Pain chest due to pleuritis if pleura involved • May present with symptoms of underlying disease, e.g. tuberculosis, amebic liver abscess, malignancy lung • May present with complication, e.g. meningitis, empyema thoracis	• All the signs present in a cavity filled with secretion/necrotic material will be present as discussed above • In case of rupture lung abscess, either the signs of empyema thoracis, or pyopneumothorax as discussed earlier will be present • In case of rupture amebic liver abscess, there will be history of expectoration of anchovy sauce sputum with tender hepatomegaly • In case of malignancy, there will be marked weight loss, cachexia, hemoptysis with signs of collapse or consolidation. In addition, there may be features of metastatic spread to the mediastinal lymph nodes or evidence of compression of neighbouring structures

3. Meningitis, brain abscess
4. Empyema and pyopneumothorax
5. Secondary renal amyloidosis
6. Massive hemoptysis
7. Emaciation and hypoproteinemia in long-standing cases.

Q 17. What does edema indicate in a patient with lung abscess?

Ans. 1. ***Hypoproteinemia*** due to loss of protein through massive expectoration
2. ***Malnutrition/malabsorption***
3. ***Renal amyloidosis*** leading to albuminuria and nephrotic syndrome.
4. ***Cor pulmonale and congestive cardiac failure,*** through rare, may develop in some cases when the disease is extensive or bilateral.

Q 18. How does a lung abscess lead to brain abscess?

Ans. What is the common site? Lung abscess leads to meningitis and brain abscess by hematogenous spread. These abscesses are commom in the posterior frontal region or parietal lobes and are usually multiple.

Q 19. Which is the imaging procedure for upper lobe lesions?

Ans. MRI is better for upper lobe lesions than CT scan of the chest, otherwise MRI is less useful than CT scan because of poorer imaging of lungs parenchyma and inferior spatial resolution.

Q 20. How would you treat such a case?

Ans. 1. ***Postural drainage of the cavity,*** sitting position is best for upper lobe cavity.
2. ***Antibiotics*** for pyogenic lung abscess and ATT for tubercular cavity.
3. ***Expectorants and mucolytic agents***
4. ***Surgery*** in localised lung cavity which is nidus for recurrent pulmonary infection or hemoptysis.
5. ***Chest physiotherapy.***

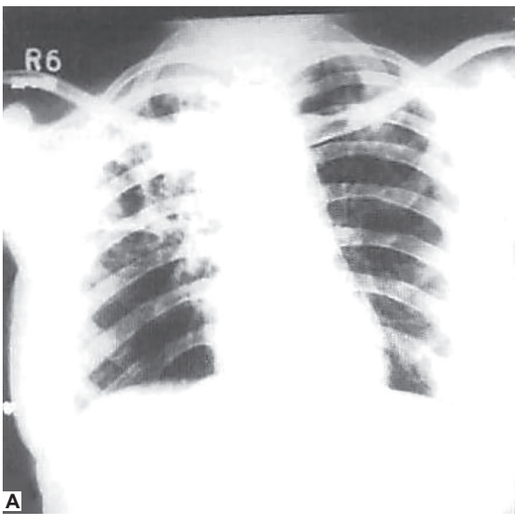
CASE 9: PULMONARY TUBERCULOSIS

The patient whose X-ray is depicted in Fig. 1.9A presented with cough, fever, hemoptysis, pain chest and weakness for the last 8 months. There was history of loss of weight, appetite and night sweats. There were crackles in the right infraclavicular region without bronchial breathing.

Clinical Presentations (Fig. 1.9B)

Major manifestations:

1. A cavity
2. Consolidation or collapse
3. Pleural effusion/empyema
4. Miliary tuberculosis
5. Hydropneumothorax or bronchopleural fistula
6. Hilar lymphadenopathy
7. Bronchiectasis.



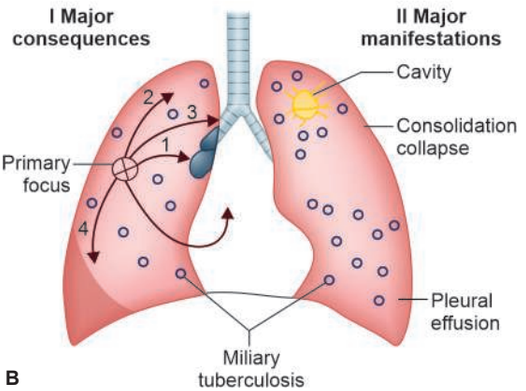


Fig. 1.9A and B: A. Primary pulmonary tuberculosis. Consequences if left untreated are **(Fig. 1.9B)**:

1. The primary focus may spread to hilar or mediastinal lymph node to form primary or Ghon's focus
2. Direct extension of primary focus into other part of lung
3. Extension of primary focus to bronchus
4. Extension of primary focus to pleura
5. Dissemination into bloodstream leading to miliary tuberculosis

History

Point to be Noted

- Write chief complaints in chronological order
- Note the onset and progression of the symptoms
- History of fever, cough, hemoptysis, breathlessness, pain chest/discomfort, any neurological deficit
- Any history of weight loss, decreased appetite, night sweats or evening rise in temperature
- Ask complaints pertaining to other systems.

Examination

Proceed as follows:

I. General Physical Examination

- Ill-look
- Phlyctenular conjunctivitis
- Cervical or axillary lymphadenopathy
- Look for anemia, jaundice, cyanosis and edema feet
- Look for JVP, trachea, etc.
- Note any clubbing of the fingers
- Any joint involvement.

II. Systemic Examination

Inspection

- Shape and symmetry of chest, note any bulging or retraction.
- Look at the movements of chest at every quadrant of chest. Compare both sides with each other.
- Look at the apex beat, e.g. location.
- Look for any distended veins or scar mark or mark for aspiration over the chest.
- Count the respiratory rate and note the type of breathing.
- Look for pulsations in supraclavicular fossa, epigastrium or other sites.

Palpation

- Palpate the apex beat to confirm its position.
- Palpate the trachea for any deviation.
- Note the expansion of the chest and measure it.
- Compare the vocal fremitus on both the sides.
- Palpate the intercostal space for any widening or narrowing.
- Palpate the crepitus or crackles or rub if any.

Percussion

- Percuss the lungs for resonance.
- Define cardiac and liver dullness.
- Percuss 2nd left and right intercostal spaces for dullness or resonance.
- Percuss directly the clavicles and supraclavicular areas for resonance.

Auscultation

- Hear the breath sounds and note the character and intensity and compare them on both the sides.
- Hear for any added sounds, e.g. crackles, wheezes rub, etc.
- Vocal resonance to be compared on both sides for increase or decrease.
- Elicit other specific signs depending on the underlying disease, e.g. succussion splash, coin test, etc.

Other Systems

- Examine the spine for deformity and tenderness
- Examine abdomen for fluid or any organ enlargement
- Examine eyes for phlyctenular conjunctivitis or choroid tubercles.
- Elicit the signs of meningitis if suspected.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. Postprimary pulmonary tuberculosis (fibroexudative apical tuberculosis).

Q 2. What is fibroexudative apical tuberculosis?

Ans. It is a common local infiltrative lesion of tuberculosis involving the apex of the lung. The features are:

- Depressed chest in the infraclavicular region
- Trachea may/may not be shifted to the same side
- No mediastinal shift
- Percussion note over the area involved is impaired
- Coarse/medium/fine crackles are heard at the apex
- No bronchial breath sounds.

Only crackles at the apex clinch the diagnosis.

Q 3. What do you understand by the term primary pulmonary tuberculosis? How does it differ from postprimary tuberculosis?

Ans. Infection with *M. tuberculosis* occurring most frequently through inhalation of infected droplets with the primary involvement of the lung is called *primary pulmonary tuberculosis.*

- Following inhalation, of *M tuberculosis,* a subpleural lesion (*Ghon's focus)* develops that causes a rapid transport of bacilli to the regional (hilar) lymph nodes leading to development of primary complex (Table 1.28). The fate of the primary complex is as follows:
  1. It may heal spontaneously within 1–2 months and tuberculin skin test becomes positive.
  2. Spread of the primary focus to hilar and mediastinal lymph nodes to form primary complex which in most cases heals spontaneously.
  3. It may remain dormant, becomes reactivated when the body defenses are lowered.
  4. Direct extension of primary focus—called progressive pulmonary tuberculosis merging with postprimary TB.
  5. Hematogenous spread leading to miliary tuberculosis, or tubercular meningitis.

Table 1.28: Primary tuberculosis

- Subpleural lesion ***(Ghon's focus)***
- Draining lymphatics from this focus to hilar lymph nodes
- Hilar lymphadenopathy

Clinical Features of Primary Tuberculosis

I. **Symptoms and signs of infection,** i.e. fever, influenza like illness, primary complex, skin test conversion (positive Mantoux test).

II. **Symptoms and signs of the disease,** i.e. lymphadenopathy (hilar, paratracheal, mediastinal), collapse or consolidation (right middle lobe), obstructive emphysema, pleural effusion, endobronchial tuberculosis, miliary tuberculosis or, meningitis and pericarditis.

III. **Symptoms and signs of hypersensitivity**, e.g. erythema nodosum, phlyctenular conjunctivitis, dactylitis.

Clinical Features of Postprimary Pulmonary Tuberculosis

However, 85–90% of patients develop latent infection (positive tuberculin test or radiographic evidence of self-healed tuberculosis); and within this group 5–10% reactivate during their lifetime resulting in post-primary disease, predominantly pulmonary (50% smear positive). Re-exposure to the smear positive pulmonary tuberculosis may result in postprimary disease/tuberculosis. The differences between progressive primary complex and postprimary tuberculosis are enlisted in Table 1.29.

Table 1.29: Differences between progressive primary and postprimary tuberculosis

Progressive primary complex	*Postprimary tuberculosis*
Common in children	Common in adults
1. Hilar lymphadenopathy	Absence of lymph node enlargement
2. Subpleural focus or focus in any part of the lung	Usually apical fibrosis
3. Cavitation rare	Cavitation common
4. Fibrosis uncommon	Fibrosis common
5. Miliary tuberculosis common	Miliary tuberculosis uncommon
6. Direct extension of primary focus	Re-exposure to smear positive pulmonary disease

Q 4. What are clinical presentations of postprimary pulmonary tuberculosis?

Ans. Clinical presentations are as follows:

- Chronic cough, hemoptysis with signs and symptoms of exudative/infiltration or a cavity or collapse/fibrosis
- Pyrexia of unknown origin (PUO)
- Unresolved pneumonia (consolidation)
- Pleural effusion
- Asymptomatic (diagnosed on chest X-ray)
- Weight loss, night sweats, evening rise of temperature, general debility (cryptic tuberculosis)
- Spontaneous pneumothorax.

Q 5. What is time table of tuberculosis?

Ans. As already described, in 85–90% cases the primary complex heals spontaneous with or without calcification. In 10–15% cases, multiplication of tubercular bacilli is not contained and lymph nodes enlargement results in either local pressure effects or lymphatic spread to the pleura or pericardium or rupture into adjacent bronchus or pulmonary blood vessel. The time table of tuberculosis is given in Table 1.30.

Table 1.30: Time table of tuberculosis

Time from infection	*Manifestations*
3–8 weeks	× Primary complex, positive tuberculin skin test, erythema nodosum
3–6 months	× Collapse and bronchiectasis, adult pulmonary tuberculosis, miliary tuberculosis
Within 1 year	× Pneumonia, pleural effusion
Within 3 years	× Tuberculosis affecting bones, lymph node, joints, GI tract and genitourinary
From 3 years onwards	× Postprimary disease due to reactivation or reinfection
Around 8 years	× Urinary tract disease

Q 6. Who are at high-risk of tuberculosis?

Ans.
- Asian immigrants
- Older persons
- Alcoholic and debilitated persons or destitute
- Immunocompromised individuals, i.e. AIDS, diabetic patients
- Professional, e.g. doctor, nurses, physiotherapists
- Close contacts, i.e. family members of a case with tuberculosis.

Q 7. What is cryptic tuberculosis? What is its presentation?

Ans. The term 'cryptic' means 'hidden'. A patient of tuberculosis with normal chest radiograph is called *cryptic tuberculosis*. Its presentation is as follows:
- Age over 60 years
- Intermittent low grade fever (PUO) with night sweats and evening rise
- Unexplained weight loss, general debility
- Hepatosplenomegaly (seen in 25% cases only)
- Normal chest X-ray
- Negative tuberculin skin test
- Leukemoid reaction or pancytopenia
- Confirmation is done by biopsy (liver or bone marrow).

Q 8. What are the stigmata of tuberculosis (evidence of present or past infection or disease)?

Ans. Stigmata attached with the tuberculosis are as follows:
- Phlyctenular conjunctivitis
- Erythema nodosum
- Tubercular lymphadenopathy with or without scars and sinuses
- Thickened, beaded spermatic cord
- Scrofuloderma
- Positive Mantoux test
- Localised gibbus, spinal deformity, paravertebral soft tissue swelling.

Q 9. What are the chronic complications of pulmonary tuberculosis?

Ans. Common complications of pulmonary TB include:

I. **Pulmonary complications**
1. Massive hemoptysis
2. Cor pulmonale
3. Fibrosis/emphysema (compensatory)
4. Recurrent infections
5. Tubercular empyema
6. Lung/pleural calcification
7. Obstructive airway disease (endobronchial)
8. Bronchiectasis
9. Bronchopleural fistula.

II. **Nonpulmonary complications**
1. Empyema necessitans
2. Laryngitis
3. Enteritis following ingestion of infected sputum
4. Anorectal disease following ingestion of infected sputum
5. Amyloidosis (secondary)
6. Poncet's polyarthritis.

Q 10. How will you investigate a case of pulmonary tuberculosis?

Ans. Investigations are as follows:
1. ***Routine blood examination,*** i.e. TLC, DLC, ESR for anemia, leucocytosis. Raised ESR and C-reactive protein suggest tuberculosis.
2. ***Mantoux test*** is nonspecific (low sensitivity and specificity).
3. ***Sputum*** (induced by nebulized hypertonic saline, if not expectorated), or gastric lavage (mainly used for children) or *bronchoalveolar lavage* for acid-fast bacilli isolation (Ziehl-Neelsen stain) and culture.
4. ***Chest X-ray*** (AP, PA and lateral and lordotic views) for radiological manifestations of tuberculosis in the lungs. The varied manifestations are:
   - Soft **fluffy** shadow (confluent)
   - Apical infiltration
   - Dense nodular opacities
   - Miliary mottling shadows (miliary tuberculosis)
   - A cavity or multiple cavities (irregular, thin walled)
   - Fibrocaseous lesions
   - Tuberculoma
   - Calcification—lung and/or pleura
   - Bronchiectasis especially in the upper zones
   - Mediastinal (unilateral) lymphadenopathy (enlarged hilar lymph nodes)
   - Primary complex (Ghon's focus) in children.
5. ***CT scan*** for diagnosis and differential diagnosis.

6. ***PGR (polymerase chain reaction)*** with blood or any other fluid.
7. ***ADA (adenosine deaminase)*** levels increase in tuberculosis.
8. ***Transbronchial biopsy.***

Q 11. Which test gives an early diagnosis of tuberculosis?

Ans. Polymerase chain reaction (PCR) gives rapid diagnosis.

Q 12. How would you investigate close contacts of a patient with tuberculosis?

Ans. Close contacts are investigated as follows:

- First confirm the history of close contacts with the patient having open tuberculosis
- Enquire about BCG vaccination
- Perform Mantoux or Heaf testing
- Advise chest X-ray examination.

Q 13. How would you treat newly diagnosed sputum positive tuberculosis?

Ans. 1. Isolation of the patient in a single room for 2 weeks if smear positive.
2. Barrier nursing care.
3. For new smear positive or new cases of pulmonary tuberculosis are put on WHO DOTS regimen category I which comprises
   - HRZE daily/thrice a week for 2 months
   - Assess sputum for AFB. If negative use two drugs (HR) for 4 months.
   - If sputum remains positive, extend four drugs regimen for one month more, then use 2 drugs (HR) for 2 months and if sputum is negative continue it for 2 months more or if positive, shift to category II.

Q 14. What are various categories of WHO-DOTS regimen?

Ans. Read *Textbook of Medicine*.

Q 15. What are the toxic effects of antitubercular drugs.

Ans. Read Commonly used Drugs, Unit 3 of this book.

Q 16. Name second-line antitubercular drugs.

Ans. Para-aminosalicylic acid, ethionamide, capreomycin, cycloserine, ciprofloxacin.

Q 17. What are indications of BCG vaccination?

Ans.
- Previous unvaccinated contacts.
- Persistently Mantoux test negative contacts below 35 years of age.

Q 18. What are indications of chemoprophylaxis?

Ans. 1. Mantoux test positive persons with no clinical or radiological evidence of tuberculosis.
2. Children under 5 years of age who are close contacts of smear positive adult patient.
3. Immunocompromised contacts irrespective of immune status.

Q 19. Which drug is used for chemoprophylaxis?

Ans. Isoniazid is used in usual dosage for one year.

Q 20. What is miliary tuberculosis? What is the status of immunity in this disease?

Ans. It is defined as dissemination of tuberculosis through the bloodstream producing miliary tubercles in various organs. Immunity is lowered in it, hence, dissemination occur. Mantoux test is negative which confirms lowered immunity.

Q 21. What is treatment of multidrug resistant tuberculosis?

Ans. Drug resistant tuberculosis may be primary or acquired during treatment with inappropriate regimen or due to irregular treatment. MDR (multidrug resistant) tuberculosis is a big problem in Asia. Although 6-month regimen of RZE (excluding H) is effective for patients with initial isoniazid resistance, all the 3 drugs to be continued for 6 months.

For patients resistant to isoniazid (H) and rifampicin (R), combinations of a fluoroquinolones, ethambutol (E), pyrazinamide (Z) and streptomycin (S) is given for 18–24 months and for at least a month after sputum culture conversion. For those resistant to streptomycin, injectable amikacin can be used in its place.

For patients resistant to all first line drugs, cure may be obtained with combination of 4 second line drugs (ethionamide, cycloserine, quinolone and PAS) including one injectable agent for full 24 months.

Q 22. Name new antitubercular drugs.

Ans. Following drugs are being evaluated.

- Rifapentine—a rifamycin antibiotic, is bacteriostatic similar to rifampicin. Other drugs include *gatifloxacin*, *moxifloxacin*, *clarithromycin*, linezolid and *oxazolidinones*.

CASE 10: BRONCHIAL ASTHMA

The patient (Fig. 1.10A) presented with acute attack of breathlessness and cough. There was no history of pain chest or hemoptysis. There was history of such attacks in the past. On examination, wheezes were heard all over on both sides of the chest.

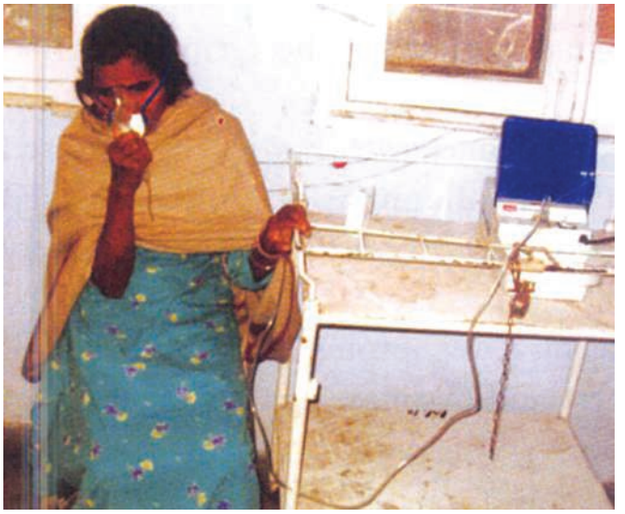


Fig. 1.10A: A patient of acute severe asthma being nebulized

Clinical Presentations

- **Typical symptoms** include wheeze, breathlessness, cough and tightness of chest. These symptoms may occur for the first time at any age and may be episodic or persistent.
- **Episodic asthma** presents with intermittent acute attacks, remains asymptomatic between attacks. The precipitating factor is either respiratory viral infection or exposure to allergens. This type of asthma occurs in children or young adults who are atopic.
- **Persistent** asthma presents with chronic wheezing and breathlessness, has to be differentiated from left heart failure (cardiac asthma). This is called adult onset asthma seen in older nonatopic individuals. Typically there is diurnal pattern in symptoms and PEF shows morning diping. Cough and wheezing are nocturnal and disturb the sleep—hence called nocturnal asthma.

History

Important Points to be Noted in History

- **Present history** should cover the present symptoms in details. Note seasonal or nocturnal attacks of asthma. Is there worsening of symptoms in the morning (morning diping)?
- **Past history** should include any history of cough and cold in the childhood, chronic exposure to dust and smoke. Any history of recurrent attacks of nasal discharge, sneezing and angioneurotic edema.
- **Personal history,** e.g. smoking, alcohol, occupation, habits, diet (food allergy).
- **Family history** of bronchial asthma, hay fever and eczema.
- Ask about any precipitant.

Examination

Proceed as follows:

I. General Physical Examination

- *Resting position:* Patient is dyspneic and tachypneic during acute attack, sits in prop up position and uses extrarespiratory muscles for respiration.
- *Pulse:* Tachycardia is usually present in acute attack. Marked tachycardia and bounding pulses indicate CO_2 narcosis (retention). Presence of pulsus paradoxus indicates severe acute asthma
- *BP* and *temperature* normal
- *Cyanosis* is present in severe acute asthma
- *Level of consciousness:* Patients with mild attacks are fully conscious but anxious looking. Marked anxiety, drowsiness and restlessness indicate increasing severity of airway obstruction.
- *Respiration:* Rate is more, respiration is rapid and shallow.
- *Speech:* If the patient can speak easily and in full sentences, the dyspnea is mild. Monosyllabic speech suggests moderate dyspnea. Inability to speak sentences without stopping to take a breath indicate severe asthma.
- *Flapping tremors* (asterixis) on outstretched hands, papilledema, and bounding pulses indicate CO_2 narcosis.
- *Nasal examination* for polyp or allergic rhinitis. Throat examination for septic focus.
- *Skin examination* for allergic.

II. Systemic Examination

Inspection

- Patient is dyspneic at rest
- Accessory muscles of respiration and alae nasi are working
- Respiratory rate is increased
- Audible wheezing
- Excavation of suprasternal notch and supraclavicular fossae may be present with recession of intercostal spaces during inspiration
- Shape of the chest normal, but there may be pigeon-shape chest in long-standing childhood asthma
- Tracheal tug absent.

Palpation

- Trachea is central
- Apex beat may not be palpable due to overinflated lungs
- Movements of the chest are bilaterally and symmetrically decreased
- Expansion of the chest on the measurement is reduced
- Vocal fremitus is reduced uniformly on both the sides
- Wheeze/rhonchi may be palpable.

Percussion

- Resonant note all over the chest
- Liver dullness intact at normal 5th intercostal space in right midclavicular line
- Normal cardiac dullness.

Auscultation

- Vesicular breathing with prolonged expiration present all over the chest
- Vocal resonance reduced uniformly all over the chest

- Polyphonic expiratory and inspiratory wheezes (rhonchi) are heard over the chest
- Coarse crackles at both the bases
- No pleural rub.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. Sir, my clinical diagnosis is bronchial asthma.

The points in favour of diagnosis are:

i. ***Episodic nature*** of cough, wheeze, breathlessness and tightness in chest
ii. ***Exacerbation of cough or wheeze*** at night or after exercise
iii. ***Precipitation of attacks*** during summer, dusty and rainy seasons (seasonal attacks)
iv. ***History of atopy*** (eczema, hay fever) or rhinitis (seasonal) present
v. ***Examination of chest shows***
   - Tachypnea
   - Excavation of suprasternal and supraclavicular, fossa
   - Reduced movements and expansion of chest
   - Indrawing of intercostal spaces
   - Resonant percussion note on both sides
   - Bilateral scattered wheezes and rhonchi.

Q 2. What is your differential diagnosis?

Ans. The differentiation of asthma from other diseases associated with dyspnea and wheezing is not difficult, following conditions have to be kept in mind during an attack of asthma.

1. **Chronic bronchitis/COPD.** The differences between asthma and chronic bronchitis have been discussed as a separate question (read the differences).
2. **Upper airway obstruction by tumor or laryngeal edema.** In this condition, there is usually stridor and there are harsh respiratory sounds limited to the area of trachea not all over the chest as heard in bronchial asthma. Diffuse wheezing is absent. Indirect laryngoscopy and bronchoscopy confirms the diagnosis.
3. **Endobronchial disease** due to tumor, tuberculosis, foreign body or bronchostenosis produces paroxysms of coughing with persistent wheezing limited to one area of the chest.
4. **Left ventricular failure** (cardiac asthma) produces cough, dyspnea, PND with moist basal rales, gallop rhythm, bloodstained sputum and other signs of heart failure.
5. **Carcinoid syndrome,** episodic flushing, diarrhea, pruritus, salivation along with diffuse wheezing in the chest are characteristics. Cardiac lesions may also occur. The diagnosis is confirmed by measurement of urinary or plasma serotonin or its metabolites in urine.
6. **Recurrent pulmonary thromboembolism:** Recurrent episodes of dyspnea, particularly on exertion with or without hemoptysis can occur in pulmonary embolism. Sometimes, widespread wheezing simulating asthma may occur causing confusion with it, lung scans and pulmonary angiography may be necessary to confirm the diagnosis.
7. **Eosinophilic pneumonia.** Acute eosinophilic pneumonia is characterised by episodes of cough, fever, chills, dyspnea and wheezing following an exposure to an antigen. Neutrophila, eosinophilia and lymphopenia can occur. Chest X-ray shows nodular infiltrates or reticulonodular opacities. Pulmonary function tests reveal restrictive defect. High resolution CT scan is diagnostic.

Q 3. What do you understand by the term bronchial asthma?

Ans. *Bronchial asthma* is defined as a disorder characterised by chronic airway inflammation and increased responsiveness of tracheobronchial tree to a variety of stimuli resulting in temporary narrowing of the air passages leading to symptoms of cough, wheeze, tightness of chest and dyspnea. Airflow obstruction is transient and reversible with treatment. It is not a uniform disease but rather a dynamic clinical syndrome comprising of two common distinct patterns:

i. Episodic asthma in which acute attacks are precipitated by allergens or infection by respiratory virus. These attacks are short-lived and patient in between attacks is symptom free. These attacks are common in children who are atopic hence, called *extrinsic asthma.*
ii. The other pattern is *persistent form* in which there is chronic wheeze and breathlessness, these cases resemble patients of COPD. These individuals are nonatopic, and asthma develops in old age—called *intrinsic asthma.*

Q 4. What are causes of wheezes?

Ans.
1. Bronchial asthma
2. COPD, predominantly chronic bronchitis
3. Left ventricular failure (cardiac asthma)
4. Bronchial tumor
5. Eosinophilic lung disease (pulmonary eosinophilia)
6. Carcinoid syndrome
7. Recurrent thromboembolism
8. Anaphylaxis
9. Systemic vasculitis with pulmonary involvement
10. Mastocytosis.

Q 5. What are the differences between extrinsic and intrinsic asthma?

Ans. Table 1.31 differentiates atopic (extrinsic) and nonatopic intrinsic asthma.

Table 1.31: Differentiating features of extrinsic and intrinsic asthma

Extrinsic asthma (atopic)	*Intrinsic asthma (nonatopic)*
Episodic, sudden onset	Nonepisodic, chronic or persistent
Early onset or childhood asthma	Late onset or adult asthma
More wheeze, less cough	More cough, less wheeze
Mostly seasonal	Mostly nonseasonal
Attacks may occur at any time of the day or night	Mostly attacks occur at night (nocturnal)
Diurnal pattern, e.g. symptoms and peak expiratory flow show morning dipping with subsequent recovery	Nondiurnal pattern
Nonexercise-induced attacks	Exercise-induced attacks
Positive family history of an allergic disorder	No family history
Skin hypersensitivity tests positive	Skin tests negative
Sodium cromoglycate is most effective	Not effective

Q 6. What is acute severe asthma?

Ans. This term has replaced the previous horrifying term status asthmaticus. It is defined as either an acute attack of prolonged asthma or paroxysmal attacks of acute asthma where there is no remission of attacks in between and they are not controlled by conventional bronchodilators. It is a life-threatening emergency, needs proper diagnosis and urgent treatment.

The *diagnosis* is suggested by:

- Acute dyspnea, orthopnea with wheeze, tachycardia, tachypnea and perspiration
- Central cyanosis
- Dry (unproductive) cough with mucoid expectoration
- Respiratory distress with hyperactivity of extrarespiratory muscles (accessory muscles of respiration)
- Pulsus paradoxus
- Diminished breath sounds due to reduced air entry and minimal or absence of high-pitched polyphonic rhonchi (wheezes)

Silent chest is a characteristic feature of acute severe asthma and is an ominous sign.

- PEFR (peak expiratory flow rate) is <50% of predicted or patient's best.

Q 7. What are the parameters of assessment of severity of asthma?

Ans. The parameters of life-threatening asthma are:

1. **Bedside parameters**
   - Pulse rate >110/min, respiratory rate >25 min.
   - Pulsus paradoxus
   - Tachypnea (rapid shallow respiration)
   - Unable to speak in sentences (i.e. one sentence in one breath)
   - PEF <50% of predicted or <100 L/min.
2. **Clinical parameters**
   - Cannot speak
   - Central cyanosis
   - Exhaustion, confusion, obtunded consciousness
   - Bradycadia, hypotension
   - *'Silent chest', feeble respiratory effort.*
   - Uncontrolled PEF or PEF <33% of predicted or best.
3. **Investigative parameters of life-threatening asthma**
   - Arterial blood gas analysis
   - A normal (5–6 kPa) or high CO_2 tension
   - Severe hypoxemia (<8 kPA) especially if being treated with O_2
   - A low pH or acidosis.

Q 8. What are various allergens for asthma and how to avoid them?

Ans. It is a hard fact that certain allergens/drugs can precipitate asthma in sensitised individual, their knowledge is essential so as to prevent the development of life-threatening situation. The allergens encountered at home or at work place are listed along with preventive measures (Table 1.32).

Table 1.32: Various allergens and other substances likely to provoke an attack of asthma

Allergen	*Efficacy/propensity*	*Preventive measures*
1. **More common**		
Pollens	Low	Try to avoid exposure to flowering vegetation Keep bedroom windows closed
House dust	Low/doubtful	Vacuum cleaning of the matress daily Shake out the blankets and bedsheets daily Dust bedroom thoroughly
Animal dander	High	Avoid contact with animal pets, e.g. dogs, cats, horses, etc.
Feathers in pillows or quilts	High	Substitute foam pillows and terylene quilts
Drugs	High	Avoid all preparations of relevant drugs
Insect web	High	Do not allow the insect web to collect
2. **Less common**		
Food/food items	Low	Identify and eliminate them from diet
Chemicals/pollutants	High	Avoid exposure to chemicals/pollutants and/or change of an occupation

Q 9. What is persistent rhonchi/wheeze? What are its causes?

Ans. A localised wheeze persisting in a localised area could be due to:
- Bronchostenosis
- Foreign body obstruction
- Bronchial adenoma.

Q 10. What are the causes of pulsus paradoxus?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 11. What are precipitating factors for acute attack of asthma?

Ans. 1. **Allergens (Read** Table 1.32**)**
2. **Pharmacological stimuli,** e.g. drugs such as;
   - Aspirin and NSAIDs
   - Beta blockers
   - Colouring agents, e.g. tartrazine
   - Sulfiting agents, e.g. potassium metabisulfite, potassium and sodium bisulfite, sodium sulfite and SO_2 which are used in food industries. Exposure usually follows ingestion of these compouds in food and beverages, e.g. salads, fresh fruit, potatoes, shellfish and wine.
3. **Environmental and air pollutions.**
   - Ozone, nitrous dioxide and SO_2
   - Dust, fumes, pollens.
4. **Occupational factors**
   - Metal salts, e.g. platinum, chromium, nickel
   - Wood and vegetable dusts e.g. grain, flour, cast or bean, coffee beans, gum acacia, etc.
   - Drugs, e.g. antibiotics, piperazine.
   - Industrial chemicals and plastics, e.g. dyes
   - Biological enzymes, e.g. laundry detergents and pancreatic enzymes
   - Animal and insect dusts and secretions.
5. **Infections,** e.g. viral, bacterial.
6. **Exercise** (exercise-induced asthma).
7. **Emotional stress.**

Q 12. What is wheeze? What are its types? What are its causes?

Ans. Read *Clinical Methods* of Prof SN Chugh.

Q 13. What are the causes of recurrent bronchospasm?

Ans. 1. Bronchial asthma
2. Carcinoid tumor
3. Recurrent pulmonary emboli
4. Chronic bronchitis with acute exacerbation
5. Recurrent LVF (cardiac asthma).

Q 14. What are the complications of asthma?

Ans. 1. Severe acute asthma (status asthmaticus)
2. Recurrent pulmonary infection leading to superadded bronchitis and pneumonia.
3. Sputum retention syndrome leading to atelectasis of lung
4. Pneumothorax
5. Emphysema, can occur in long-standing asthma
6. Respiratory failure (type II common)
7. Chronic cor pulmonale
8. Precipitation of syncope, hernias, prolapse, subconjunctival hemorrhage due to repeated coughing.

Q 15. How does bronchial asthma differ from chronic bronchitis?

Ans. See Table 1.33.

Q 16. What are indications of steroids in asthma?

Ans. 1. Nocturnal asthma (sleep is disturbed by wheeze)
2. Persistence of morning tightness until mid-day
3. Symptoms and peak expiratory flow deteriorates progressively each day
4. Maximum treatment with bronchodilators
5. When there is need of emergency nebulizers.

Q 17. Name the inhalational steroids.

Ans. Beclomethasone
Budesonide
Ciclesonide
Fluticasone
Triamcinolone.

Q 18. What are the indications for mechanical ventilation with intermittent positive-pressure ventilation?

Ans.
- Worsening hypoxia (PaO_2 <8 kPa) despite 60% inspired O_2

Table 1.33: Differences between bronchial asthma and chronic bronchitis

Feature	*Bronchial asthma*	*Chronic bronchitis*
Onset	Acute	Slow, insidious
Age	Childhood, adolescents and middle age	Usually middle age or old patients
Pathogenesis	Allergic	Allergic-inflammatory
History of smoking	Absent	Present
Family history	May be positive	Negative
History of allergy, e.g. rhinitis, hay fever, eczema	Present	Absent
Duration of symptoms	No fixed duration	At least of 2 years duration
Nature of symptoms and signs	Intermittent episodic	Persistent, acute exacerbation can occur
Seasonal variation	Present	Absent
Symptoms	Dyspnea > cough	Cough > dyspnea
Signs	Wheezes/rhonchi are more pronounced than crackles	Both wheezes and crackles are present
Sputum and blood eosinophilia	Common	Uncommon
Pulmonary function tests	Usually normal	Usually abnormal

- Hypercapnia (PaO_2 >6 kPa)
- Drowsiness
- Coma.

Q 19. How will you manage a case of severe acute asthma?

Ans.
- Nebulized beta-agonists, e.g. terbutaline or salbutamol
- High concentration of O_2
- High doses steroids, e.g. IV hydrocortisone or oral prednisolone or both
- Order immediately blood gases and X-ray chest to rule out pneumothorax
- When life-threatening features are present:
  - Add ipratropium bromide to nebulized beta-agonist
  - IV aminophylline or salbutamol or terbutaline.

Q 20. What is step-care regimen for management of chronic asthma in adults?

Ans. British thoracic society regimen is depicted in Fig. 1.10B.

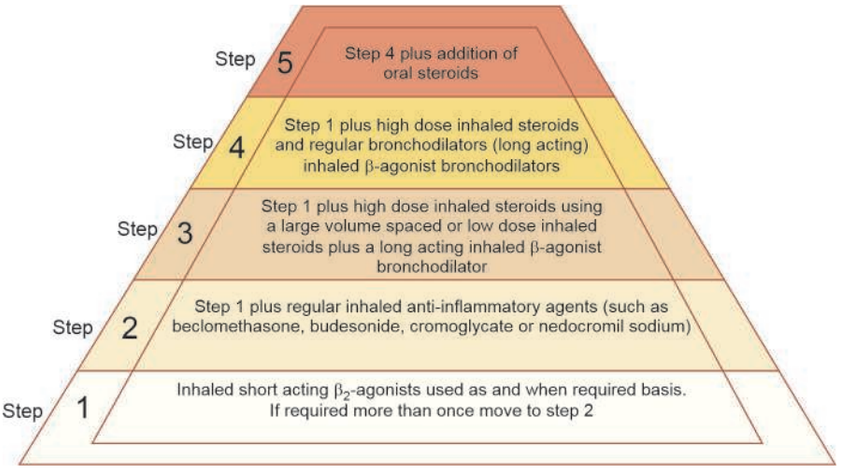


Fig. 1.10B: Pyramid of step care treatment of chronic bronchial asthma

CASE 11: BRONCHIECTASIS

The patient (Fig. 1.11A) presented with history of cough with massive purulent (foul smelling) expectoration more than 250 ml a day with frequent streaking of the sputum with blood. The cough and expectoration was more in the morning in left lateral position. Chest examination revealed coarse crackles in right infra-axillary and infrascapular region.

Clinical Presentations

- Chronic cough, massive expectoration related to diurnal variation and posture
- Recurrent hemoptysis
- Recurrent pneumonias (fever, cough, pain chest due to pleurisy)
- Dyspnea and wheezing
- Associated systemic symptoms, e.g. fever, weight loss, anemia, weakness
- Edema feet due to development of either cor pulmonale or involvement of kidneys by secondary amyloidosis.

History

Points to be Noted in the History

- Write the complaints in chronological order and detail them.
- Ask specifically about the amount of sputum, colour, consistency, smell, etc.
- Is there any relationship between posture and cough?
- Past history of tuberculosis or childhood measles, mumps or whooping cough.
- Past history of recurrent fever or chest infection or asthma.
- Any history of edema feet, swelling of the abdomen, etc.
- Any history of fever, headache, vomiting, or neurological deficit.

EXAMINATION

Proceed as follows:

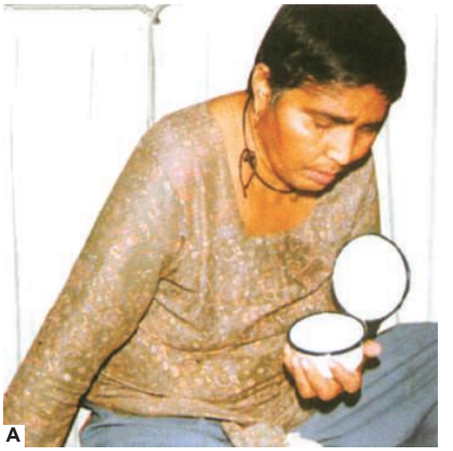
I. General Physical Examination

- Patient may be dyspneic and has lots of coughing (coughing-coughing-coughing)
- Toxic look and fever if patient develops severe infection
- Pulse rate increased
- Respiratory rate may be high
- Nutrition may be poor due to hypoproteinemia as a result of massive expectoration
- Cyanosis may be present, if disease is bilateral and severe or patient develops respiratory failure or cor pulmonale
- Clubbing of fingers and toes common; may be grade I to IV
- Edema feet if there is cor pulmonale or hypoproteinemia.

II. Systemic Examination

Inspection

- The affected side of the chest may be retracted (right side in this case)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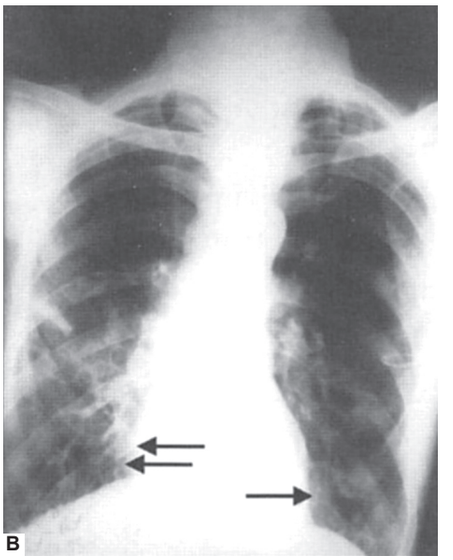
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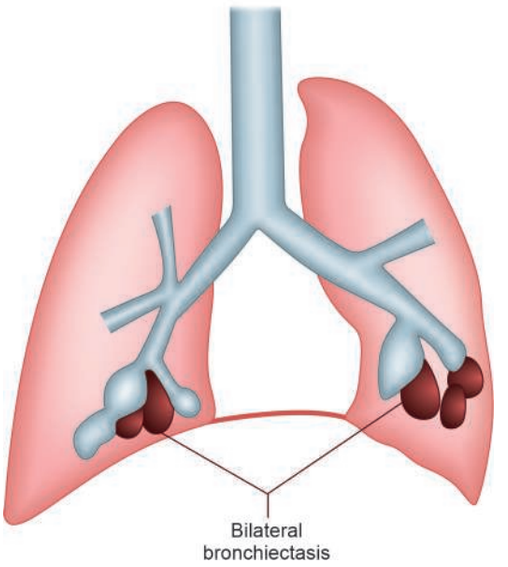


C

Fig. 1.11A to C: **A.** A patient with bronchiectasis bringing out massive mucoid expectoration; **B.** X-ray chest; **C.** Diagram

- There may be diminished movement on the side involved
- There is wasting of muscles of thorax
- Look for the apex beat for dextrocardia.

Palpation

- Chest may be retracted with diminished movements and crowding of the ribs in the lower part(s). There may be palpable wheeze or rhonchi and coarse mid-inspiratory and expiratory crackles.

Percussion

The percussion note is impaired over the area involved.

Auscultation

- Breath sounds may be bronchial, with coarse, bubbling leathery mid inspiratory and expiratory crackles (right lower zone in this case)
- Vocal resonance may be increased.

N.B.: All the signs will be seen on both sides in bilateral disease.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. In view of long history of cough with massive purulent expectoration, more in the morning and in left lateral position; with retraction of chest on right side and diminished movements and presence of coarse, mid and late inspiratory crackles, bubbling in nature, rhonchi and wheezes in right infra-axillary and infrascapular region, my provisional diagnosis is right-sided bronchiectasis.

Q 2. What are your other possibilities?

Ans.
1. **Lung abscess:** Read case discussion in lung abscess
2. **Tubercular cavity filled with exudate** (read case discussion)
3. **Resolving pneumonia**
4. **Empyema thoracis** with bronchopleural fistula.

Q 3. What are the causes of massive expectoration?

Ans.
1. Bronchiectasis
2. Lung abscess
3. Necrotising pneumonia
4. A tubercular cavity filled with exudates
5. Empyema thoracis or ruptured amebic liver abscess with communication to exterior through patent bronchus
6. Cystic fibrosis
7. Chronic bronchitis.

Q 4. What do you understand by the term bronchiectasis?

Ans. ***Bronchiectasis*** is a localised irreversible dilatation and distortion of bronchi. Although die definition is based on histopadiological changes, yet clinical diagnosis is applied when chronic and recurrent infections occur in the dilated airways resulting in collection of secretions within them leading to massive expectoration, more so in the morning. It may be focal and unilateral (involvement of airway within limited region of the lung parenchyma) or diffuse and bilateral.

Q 5. What are its pathological types (Reid's classification)?

Ans. Pathological types of bronchiectasis are:
1. **Cylindrical bronchiectasis.** The bronchi are uniformly dilated
2. **Varicose bronchiectasis.** The affected bronchi have irregular or beeded pattern of dilatation.
3. **Saccular (cystic) bronchiectasis.** The bronchi have ballooned or cystic appearance.

These pathological shapes can only be seen on bronchoscopy and CT scan.

Q 6. What are the causes of bronchiectasis?

Ans. The causes of bronchiectasis are enlisted in Table 1.34. The most common cause is infection of bronchi with or without obstruction. Impaired pulmonary defense mechanisms such as immunoglobulin deficiency, cystic fibrosis may lead to bronchiectasis by repeated infections without obstruction. Some noninfective causes also lead to bronchiectasis.

Table 1.34: Causes of bronchiectasis

1. Postinfective, e.g. postpneumonic, following, measles, whooping cough and post-tubercular (tubercular bronchiectasis common in upper-lobe)
2. Mechanical bronchial obstruction (obstructive bronchiectasis) as in endobronchial tuberculosis, carcinoma, extrinsic lymph node compression
3. Allergic bronchopulmonary aspergillosis
4. γ-globulin deficiency, e.g. congenital or acquired
5. Immobile cilia syndrome (Kartagener's syndrome)
6. Cystic fibrosis
7. Neuropathic disorders, namely Riley-Day syndrome (Chagas' disease)
8. Idiopathic

Q 7. What are major pathogens in bronchiectasis?

Ans. Major pathogens are:
- *S. aureus*
- *H. influenzae*
- *Pseudomonas aeruginosa.*

Q 8. What are common sites for localised disease?

Ans. Left lower lobe and lingula.

Q 9. What is Kartagener's syndrome?

Ans. It consists of the following:
- Sinusitis
- Dextrocardia
- Bronchiectasis
- ***Primary ciliary dyskinesia.*** The normal sperm motility also depends on proper ciliary function, males are generally infertile.

Q 10. Where does bronchiectasis occurs in allergic bronchopulmonary aspergillosis?

Ans. The bronchial dilatation occurs in more proximal bronchi due to type III immune complex reactions.

Q 11. What other abnormalities may be associated with bronchiectasis?

Ans. 1. Congenital absence of bronchial cartilage (*Campbell syndrome*)
2. Tracheobronchomegaly
3. Azoospermia
4. Chronic sinopulmonary infection
5. Congenital kyphoscoliosis
6. Situs inversus and paranasal sinusitis (Kartagener's syndrome).

Q 12. What is dry or wet bronchiectasis?

Ans. Chronic cough with massive purulent sputum, more in the morning and in one of die lateral or lying down position (postural relation depends on the side(s) involved), hemoptysis, and dilated airways on the bronchoscopy or high resolution CT scan are characteristic features of *wet bronchiectasis*.

The term *dry bronchiectasis* refers to either asymptomatic disease or a disease with recurrent nonproductive cough associated with intermittent episodes of hemoptysis and bronchiectasis in an upper lobe. The hemoptysis can be life-threatening as bleeding occurs from the bronchial vessels under systemic pressure. There is usually a past history of tuberculosis or granulomatous infection.

Q 13. How will you investigate a case of bronchiectasis?

Ans. Following investigations are to be done:

- **Hemoglobin,** TLC, DLC, ESR. Polymorphonuclear leucocytosis with raised ESR suggest acute infection. There may be normocytic normochromic anemia due to repeated infections.
- **Sputum for culture and sensitivity.** The sputum volume, colour, cellular elements are useful guide for active infection. Sputum for eosinophilia provides a clue to asthma and/or bronchopulmonary aspergillosis.
- **Urine examination** for proteinuria if amyloidosis is being suspected.
- **Blood culture and sensitivity** if there is evidence of bacteremia or septicemia.
- **Chest X-ray (PA view).** The chest X-ray (Fig. 1.11B) may be normal with mild disease or may show prominent (dilated) cystic spaces (saccular bronchiectasis) either with or without airfluid levels, corresponding to the dilated airways. These dilated airways are often crowded together in parallel, when seen longitudinally, appear as '*tram-tracks*', and when seen in cross section appear as, '*ring shadows*'. These may be difficult to distinguish from enlarged airspaces due to bullous emphysema or from regions of honeycombing in patients with severe interstitial lung disease. Because these spaces may be filled with secretions, the lumen may appear dense rather than radiolucent, producing opaque tubular or branched tubular structures.
- **Bronchography a gold standard for diagnosis** shows an excellent visualization of bronchiectatic airways, but, nowadays is not done because of availability of high resolution CT scan.
- **High resolution CT scan** will show dilated airways in one or both of the lower lobes or in an upper lobe. When seen in cross-section, the dilated airways have a ring-like appearance.
- **Fiberoptic bronchoscopy.** It is done to find out the cause. When the bronchiectasis is focal, fiberoptic bronchoscopy may show an underlying endobronchial obstruction. Bronchiectasis of upper lobe is common either due to tuberculosis or bronchopulmonary aspergillosis.
- **Pulmonary function tests.** These tests demonstrate airway obstruction as a consequence of diffuse bronchiectasis or associated COPD. Pulmonary function tests are useful to define the extent, severity of the disease, need for bronchodilators and to plan surgery.
- **Specific tests for aspergillosis,** i.e. precipitin test and measurement of serum IgE.

Q 14. What are the complications of bronchiectasis?

Ans. Common complications are as follows:
1. Recurrent pneumonias (e.g. repeated infections)
2. Bacteremia and septicemia
3. Massive hemoptysis (from dilated bronchial vessels) leading to pulmonary apoplexy
4. Right ventricular failure or cor pulmonale
5. Secondary amyloidosis
6. Meningitis or brain abscess
7. Aspergilloma (fungal ball) in a bronchiectatic cavity.

Q 15. What is difference between standard and high resolution CT?

Ans. In standard CT, the resolution (the slice thickness) is 10 mm thick, whereas in high resolution CT the slice thickness is 1–2 mm and high spatial resolution algorithms are used to reconstruct images.

Q 16. What do you know about spiral CT?

Ans. This is a rapidly evolving technique to image the chest which has the advantage of imaging truly contiguous sections; with the result completely seamless reconstructions are possible. This may allow virtual-reality bronchoscopy imaging.

Q 17. How would you treat bronchiectasis?

Ans.
- Postural drainage
- Antibiotics
- Bronchodilators and mucolytics
- Surgery in selected cases
- Treat the complication when they arise.

Q 18. What is indication of surgery in bronchiectasis?

Ans.
- ***Localised disease*** involving a segment or a lobe without involvement of other parts of the lung on bronchographic or CT evidence.
- ***Recurrent hemoptysis.***

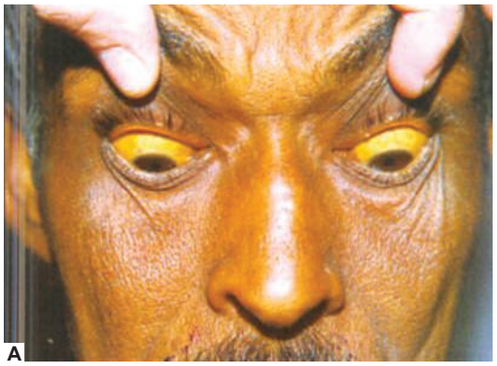
CASE 12: JAUNDICE

The patient (Fig. 1.12A) presented with fever for a few days followed by jaundice and dark colouration of urine. There was history of pain abdomen, and distaste to food.

Clinical Presentations

The clinical presentation of a case with jaundice varies according to the cause:

1. Patients with hepatitis present with fever, abdominal pain, jaundice, tender hepatomegaly, anorexia, distaste to food and smoking.
2. Patients with hemolytic jaundice complain of insidious onset and long duration of jaundice with dark coloured urine and stools.
3. Patients with obstructive jaundice present with abdominal pain, pruritus and acholic stools in case the bile duct stone is the cause; while carcinoma of the pancreas produces painless progressive jaundice with palpable gallbladder.
4. Patients with cirrhosis of liver present with features of portal hypertension (ascites, hematemesis, melena, splenomegaly) and jaundice develops during decompensation of liver disease, i.e. hepatic encephalopathy (mental features will be present).
5. Jaundice may present during each pregnancy in a patient with benign intrahepatic cholestatic jaundice of pregnancy.
6. A young patient with recurrent jaundice of long duration usually suffer from congenital hyperbilirubinemia.



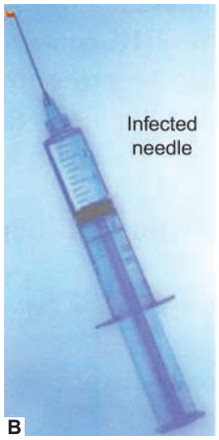


Fig. 1.12A and B: **A.** A patient with jaundice; **B.** Infected needle—a common cause of hepatitis B

History

Points to be Noted in History

A complete medical history is perhaps the most important part of evaluation. Ask for the following:

- ***Duration*** of jaundice
- ***Sore throat*** and ***rash*** (infectious mononucleosis)
- ***Occupation*** (Weil's disease in sewerage workers and farmers)
- ***Abdominal pain*** (cholecystitis, gallstones, cholangitis, carcinoma of pancreas)
- ***Pruritus*** (cholestatic hepatitis, primary biliary cirrhosis)
- ***Triad of fever***, rigors and upper abdominal pain (cholangitis)
- ***Any change in appetite, taste, weight*** and ***bowel habits*** (hepatitis)
- ***Any history of blood transfusions***, IV injections (Fig. 1.12B), tattooing, unprotected sexual activity (hepatitis B)
- ***Recent travel*** history
- ***Exposure to people with jaundice*** either in the family, or locality or outside (hepatitis)
- ***Exposure to possibly contaminated food***
- ***Occupational exposure*** to hepatotoxins or chemicals
- ***Detailed drug history*** (especially oral contraceptive and phenothiazines), i.e. taken in the past or are being taken. History of taking herbal or indigenous medicine
- ***History of alcohol*** intake
- History of pregnancy (pregnancy-induced or pregnancy associated jaundice)
- History of epistaxis, hematemesis or bleeding tendency (pale stool in obstructive jaundice)
- Family history for congenital hyperbilirubinemia, i.e. Gilbert's, Crigler-Najjar and Dubin-Johnson and Rotor syndromes
- Presence of any accompanying symptoms, such as arthralgias, myalgias, weight loss, fever, pain in abdomen, pruritus and change in colour of stool or urine
- Symptoms of encephalopathy, i.e. mental features.

EXAMINATION

Proceed as follows:

I. General Physical Examination

- Assess the patient's nutritional status (muscle mass, wasting), deficiency of vitamins and nutrients

- Look for stigmatas of chronic liver disease. These are commonly seen in alcoholic cirrhosis:
  - Spider nevi
  - Palmar erythema
  - Gynecomastia
  - Caput medusae
  - Dupuytren's contracture
  - Pigmentation
  - Parotid glands enlargement
  - Testicular atrophy, axillary and pubic hair loss
- *Look for enlarged lymph nodes:* An enlarged left supraclavicular node (Virchow's node) or periumbilical nodule (Sister Mary Joseph's nodule) suggests an abdominal malignancy
- *JVP and other signs of right heart failure*
- *Look for pulse* rate (bradycardia in obstructive jaundice), anemia and scratch marks, xanthelasma/xanthomatosis occur due to hypercholesteremia in obstructive jaundice.
- Look for any mark for drainage of ascites.

II. Systemic Examination

Abdominal examination for

- *Hepatomegaly*, e.g. note, size, shape, surface, movement with respiration, consistency and whether pulsatile or not. Elicit tenderness
- *Splenomegaly*—define its characteristics
- *Ascites*—Elicit all the signs for detection of fluid
- *Prominent venous collaterals* or veins must be looked for determine the flow of blood
- Look at the *hernial sites*
- Look for *scratch marks*.

Other Systems Examination

Cardiovascular, i.e. valvular heart disease, pericardial effusion.

Respiratory System

Pleural effusion especially right-sided

Examination of Excreta

- Urine
- Stool.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your provisional diagnosis and why?

Ans. The provisional diagnosis of this case is acute hepatitis probably viral. The *points in favour of diagnosis are*:

i. *Presence of prodromal symptoms,* i.e. fever, malaise, distaste for food, anorexia
ii. *Acute onset of jaundice* with dark coloured urine and stool with no pruritus
iii. *Tender moderate hepatomegaly* which is soft, smooth.

Q 2. How do you define jaundice? Where will you look for jaundice?

Ans. **Jaundice or icterus** refers to yellow disolouration of sclera, conjunctiva, mucous membrane of the tongue and skin due to raised serum bilirubin.

- Normal serum bilirubin is 0.3–1.5 mg%.
- Scleral staining or jaundice becomes clinically evident when serum bilirubin is at least 3.0 mg/dl.
- Raised bilirubin in between 1.5 and 3 mg/dl indicates subclinical jaundice.

Sites to be seen for Jaundice

Jaundice should be seen in sclera in broad day light because icterus is difficult to examine in the presence of tube light or fluorescent light because of yellow reflection. The sclera provides white background.

> Jaundice first appears in sclera due to affinity of bilirubin to stain elastin in sclera. A second place to examine the jaundice is underneath tongue.

Q 3. What is differential diagnosis in your case?

Ans. A large number of conditions that produce fever, jaundice and tender hepatomegaly come into differential diagnosis of viral hepatitis such as:

1. **Infectious mononucleosis**: Fever, lymphadenopathy, jaundice and hepatomegaly constitute clinical hallmark. Peripheral blood film will show atypical lymphocytosis. Serology (*Paul-Bunnel test*) helps in the diagnosis.
2. Nonviral hepatitis such as toxoplasmosis and nocardiosis can produce similar picture. Serology can differentiate the non-viral conditions from viral hepatitis.
3. **Autoimmune hepatitis**—Read Table 1.34
4. **Alcoholic and drug-induced/hepatitis**—Read Table 1.34.
5. **Amebic liver abscess.** Acute amebic liver abscess produces, fever, large tender hepatomegaly. Jaundice can occur occasionally. There may or may not be past history of dysentery. USG is diagnostic which reveals an abscess.
6. **Congestive hepatomegaly.** Signs of right ventricular failure, e.g. raised JVP, cyanosis, oedema feet and signs of pulmonary hypertension (loud P2, narrow split of S2 and Grahm-Steell murmur) separates congestive hepatomegaly from viral hepatitis.
7. **Budd-Chiari syndrome** (occlusion of hepatic vein or inferior vena cava) and veno-occlusive disease (involvement of small hepatic veins and venules due to consumption of bush tea) also produce massive hepatomegaly, jaundice but presence of ascites and signs of portal hypertension differentiate it from viral hepatitis. The absence of signs of congestive heart failure differentiates it from congestive hepatomegaly.
8. **Malignancy of liver**—Read Table 1.35.
9. **In pregnant women, acute fatty liver of pregnancy** and cholestasis of pregnancy and eclampsia constitute differential diagnosis of viral hepatitis.

Q 4. To which group of viral hepatitis your case belong?

Ans. Hepatitis A (short incubation, epidemic form of hepatitis)

Q 5. Name the types of viral hepatitits?

Ans. Viral hepatitis A, B, non-A, non-B (hepatitis C), hepatitis D and E.

Q 6. What is the source of infection in your case?

Ans. Contaminated food, milk, water or other food items.

Q 7. How does hepatitis A spread?

Ans. Feco-oral route (common), percutaneous and sexual transmission rare.

Q 8. How would you confirm the diagnosis?

Ans. The **diagnosis of hepatitis A** is made during an acute illness by demonstrating anti-HAV of IgM class. After acute illness, anti HAV of IgG class remains detectable indefinitely indicating past or previous infections.

Q 9. What is prophylaxis of hepatitis A?

Ans. **Both passive immunization** with IG (immunoglobulin) and **active immunization** with vaccines are available. All preparations of IG contain anti-HAV concentration sufficient to be protective. It gives immediate protection, formalin-inactivated vaccine used for pre-exposure prophylaxis gives long lasting protection.

Q 10. What are the indications of hepatitis A prophylaxis?

Ans. I. **Passive immunization with IG (immunoglobulin)** is indicated in:
- Pre-exposure prophylaxis or early incubation period prophylaxis.
- For postexposure hepatitis of intimate contact (household, sexual, institutional). Dose is 0.02 ml/kg intramuscular

II. **Active immunization by vaccine**
- It is indicated as pre-exposure prophylaxis for travellers to tropical countries, developing countries or other areas outside standard tourist routes.

III. **Both passive and active immunization**
- Passive immunization with IG at different site and active immunization with vaccine at another site are indicated during imminent travel or immediate travel.
- Two doses of vaccine are given at 0 month and at 6–12 months.

Q 11. Which hepatitis spread by blood transfusion?

Ans. Hepatitis B, C, D.

Q 12. Which hepatitis is most dangerous?

Ans. Hepatitis B.

Q 13. What would be the color of other fluids in jaundice?

Ans. Body fluids (CSF, tears, joint fluid) become **yellow coloured** if there is predominant conjugated hyperbilirubinemia as conjugated bilirubin being water-soluble gets excreted into these secretions.

Q 14. What are other causes of yellow discoloration of tissue?

Ans. Besides jaundice, other causes are:
- ***Carotenoderma (hypercarotenemia)*** due to excessive consumption of fruits and vegetables rich in carotene (e.g. carrots, oranges, squash, peeches).
- ***Use of antimalarial drug***, e.g. mepacrine, quinacrine. They are not used nowadays.
- ***Excessive exposure*** to phenols carotenoderma can be distinguished from jaundice by sparing of the sclera and normal coloured urine while it stains all other tissues. On the other hand, quinacrine stains the sclera and produces yellow discolouration of urine.

Q 15. What are the causes of jaundice?

Ans. Jaundice reflects hyperbilirubinemia, indicates an imbalance between bilirubin production and clearance. Increased production and decreased clearance are the underlying mechanisms for production of jaundice. Hyperbilirubinemia may result from:

i. Overproduction of bilirubin
ii. Impaired uptake, conjugation or excretion of bilirubin
iii. Regurgitation of unconjugated or conjugated bilirubin from damaged hepatocytes or bile ducts.

- *Unconjugated hyperbilirubinemia* results from either overproduction or impaired uptake or conjugation of bilirubin.
- On the other hand, *conjugated hyperbilirubinemia* is due to decreased excretion into the bile ductules or backward leakage of the pigment.
- The causes of jaundice are tabulated (Table 1.35).

Q 16. How do you classify jaundice?

Ans. Jaundice is classified in different ways:

1. **Based on colouration of sclera**
   - *Medical jaundice* (yellow colouration)
   - Surgical jaundice (greenish yellow colouration). The green colour is produced by oxidation of bilirubin to biliverdin in long-standing cases of jaundice.
2. **Based on the etiology**
   - *Hemolytic or prehepatic* (excessive destruction of RBCs)
   - *Hepatic* (cause lies inside the liver)
   - *Obstructive or posthepatic* (cause lies outside the liver in extrahepatic biliary system).
3. **Based on chemical nature of bilirubin**
   - *Unconjugated hyperbilirubinemia*
   - *Conjugated hyperbilirubinemia* (conjugated bilirubin is >50% of total bilirubin. The normal conjugated bilirubin is just 15–20%).

Table 1.35: Causes of jaundice depending on the type of hyperbilirubinemia

Jaundice with predominanty unconjugated hyperbilirubinemia
1. ***Hemolysis* (excessive destruction of RBCs and/or ineffective erythropoiesis)**
× Intracorpuscular or extracorpuscular defects
× Drug-induced especially in patients with G6PD deficiency
× Infections, e.g. malaria, viral
× Immune hemolysis
× Microangiopathic hemolytic anemia
× Paroxysmal nocturnal hemoglobinuria
× Ineffective erythropoiesis due to folate, vitamin B_{12} and iron deficiency and thalassemia
2. **Decreased uptake of bilirubin**
× Drugs, sepsis
× Hepatitis (acute or chronic), decompensated cirrhosis
× Gilbert's syndrome (congenital defect)
3. **Decreased conjugation of bilirubin**
× Neonatal jaundice
× Gilbert's and Crigler-Najjar syndrome—type I (complete absence), type II (partial deficiency of enzyme glucuronyl transferase)
Jaundice with predominantly conjugated hyperbilirubinemia
1. **Cholestasis**
A. Intrahepatic
× Congenital (Dubin-Johnson and Rotor syndrome)
× Benign intrahepatic cholestasis
× Cholestatic jaundice of pregnancy
× Drugs and alcohol
× Hepatitis (acute and chronic)
× Primary biliary cirrhosis
× Hodgkin's lymphoma
× Postoperative
B. Extrahepatic
× Bile duct stone, stricture, cholangitis
× Parasite (roundworm)
× Trauma to bile duct
× Bile duct obstruction due to tumor (bile duct, pancreas, duodenum)
× Secondaries in liver or at portahepatis
× Pancreatitis
× Choledochal cyst

Q 17. What are characteristic features of hemolytic jaundice?

Ans. These are as follows:

i. Anemia with mild jaundice.
ii. Freshly voided urine is not yellow, becomes yellow on standing due to conversion of excessive urobilinogen in the urine to urobilin on oxidation.
iii. Preceding history of fever (malaria, viral), or intake of drugs if patient is G6PD deficient or intake of heavy metals.
iv. Typical facies, e.g. chipmunk facies seen in thalassemia due to excessive marrow expansion leading to frontal bossing and maxillary marrow hyperplasia.
v. Mild hepatosplenomegaly. The liver is nontender.
vi. No pruritus or itching. No xanthelasma/xanthomatosis.
vii. Peripheral blood film examination and other tests for hemolysis will confirm the diagnosis.

Q 18. What is differential diagnosis of hepatocellular jaundice?

Ans. Common causes of hepatocellular jaundice are differentiated in Table 1.36.

Q 19. List few differences between intrahepatic and extrahepatic obstructive jaundice?

Extrahepatic jaundice (surgical jaundice)	*Intrahepatic obstruction (medical jaundice)*
× Common in old and middle age	× Common in young
× Associated history of dyspeptic symptoms (gallbladder dyspepsia)	× History of hepatitis (contacts, blood transfusion in injections) or intake of drugs
× Jaundice is slow to develop, intermittent with pain	× Transient painless Jaundice of sudden onset
× Pruritus is characteristic (scratch marks may be present)	× Pruritus is minimal
× Hepatomegaly is usually present due to dilated biliary sytem	× No hepatomegaly. Splenomegaly can occur in 5–10% cases of hepatitis
× Gallbladder may be palpable due to obstruction below the cystic duct	× Gallbladder is not palpable as obstruction is within liver above the cystic duct
× Signs of infection or inflammation absent	× Fever, alteration in WBC count may be present
× Serum bilirubin is usually high (>10 mg%)	× Varies with the severity
× Serum lipids (triglyceride, cholesterol) and alkaline phosphatase are very high	× They are mildy raised
× Ultrasonography and CT scan are diagnostic and help to find out the cause	× They show just altered echotexture
× Stone, tomor, parasite are common causes	× Viral infection, autoimmunity and drugs are common causes

Q 20. What are clinical characteristic of obstructive jaundice?

Ans. The clinical characteristics are:

i. Deep yellow or greenish yellow jaundice—called *surgical jaundice*
ii. *Pruritus or itching* present due to retention of bile salts
iii. *Urine is dark coloured* due to excretion of bile pigments but stools are clay-coloured (acholic)
iv. There may be *associated pain abdomen*, *severe*, colicky with *intermittent jaundice, if bile duct stone is the cause*
v. *Gallbladder is palpable* if bile duct is obstructed either by an impacted stone or by carcinoma of head of pancreas. A palpable gallbladder in obstructive jaundice unlikely due to chronic cholecystitis (Courvosier's law)
vi. *Slowing of pulse rate or bradycardia* may occur due to retention of bile salts
vii. *Fever, shaking chills and rigors* with jaundice indicate cholangitis and biliary obstruction (Charcot's fever)

Table 1.36: Differential diagnosis of hepatocellular jaundice

Viral hepatitis	*Autoimmune hepatitis*	*Alcoholic hepatitis*	*Carcinoma of liver*	*Drug-induced*
× Fever followed by jaundice. As the jaundice appears, fever disappears × Anorexia, nausea and vomiting, distaste to food and smoking × Arthralgia, myalgia, headache, pharyngitis, cough, fatigue, malaise × Dark coloured urine and clay-coloured or norma! coloured stool × History of exposure to a patient with jaundice or use of contaminated food or IV injection/ blood transfusion or sexual contact, etc. × *Hepatomegaly*. Liver is moderately enlarged, soft, tender, smooth	× Splenomegaly in 20% cases only × Insidious onset. Chronic course × Common in females × Fever with jaundice, anorexia, fatigue, arthralgia, vitiligo, epistaxis. Amenorrhea is the rule × Sometimes a '*cushingoid*' face with acne, hirsutism, pink cutaneous striae × Bruises may be seen × Hepatosplenomegaly, spider telangiectasis are characteristic × Other autoimmune disorders may be associated × Serological tests for specific autoantibodies confirm the diagnosis	× History of alcoholism × Anorexia, weight loss × Stigmata of chronic liver disease (spider nevi, palmar erythema, gynecomastia, testicular, atrophy, Dupuytren's contractures, parotid enlargement) may be present × Jaundice with enlarged tender liver × May be associated with other manifestations of alcoholism, e.g. cardiomyopathy, peripheral neuropathy	× Common in old age × Progressive jaundice with loss of appetite and weight × Liver enlarged, tender, hard, nodular. Hepatic rub may be heard × Anemia, fever lympha-denopathy in neck and marked cachexia present × Jaundice is deep yellow or greenish × Ascites may be present × Evidence of metastatic spread to lungs, bone, etc. × USG and liver biopsy will confirm the diagnosis	× History of intake of hepatotoxic drugs, e.g. INH, rifampicin oral contraceptives × Malaise before the onset of jaundice × Occasionally rash, fever, arthralgia present × Liver is enlarged and tender × Tests for viral hepatitis are negative

viii. In long-standing obstructive jaundice, *xanthomas*, *weight loss*, *malabsorption* or steatorrhoea may occur

ix. *Conjugated hyperbilirubinemia* with dilatation of intrahepatic or extrahepatic ducts on USG confirm the diagnosis.

Q 21. Name the few causes of postoperative jaundice.

Ans. 1. *Hemolysis and reabsorption of hematoma*, hemoperitoneum or blood transfusions.
2. *Impaired liver functions* due to sepsis, anesthesia, shock.
3. *Extrahepatic biliary obstruction* due to biliary stones or unsuspected injury to biliary tree.

Q 22. What are medical causes of extrahepatic obstruction?

Ans. Read causes of extrahepatic obstruction in Table 1.35.

Q 23. What are characteristics of various viral hepatitis?

Ans. The characteristics of viral hepatitis are enlisted in Table 1.37.

Q 24. What are causes of acute hepatitis?

Ans. Hepatitis occurs due to a variety of infective and noninfective causes (Table 1.38).

Q 25. Name the familial congenital hyperbilirubinemia.

Ans.
- **Gilbert's syndrome** (predominantly unconjugated hyperbilirubinemia)
- **Crigler-Najjar syndrome** (type I: Complete absence of glucuronyl transferase, type II: Partial deficiency of enzyme)
- **Dubin-Johnson** (decreased excretion of bilirubin/ syndrome
- **Rotor**—excretory defect of bilirubin with pigmentation of liver.

Q 26. What is Dubin-Johnson syndrome?

Ans. It is familial conjugated hyperbilirubinemia in which there is excretory defect of bilirubin excretion and there is pigmentation of liver due to melanin (rotor syndrome) detected on liver biopsy. It is detected by delayed bromosulphthalein excretion test.

Q 27. What are causes of prolonged jaundice (i.e. duration >6 months)?

Ans. Causes of prolonged jaundice are as follows:
1. Chronic hepatitis or cholestatic viral hepatitis, chronic autoimmune hepatitis
2. Cirrhosis of the liver
3. Malignancy of liver
4. Hemolytic jaundice (e.g. thalassemia)
5. Congenital hyperbilirubinemia
6. Drug-induced
7. Alcoholic hepatitis
8. Primary biliary cirrhosis
9. Wilson's disease
10. Obstructive jaundice (extrahepatic biliary obstruction).

Q 28. What are complications of acute viral hepatitis?

Ans. Complications are common in type B or type C viral hepatitis; type A hepatitis usually resolves spontaneously. The complications are:
- *Fulminant hepatitis*—a dreadful complication
- *Cholestatic viral hepatitis*
- *Relapsing hepatitis* (transient subclinical infection)
- *Chronic carrier state*
- *Chronic hepatitis*
- *Posthepatitis syndrome* (symptoms persist but biochemical investigations normal)
- *Cirrhosis of the liver*
- *Hepatocellular carcinoma*.

Table 1.37: Distinguishing features of main hepatitis viruses

Virus	*A*	*B*	*C*	*D*	*E*
Group	Enterovirus	Hepadna	Flavivirus	Delta particle (incomplete virus)	—
Nucleic acid	RNA	DNA	RNA	RNA	RNA
Size	27 nm	40–42 nm	30–35 nm	35 nm	27 nm
Incubation period in weeks	2–6	4–26	2–20	5–9	3–8
Spread					
Faeco-oral	Yes	No	No	No	Yes
Parenteral (blood)	Uncommon	Yes	Yes	Yes	Yes
Saliva (kissing)	Yes	Yes	Yes	—	—
Sexual act	Uncommon	Yes	Uncommon	Yes	Unknown
Vertical transmission	No	Yes	Uncommon	Yes	No
Chronic infection					
Incidence	Not known	5–10%	>50%	—	—
Severity	Mild	Often severe	Moderate	Unknown	Mild to moderate
Prevention					
Active	Vaccine	Vaccine	No	Prevented by hepatitis B	No
Passive	Immune serum globulins	Hyperimmune serum globulins	No	Virus infection	No
Prognosis	Good	Worst with age and debility	Moderate	Same as with hepatitis B	Good

Table 1.38: Causes of acute hepatitis

Infective

- *Viral*, e.g. hepatitis A, B, C, D, E, Epstein-Barr virus, cytomegalovirus, herpes simplex and yellow fever virus
- *Postviral*: Reye's syndrome in children (aspirin-induced)
- *Nonviral*, e.g. Leptospira, Toxoplasma, Coxiella

Noninfective

- *Drugs*, e.g. paracetamol, halothane, INH, rifampicin, chlorpromazine, methyldopa, oral contraceptives
- *Poisons*, e.g. carbon tetrachloride, mushrooms, anatoxin
- *Metabolic*, e.g. Wilson's disease, pregnancy
- *Vascular*, e.g. CHF, Budd-Chiari syndrome, oral contraceptives

Q 29. What is carrier state in hepatitis?

Ans. Some asymptomatic patients carrying the HbsAg for more than 6 months after the episode of acute hepatitis B are called *chronic carriers*. Carrier stage does not exist in hepatitis A and E. These carriers are potential source of transmission of infection.

Q 30. How will you investigate a case with acute viral hepatitis?

Ans. Following are the investigations:

1. **TLC and DLC** may show leucopenia or lymphopenia, atypical lymphocytes may be seen. The ESR may be high.
2. **Hepatic profile**
   - ***Serum bilirubin raised***, equally divided between conjugated and unconjugated fractions, or sometimes conjugated fraction may predominate (cholestatic phase).
   - ***Serum transaminases*** (SGOT/SGPT) are raised more than ten times (400–4000 IU).
   - ***Serum alkaline*** phosphatase may or may not be raised; if raised, indicates cholestasis.
   - ***Plasma albumin*** is normal, may become low if jaundice is prolonged.
   - ***Prothrombin time*** is normal, if increased, indicates extensive hepatocellular damage and bad prognosis.
   - ***Urine*** may show:
     - Urobilinogen in urine, appears during preicteric phase, disappears with onset of jaundice and reappears during recovery
     - Bilirubinuria occurs during subclinical stage
     - Presence of bile salt and bile pigment indicates cholestasis
     - Stool may be normal coloured or clay-coloured (obstructive jaundice).
3. **Ultrasound of liver** may reveal hepatomegaly with normal echotexture. CT scan is not superior to USG.
4. **Serological tests** (Table 1.39): These are done in acute hepatitis.
5. **Special investigations,** e.g. mitochondrial antibodies, ERCP, CT scan and liver biopsy (if needed).

Table 1.39: Diagnostic serology of acute hepatitis

Hepatitis	Serology			
	Hbs Ag	IgM anti-HAV	IgM anti-HBC	Anti-HCV
Acute hepatitis A	–	+		–
Acute hepatitis B	+	–		+
Acute hepatitis A	+	+		–
Super imposed on chronic hepatitis B	+	–		–
Acute hepatitis A and B	+	+	+	–
Acute hepatitis C	–	–	–	–

Q 31. Which hepatitis produces extrahepatic manifestations? What are these manifestations?

Ans. Hepatitis B produces extrahepatic manifestations are as follows:

- Serum sickness like syndrome
- Polyarthritis
- Acute glomerulonephritis (immune-complex)
- Atypical pneumonia
- Aplastic anemia or agranulocytosis
- Autoimmune hemolytic anemia
- Guillain-Barré syndrome
- Skin rashes (urticaria).

Q 32. What is acute fulminant hepatitis? How does it present clinically?

Ans. **Acute fulminant hepatitis** is said to be present when a previously healthy person develops acute hepatitis and goes into acute hepatic insufficiency/failure within 2 weeks of illness. This is due to acute massive necrosis (acute yellow atrophy) with shrinkage of liver (liver span <10 cm on USG).

The causes are:

1. Type B, C and D viral infection
2. Drugs
3. Pregnancy
4. Wilson's disease and liver poisons (mushrooms, carbon tetrachloride, phosphorous)
5. Reye's syndrome in children.

The symptoms and signs of acute fulminant hepatitis are due to acute hepatic encephalopathy without stigmatas of the liver disease and signs of portal hypertension.

Q 33. What is chronic hepatitis? What are its causes?

Ans. It is defined as an inflammation of the liver (acute viral hepatitis) lasting for 6 months. The causes are:

- Autoimmune hepatitis
- Hepatitis B, C, D
- Drug-induced hepatitis
- Wilson's disease
- Alcoholic hepatitis
- Alpha-1 antitrypsin deficiency.

The **diagnosis of chronic hepatitis** is made when clinical and biochemical evidence of hepatitis (e.g. jaundice, raised liver enzymes) persists for >6 months. The diagnosis is confirmed by liver biopsy and blood serology.

Q 34. Whom will you advise prophylaxis against hepatitis B (Table 1.40)?

Ans. The indications are given in Table 1.40. Recently there has been mass prophylaxis program for hepatitis B in general population in India.

Table 1.40: Indications for hepatitis B vaccination in endemic areas

- **Parenteral drug abusers**
- *Male homosexuals*
- *Close contacts (relatives or sexual partners) of infected persons*
- *Patients receiving maintenance dialysis*
- *Laboratory staff*
- *Medical personnel*
  - Dentists
  - Surgeons/obstetricians
- *Medical/paramedical staff of:*
  - Intensive care department
  - Accident and emergency department
  - Endoscopy units
  - Oncology units
- *Nursing staff* involved in care of such patients

CASE 13: ASCITES

The patient (Fig. 1.13) presented with progressive distension of abdomen with abdominal discomfort and dyspnea. No history of jaundice or hematemesis. No history of edema feet or puffiness of face. No history of palpitation, PND or orthopnea. No past history of jaundice or rheumatic fever. No history of pain chest, cough with expectoration or hemoptysis. Examination revealed flanks full, positive fluid thrill and shifting dullness.

Clinical Presentations

- ***Often considerable number of patients with ascites*** may go unnoticed for weeks or months either because of coexistent obesity or because the ascites formation has been insidious, without pain or localising symptoms.
- ***Ascites may first be noticed by the patient as an abdominal swelling*** with progressive increase in belt or size of clothing.
- ***Progressive abdominal distension due to ascites*** produces sensation of stretching or pulling of the flanks or groins and vague low back pain.
- ***Tense ascites*** may produce an increase in intra-abdominal pressure resulting in indigestion and heart burn due to gastroesophageal reflux; or dyspnea, orthopnea and tachypnea due to elevated domes of diaphragm and abdominal wall hernias (inguinal or abdominal).
- ***Patient may complain of respiratory embarrassment*** due to massive ascites or right-sided pleural effusion due to leakage of ascitic fluid through lymphatic.

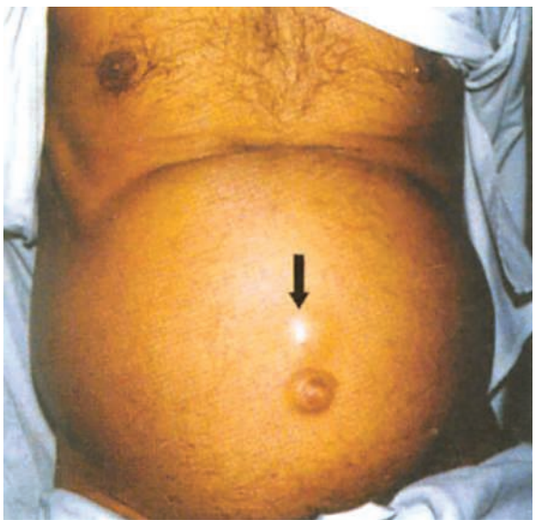


Fig. 1.13: A patient with ascites. Note the distended abdomen with everted umbilicus and a ventral hernia (↓) above the small umbilical hernia channels in diaphragm. A large pleural effusion obscuring the most of the lung may occasionally develop, is known as hepatic hydrothorax

History

Points to be Noted on History

- *Onset* and *progression* of symptoms
- *Past history* of jaundice, hematemesis and melena, CHF, tuberculosis, rheumatic fever, renal failure, polyarthritis
- *Personal history*—alcoholism, diet
- *History of malignancy* (mesothelioma, secondaries in liver) e.g. loss of appetite and weight
- *Family history*, e.g. cirrhosis, Wilson's disease, hemochromatosis
- *History of pain in abdomen* (spontaneous bacterial peritonitis, malignancy).

EXAMINATION

Proceed as follows:

I. General Physical Examination

Look for the fallowings:

- **Face:** Vacant look, emaciated face and sunken cheeks indicate cirrhosis of the liver (cirrhotic fades)
- **Mental features,** e.g. confusion, disorientation, disturbed sleep pattern, bizarre handwriting, disturbed speech with jaundice indicate hepatic encephalopathy
- **Puffiness of face** with periorbital edema. It occurs in nephrotic syndrome
- ***Generalised or localised lymphadenopathy*** (e.g. tubercular, malignancy collagen vascular disorders)
- ***Raised JVP and cyanosis*** (congestive heart failure, constrictive pericarditis)
- ***Cyanosis, clubbing of fingers*** (e.g. bacterial endocarditis, hepatic encephalopathy)
- ***Stigmatas of chronic liver disease,*** e.g. muscle wasting, gynecomastia, testicular atrophy, loss of axillary and pubic hair, parotid enlargement and Dupuytren's contractures)
- ***Palmar erythema*** or ***painful fingertips*** or ***gangrene*** or ***flapping tremors***
- ***Pedal edema,*** sacral edema, scrotal edema
- ***Signs of multiple nutrients deficiency,*** e.g. angular stomatitis, cheilosis, anemia, atrophic or bald tongue, muscle flabbyness, wasting and pigmentation of tongue and mucous membranes.

II. Systemic Examination

Inspection

- Fullness of flanks or tense abdominal distension
- The umbilicus is either transversely slit, e.g. smiling umbilicus (moderate ascites) or everted with or without umbilical hernia (massive ascites)
- Prominent distended veins over the abdomen or around umbilicus (caput medusae) in a patient with cirrhotic portal hypertension or inferior vena cava obstruction
- Ventral, umbilical or inguinal hernia may or may not be seen
- There may be a mark of tapping of ascites (a mark with staining of tincture).

Palpation

- Increased abdominal girth
- Tenderness of abdomen in peritonitis with ascites
- Flow of blood in distended veins is away from the umbilicus in portal hypertension and from below upwards in IVC obstruction
- Palpable spleen in a patient with ascites (by dipping method) indicate portal hypertension

- Hepatomegaly. It indicates Budd-Chiari syndrome (malignancy or postnecrotic nodular conolasis)
- Elicit for abdominal wall edema.

Percussion

- Percussion note is dull. Dullness is more marked in flanks with central sparing
- Shifting dullness is present in moderate ascites but becomes absent in huge ascites
- Fluid thrill is present in huge ascites, moderate ascites and localised ascites but absent in mild ascites
- Puddle's sign (dullness around umbilicus in knee-elbow position) is positive in mild ascites.

Auscultation

- A venous hum around umbilicus indicate cirrhotic portal hypertension (Cruveihlier-Bombgarten's syndrome)
- A bruit over the liver indicates malignancy or recently done biopsy.

Other system examination

- Cardiovascular
- Urogenital system.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your provisional diagnosis?

Ans. My provisional diagnosis is ascites. *The points in favour are:*

- Distended abdomen with full flanks and transverse slit (smiling) umbilicus.
- Presence of both fluid thrill and shifting dullness.
- Flanks are dull with central sparing.
- Intestinal sounds are heard in the centre of abdomen.

Q 2. How do you define ascites?

Ans. Normal amount of fluid in the peritoneal cavity is 100–150 ml of lymph, not detected by any means:

- Abnormal collection of fluid (>300 ml) in the peritoneum is called ascites.
- This amount is detected on USG abdomen.
- Significant amount of fluid (>500 ml) produces fullness of flanks on lying down position, is detected clinically.
- Larger amount of fluid (e.g. 1 L) produces horseshoe shape of the abdomen.
- Tense ascites means the peritoneal cavity is filled with free fluid producing cardio-respiratory embarrassment.

Q 3. What are causes of distended abdomen?

Ans. ***Five "F"*** denotes distension such as ***Fat***, ***Fluid***, ***Flatus***, ***Feces*** and ***Fetus***.

Q 4. What important points will you ask in history from a patient with ascites?

Ans. The following points are to be noted in a case of ascites:

- Onset, e.g. sudden or gradual
- Past history of rheumatic fever, joint pain, jaundice, alcoholism, hematemesis or melena. Low grade fever or past history of tuberculosis or polyarthritis
- History of heart failure, liver disease, malignancy
- Decrease or loss of appetite
- Diet and nutrition
- Cough and hemoptysis (present or past)
- Loss of weight, malignant cachexia
- Prolonged history of diarrhea >3 months, alteration in bowel habits
- Pain abdomen (acute pancreatitis) spontaneous bacterial peritonitis
- History of puffiness of face or edema or chronic renal failure.

Q 5. What are the causes of ascites?

Ans. Ascites occurs due to **transudation** of fluid into peritoneum in hypoproteinemic states or **exudation** into peritoneum by inflammation or infiltration of peritoneum by malignant process. The common **causes** are given in Tables 1.41 and 1.42.

Table 1.41: Causes of ascites

Systemic (ascites with edema)	*Local (ascites only without edema)*
× Nephrotic syndrome	× Peritonitis (serous, exudative)
× Cirrhosis of the liver	× Tuberculosis
× Hypoproteinemia: Nutritional or following chronic diarrhea or malabsorption	× Malignancy with secondaries in peritoneum
× Congestive heart failure or constrictive pericarditis	× Pancreatitis
× Malignancy of liver	× Spontaneous bacterial peritonitis
× Meig's syndrome (ovarian tumor)	× Portal vein thrombosis
× Hypothyroidism	× Hepatic vein thrombosis (Budd-Chiari syndrome)
	× Chylous ascites

Q 6. What is differential diagnosis of ascites?

Ans. The differential diagnosis of ascites depends on the cause of ascites and whether ascites is a part of generalised *anasarca* (ascites, edema, fluid in serous cavities) or is localised.

1. **Ascites of nephrotic syndrome:** Puffiness of face in the morning, pitting ankle edema, slowly developing ascites with or without anemia indicate ascites to be of renal origin. The massive albuminuria confirms the diagnosis.
2. **Ascites due to cirrhosis of the liver:** Past history of jaundice or chronic liver disease, with history of recent episode of hematemesis and jaundice in a patient with ascites suggest cirrhosis. The gynecomastia, loss of axillary and pubic hair, weakness, weight loss are stigmata of chronic liver disease. Prominent

Table 1.42: Causes of ascites depending on the nature of fluid

Transudate (serum ascitic fluid albumin gradient >1.1)

- Noninflammatory fluid, serous or straw coloured
- Fluid protein content <3.0 g/dl (or <50% of serum proteins)
- Specific gravity low or normal
- Occasional cell, mostly mesothelial
- Serum-ascites albumin gradient >1.1 g/dl (serum albumin minus ascitic fluid albumin)

Causes

- Nephrotic syndrome
- Congestive heart failure, pericardial effusion
- Hypoproteinemia, protein-losing states
- Cirrhosis of the liver
- Meig's syndrome

Exudate (serum/ascitic fluid albumin gradient >1.1)

- Inflammatory thick, turbid or mucinous, hemorrhagic or straw coloured fluid
- Protein content >3.0 g/dl (>50% of serum proteins)
- Specific gravity is high
- Cell count (100–1000 cells/mm^3), mostly either mononuclear or neutrophils
- Serum-ascites albumin gradient <1.1 g/dl

Causes

- Peritonitis, e.g. pyogenic, tubercular, malignant, subacute bacterial
- Leukemias, lymphomas
- Chylous ascites
- Budd-Chiari syndrome
- Pancreatitis (pancreatic ascites)

abdominal veins, splenomegaly suggest portal hypertension due to cirrhosis.

3. **Ascites due to hypoproteinemia:** Anemia, multiple deficiencies, muscle flabbyness and atony of muscles with ascites and edema indicate hypoproteinemia to be its cause. The patient may have history of chronic diarrhea or recurrent diarrhea.
4. **Ascites of congestive heart failure:** Raised JVP, tender hepatomegaly, dyspnea, orthopnea, paroxysmal nocturnal dyspnea (PND), cardiomegaly with or without murmurs, ascites, edema with or without peripheral cyanosis are points in favour of congestive heart failure as the cause of ascites.
5. **Tubercular ascites:** A slow developing ascites with anorexia, low grade fever, common occurrence in females than males, night sweats and evening rise of fever with or without any evidence of tuberculosis elsewhere are points in favour of tubercular ascites if it develops in young age.
6. **Malignant ascites:** Rapid filling tense ascites in old age with decrease or loss of appetite, marked cachexia, hemorrhagic nature of ascites could be due to malignancy anywhere in the abdomen with secondaries in the peritoneum (e.g. ovary, uterus, stomach pancreas, lung, breast).
7. **Pancreatic ascites** is due to collection of a large amount of pancreatic secretions either due to disruption of pancreatic duct or pseudocyst formation. It is painless, mild to moderate collection seen in patients with chronic pancreatitis. The ascitic fluid is exudate with low SAAG (<1.1) and high, fluid amylase levels (>1000 unit/L).

Q 7. What is chylous ascites? What are its causes?

Ans. It is the presence of milky fluid containing lymph in the peritoneal cavity. Milky fluid (turbidity) may be due to large number of cells (e.g. leucocytes, degenerated cells or tumor cells) or due to increased amount of protein content called *pseudochylous*.

Causes: Chylous ascites is most commonly due to obstruction to the lymphatics or thoracic duct especially by lymphoma, contains a large amount of triglycerides (>1000 mg/dl), and results from:

1. ***Trauma or penetrating abdominal injury*** to the thoracic duct
2. ***Tumors*** (malignant tumors of lymph nodes or others infiltrating the lymphatics)
3. ***Tuberculosis*** with lymphadenitis
4. ***Filariasis*** (filarial worms obstructing the lymphatics)
5. Occasionally ***cirrhosis and pancreatitis***. Turbidity of fluid disappears after extraction with ether; a diagnostic clue to the presence of fat and differentiates it from pseudochylous ascites.

Pseudochylous ascites refers to increased amount of proteins and calcium in the fluid leading to turbidity which is not dissolved by ether.

Chyliform ascites means a large number of cells (leucocytes, degenerated epithelial cells or tumor cells) as the cause of turbidity which disappears on extraction with alkali.

Q 8. What would be nature of ascites when both fluid thrill and shifting dullness are absent?

Ans. Mucinous ascites.

Q 9. What is mucinous ascites?

Ans. Rarely, ascitic fluid may be mucinous (gelatinous) in character, giving lobulated (jelly-like mass) appearance to the ascites.

- The fluid thrill and shifting dullness are absent.
- It is difficult to aspirate (ascitic tap is dry).
- It may be either due to pseudomyxoma peritonei (rupture of mucocele of appendix or mucinous ovarian cyst)
- Rarely, it is due to colloid carcinoma of stomach or colon with peritoneal metastases.

Q 10. What it serum ascitic albumin gradient (SAAG)?

Ans. It is calculated by subtracting the ascitic fluid albumin concentration from serum albumin concentration from samples obtained at the same time. This gradient correlates directly with portal

pressure; those whose gradient is >1.1 g/dl have portal hypertension and those with gradients <1.1 g/dl do not. The accuracy of such determination is 97%. The gradient has nothing to do with nature of ascites, i.e. transudative or exudative.

Q 11. What is refractory ascites?

Ans. Ascites is said to be refractory if it persists inspite of the maximum dose of diuretics (400–600 mg of spironolactone and 120–160 mg of furosemide) and salt restriction.

i. Noncompliance of salt restriction
ii. Hepatorenal syndrome, e.g. functional renal failure in cirrhosis of the liver
iii. Low serum sodium or failure of diuretic therapy
iv. Infections or subacute bacterial peritonitis
v. Superimposition of hepatoma
vi. GI bleeding
vii. Development of hepatic or portal vein thrombosis.

Q 12. What is genesis of ascites in cirrhosis?

Ans. Increased hydrostatic pressure due to splanchnic vascular dilatation and increased portal venous flow.

- Sodium retention due to hyperaldosteronism as a result of activation of renin-angiotensin aldosterone system
- Decreased oncotic pressure due to hypoalbuminemia
- Increased formation of lymph due to vascular dilatation and increased portal venous blood flow
- Stimulation of antidiuretic hormone due to hypoperfusion of kidneys.

Q 13. What are physical signs of ascites?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 14. How would you differentiate ascites from ovarian cyst?

Ans.

Ascites	*Ovarian cyst*
× Generalised distention	× Localised distension
× Flanks fall	× Centtal or aniliac fossa swelling
× Umbilicus is transurgery slit or everted	× Vertically slit or everted umbilicus
× Umbilicus to symphysis pubis distance is more than xiphisternum to umbilicus	× The distances from umbilicus to pubis is smaller than umbilicus to xiphisternum
× Swelling does not have well defined demarcation	× Swelling is rounded with well defined upper border, i.e. you can reach above the swelling
× Horseshoe shape dullness on percussion (flanks dull, centre spares)	× Dullness is limited to midline or in one or two quadrants (quardrantic dullness)
× Shifting dullness present and characteristic	× Shifting dullness absent
× Vaginal examination is negative	× Vaginal examination is diagnosis
× USG is diagnostic, defects free fluid and its cause	× USG defects localised fluid and confirms the ovarian cyst

Q 15. What does presence of fluid thrill and absence of shifting dullness indicate?

Ans. Fluid thrill is present while shifting dullness is absent in following situations in the abdomen.

1. Mild ascites (≤500 ml of fluid)
2. Huge or massive ascites where there is no space for fluid to get shifted
3. Localised ascites
4. Ovarian cyst
5. Distended bladder.

Q 16. What are physical signs of mild, moderate and massive ascites?

Ans. The signs are given in Table 1.43.

Table 1.43: Physical signs in various grades of ascites

Grades	*Signs*
0 Minimal	Puddle's sign
1 Mild	Shifting dullness present fluid thrill absent
2 Moderate	Shifting dullness and fluid thrill present
3 Massive	Fluid thrill present, shifting dullness absent

N.B.: Localised ascites will behave like massive ascites, hence, in this also fluid thrill will be present and shifting dullness absent.

Q 17. What are the causes of rapid filling of ascites?

Ans. Malignancy (primary and secondary)

- Tuberculosis
- Chylous
- Spontaneous bacterial peritonitis
- Budd-Chiari syndrome.

Q 18. What are causes of purulent and hemorrhagic ascites?

Ans. They are depicted in Table 1.44.

Table 1.44: Purulent vs hemorrhagic ascites

Purulent ascites	*Hemorrhagic ascites*
× Pyogenic peritonitis	× Abdominal trauma or trauma during tapping of ascites
× Septicemia	× Malignancy of peritoneum (primary or secondary)
× Ruptured amebic liver abscess	× Tubercular peritonitis
× Pelvic inflammatory disease	× Bleeding diathesis
× Penetrating abdominal trauma with introduction of infection	× Acute hemorrhagic pancreatitis

Q 19. What are the causes of ascites disproportionate to edema feet (ascite precoax)?

Ans. These are as follows:

- Constrictive pericarditis
- Restrictive cardiomyopathy
- Hepatic vein thrombosis
- Cirrhosis of liver
- Tubercular peritonitis

- Intra-abdominal malignancy
- Meig's syndrome.

Q 20. What are the causes of hepatosplenomegaly with ascites?

Ans. Hepatosplenomegaly with ascites indicates:

i. Lymphoreticular malignancy
ii. Leukemia
iii. Malignancy of liver
iv. Secondaries in the liver
v. Hepatic vein thrombosis (Budd-Chiari syndrome)
vi. Postnecrotic cirrhosis
vii. Congestive heart failure
viii. Pericardial effusion.

Q 21. How will you investigate a patient with ascites?

Ans. Investigations are done to confirm the diagnosis and to find out its cause. These include:

1. **Blood examination:** Anemia may be present. Presence of neutrophilic leukocytosis indicates infection.
2. **Urine examination:** Massive albuminuria (>3.5 g/day) is present in nephrotic syndrome. Small amount of proteinuria occurs in pericardial effusion and congestive heart failure.
3. **Stool for occult blood:** If present, may indicate gastrointestinal malignancy as the cause of ascites.
4. **Ultrasonography:** It is of proven value in detecting ascites, presence of a masses, evaluation of size of liver and spleen, portal vein diameter and presence of collaterals and enlargement of caudate lobe.
5. **Plain X-ray abdomen** in standing position is useful. It may show ground glass opacity or diffuse haziness with loss of psoas muscle shadow. It may show intestinal obstruction (3–5 fluid levels in step-ladder pattern), raised right dome suggests either amebic liver abscess or hepatoma.
6. **Diagnostic paracentesis:** 50–100 ml of ascitic fluid is withdrawn with the help of a needle and biochemically analysed to establish the etiology of ascites and to plan its treatment. It is also sent for bacteriological examination. The differences between transudative and exudative ascites with their respective causes have already been discussed.
7. **Serum-ascites albumin gradient:** The albumin in serum and ascitic fluid is determined to calculate the gradient. The serum albumin minus ascitic fluid albumin determines the gradient. The gradient >1.1 g/dl indicates transudative ascites with portal hypertension and <1.1 g/dl indicates exudative ascites without portal hypertension. The fluid protein <50% of serum protein also indicates transudate; while >50% indicates exudate.
8. **Further investigations** are done to find out the cause, e.g. serum proteins, serum cholesterol for nephrotic syndrome, X-ray chest, ECG, echo for congestive heart failure/pericadial effusion, liver function tests and tests for portal hypertension.

Q 22. What does paracentesis mean? What are its indications?

Ans. **Paracentesis** means removal of fluid. Paracentesis of ascitic fluid is indicated as follows:

i. **Diagnostic:** A diagnostic tap of ascitic fluid is done by putting the needle in the flank in one of lateral positions. The fluid removed is 50–100 ml for diagnostic purpose, i.e. for biochemical, cytological and bacteriological analysis.
ii. **Therapeutic:** It is done as a part of treatment. Ascitic fluid is rich in proteins, hence should not be routinely tapped. It is removed if patient has cardiorespiratory embarrassment (acute respiratory distress with tachycardia). The amount of fluid removed depends on the relief of symptoms or maximum of 3–5 litres of fluid may be removed in one setting. Repeated tapping should be avoided unless absolutely necessary as this may predispose to secondary infection of peritoneum and also causes protein loss.
iii. **Refractory ascites** (nonresponse to treatment)
iv. **Paracentesis** is attempted before *needle biopsy* of liver, *ultrasonography* or for *better palpation* of *underlying viscera*.

Q 23. What would you see on ultrasound in cirrhotic ascites?

Ans. i. To detect presence of ascites (free or loculated)
ii. To detect splenomegaly
iii. To detect portal vein thrombosis or formation of collaterals
iv. To measure die portal vein diameter.
v. Condition of liver and its echotexture

Q 24. How does ultrasound help in the diagnosis of tubercular ascites?

Ans. It may reveal:

- Enlargement of mesenteric, preaortic and para-aortic lymph nodes
- Thick fibrinous septae may be seen traversing ascites (septate ascites)
- Thickened mesentery or *rolled up omentum*
- Tuberculosis of the liver, spleen, etc.

Q 25. What are ultrasound findings in Budd-Chiari syndrome?

Ans.

- Altered echotexture of liver
- Enlargement of caudate lobe
- Presence of ascites
- Reversal of portal blood flow on Doppler study.

Q 26. What are complications of paracentesis?

Ans. Common complications of paracentesis are as follows:

1. Sudden withdrawal of a large amount of fluid may lead to dilatation of splanchnic blood

vessels with subsequent **development of shock**.

2. **Introduction of infection (peritonitis)** if sterile precautions are not observed.
3. **Hypoproteinemia.** Ascitic fluid is rich in proteins, repeated large amount of aspiration may lead to development of hypoproteinemia.
4. **Precipitation of hepatic coma.** Sudden withdrawal of ascites in a patient with cirrhotic portal hypertension may precipitate hepatic encephalopathy.
5. **Constant oozing of the ascites** due to formation of a track (especially in tense ascites).

Q 27. What are sequelae/complications of ascites?

Ans. These are as follows:

- **Cardiorespiratory embarrassment**
- **Right-sided pleural effusion** due to leakage of ascitic fluid through lymphatic channels in the diaphragm
- **Spontaneous bacterial peritonitis**
- **Abdominal hernia** (umbilical, inguinal) and diverication of recti due to tense ascites as a result of increased intra-abdominal pressure
- **Functional renal failure**
- **Mesenteric venous thrombosis.**

Q 28. How would you manage a case with ascites?

Ans. 1. Rest in bed.

2. **Dietary salt restriction.** In severe ascites, sodium should be strictly restricted to less than 10 mEq/dl.
3. **Diuretics:** A combination of frusemide/torsemide with spironolactone is better than either alone.
4. **Fluid restriction in severe ascites.**
5. **Paracentesis:** It should be done for therapeutic purpose when there is an evidence of cardiorespiratory embarrassment. Repeated tapping should be avoided as far as possible.
6. **Salt-free albumin infusion.**
7. **Treatment of the underlying cause,** i.e. ATT for tuberculosis, appropriate treatment of CHF, nephrotic syndrome, pericardial effusion.
8. **If cirrhotic portal hypertension** is the cause then peritoneovenous shunting or TIPS may be employed (read the case discussion on cirrhotic portal hypertension and ascites).

Q 29. What is treatment of refractory ascites?

Ans. 1. Dietary sodium restriction plus diuretic.
2. Large volume paracentesis plus albumin.
3. Transjugular intrahepatic portosystemic shunt.
4. Liver transplantation.

CASE 14: HEPATOMEGALY

The patient (Fig. 1.14) presented with pain in the abdomen especially in right hypochondrium with swinging temperature, chills and rigors of 2 weeks duration. There was past history of loose motions and blood. Pain was more marked in left lateral position.

Clinical Presentations

Patients having hepatomegaly present with:

1. No symptoms (***asymptomatic***), hepatomegaly is detected during routine examination.
2. ***Pain in right upper quadrant***: It occurs in acute hepatomegaly due to stretching of the capsule of the liver which is pain-sensitive structure.
3. ***Mass in right hypochondrium.***
4. Patients may present with ***fever, jaundice, distaste for food, dark urine*** and ***sometimes pruritus***.
5. ***Patient may present, acute pain with fever and chills.*** This may occur following an episode of dysentery.
6. ***Patients with alcoholic liver disease may present with*** other toxic manifestations of alcoholism, e.g. peripheral neuropathy, proximal sympathy, cerebellar ataxia.

Wernicke's encephalopathy (ocular nerve palsy) and Korsakoff's psychosis (loss of recent memory and confabulation).

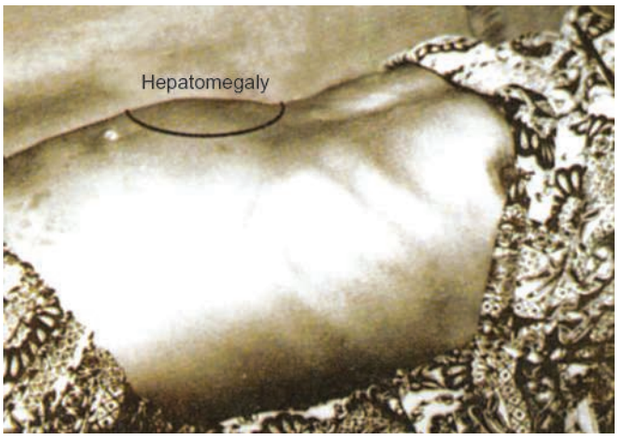


Fig. 1.14: A patient with hepatomegaly

History

Points to be Noted in History

- Present history of dysentery or GI disorder
- Any history of bleeding from any site
- History of fever, pigmentation, neck swelling, jaundice, anorexia, weight loss
- Full drug history
- Past history of tuberculosis, jaundice, diabetes, RHD (congestive heart failure)
- Personal history, e.g. alcoholism
- Nutritional history
- Family history of polycystic disease.

EXAMINATION

Proceed as follows:

I. General Physical Examination

- Assess the nutritional status
- Examine neck for lymph nodes, JVP
- Look at the skin for purpuric spots, ecchymosis, bruises, pigmentation
- Note anemia, cyanosis, jaundice, palmar erythema, spider angiomata
- Look for stigmatas of chronic liver disease and hepatic flap
- Note pedal edema
- Examine vitals, e.g. respiration, pulse, temperature and BP.

II. Systemic Examination

Inspection

- A right upper quadrantic fullness due to mass that moves with respiration (present in this case)
- Umbilicus is normal unless ascites present
- Normal abdominal movements
- Hernia sites are usually normal
- Prominent abdominal veins and collateral with flow away from umbilicus suggest portal hypertension.

Palpation

- Define the mass and study its characteristics, e.g. solid or cystic, smooth or irregular, soft, firm or hard, tender or nontender, etc. Note whether it is pulsatile or not
- Elicit intercostal tenderness (thumbing sign). It was positive in this case
- Elicit the signs of ascites if suspected
- Palpable the abdomen for other mass or masses such as spleen or lymph nodes.

Percussion

- Define upper and lower borders of the liver and calculate the liver span. It was 22 cm in this case
- Hydatid sign if hydatid cyst is suspected
- Percuss flanks for ascites.

Auscultation

- A bruit indicates a vascular hepatic tumor or hemangioma
- A rub indicates hepatic infarction or a nodular liver
- A venous hum around umbilicus indicates portal hypertension
- Auscultate for bowel sounds.

III. Cardiovascular Examination

- Cardiovascular system for heart failure
- CNS examination for alcoholism.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. In view of painful and tender mass in right hypochondrium with swinging temperature and chills, positive intercostal tenderness with massive hepatomegaly without jaundice and signs of portal hypertension; and past history of dysentery the diagnosis of amebic liver abscess is most likely in this case.

Q 2. What is differential diagnosis?

Ans. The following are differential conditions:

I. Congestive hepatomegaly: It is due to chronic venous congestion of the liver as a result of congestive heart failure due to any cause, i.e. constrictive pericarditis, pericardial effusion and hepatic vein thrombosis (*Budd-Chiari syndrome*). Symptoms of dyspnea, orthpnea, paroxysmal nocturnal dyspnea and cough with physical signs, such as raised JVP, cyanosis, peripheral edema, crackles at both lung bases, heart murmurs, cardiomegaly and hepatomegaly indicate congestive heart failure. Nonvisible apex, pulsus paradoxus, low pulse pressure, widening of cardiac dullness and dullness of 2nd and 3rd left space, feeble heart sounds with other peripheral signs of congestive heart failure indicates hepatomegaly due to either constrictive pericarditis or pericardial effusion. In hepatic vein thrombosis (*Budd-Chiari syndrome*), there is an intractable ascites, jaundice, prominent abdominal veins and collaterals formation due to development of portal hypertension. Hepatomegaly is a part of the syndrome.

In these congestive states, liver is moderately or massively enlarged, tender, has smooth surface and round well-defined edge. Further investigations should be done to confirm the diagnosis.

II. Inflammatory hepatomegaly: Inflammation of liver due to hepatitis or typhoid fever produces enlargement of liver. In hepatitis, there is history of fever, distaste for food, nausea, vomiting followed by jaundice and pain in right hypochondrium. Typhoid fever is characterised by moderate to high grade fever, abdominal symptoms (nausea, vomiting, diarrhea with or without blood), tenderness of abdomen, rose spots and slow pulse rate. At about 7 to 10th day of illness, spleen also becomes enlarged.

Liver in inflammatory disorders shows mild to moderate enlargement, is tender and has smooth surface. Further investigations are required to confirm the respective inflammatory cause.

III. Infiltrative hepatomegaly: Liver becomes enlarged when it gets infiltrated with leukemic cells or lymphoma cells or with fat and glycogen. Fatty infiltration of liver occurs in pregnancy, malnutrition, diabetes mellitus and alcoholism. Fatty liver is mildly enlarged, nontender and has smooth surface. In leukemia, there is evidence of anemia, bleeding tendency (purpuric spots, ecchymosis, epistaxis, bruising, etc.), fever, lymph node enlargement and splenomegaly; while fever with hepatosplenomegaly and lymphadenopathy are characteristics of lymphoma. Peripheral blood film examination will confirm the diagnosis. In these disorders, liver is moderately enlarged, soft to firm in consistency, nontender with smooth surface. Further investigations are needed to confirm the diagnosis.

IV. Hepatomegaly due to parasitic infection/ infestations: Malaria, kala-azar, hydatid disease and amebic infection can produce hepatomegaly by various mechanisms. Chronic malaria produces massive enlargement of liver along with other characteristics, such as fever of several days duration with classical bouts on alternate days with shaking chills and rigors. Jaundice is also common due to hepatitis or hemolysis. There is splenomegaly. Hepatomegaly is nontender. Peripheral blood film will confirm the diagnosis of this condition.

Fever, hyperpigmentation of skin, especially face and hands, hepatosplenomegaly and anemia support the diagnosis of kala-azar in endemic area. The diagnosis can easily be confirmed by demonstrating the parasite in stained smears of aspirate of bone marrow, lymph nodes, spleen or liver or by culture of these aspirates.

Hydatid disease of liver produces cystic enlargement with positive hydatid sign on percussion with peripheral eosinophilia. **USG is useful for confirming the diagnosis.**

V. Hematological disorders: All types of anemia, especially hemolytic anemia, lead to mild to moderate nontender hepatomegaly. The presence of mild jaundice, dark coloured urine and stools with mild to moderate hepatosplenomegaly support the diagnosis of hemolytic anemia. The diagnosis is further confirmed by tests for hemolysis and peripheral blood film examination. Malaria can also produce hemolysis, jaundice and hepatomegaly as already discussed.

Tumors of liver: The tumors (primary or secondary) can enlarge the liver. Liver in malignancy is massively enlarged, tender and has nodular surface and hard consistency.

Friction rub may be audible in some cases. Jaundice, pruritus may or may not be present, depending on the presence or absence of cholestasis. USG and biopsy of liver will confirm the diagnosis.

VI. Hepatomegaly due to diseases of liver: Posthepatic or postnecrotic cirrhosis can produce nontender, mild to moderate hepatomegaly with other stigmatas of cirrhosis and portal hypertension (muscle wasting, loss of axillary and pubic hair, gynecomastia, palmar erythema, spider angiomata, ascites, caput medusae and splenomegaly). The diagnosis is confirmed by liver biopsy and by biochemical and radiological tests.

Q 3. How do you define hepatomegaly?

Ans. Liver is placed just below the right dome of diaphragm and its edge is normally palpable on deep inspiration in right hypochondrium in some people and in children. The palpable liver does not mean hepatomegaly because if liver is displaced downwards due to any cause (emphysema, subphrenic abscess) it becomes palpable. Therefore, before commenting on hepatomegaly, the upper border must be defined by percussion in midclavicular line. Upper border of liver dullness is in 5th intercostal space.

Definition: Hepatomegaly refers to actual enlargement of liver (enlarged liver span) without being displaced downwards, i.e. the upper border of liver dullness stays as normal.

N.B.: Always tell liver span in a case of hepatomegaly instead of commenting palpable liver by so many centimetres.

Q 4. What are the causes of palpable liver without its actual enlargement?

Ans. This denotes downwards displacement of normal liver due to:

- Emphysema
- Thin and lean person
- Subphrenic abscess (right side)
- Visceroptosis (liver descends down during standing due to weak support)
- Any mass or fluid interposed between liver and the diaphragm will push liver downwards, e.g. subpulmonic effusion. Massive right-sided pleural effusion or pneumothorax.

Q 5. What are the causes of hepatomegaly?

Ans. Table 1.45 explains the causes of hepatic enlargement.

Q 6. Where are the points to be noted in hepatic enlargement?

Ans. Following are important points:

1. **Extent of enlargement.** Liver span should be defined. Normal liver span is 10–14 cm. Less than 10 cm is considered as acute fulminant hepatitis (acute yellow atrophy) and >14 cm is taken as hepatomegaly.
2. **Movements with respiration.** Liver always moves with respiration, i.e. descends 1–3 cm downwards with deep inspiration.
3. **Tenderness** (tender or nontender). Tender hepatomegaly suggests acute enlargement or infarction.
4. **Edge** (sharp or blunt)
5. **Surface** (smooth, irregular or nodular)
6. **Consistency** (soft, firm, hard)
7. **Upper border of liver dullness** (normal or shifted)
8. **Whether left lobe** is enlarged or not. Is there any enlargement of caudate lobe?
9. Any **rub, bruit, venous hum.**
10. Any **pulsation** (intrinsic or transmitted).

Table 1.45: Etiology of hepatic enlargement

1. Vascular
× Congestive heart failure (CHF)
× Pericardial effusion or constrictive pericarditis
× Hepatic vein thrombosis (Budd-Chiari syndrome)
× Hemolytic anemia
2. Bile duct obstruction (cholestasis)
× Bile duct stone
× Tumor
3. Infiltrative
× Leukemias (acute and chronic leukemia especially chronic myeloid leukemia)
× Lymphoma
× Fatty liver (e.g. alcoholism, diabetes, malnutrition)
× Amyloidosis
× Fat storage diseases, such as Gaucher's disease, Niemann-Pick's disease in children
× Granulomatous hepatitis (e.g. typhoid, tuberculosis and sarcoidosis)
4. Parasitic
× Malaria
× Kala-azar
× Hydatid disease
× Amebic liver abscess
5. Infective/inflammatory
× Hepatitis
× Typhoid fever
6. Tumors
× Hepatocellular carcinoma
× Secondaries or metastatic deposits in liver
7. Rare
× Polycystic disease of the liver
× Hemangioma of liver
× A large hepatic cyst

Q 7. What are the common causes of mild to moderate hepatomegaly?

Ans. They are:

- Typhoid fever, tuberculosis
- Leukemias
- Congestive splenomegaly (e.g. CHF, pericardial effusion)
- Budd-Chiari syndrome

- Hemolytic anemia
- A hemangioma or congenital cyst
- Fatty liver
- Postnecrotic cirrhosis.

Q 8. What are the causes of tender hepatomegaly?

Ans. Causes are as below:

- Acute viral hepatitis
- Amebic liver abscess
- Congestive hepatomegaly (e.g. CHF, constrictive pericarditis, pericardial effusion, Budd-Chiari syndrome)
- Pyogenic liver abscess
- Malignancy of the liver
- Perihepatitis (e.g. after biopsy or hepatic infarct)
- Infected hydatid cyst.

Q 9. What are the causes of enlargement of left lobe?

Ans. Causes are as below:

- Amebic liver abscess (left lobe abscess)
- Hepatoma
- Metastases in liver.

Q 10. What are different consistencies of the liver?

Ans. Table 1.46 explains the answer.

Table 1.46: Differential diagnosis of hepatomegaly depending on consistency of liver

Consistency	*Causes*
Soft	Congestive heart failure, viral hepatitis, fatty liver, acute malaria, visceroptosis (drooping of liver)
Firm	Cirrhosis, chronic malaria and kala-azar, hepatic amebiasis, lymphoma
Hard	Hepatocellular carcinoma, metastases in liver, chronic myeloid leukemia, myelofibrosis

Q 11. What are the causes of irregular surface of liver?

Ans. Following are causes:

- Cirrhosis (micronodular or macronodular)
- Secondaries in the liver
- Hepatocellular carcinoma
- Hepatic abscesses (pyogenic, amebic)
- Multiple hepatic cysts.

Q 12. What are the causes of massive hepatomegaly?

Ans. Massive hepatomegaly means enlargement >8 cm below die costal margin. The **causes** are:

1. Malignancy liver (primary or secondary)
2. Amebic liver abscess
3. Chronic malaria and kala-azar
4. Hepatitis (sometimes)
5. Hodgkin's disease
6. Polycystic liver disease.

N.B.: Acute malaria does not produce hepatomegaly.

Q 13. What are the causes of hepatic bruit and rub?

Ans. Following are the causes:

- **Bruit**
  - Hepatocellular carcinoma
  - Hemangioma liver
  - Alcoholic hepatitis/liver disease
- **Rub**
  - Infections of liver
  - Following liver biopsy
  - Hepatic infarction (embolic)
  - Perihepatitis due to any cause (gonococcal perihepatitis in women)
  - Carcinoma of liver.

Q 14. What does the presence of abdominal venous hum medicate?

Ans. It is virtually diagnostic of cirrhotic portal hypertension. When present with hepatic arterial bruit in the same patient, then it suggests cirrhosis with either alcoholic hepatitis or malignancy liver.

Q 15. What is Cruveilhier-Baumgarten syndrome?

Ans. It is the presence of the abdominal venous hum in portal hypertension secondary to cirrhosis.

Q 16. What does a presence of hepatic rub, bruit and venous hum indicate?

Ans.

1. The presence of hepatic rub with bruit indicates cancer of the liver.
2. The presence of the hepatic rub, bruit and venous hum indicates that a patient with cirrhosis has developed a hepatoma.

Q 17. What do you understand by pulsatile liver? How will you demonstrate it?

Ans. Pulsatile liver means pulsations felt over the liver which could be:

1. *Intrinsic pulsations* due to:
   - Tricuspid regurgitation (systolic pulsations) either organic or functional
   - Hemangioma of the liver
2. *Transmitted pulsation from right ventricle* due to: Right ventricular hypertrophy.

Method of demonstration of pulsations of liver:
The presystolic or systolic pulsations of the heart can be transmitted to venous circulation in the liver in the presence of tricuspid incompetence, which can be detected as follows:

- Make the patient to sit in a chair, stand on the right side of the patient
- Place your right palm over liver in right hypochondrium and left palm over the back in the same manner as used for bimanual palpation
- Ask the patient to hold his breath after taking deep inspiration
- Observed the lifting and separation of hands from the side with each heartbeat.

In case of pulsatile liver, the hands are lifted and separated to some extent.

Clinical Tip

In case of pulsatile liver, always look for other signs of tricuspid regurgitation (engorged pulsatile neck veins, v and y collapse and a pansystolic murmur) and congestive heart failure (cyanosis, dyspnea, edema).

Q 18. What do you understand by the term liver span? What is its significance?

Ans. The liver span is the vertical distance between the upper and lower borders of the liver which is defined either clinically (on percussion) or on ultrasound. Normal liver span in an adult is variable (10–14 cm), greater in men than in women, greater in tall people than in short.

Significance

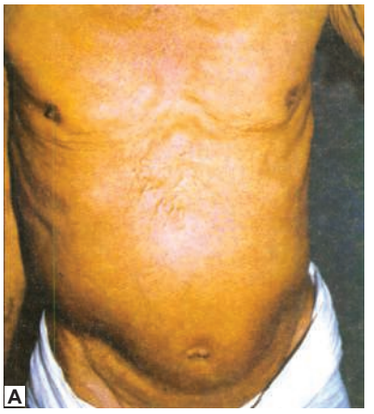
- Liver span is actually reduced when liver is small and shrunken (acute fulminant hepatitis) or masked when free air is present below the diaphragm as from a perforated viscus (liver dullness is masked, hence, span appears to be reduced).
- Liver span is increased when liver is enlarged not when liver is displaced.
- Serial observations may show a decreasing span of dullness with resolution of hepatitis, CHF or less commonly with progression of fulminant hepatitis.
- It is used to define actual *vs* apparent enlargement of liver.
  - Actual or real enlargement means palpable liver with increase in liver span.
  - Apparent enlargement means liver is palpable without being actually enlarged (liver span is normal). It is displaced downwards by right-sided pleural effusion, pneumothorax, COPD or low diaphragm.

Q 19. What is Reidle lobe of the liver?

Ans. **Reidle lobe of liver** is a tongue-like projection of the right lobe of the liver, represents a variation in shape of the normal liver. It is commonly found in females or those with a lanky built. It is usually mistaken for a gall bladder or right kidney, can be differentiated on ultrasound.

CASE 15: PORTAL HYPERTENSION

The patient (Fig. 1.15A) presented with distension of abdomen, weakness, dull abdominal ache and mild exertional dyspnea for the last 3 months. There was history of hematemesis and jaundice in the past.



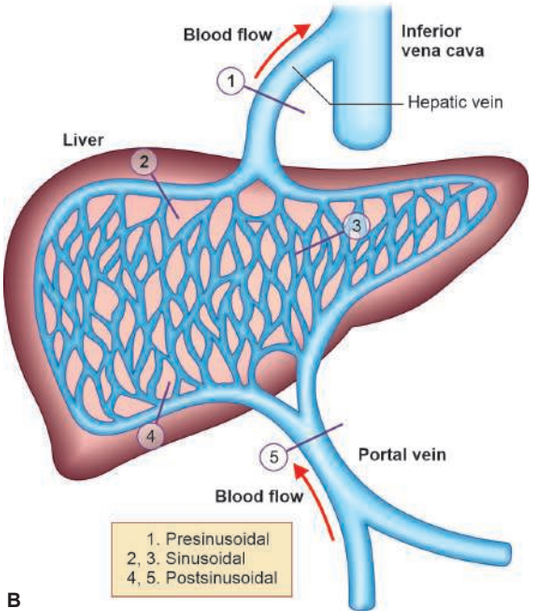


Fig. 1.15A to C: **A.** Patient with symptoms and signs of portal hypertension due to cirrhosis of the liver; **B.** Classification of portal hypertension depending on the site of obstruction; **C.** Cirrhotic liver—a common cause of portal hypertension

Clinical Presentations

Patients usually present with:

- Progressive distension of abdomen, swelling of legs, hematemesis and melena (e.g. portal hypertension)
- Fatigue, weight loss, flatulent dyspepsia, anorexia, malnutrition, muscle wasting drowsiness, disturbed sleep pattern (e.g. hepatic encephalopathy).

Points to be Noted in the History

- History of fever, jaundice, bleeding from any site
- History of disturbance in consciousness, sleep or behaviour problem
- Past history of alcoholism, drug intake, jaundice, delivery (in female)
- Family history of jaundice or similar illness
- Nutritional history.

EXAMINATION

General Physical Examination

- Look for hepatic facies, e.g. earthy look, sunken (hollow) cheek and malar prominence—present in this case.
- Assess nutritional status—poor in this case
- Look for stigmatas of cirrhosis (wasting of muscles, palmar erythema, spider angiomas, testicular atrophy, gynecomastia, bilateral parotid enlargement and Dupuytren's contractures). Few stigmatas were present.
- Look for signs of hepatic insufficiency, i.e. mental features, jaundice, bleeding (purpura, ecchymosis and bruising) clubbing of fingers, flapping tremors.
- Look for signs of portal hypertension, e.g. ascites, collaterals formation and fetor hepaticus, splenomegaly. Ascites and splenomegaly present.
- Look for anemia, jaundice, Keyser-Fleischer's rings.
- Look for signs of malnutrition and vitamin deficiency.
- Look for peripheral pitting edema, which was present.
- Look for signs of CHF or pericardial effusion, e.g. raised PVP, cyanosis, neck pulsations, etc.
- Note the vital signs, e.g. temperature, respiration, BP and pulse.

Systemic Examination

Inspection

- Skin over the abdomen may be thin, shiny due to edema of abdominal wall
- Abdominal distension with increased abdominal girth—present in this case
- Prominent veins with flow of blood away from umbilicus
- Hernias (umbilical or inguinal) may or may not be present
- Umbilicus may be everted or transversely slit (smiling umbilicus) in presence of ascites (umbilicus was transversely slit in this case).

Palpation

- Liver was palpable, nontender, firm with sharp irregular margins. Left lobe was enlarged. In some cases, liver may not be palpable
- Spleen was also palpable, nontender, soft to firm
- Ascites was detected by fluid thrill
- Flow of blood in dilated veins was away from umbilicus.

Note: Palpate the liver and spleen by dipping method in presence of ascites.

Percussion

- Shifting dullness confirmed the presence of ascites
- Flanks were dull with central sparing
- Liver and splenic areas were dull.

Auscultation

Hear for:

- *Bruit* over liver. It indicates malignant liver
- *Rub*. It indicates perihepatitis due to infarction or may be heard over a nodule
- *Venous hum* around umbilicus. Its presence indicates portal hypertension *(Cruveilhier-Baumgarten's syndrome)*.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. The clinical diagnosis is ***cirrhotic portal hypertension without hepatic encephalopathy***. The points in favour are:

- Long history of illness
- Past history of jaundice and hematemesis
- Poor nutritional status, e.g. sunken cheeks
- Presence of stigmata of cirrhosis
- Presence of ascites, splenomegaly and collaterals with flow of blood away from umbilicus
- Pitting edema.

Q 2. What is portal hypertension? How do the patients present with it?

Ans. Normal portal venous pressure is low (5–10 mmHg) because vascular resistance in hepatic sinusoids is minimal.

- ***Portal hypertension is defined*** as elevated portal venous pressure more than 10 mmHg, results írom increased resistance to portal blood flow. As the portal venous system lacks valves, therefore, obstruction at any level between right side of the heart and portal vein will result in retrograde transmission of elevated blood pressure.
- Portal hypertension results in congestion of viscera (stomach and intestine), formation of collaterals and subsequent rupture, and precipitation of hepatic failure.
- Patient commonly present with:
  i. **Variceal bleeding**, e.g. hematemesis; melena, piles.
  ii. **Chronic iron deficiency anemia** due to congestive gastropathy and repeated minor bleeding.
  iii. **Abdominal distension** (ascites), splenomegaly.
  iv. **Spontaneous bacterial peritonitis**.
  v. Symptoms and signs of **hepatic encephalopathy** (discussed below) may be associated with portal hypertension.
  vi. Oliguria/anuria due to **hepatorenal syndrome.**
  vii. **Hypersplenism** leading to pancytopenia.

Q 3. How do you classify portal hypertension?

Ans. Increased portal pressure can occur at three levels relative to hepatic sinusoids (Fig. 1.15B).

1. **Presinusoidal:** It means obstruction in the presinusoidal compartment outside the liver (between sinusoids and portal vein).
2. **Sinusoidal:** Obstruction occurs within the liver itself at the level of sinusoids.
3. **Postsinusoidal:** Obstruction is outside the liver at the level of hepatic veins, inferior vena cava or beyond sinusoids within liver (veno-occlusive disease).

Q 4. What are the causes of portal hypertension?

Ans. Cirrhosis is the most common cause, accounts for >90% of cases (Table 1.47).

Table 1.47: Causes of portal hypertension depending on the site of obstruction

1. **Postsinusoidal** (Fig. 1.15B)
× *Extrahepatic postsinusoidal*, e.g. Budd-Chiari syndrome
× *Intrahepatic postsinusoidal*, e.g. veno-occlusive disease
2. **Sinusoidal**
× Cirrhosis of the liver (Fig. 1.15C)
× Cystic liver disease
× Metastases in the liver
× Nodular transformations of the liver
3. **Presinusoidal**
× *Intrahepatic presinusoidal*, e.g. schistosomiasis, sarcoidosis, congenital hepatic fibrosis, drugs and toxins, lymphoma, leukemic infiltrations, primary biliary cirrhosis.
× *Extrahepatic presinusoidal*, e.g. portal vein thrombosis, abdominal trauma, compression of portal vein at porta hepatis by malignant nodules or lymph node, pancreatitis

Q 5. Define noncirrhotic portal hypertension. What are its causes?

Ans. This is defined as portal hypertension without hepatocellular damage and lack of nodular regeneration activity in the liver.

- These cases manifest usually with splenomegaly, anemia, recurrent variceal bleed and chances of hepatic encephalopathy are remote.

This disorder is usually associated with either congenital or acquired hepatic fibrosis, which may be localised or generalised. Some causes of noncirrhotic portal fibrosis are given in Table 1.48.

Q 6. What are differences between cirrhotic and noncirrhotic portal hypertension?

Ans. Differences between cirrhotic and noncirrhotic portal hypertension are given in Table 1.49.

Table 1.48: Causes of noncirrhotic portal fibrosis

1. **Idiopathic portal hypertension (noncirrhotic portal fibrosis, Banti's syndrome)**
   - Intrahepatic fibrosis and phlebosclerosis
   - Portal and splenic vein sclerosis
   - Portal and splenic vein thrombosis
2. **Schistosomiasis** (pipe-stem fibrosis with presinusoidal portal hypertension)
3. **Congenital hepatic fibrosis**
4. **Lymphomatous infiltration** around portal triad
5. **Chronic arsenic poisoning** (deposition of arsenic in liver)

Table 1.49: Differentiation between cirrhotic and noncirrhotic portal hypertension

Cirrhotic	*Noncirrhotic*
Slow insidious onset	Acute or sudden
Ascites present	Ascites absent
Recurrent hematemesis uncommon	Recurrent hematemesis is common and presenting feature
Anemia moderate	Anemia severe
Hepatic encephalopathy common	Hepatic encephalopathy uncommon
Edema present	No edema
Liver biopsy shows cirrhosis	No evidence of cirrhosis; only portal fibrosis seen

Q 7. Why does ascites absent in noncirrhotic portal hypertension?

Ans. Ascites is sign of cirrhosis (liver cell dysfunction), hence, absent in noncirrhotic portal hypertension.

Q 8. What are pathological types of cirrhosis?

Ans.
- Micronodular
- Macronodular
- Mixed.

Q 9. What are clinical types of cirrhosis?

Ans.
- Posthepatitis
- Alcoholic
- Cardiac
- Biliary
- Cryptogenic.

Q 10. Define cirrhosis of the liver. What are its clinical characteristics?

Ans. Cirrhosis is the pathological term, denotes irreversible destruction of liver cells (necrosis) followed by fibrosis and nodular regeneration of the liver cells in such a way that the normal liver architecture is lost.

Clinical features of cirrhosis

- Cirrhosis may be totally asymptomatic, and in lifetime may be found incidentally at surgery or may just be associated with isolated hepatomegaly. The liver in cirrhosis is usually small but may become large due to nodular transformation. When palpable, it is firm, nodular, nontender with sharp and irregular borders.
- It may present with nonspecific complaints, such as weakness, fatigue, muscle cramps, weight loss, nausea, vomiting, anorexia and abdominal discomfort.
- The common clinical features of the cirrhosis are due to *either liver cell failure* with or without hepatic encephalopathy or *portal hypertension*. (read liver cell failure, next question).

Q 11. What are signs and symptoms of liver cell failure?

Ans. Signs of liver cell failure are:

- **Hepatomegaly or small shrunken liver**
- **Jaundice, fever**
- **Circulatory changes,** e.g. palmar erythema, spider angiomas, cyanosis (due to AV shunting in lungs), clubbing of the fingers, tachycardia, bounding pulses, hyperdynamic circulation.
- **Endocrinol changes**, e.g.
  - Loss of libido, hair loss
  - Gynecomastia, testicular atrophy, impotence in males
  - Breast atrophy, irregular menses, amenorrhoea in females
- **Hemorrhagic manifestations,** e.g. Bruises, epistaxis, purpura, menorrhagia
- **Miscellaneous**
  - Diffuse pigmentation
  - White nails
  - Dupuytren's contractures
  - Parotid enlargement.
- **Hepatic encephalopathy:** Read below.

Q 12. What are signs of portal hypertension?

Ans. Signs of portal hypertension

- **Splenomegaly.**
- **Collateral vessels** formation at gastroesophageal junction, around the umbilicus, behind the liver and in the rectum.
- **Variceal bleeding** (hematemesis and melena).
- **Fetor hepaticus** due to excretion of mercaptans in breath.

Q 13. What are signs of hepatic encephalopathy?

Ans. It comprises features of liver cells failure described above plus mental feature described below:

- ***Mental features*** (e.g. reduced alertness, restlessness, behavioural changes, bizarre handwriting, disturbance in sleep rhythm, drowsiness, confusion, disorientation, yawning, and hiccups). In late stages, convulsions may occur and patient lapses into coma.

Q 14. What are precipitating factors for hepatic encephalopathy?

Ans. There are certain factors that push the patient with compensated cirrhosis of the liver into decompensation phase (hepatic encephalopathy). These include:

1. Drugs, e.g. sedatives, hypnotics
2. Gastrointestinal bleeding (e.g. varices, peptic ulcer, congestive gastropathy)
3. Excessive protein intake
4. Diuretics producing hypokalemia and alkalosis
5. Rapid removal of large amount of ascitic fluid in one setting (>3 L)

6. Acute alcoholic bout
7. Constipation
8. Infections and septicemia, surgery
9. Azotemia (uremia)
10. Portosystemic shunts, e.g. spontaneous or surgical.

Q 15. What is probable pathogenesis of hepatic encephalopathy?

Ans. Although, hepatic encephalopathy is called *ammonia encephalopathy* but NH_3 is not only the culprit. The possible mechanisms are:

i. Increased NH_3 levels in blood
ii. Increased levels of short-chain fatty acids
iii. Increase in false neurotransmitters like octopamine and rise in GABA level (true neurotransmitter)
iv. Rise in methionine levels
v. Rise in certain amino acids (ratio of aromatic amino acids to branched chain amino acids is increased) and mercaptans.

All these products described above are retained in blood in higher concentration due to combined effect of liver cell failure (decreased metabolism) and portosystemic shunting (delivery of these substances into circulation by bypassing the liver).

Q 16. How do you stage/grade the hepatic encephalopathy?

Ans. Clinical staging of hepatic encephalopathy is important in following the course of illness and to plan the treatment as well as to assess the response to therapy (Table 1.50).

Table 1.50: Clinical staging of hepatic encephalopathy

Stage	*Mental features*	*Tremors*	*EEG change*
I	Euphoria or depression, confusion, disorientation, disturbance of speech and sleep pattern	+/–	Normal EEG
II	Lethargy, moderate confusion	+	High voltage triphasic slow waves (abnormal EEG)
III	Marked confusion, incoherent speech, drowsy but arousable	+	High voltage triphasic waves (2–5/sec) (abnormal EEG)
IV	Coma, initially responsive to noxious stimuli, later unresponsive		Delta activity (abnormal EEG)

Q 17. What are diagnostic criteria for hepatic encephalopathy?

Ans. The four major criteria are:

1. ***Evidence of acute or chronic hepatocellular disease*** (jaundice, palmar erythema, spider angiomas) with extensive portosystemic collaterals (caput medusae)
2. ***Slowly deterioration of consciousness*** from reduced awareness to confusion, disorientation, drowsiness or stupor and finally into coma.
3. ***Shifting combination of neurological signs including*** asterixis (tremors), rigidity, hyperreflexia, extensor plantar response and rarely seizures.
4. ***EEG changes.*** Symmetric high voltage triphasic waves changing to delta slow activity.

Q 18. What will you look on general physical examination in a patient with alcoholic cirrhosis of the liver?

Ans. Examination of a patient with cirrhosis is as follows (read case summary also in the beginning).

General physical signs

Look for:

- Malnutrition, vitamin deficiency
- Anemia
- Jaundice (icterus)
- Hepatic facies, e.g. earthy look, sunken shiny eyeballs, muddy facial expression, sunken cheeks with malar prominence, pinched up nose and parched lips, icteric tinge of conjunctiva
- Edema feet
- Obvious swelling of abdomen
- Wasting of muscles
- Foul smell (fetor hepaticus)
- Flapping tremors
- Cyanosis.

Signs of chronic alcoholism (alcoholic stigmata)

- Red tip of nose and redness of cheeks
- Spider nevi
- Pigmentation of skin; may or may not be present
- Gynecomastia and testicular atrophy in males
- Palmar erythema
- Scanty axillary and pubic hair in male, breast atrophy in females
- White nails
- Dupuytren's contracture.

Q 19. What are alcoholic stigmata?

Ans. These stigmata precede the development of cirrhosis, hence, are usually present in alcoholic cirrhosis. They have been discussed above.

Q 20. What are the stages of alcoholic cirrhosis?

Ans.
1. Fatty liver
2. Alcoholic hepatitis/steatohepatitis
3. Alcoholic cirrhosis.

Q 21. What are complications of cirrhosis?

Ans. Following are complications:

1. *Portal hypertension* (fatal variceal bleeding)
2. *Hepatocellular failure* and subsequent hepatic encephalopathy
3. *Spontaneous bacterial peritonitis* (ascitic fluid leukocytes count >500 cells/µl or >250 polymorphs/µl)
4. *Septicemia*
5. Increased incidence of *peptic ulcer* and *hepatocellular carcinoma*

6. *Nutritional debility* (e.g. anemia, hypoproteinemia)
7. *Hepatorenal* and *hepatopulmonary syndromes*. It is functional acute renal failure in a patient with cirrhosis of the liver, develops due to circulatory or hemodynamic changes. The exact etiology is unknown. The kidneys structurally are normal but functionally abnormal, hence called functional renal failure. The prognosis is poor. Hepatorenal syndrome rarely can develop in hepatitis also.
   Hepatopulmonary syndrome is development of cyanosis and clubbing of the fingers due to arteriovenous shunting in the lungs.
8. Hemorrhagic tendency.

Q 22. What are the causes of death in cirrhosis?

Ans. Common causes are as follows:

1. Most common cause is fatal septicemia (gram-negative)
2. Hepatic encephalopathy
3. Cerebral edema
4. Fatal bleeding
5. Renal failure (hepatorenal syndrome)
6. Hypoglycemia, hypokalemia, etc.

Q 23. What are the causes of upper GI bleed in cirrhosis of the liver?

Ans. The causes are:

1. Esophageal varices
2. Gastric varices/erosions
3. Congestive gastropathy
4. Gastroduodenal ulcerations
5. Mallory-Weiss tear
6. Bleeding tendencies.

Q 24. How will you investigate a case with cirrhosis of the liver?

Ans. Investigations of cirrhosis are as follows:

1. **Complete hemogram and ESR**
   - ***Anemia:*** Anemia in cirrhosis is due to hematemesis, melena, anorexia with poor intake of nutrients, piles, malabsorprtion and hypersplenism. Anemia is commonly microcytic and hypochromic.
   - ***Pancytopenia*** (anemia, leukopenia and thrombocytopenia) is due to hypersplenism.
   - ***Raised ESR*** indicates infections.
2. **Stool for occult blood (guaiac test)** may be positive. Bleeding in cirrhosis is intermittent, hence, test may be performed at least for 3 consecutive days. Vitamin C intake may give false positive result.
3. **Rectal examination** for internal piles.
4. **Chest X-ray** for lung pathology or pleural effusion.
5. **Hepatic profile**
   - Total serum proteins and albumin may be low. The albumin/globulin ratio is altered.
   - Serum bilirubin is normal or raised.
   - Serum transaminases are normal or mildly elevated.
   - Alkaline phosphatase is mildly elevated.
   - Serum cholesterol is low.
   - Prothrombin time is normal or increased and does not return to normal with vitamin K therapy. Low PT is bad prognostic sign.
   - Viral markers (HbsAg) are negative.
   - Serum autoantibodies, antinuclear, anti-smooth muscle and antimitochondrial antibodies level increase in autoimmune hepatitis, cryptogenic cirrhosis and biliary cirrhosis.
   - Serum immunoglobulins, e.g. IgG is increased in autoimmune hepatitis, IgA increased in alcoholic cirrhosis and IgM in primary biliary cirrhosis.
6. **Other blood tests,** e.g. serum copper (Wilson's disease), iron (hemochromatosis), serum alpha-1-antitrypsin (cystic fibrosis) and serum alpha-fetoprotein (hepatocellular carcinoma).
7. **Imaging**
   - *Ultrasound for liver* may reveal change in size, shape and echotexture of the liver. Fatty change and fibrosis produce diffuse increased echogenicity. The presence of ascites, portal vein diameter (>14 mm indicates portal hypertension), presence of varices and splenomegaly can be determined on USG.
   - *Barium swallow for esophageal varices* (worm-eaten appearance due to multiple filling defects).
   - *CT scan* is not better than USG in cirrhosis of liver.
8. **Upper GI endoscopy** shows esophageal and gastric varices, peptic ulcer or congestive gastropathy (petechial hemorrhages both old and new, seen in gastric mucosa—mosaic pattern of red and yellow mucosa).
9. **Pressure measurement studies**
   - *Percutaneous intrasplenic pressure* is increased in portal hypertension.
   - Wedged hepatic venous pressure is increased.
10. **Dynamic flow studies**. These may show distortion of hepatic vasculature or portal vein thrombosis:
    - *Doppler ultrasound for visualisation of portal venous system* and duplex Doppler for measurement of portal blood flow and flow reversal in portal and splenic vein.
    - *Portal venography* by digital subtraction angiography.
11. **Electroencephalogram (EEG)** may show triphasic pattern in hepatic encephalopathy.
12. **Liver biopsy:** It is a gold standard test to confirm the diagnosis of cirrhosis and helps to find out its cause. Special stains can be done for iron and copper.
13. **Tapping of the ascites:** Ascites is transudative due to presence of portal hypertension (serum

albumin/ascites albumin gradient >1.1). The fluid should be sent for cytology, biochemistry and for culture if bacterial peritonitis is suspected.

Q 25. How would you manage a patient of cirrhosis and ascites?

Ans. The steps of management would be:

- **Sodium restriction** to 80–90 mEq/day.
- **Diuretics:** A combination of frusemide and spironolactone is effective, serial monitoring of Na^+ concentration helps to determine the optimal dose of diuretic; doses are increased until a negative sodium balance is achieved.
- **Paracentesis:** About 3–5 litres of fluid can be removed in a patient with cardiorespiratory embarrassment to relieve symptoms.
- **If ascites is diuretic resistant,** then
  - *Therapeutic paracentesis with infusion of salt-free albumin.*
  - *Peritoneovenous shunting* (*Laveen shunt*) is of limited use nowadays because of high rate of infection and development of DIC.
  - *Transjugular intrahepatic portosystemic shunt (TIPS)*. It is side to side shunt consisting of stented channel between portal vein and hepatic vein.
  - *Extracorporeal ultrafiltration of ascitic fluid* with reinfusion.
  - *Liver transplantation.*

Q 26. What are indications of TIPS?

Ans.
- A huge or tense ascites refractory to treatment
- Recurrent ascites.

CASE 16: CHRONIC DIARRHEA AND MALABSORPTION

The 14 years male adolescent (Fig. 1.16) was brought by the mother with complaints of stunted growth and reduction in weight. There was history of chronic diarrhea since childhood. There was history of intermittent loose motion since then.

Clinical Presentations (Fig. 1.16)

These patients present with:

1. ***Passage of loose stools >3 per day*** for the last 3 months.
2. ***Patients may complain of nonspecific symptoms***, e.g. ill health, weakness, fatigue, weight loss with signs and symptoms of malnutrition, anemia, vitamins and mineral deficiency.
3. ***Specific symptoms and signs depending on the underlying cause;***
   - *Fever, pain abdomen, diarrhea with or without blood* may suggest underlying inflammatory bowel disease.

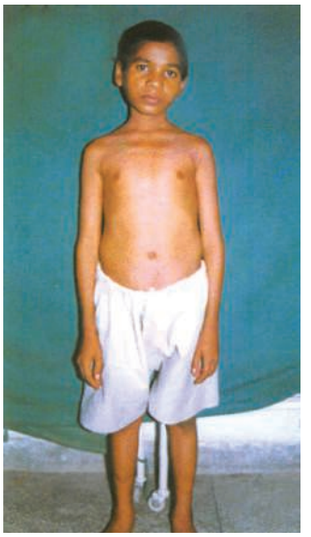


Fig. 1.16: An adolescent male with stunted growth and chronic diarrhea. There was anemia, edema feet and signs of multiple nutrient deficiency

- *Presence of edema face and feet, anemia, muscle wasting* and ***weight loss*** indicate hypoproteinemia due to protein-losing enteropathy.
- *The presence of steatorrhea* (large, offensive stools with increased fat content) indicates either pancreatic or hepatic cause of malabsorption.
- *Diarrhea with features of vitamin$_{12}$ deficiency* (red tongue—glossitis, macrocytic anemia, peripheral neuropathy and subacute combined degeneration of the cord) indicate chronic gastritis or malabsorption due to involvement of terminal ileum (site of vitamin B_{12} absorption) due to any cause or bacterial proliferation in blind loop syndrome or stricture of bowel.
- *Diarrhea following ingestion of milk or milk product* indicates milk allergy or milk intolerance.

Points to be Noted in History

- Ask about onset, duration, frequency, nature and any associated symptoms, e.g. nausea, vomiting or pain in abdomen.
- Whether or not it is nocturnal? Is there any blood in stool?
- History of fever, worm expulsion or recurrent episodes of diarrhea
- Any relation of diarrhea with food or milk
- History of edema feet, distension of abdomen, loss of appetite or weight
- Developmental history including milestones
- Nutritional history
- Family history
- Any history of foreign travel.

EXAMINATION

General Physical Examination

- Record height and weight, and calculate BMI
- General appearance, e.g. facial puffiness, protuberant abdomen
- Look for deficiency signs of nutrients, e.g. protein (weakness, muscle wasting, flabbyness, edema, protuberant abdomen, thin-peppary skin), fat (thin extremities, sunken cheeks, flat buttocks and thin chest, etc.)
- Look for signs of vitamin deficiency, e.g. xerosis, Bitot's spots, cheilosis, angular stomatitis, aphthous ulcers, spongy and bleeding gums, bowing of the legs, rickety rosary, purpuric or ecchymotic patches, peripheral neuropathy and anemia
- Record pulse, BP, temperature and respiration
- Look for lymphadenopathy any where in the body, e.g. neck, axilla, groin, etc.

Systemic Examinations

All the major systems have to be examined.

I. Abdomen

- Note abdominal protuberance, flabby abdominal muscle and edema of abdominal wall
- Look for the signs of ascites due to hypoproteinemia
- Look for enlargement of spleen, liver due to anemia or intercurrent infection
- Look for any abdominal lymph nodes
- Rectal examination.

II. CVS Examination

Examine the heart for any enlargement, murmur, rub or abnormal sound.

III. Examination of Nervous System

Look for evidence of beriberi, Korsakoff psychosis, Wernicke's encephalopathy, peripheral neuropathy or mental subnormality.

IV. Endocrine and Metabolism

Look for signs of hypopituitarism, hypothyroidism, rickets.

V. Other Systems

- *Respiratory system* for any evidence of tuberculosis or infection
- *Skin* for any dryness, bleeding, etc.
- *Joints*
- *Hematopoietic system* for anemia, bleeding.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is probable diagnosis of the patient in picture?

Ans. In an adolescent child with diarrhea since childhood, reduced weight and height, history of delayed milestones, presence of anemia, protuberant abdomen, muscle wasting, edema feet, signs of multiple nutrients and vitamins deficiency, die clinical diagnosis of malabsorption syndrome is most likely.

Q 2. How do you define diarrhea?

Ans. **Diarrhea is defined** as passage of frequent loose stools, i.e. more than 3 in a day. Quantitatively it is defined as fecal output >200 mg/day when dietary fibre content is low.

Acute diarrhea means rapid onset of diarrhea occurring in an otherwise healthy person not lasting for more than 2 weeks. It is usually infective in origin (viral or bacterial).

Chronic diarrhea refers to slow onset of diarrhea persisting for more than 3 months. It is usually a symptom of some underlying disease or malabsorption syndrome.

Malabsorption syndrome refers to defective absorption of one or more essential nutrients through the intestine. The malabsorption may be specific or generalised. The examples of specific malabsorption include lactose intolerance, vitamin B_{12} malabsorption, etc.

Q 3. What are the causes of malabsorption?

Ans. Malabsorption may be due to diseases of pancreas, GI tract and the liver. The causes of malabsorption are given in Table 1.51.

Q 4. What are the common causes of chronic diarrhea?

Ans. The causes are:

- *Inflammatory bowel disease*, e.g. ulcerative colitis, Crohn's disease
- *Celiac disease* (gluten-induced) or *tropical sprue*
- *Intestinal diseases*, e.g. tuberculosis, stricture, fistula
- *Worm infestations*, e.g. giardiasis
- *Pancreatic disease*, e.g. chronic pancreatitis, malignancy
- *Endocrinal causes*, e.g. diabetes, Addison's disease, thyrotoxicosis, etc.

Q 5. How will you diagnose malabsorption?

Ans. Diagnosis of malabsorption is based on:

1. **Symptoms and signs suggestive of malabsorption** (diarrhea >3 months with deficiency signs of one or more nutrients).
2. **Biochemical tests** or other investigations documenting the evidence of malabsorption to one or more nutrients.
3. **Radiology of small intestine** may show either gastrointestinal motility disorder, fistula, stricture, Zollinger-Ellison's syndrome or characteristic intestinal changes of malabsorption, i.e. breaking up of barium

Table 1.51: Causes of malabsorption syndrome

A. Pancreatic disorders (disorders of maldigestion)
1. Chronic pancreatitis
2. Cystic fibrosis
3. Malignancy pancreas
4. Ulcerogenic tumors of pancreas (Zollinger-Ellison's syndrome)

B. Disorders causing deficiency of bile acids/bile salts
1. *Interruption of enterohepatic circulation of bile acids/salts or reduced bile salt concentration.*
   a. Ileal resection or inflammatory bowel disease
   b. Parenchymal liver disease or cholestasis (intra- or extrahepatic)
2. *Abnormal bacterial proliferation in small intestine leading to bile salt deconjugation*
   a. Blind loop (stagnant loop) syndrome
   b. Strictures or fistulas of small intestine
   c. Hypomotility of small intestine due to diabetes
3. *Drugs causing sequestration or precipitation of bile salts, e.g. neomycin and cholestyramine*
4. *Inadequate absorptive surface:* Intestinal resection or bypass surgery of intestine.
5. *Mucosal defects of absorption (inflammatory, infiltrative or infective disorders)*
   a. Tropical sprue
   b. Lymphoma
   c. Whipple's disease
   d. Radiation enteritis
   e. Amyloidosis
   f. Giardiasis
   g. Scleroderma
   h. Eosinophilic enteritis
   i. Dermatitis herpetiformis

C. Biochemical or genetic abnormalities
1. Celiac disease (gluten-induced enteropathy)
2. Disaccharidase deficiency
3. Hypogammaglobulinemia
4. Abetalipoproteinemia

D. Endocrinal or metabolic defects
1. Diabetes mellitus
2. Addison's disease
3. Carcinoid syndrome
4. Hyperthyroidism

E. Specific malabsorption (mucosa is histologically normal)
1. Lactase deficiency
2. Vitamin B_{12} malabsorption

column with segmentation, clumping and coarsening of mucosal folds (Moulage's sign).

4. **Biopsy and histopathology of small intestine** shows partial villous atrophy with lymphocytic infiltration.

Q 6. How will you investigate a case of malabsorption?

Ans. The various tests of malabsorption of different nutrients are enlisted in Table 1.52.

Q 7. What are diagnostic criteria for nontropical sprue?

Ans. Diagnostic clues to nontropical sprue (celiac disease) are given in Table 1.53.

Q 8. What are symptoms and signs of malabsorption syndrome?

Ans. Due to fecal loss of certain nutrients, vitamins and minerals, their deficiency symptoms and signs appear (Table 1.54).

Q 9. What are symptoms and signs of various vitamins deficiency?

Ans. Read Table 1.54.

Q 10. What are signs of iron deficiency?

Ans. Read Table 1.54.

Q 11. What are signs of vitamin B complex deficiency?

Ans. Read Table 1.54.

Q 12. What are deficiency signs of vitamin B_1?

Ans. Beriberi, e.g. wet beriberi (high cardiac output state) and dry beriberi (peripheral neuropathy).

Table 1.52: Investigations for malabsorption

Test	*Normal values*	*Malabsorption (non-tropical sprue)*	*Maldigestion (pancreatic insufficiency)*
I. Tests for fat absorption			
1. Fecal fat (24 hours excretion)	<6.0 g/day	>6.0 g/day	>6.0 g/day
2. Fat in stools (%)	<6	<9.5 and >6	>9.5 (steatorrhea)
II. Tests for carbohydrate absorption			
1. D-xylose absorption (25.0 g oral dose)	5 hours urinary excretion >4.5 g	Decreased	Normal
2. Hydrogen breath test (oral 50.0 gm lactose and breath H_2 measured every hour for 4 hours)	Less than 10 ppm above baseline in any sample	Increased	Normal
III. Tests for protein absorption			
1. Fecal clearance of endogenous alpha-1 antitrypsin measured in three days collection of stools	Absent in stools	Increased	Increased
2. Nitrogen excretion (3–5 days collection of stools)	<2.5 g/day	>2.5 g/day	>2.5 g/day
IV. Tests for vitamins absorption			
1. Radioactive B_{12} absorption test (0.5 mg of labelled vitamin B_{12} is given orally followed 2 hours later by 1000 µg of nonlabelled B_{12} given by IM injection. Radioactivity in the urine is seen after 24 hours)	>16% radioactivity in urine	Frequently decreased	Frequency decreased
V. Other tests			
1. *Breath tests*			
a. Breada $14CO_2$ (14C xylose)	Minimal amount	Decreased	Normal
b. Bile salt breath test (radioactive)	<1% dose excreted		
	$^{14}CO_2$ in 4 hrs	Normal	Normal
2. *Blood tests*			
a. Serum calcium	9–11 µg/dl	Frequently decreased	Normal
b. Serum albumin	3.5–5.5 g/dl	Frequendy decreased	Normal
c. Serum iron	80–150 µg/dl	Decreased	Normal
d. Serum vitamin A	>100 IU/dl	Decreased	Decreased
VI. Miscellaneous tests			
1. Bacterial (culture)	<105 organisms/ml	Normal but abnormal in blind loop syndrome	Normal
2. Secretin test	Volume (1.8 ml/kg/hr) and bicarbonate (>80 mmol/L) Concentration in duodenal aspirate	Normal	Abnormal
3. Barium study (follow through)	Normal pattern	Flocculations and segmentations of barium column (malabsorption pattern—see text)	Normal pattern
4. Small intestine biopsy	Normal mucosa	Abnormal	Normal

Table 1.53: Diagnostic criteria for nontropical sprue

1. **Clinical**	Symptoms and signs of long duration suggestive of malabsorption (Table 1.54)
2. **Biochemical**	Positive evidence of fat, carbohydrate, protein, vitamin B_{12}, folate malabsorption (Table 1.52)
3. **Immunological**	Antigliadin, antireticulin and antiendomysial antibodies are seen in high titres in majority of patients
4. **Histopathology of small intestine**	Villous or subvillous atrophy with mononuclear cells infiltration of lamina propria and submucosa
5. **Therapeutic response**	Clinical, biochemical and histopathological improvement on gluten-free diet

Table 1.54: Deficiency signs in malabsorption syndrome

Deficiency	*Signs and symptoms*
Vitamin A	× Night blindness, xerosis, Bitot's spots, keratomalacia, dryness of eyes and follicular hyperkeratosis of skin
Vitamin C	× Scurvy
Vitamin D	× Rickets in children and osteomalacia in adults
Vitamin K	× Bleeding tendencies
Vitamin B complex	× Bald tongue, angular cheilosis, stomatitis, glossitis, peripheral neuropathy, subacute combined degeneration, megaloblastic anemia, dermatitis and dementia (pellagra)
Deficiency of nutrients (carbohydrate, proteins, loss of fats)	× Vague ill health, fatigue, weight × Muscle wasting and edema
Iron deficiency	× Anemia
Calcium deficiency	× Bone pain, tetany, paresthesias, muscle wasting
Potassium deficiency	× Distension of abdomen, diminished bowel sounds, vomiting, muscle weakness and EKG changes
Sodium and water depletion	× Nocturia, hypotension

Q 13. What are deficiency signs of vitamin B_2?

Ans. Cheilosis and angular stomatitis

Q 14. What are signs of pellagra?

Ans. It is due to niacin deficiency. It produces diarrhea, dermatitis, dementia and rarely death can occur.

Q 15. What is Traveller's diarrhea?

Ans. It is an acute infective diarrhea frequently seen in tourists caused by the following pathogenic organisms:

- *Enterotoxigenic E. coli*
- *Shigella*
- *Salmonella*
- *Campylobacter*
- *Rotavirus*
- *Giardia intestinalis*
- *Entamoeba histolytica.*

It is characterised by sudden onset of diarrhea with watery stools, fever, nausea, vomiting, abdominal pain which lasts for 2–3 days.

- On examination, there may be diffuse tenderness of abdomen.
- Treatment is tetracycline or ciprofloxacin plus metronidazole combination with correction of dehydration.

Q 16. What is pseudomembranous colitis?

Ans. It is an antibiotic-induced diarrhea caused by an opportunistic commensal *Clostridium difficile*. It can occur in immunocompromised state also. The antibiotics incriminated are: Ampicillin, clindamycin and cephalosporins.

Q 17. What is spurious diarrhea?

Ans. It occurs following fecal impaction in constipated patients, seen in old persons, characterized by sense of incomplete evacuation and gaseous distension with diarrhea. It is relieved by enema.

Q 18. What do you know about blind-loop syndrome? What are its causes?

Ans. The term refers to small intestinal abnormality associated with outgrowth of bacteria (bacterial count is >108/ml) causing steatorrhea, and vitamin B_{12} malabsorption, both of which improve dramatically after oral antibiotic therapy. This also called '*contaminated bowel syndrome*', or '*small intestinal stasis syndrome*'.

N.B.: Normally the small intestine is either sterile or contain $<10^4$ organism/ml.

The **causes** are:

- Gastric surgery
- Diverticulosis
- Fistulae
- Bowel resection
- Diabetic autonomic neuropathy
- Hypogammaglobulinemia.

All these structural abnormalities lead to delivery of the coliform bacteria from colon to small intestine and predispose to their proliferation.

The triphasic malabsorption test for vitamin B_{12} as detailed below is diagnostic.

Stage 1. Malabsorption without replacement of intrinsic factor.

Stage 2. Malabsorption persists with replacement of intrinsic factor.

Stage 3. Malabsorption to B_{12} improves after a 5–7 days course of antibiotic therapy.

Q 19. What is lactose intolerance?

Ans. It occurs due to deficiency of an enzyme lactase—a disaccharidase which normally hydrolyses lactose to glucose and galactose. The deficiency may be *primary* (inherited) or *secondary* (acquired), is characterised by abdominal colic, distension of abdomen and increased flatus followed by diarrhea on ingestion of milk; withdrawal or substitution therapy with enzyme lactase improves the condition.

Q 20. What do you understand by the term protein-losing enteropathy?

Ans. The term implies excessive loss of proteins through the GI tract leading to hypoproteinemia

and its clinical manifestations such as edema face and feet, muscle wasting (flabbiness of muscles) and weight loss.

A variety of disorders lead to it (Table 1.55). The diagnosis of protein-losing enteropathy is confirmed by measurement of fecal nitrogen content (increased) and fecal clearance of alpha-1-antitrypsin or ^{51}Cr labelled albumin after IV injection. Excessive intestinal clearance of alpha-1-antitrypsin >13 ml/ day (normal <13 ml/day) confirms the diagnosis.

Table 1.55: Disorders producing protein-losing enteropathy

1. Disorders of stomach
a. Hypertrophic gastritis (Menetrier's disease)
b. Gastric tumors
2. Disorders of intestine
a. Intestinal lymphangiectasia
b. Whipple's disease
c. Tropical sprue
d. Celiac disease (nontropical sprue)
e. Intestinal tuberculosis
f. Parasitic infections
g. Lymphoma
h. Allergic gastroenteropathy
i. Inflammatory bowel disease, e.g. regional enteritis
3. Cardiac disorders
a. Congestive heart failure
b. Constrictive pericarditis

Q 21. What is the difference between food intolerance and food allergy?

Ans. **Food intolerance** is an adverse reaction to food. It is not immune-mediated and results from a wide range of mechanisms such as contaminants in food, preservatives, lactase deficiency, etc.

Food allergy is an immune-mediated disorder due to IgE antibodies and type I hypersensitivity reaction to food. The most common food associated with allergy are; milk, egg, soya bean and shellfish. Food allergy may manifest as:

- *Oral allergy syndrome*—contact with certain fruit juices results in urticaria and angioedema of lips and oropharynx.
- *Allergic gastroenteropathy* leading to diarrhea with discharge of eosinophils in the stools.
- *Gastrointestinal anaphylaxis* leading to nausea, vomiting, diarrhea, and sometimes cardiovascular or respiratory collapse.
- *Diagnosis* is confirmed by double-blind placebo-controlled food challenges.

Q 22. What are inflammatory bowel disorders?

Ans. These are nonspecific inflammatory disorders of bowel having similar etiopathogenesis, pathology, investigations, complications and treatment. Exact causes of these disorders are unknown. Two common disorders are:

- Crohn's disease
- Ulcerative colitis

The clinical characteristics of both these disorders are compared in (Table 1.56).

Table 1.56: Clinical features of two common inflammatory bowel disorders

Features	*Crohn's disease*	*Ulcerative colitis*
Presenting symptoms	Diarrhea and pain abdomen in right lower quadrant with tenderness and guarding	Diarrhea with blood, mucus and pus. Pain in left lower abdomen and fever may be present. Tenderness in left side of abdomen or left iliac fossa
Palpation	A mass may be palpable on abdominal and/or rectal examination. It is an inflammatory mass	No mass palpable
Colics/diffuse pain	Recurrent abdominal colics are common due to obstruction	No colicky pain. Toxic megacolon may produce diffuse pain associated with distension of abdomen and stoppage of loose motions
Signs and symptoms of malabsorption	Moderate diarrhea and fever. Stools are loose or well-formed. Features of malabsorption of fat, carbohydrate, protein, vitamin D and vitamin B_{12} are common. These patients have anemia, weight loss, growth retardation (in children)	Patients have severe diarrhea with tenesmus. Anemia, weight loss present. Malabsorptive features are less common but dehydration common
Relapses or remissions	Common	Common
Stricture/anal fissure	Common	Less common
Abscess and fistulas	Common	Less common
Carcinoma in situ	Less common	More common in long-standing disease
Systemic involvement (hepatic, ocular, skin, ankylosing spondylitis, arthritis)	Less common	More common

Note: These distinctions in clinical features are arbitrary and should not be interpreted in absolute sense.

CASE 17: ACUTE NEPHRITIC SYNDROME

The female patient (Fig. 1.17A) presented with pain abdomen, puffiness of face and passed dark coloured small amount of urine <400 ml (Fig. 1.17B) following an episode of fever for 3 weeks.

Clinical Presentations

- ***The patients usually children or young adults present*** with the complaints of puffiness of face especially around the eyes in the early hours of the morning on getting out of bed (Fig. 1.17A).
- ***They may complain of reduced urine output*** or ***change in colouration of the urine*** (Fig. 1.17B).
- ***They may complain of headache, fatigue, weakness, breathlessness,*** cough, hemoptysis due to hypertension or left heart failure.
- Sometimes they may present with ***symptoms and signs of underlying disease***.
- Sometimes they may present with features of ***hypertensive encephalopathy*** (mental changes, headache, seizures) or uremia (GI symptoms or ill health).

HISTORY

Points to be Noted in History

Age: The patient is usually a child or adolescent

Ask for the following:

- ***History of fever***, sore throat, tonsillitis, pharyngitis, otitis media or cellulitis
- ***History of collagen vascular disorder*** or a hematological disorder
- ***History of vaccination*** (DPT)
- ***History of oliguria***, puffiness of face, change in colour of urine
- ***History of drug rash***, jaundice, breathlessness, headache and edema feet
- ***History of disturbance in consciousness***, lazziness, lethargy, nausea, vomiting, pruritus, palpitation (features of uremia).

EXAMINATION

General Physical Examination

Look for

- Face (periorbital edema, puffiness present)
- Pulse and BP (BP is high)
- JVP. It is raised
- Edema feet, sacral edema present
- Note the change in colour of urine (red, brown, or smoky).

Systemic Examinations

I. Examination of CVS

Look for the signs of cardiomegaly. Auscultate the heart for any murmur or rub or abnormal sound (3rd heart sound)

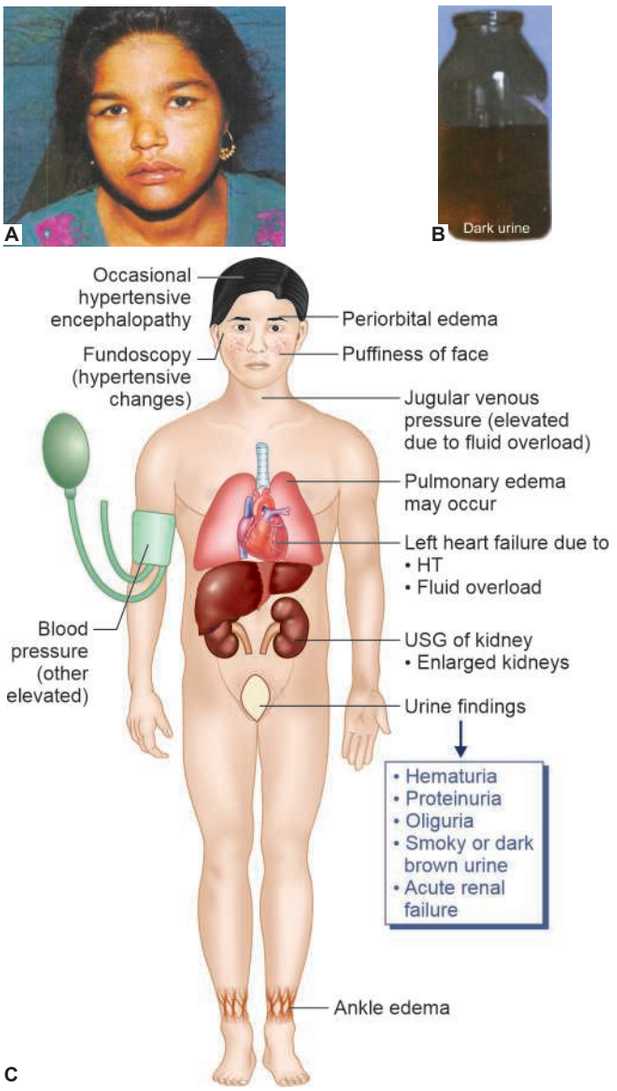


Fig. 1.17A to C: A. A young female patient having puffiness of face; **B.** 24-hour urine of the patient which is small in amount, smoky and shows RBCs and proteinuria; **C.** Clinical manifestations of acute nephritic syndrome (diagram)

II. Examination of Lungs

Auscultate the lungs for crackles or rales for fluid overload or noncardiogenic pulmonary edema due to LVF.

III. Examination of Abdomen

- Inspect the abdomen for distension or ascites
- Elicit the signs for presence of ascites or edema of abdominal wall
- Palpate the abdomen for any organ enlargement.

IV. Examination of CNS

- Note the features of hypertensive encephalopathy
- Fundoscopy.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis of the patient in picture?

Ans. The young female patient presenting with morning puffiness of face, oliguria, smoky urine and hypertension probably has acute nephritic syndrome as the first possibility due to any cause.

Q 2. What is your differential diagnosis?

Ans. The differential diagnosis lies within the causes of acute nephritic syndrome (Table 1.57A).

Q 3. How do you define acute nephritic syndrome?

Ans. **Acute nephritic syndrome** is characterised by an acute transient inflammatory process involving mainly the glomeruli and to lesser extent the tubules, manifests clinically with oliguria, hypertension, hematuria, edema and rapid renal failure. Acute glomerulonephritis (AGN) is interchangeably used as acute nephritic syndrome.

The term *rapidly proliferative glomerulonephritis* (RPGN) is used for those patients of AGN who do not go into remissions, spontaneously develop acute renal failure over a period of weeks to months. These patients belong to either a primary glomerular disease or a complicating multisystem disease (secondary glomerular disease).

Q 4. What are clinical hallmarks of acute nephritic syndrome and what is their pathogenesis?

Ans. The clinical hallmarks of acute nephritic syndrome are depicted in Fig. 1.17C. Their pathogenesis is given in the Table 1.57A.

Table 1.57A: Acute nephritic syndrome

Feature	*Mechanism (cause)*
× *Early morning puffiness or periorbital edema*	× Collection of fluid in loose periorbital tissue
× *Hematuria (gross or microscopic)*	× Glomerular inflammation
× *Hypertension*	× Retention of Na and H_2O
× *Edema*	× Retention of salt, H_2O and hypertension
× *Uremia*	× Retention of urea and creatinine
× *Oliguria*	× Reduced GFR

Q 5. What is its etiopathogenesis?

Ans. It is an *immune complex glomerulonephritis* characterised by production of antibodies against glomerular antigen, deposition of immune complexes in the walls of glomerular capillaries which modify the immune system leading to inflammation of the glomeruli. The stepwise pathogenesis is given in Table 1.57B.

Q 6. What are the causes of acute nephritic syndrome?

Ans. All the causes that lead to acute glomerular injury may lead to acute nephritic syndrome (Table 1.58).

Table 1.57B: Stepwise pathogenesis of nephritic syndrome

1. *Binding of antibodies* directed against glomerular basement membrane antigen
2. *Trapping* of soluble immune complexes in the glomerular capillary wall (subepithelial or subendothelial)
3. *In situ immune complex formation* between circulating antibody and fixed antigen or antigen planted either in the mesangium and/or in capillary wall
4. *Action of circulating primed T cells* with macrophages.

Table 1.58: Causes of AGN (acute nephritic syndrome)

I. **Infectious diseases**
   a. Poststreptococcal glomerulonephritis
   b. Nonstreptococcal glomerulonephritis
      i. *Bacterial*: Infective endocarditis, staphylococcal and pneumococcal infection, typhoid, syphilis and meningococcemia
      ii. *Viral*: Hepatitis B, infectious mononucleosis, mumps, measles, coxsackie and echoviruses
      iii. *Parasitic*—malaria

II. **Systemic disorders:** Systemic lupus erythematosus (SLE), vasculitis, Henoch-Schönlein purpura, Goodpasture's syndrome

III. **Primary glomerular diseases:** Mesangiocapillary glomerulonephritis, mesangial proliferative glomerulonephritis

IV. **Miscellaneous:** Guillain-Barré syndrome, serum sickness, DPT vaccination, IgA nephropathy

Q 7. What are the causes of rapidly proliferative glomerulonephritis (RPGN)?

Ans. It is a complication of acute glomerulonephritis or manifestation of a multisystem disease (Table 1.59).

The clinical features are summarized in Table 1.60.

Table 1.59: Causes of RPGN

I. **Infectious diseases**
   a. Poststreptococcal glomerulonephritis
   b. Infective endocarditis

II. **Multisystem diseases**
   a. Systemic lupus erythematosus (SLE)
   b. Goodpasture's syndrome
   c. Vasculitis
   d. Henoch-Schönlein purpura

III. **Primary glomerular diseases**
   a. Idiopathic
   b. Mesangiocapillary glomerulonephritis
   c. Membranous glomerulonephritis (antiglomerular basement membrane antibodies nephritis)

Table 1.60: Clinical manifestations of rapidly proliferative glomerulonephritis

1. **Signs and symptoms of azotemia**
   Nausea, vomiting, weakness. The azotemia develops early and progresses faster
2. **Signs and symptoms of acute glomerulonephritis**
   It includes oliguria, abdominal flank pain due to large kidneys, hematuria, hypertension and proteinuria

Q 8. Enumerate the complications of acute nephritic syndrome.

Ans. Complications are either due to retention of salt and water (volume overload) or hypertension or capillaritis. These include:

1. Fluid overload
2. Hypertensive encephalopathy
3. Acute left heart failure
4. Noncardiogenic pulmonary edema
5. Rapidly progressive glomerulonephritis (RPGN)
6. Uremia
7. Massive hemoptysis.

Q 9. How will you proceed to investigate a patient with acute nephritic syndrome?

Ans. The investigations to be done are given in Table 1.61.

Table 1.61: Investigations for acute nephritic syndrome

Investigation	*Positive finding*
1. ***Urine microscopy***	1. RBCs and red cell casts
2. ***Urine complete***	2. High specific gravity, proteinuria present
3. ***Blood urea and serum creatinine***	3. May be elevated
4. ***Culture (throat swab, discharge from ear, swab from infected skin)***	4. Nephrogenic streptococci—not always
5. ***ASO titre***	5. Elevated in poststreptococcal nephritis
6. ***C3 level***	6. Reduced
7. ***Antinuclear antibody (ANA)***	7. Present in significant titres in lupus (SLE) nephritis
8. ***X-ray chest***	8. Cardiomegaly, pulmonary edema—not always
9. ***Renal imaging (ultrasound)***	9. Usually normal or large kidneys
10. ***Renal biopsy***	10. Glomerulonephritis

CASE 18: NEPHROTIC SYNDROME

An 18-year-old male (Fig. 1.18) presented with complaints of puffiness of face in the morning, edema feet and distension of the abdomen for the last 1 year. Patient is passing normal amount of urine of normal colour. There is no history of headache, blurring of vision, dizziness, breathlessness or orthopnea, nausea, vomiting. There is no history of disturbance in consciousness.

Clinical Presentations

- The patients usually children, adolescents or adults present with puffiness of eyelids or periorbital edema especially in the morning on awakening followed by edema face and feet (Fig. 1.18).
- Patients with progressive disease present with ***ascites and generalised anasarca***.
- ***Patients may present with complications***, e.g. pulmonary infection, pleural effusion, thromboembolism, renal vein thrombosis, protein malnutrition and microcytic hypochromic anemia.
- ***Patients may present with symptoms and signs of underlying disorder***, i.e. infections (malaria, leprosy, syphilis, streptococcal sore throat), collagen vascular disorders, lymphomas, diabetes mellitus and toxemia of pregnancy or hypertension.

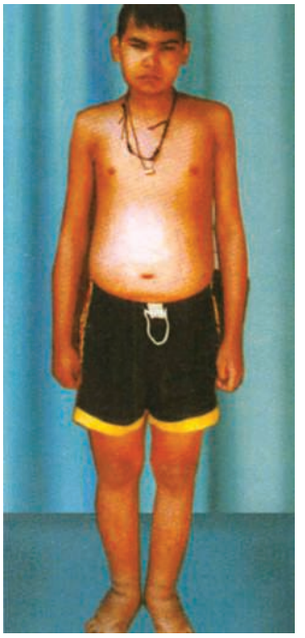


Fig. 1.18: A patient with puffiness of face and edema feet. There was ascites and scrotal edema. There was no anemia, jaundice or cyanosis. Blood pressure was normal. CVS examination was normal

HISTORY

Points to be Noted in the History

Ask the following on history:

- *Symptoms*, their *duration*, *progression*, *relapse* or *remission*, *aggravating* and *relieving factors*, *diurnal variation*
- History of *jaundice*, *sore throat*, *diabetes*, *hypertension*, neck swelling (*lymphoma*)
- *Past history of infections* (malaria, leprosy) collagen vascular disorder (SLE), skin rashes
- *Drug history* and *history of alcoholism.*

EXAMINATION

General Physical Examination

- General appearance—moon facies or puffiness of face, periorbital edema, xanthelasma
- Nutritional status
- Look for jaundice, anemia, cyanosis
- Neck veins for JVP
- Lymph nodes
- Pulse and BP
- Skin for alopecia, rash, xanthomas
- Feet for pitting edema
- External genitalia for edema and hydrocele.

Systemic Examination

1. **Abdomen**—distended, presence of ascites, edema of abdominal wall, shiny skin, nontender renal angle, scrotal (or vulval) edema, presence of hydrocele.
2. **Respiratory system:** Thoracoabdominal respiration, edema chest wall and legs, pleural effusions. Sometimes evidence of infection may be present.
3. **CVS examination:** Non-contributory.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis of the patient in picture?

Ans. Presence of morning puffiness of face followed by edema feet during daytime with ascites without hypertension in a young patient suggests the possibility of nephrotic syndrome.

Q 2. What is its differential diagnosis?

Ans. The differential diagnosis of nephrotic syndrome lies within the causes of ascites with anasarca (read differential diagnosis of ascites), such as CHF, cirrhosis of liver, hypoproteinemia, constrictive pericarditis, etc.

Q 3. How do you define nephrotic syndrome?

Ans. Nephrotic syndrome is defined as a heterogenous clinical complex comprising of following features:

1. Massive proteinuria >3.5 g/day or protein/creatinine ratio of >400 mg/mmol

2. Hypoalbuminemia/hypoproteinemia
3. Pitting pedal edema
4. Hyperlipidemia and lipiduria
5. Hypercoagulopathy.

Q 4. What are its causes?

Ans. A wide variety of disease processes including immunological disorders, toxic injuries, metabolic abnormalities, biochemical defects and vascular disorders involving the glomeruli can lead to it (Table 1.62).

Q 5. What is its etiopathogenesis?

Ans. **Massive proteinuria** >3.5 g/day is an essential criteria for the diagnosis. Other components are its consequences as described in Table 1.63.

Q 6. How will you investigate such a patient?

Ans. Investigations of nephrotic patient are as follows:

1. **Urine examination** reveals proteinuria and casts (fatty casts). Hematuria is uncommon.
2. **24 hours urine** shows excretion of albumin or proteins >3.5 g or protein/creatinine ratio >400 mg/mmol. In early stages of the disease or in patients receiving treatment, the proteinuria may be less.
3. **Serum lipids.** Low density lipoproteins and cholesterol are increased in majority of the patients. Hyperlipidemia is an integral component of the syndrome.
4. **Serum proteins or albumin.** Total serum proteins may be normal or low. Serum albumin is usually low <3 g/dl, also forms an important diagnostic criteria.
5. **Other renal function tests,** e.g. blood urea, creatinine, creatinine clearance and electrolytes are normal in uncomplicated cases, become abnormal if renal failure sets in.
6. **DNA antibody, antinuclear antibody (ANA), complement level.**
7. **Chest X-ray** may show hydrothorax.
8. **Ultrasound of abdomen:** It may show normal, small or large kidneys depending on the cause. Amyloid and diabetic kidneys are large; while kidneys in glomerulonephritis are small.
9. **Renal biopsy:** It is done in adult nephrotic syndrome to show the nature of underlying disease, to predict the prognosis and response to treatment.

Renal biopsy is not required in majority of children with nephrotic syndrome as most of them belong to minimal change disease and respond to steroids.

Q 7. What is selective and nonselective proteinuria?

Ans. **Selective proteinuria** means filtration of low molecular weight proteins especially the albumin through the glomeruli. It is seen in minimal change glomerulonephritis and early phase of other glomerulonephritis. These cases respond well to steroids.

Nonselective proteinuria means filtration of albumin along with high molecular weight proteins, e.g. globulins, antithrombin III, transferrin, immunoglobulins, thyroxine-binding globulins, calciferol-binding globulin, etc. This occurs in advanced glomerular disease and does not respond to steroids. It is a bad prognostic sign. The loss of these proteins constitute the clinical spectrum of the nephrotic syndrome in adults.

Table 1.62: Common causes of nephrotic syndrome

1. **Primary glomerular diseases**
   - a. Minimal change disease
   - b. Mesangioproliferative glomerulonephritis
   - c. Membranous glomerulonephritis
   - d. Membranoproliferative glomerulonephritis (crescents formation)
   - e. Focal glomerulosclerosis
2. **Secondary to other diseases**
   - A. *Infections*
     - a. Poststreptococcal glomerulonephritis
     - b. Poststreptococcal endocarditis
     - c. Secondary syphilis
     - d. Malaria (vivax and malariae infection)
     - e. Lepromatous leprosy
   - B. *Drugs and toxins:* Gold, mercury, penicillamine, captopril, NSAIDs antitoxins, antivenoms and contrast media
   - C. *Neoplasm*
     - a. Wilms' tumor in children
     - b. Hodgkin and non-Hodgkin's lymphoma
     - c. Leukemia
   - D. *Systemic disorders*
     - a. Systemic lupus erythematosus (SLE)
     - b. Goodpasture's syndrome
     - c. Vasculitis, e.g. polyarteritis nodosa
     - d. Amyloidosis
     - e. Diabetes mellitus
   - E. *Heredofamilial*
     - a. Congenital nephrotic syndrome
     - b. Alport's syndrome
   - F. *Miscellaneous*
     - a. Toxemia of pregnancy
     - b. Renovascular hypertension

Table 1.63: Pathogenesis of components of nephrotic syndrome

Components	*Pathogenesis*
Proteinuria	Altered permeability of GBM and the podocytes and their slit diaphragms
Hypoalbuminemia	Increased urinary protein loss not compensated by increased hepatic synthesis of albumin
Edema	Decreased oncotic pressure and stimulation of renin-angiotensin system resulting in salt and H_2O retention
Hyperlipidemia and lipiduria	Increased hepatic lipoprotein synthesis triggered by reduced oncotic pressure
Hypercoagulability	× Increased urinary loss of antithrombin III × Altered levels and/or activity of protein C and S × Hyperfibrinogenemia × Impaired fibrinolysis × Increased platelet aggregation

Q 8. What are the differences between glomerular proteinuria and tubular proteinuria?

Ans. Following are the differences:

Glomerular proteinuria. The damage to the glomeruli allows filtration of larger molecular weight proteins especially the albumin. The presence of albumin in the urine is sure sign of glomerular abnormality. The proteinuria in glomerular disease is >1 g/day. The severity of proteinuria is a marker for an increased risk of progressive loss of renal function. The glomerular proteinuria is associated with cellular casts (RBCs, WBCs) which are dysmorphic, i.e. get distorted as they pass through the glomerulus.

Tubular proteinuria is secretion of Tamm-Horsefall proteins or excretion of low molecular weight proteins especially retinol-binding proteins, β-macroglobulin. The proteinuria is <1 g/day occurs in tubulointerstitial diseases. Tubulointerstitial diseases are not the cause of either nephritic or nephrotic syndrome. The casts in tubulointestinal diseases are epithelial or granular.

Q 9. What is orthostatic proteinuria?

Ans. It occurs on standing and disappears on lying down. It is due to compression of inferior *vena cava* by liver during standing. The prognosis is good. Proteinuria is absent in the morning on rising from the bed.

Q 10. What are characteristics of minimal change disease (MCD) or lipoid nephrosis, nil disease or foot process disease?

Ans. The characteristic features are:

i. It is most common cause of nephrotic syndrome in children (70–80%) and more common in males than females.
ii. It is named so because light microscopy of renal biopsy specimen does not reveal any abnormality of glomeruli. Electron microscopy reveals effacement of the foot processes of epithelial cells
iii. Proteinuria is highly selective.
iv. Hematuria is uncommon.
v. Spontaneous relapses and remissions are common.
vi. Majority of the patients respond promptly to steroids. The disease may disappear after steroid therapy.
vii. Progression to acute renal failure is rare.
viii. Prognosis is good.

Q 11. What are characteristics of membranous glomerulonephritis?

Ans. The characteristic features are as follows:

i. It is a leading cause of nephrotic syndrome in adults (30–40%) but is a rare cause in children.
ii. It has peak incidence between the ages of 30 and 50 years, more common in males.
iii. It is named so because the light microscopy of renal biopsy specimen shows diffuse thickening of glomerular basement membrane (GBM) which is most apparent on PAS staining
iv. Proteinuria is nonselective
v. Hematuria is common (50%)
vi. Spontaneous remissions may occur in only 30–40% patients
vii. Renal vein thrombosis is a common complication
viii. Response to steroids therapy is inconsistent, it may reduce proteinuria but does not induce remission
ix. 10–20% cases progress to end-stage renal disease (ESRD) requiring transplantation of kidney.

Q 12. What are complications of nephrotic syndrome?

Ans. Common complications are as follows:

1. **Vascular**
   - Accelerated atherogenesis due to hyperlipidemia leading to accelerated hypertension and early coronary artery disease.
   - Peripheral arterial or venous thrombosis, renal vein thrombosis and pulmonary embolism due to hypercoaguable state.
2. **Metabolic**
   - Protein malnutrition
   - Iron-resistant microcytic hypochromic anemia
   - Hypocalcemia and secondary hyperparathyroidism.
3. **Infections**
   Pneumococcal and staphylococcal infections (respiratory and peritonitis) due to depressed immunity (low levels of IgG).
4. **Chronic renal failure.**

Q 13. What are causes of hypertension in nephrotic syndrome?

Ans. Hypertension is not a feature of nephrotic syndrome, but may be seen in diseases that cause nephrotic syndrome such as:

- Diabetic nephropathy
- SLE and polyarteritis nodosa
- Nephrotic syndrome complicated by CRF
- Focal glomerulosclerosis is commonly associated with hypertension.

Q 14. What is indication of renal biopsy in nephrotic syndrome?

Ans. The renal biopsy is done in adults for following reasons:

- To confirm the diagnosis
- To know the underlying pathological lesion
- To plan future treatment
- To predict the prognosis and response to treatment.

Q 15. What is the common pathological lesion in diabetic nephropathy?

Ans. **Kimmelstiel-Wilson syndrome** (diabetic nodular glomerulosclerosis) is the common pathological lesion.

- It occurs commonly in type I diabetes than type 2 diabetes
- Usually develops as a long-term microvascular complication of diabetes (duration of diabetes >10 years)
- Common presentation is moderate to massive proteinuria. Hypertension may develop later on
- With the onset of this lesion, the requirement of insulin falls due to excretion of insulin antibodies in urine
- Progresses to end-stage renal disease (ESRD) over a period of few years
- The characteristic histological lesion is nodular glomerulosclerosis.

Q 16. How does nephrotic syndrome differ from nephritic syndrome?

Ans. The differences are tabulated (Table 1.64)

Table 1.64: Differences between nephrotic and nephritic syndrome

Feature	*Nephrotic syndrome*	*Nephritic syndrome*
Onset	Slow, insidious chronic disorder	Sudden, acute renal disorder
Proteinuria	Massive >3.5 g/d	Moderate 1–2 g/d
Hyperlipidemia and lipiduria with faulty casts	Present	Absent
Hypertension	Not a feature	An important feature
Volume of urine passed in 24 hr	Normal	Oliguria
Hematuria	Not common	A common and integral component of syndrome
Acute renal failure	Uncommon	Common
Relapse and remission	Commom	Uncommon
Course	Chronic progressive disorder	70–80% cases recover completely while others pass on to RPGN

CASE 19: ANEMIA

A 19-year-old female (Fig. 1.19A) presented with pallor, fatigue, malaise, weakness and breathlessness on exertion. There was no history of fever, loose motion, blood loss, any surgery. No history of drug intake. She has generalised pallor with slight puffiness of face. Physical examination revealed pallor and koilonychia.

Clinical Presentations

- ***Patients with mild anemia are asymptomatic.*** Anemia is discovered on routine hemoglobin estimation done for some other purposes. On symptomatic enquiry, they may admit history of occasional exertional dyspnea, palpitations and fatigue.
- ***Patients with severe anemia usually*** complain of ***weakness, weight loss, dyspnea, palpitation, throbbing headache, dizziness, tinnitus*** and ***menstrual irregularity in females, tingling in extremities*** and ***GI symptoms*** (***nausea, anorexia***).
- ***Anemia may be a presenting feature of certain chronic disorders***, e.g. malabsorption, chronic renal failure, chronic blood loss (hematemesis, malena, monorrhagia) or malignant disorders.

Note: Anemia is a sign not a complete diagnosis, hence, cause of anemia must be mentioned in the diagnosis, e.g. malabsorption with anemia, CRF with anemia, etc.

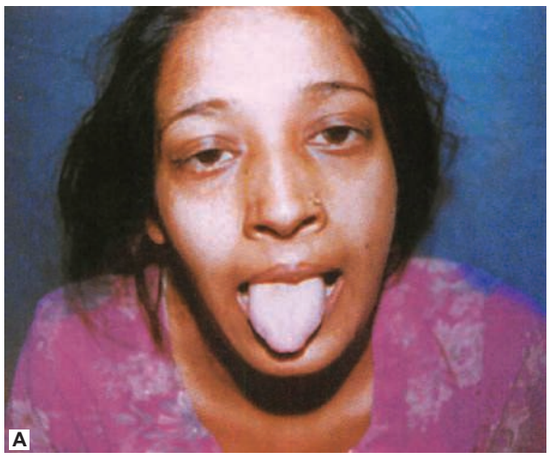
History

Points to be Noted

- Symptoms and their analysis
- History of fever, blood loss, drug intake (NSAIDs, chloramphenicol, phenytoin), loose motions, jaundice, dysphagia, vomiting
- Menstrual history, history of recent delivery and blood loss if any
- History of piles or repeated hematemesis, melena
- Nutritional history, e.g. malnutrition
- Past history of tuberculosis, bleeding, any surgery, trauma, repeated abortions/deliveries
- Personal history, e.g. alcoholism
- Family history of jaundice.

General Physical Signs

- Facial appearance or look (e.g. pallor)
- Puffiness of face or periorbital edema
- Look for anemia at different sites, nails for koilonychia, platynychia, and look for bleeding from gums or nose.
- See the tongue for glossitis (magenta coloured tongue in vitamin B_{12} deficiency, bald atrophic tongue in iron deficiency)
- Mouth for cheilosis, angular stomatitis and ulcerations (agranulocytosis)
- Neck examination for JVP, lymph nodes and thyroid



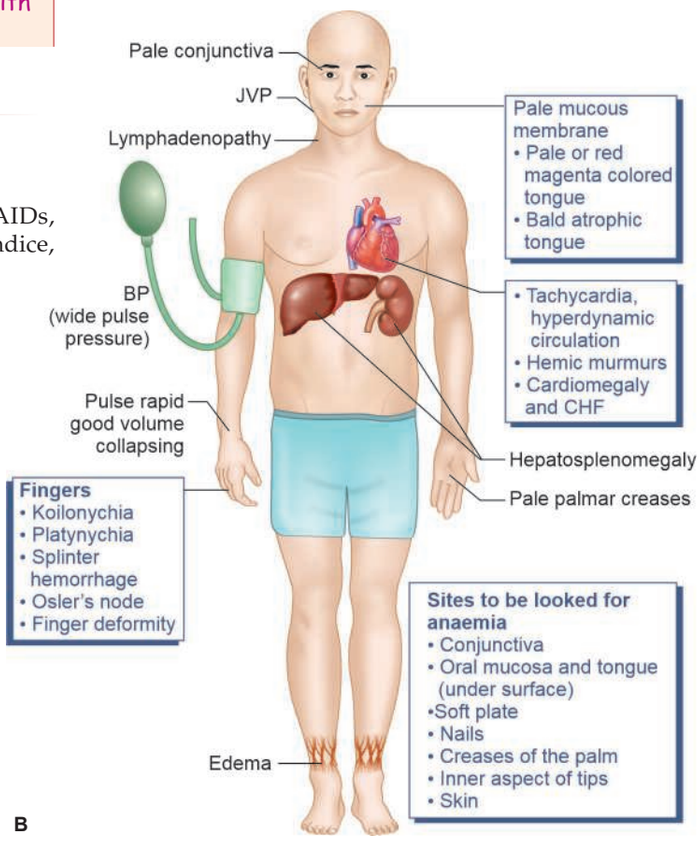


Fig. 1.19A and B: A. A patient with severe anemia; **B.** Clinical features of anemia

Systemic Examination

I. Examination of CVS

Inspection

- Look for apex beat, e.g. location, type
- Any chest deformity
- Chest movements.

Palpation

- Trachea—note any deviation
- Apex beat—confirm the findings of inspection
- Chest movements and expansion.

Percussion

- Heart borders, cardiac and liver dullness
- Lung resonance.

Auscultation

- Heart, e.g. sounds, murmurs, if any murmur, note its various characteristics
- Lung sounds, e.g. breath sounds, crackles and rales.

II. Examination of Abdomen

Inspection

Contour, shape of umbilicus, hernial sites, any swelling or mass or distension.

Palpation

- Palpate for any mass
- Pulse, BP, temperature, respiration
- Skin for any bleeding spots or rash or bruising
- Edema feet, leg ulcers (see in hemoglobinopathies)
- Look for deficiency, signs of hypoproteinemia, e.g. flabby muscles, wasting, thin skin.
- Palpate for liver, spleen and kidneys
- Elicit any tenderness.

Percussion

Define percussion note over the mass if present. Define upper border of the liver.

Auscultation

Hear for intestinal sound, bruit or rub.

III. Examination of CNS

Look for signs of neuropathy (B)

IV. Endocrine System

Look for signs of hyper- or hypothyroidism.

V. Rectal Examination

Look for piles, rectal bleeding, fissure, etc.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis of the patient in picture?

Ans. The young patient presented with exertional breathlessness, fatigue and malaise. She was found to have generalised pallor, paleness of mucous membrane and koilonychia.

The *clinical diagnosis* is anemia, the cause of which is nutritional.

Q 2. How do you define anemia?

Ans. A hemoglobin level <11.0% g in an adult female and <12.0 g% in an adult male is taken as anemia.

Q 3. What are symptoms and signs of anemia?

Ans. *For symptoms:* Read clinical presentations.
For sign—see Fig. 1.19B.

Q 4. What are the causes of anemia?

Ans. The common clinical causes of anemia in India are:

1. **Nutritional,** e.g. deficient intake of iron, folate and protein in diet
2. **Hookworm infestation**
3. **Chronic blood loss,** e.g. piles, hematemesis, menorrhagia, melena, etc.
4. **Chronic diarrhea and malabsorption**
5. **Pregnancy** associated anemia
6. **Hypoproteinemia,** e.g. nephrotic syndrome, cirrhosis of the liver
7. **Hemolytic anemia**, e.g. malarial parasite or drug-induced in G6PD deficiency
8. **Anemia of chronic infection,** e.g. tuberculosis, SLE, rheumatoid arthritis
9. **Anemia associated with malignancies,** e.g. leukemia, lymphoma, carcinoma stomach, colon, etc.
10. **Hereditary anemia.**

Q 5. What are common causes of iron deficiency anemia (microcytic hypochromic)?

Ans. Common causes are as follows:

1. **Nutritional deficiency,** e.g. inadequate iron intake
2. **Increased demands,** e.g. pregnancy and lactation
3. **Blood loss**
   - ***GI loss,*** e.g. bleeding, peptic ulcer, piles, cancer of GI tract, hematemesis, hookworm disease, angiodysplasia of colon
   - ***Uterine,*** e.g. menorrhagia, repeated abortions, dysfunctional uterine bleeding
   - ***Renal***—hematuria
   - ***Nose***—epistaxis
   - ***Lung***—hemoptysis
4. **Malabsorption** due to any cause
5. **Hereditary hemorrhagic telangiectasia.**

Q 6. What are clinical signs of iron deficiency anemia?

Ans. Clinical signs are:

- Pallor

- Glossitis (bald atrophic tongue), angular stomatitis, cheilosis
- Koilonychia
- Dysphagia (*Plummer-Vinson syndrome*)
- Mild splenomegaly
- History of *pica* (eating of strange items, e.g. coal, earth).

Q 7. What is Plummer-Vinson (Paterson-Kelly) syndrome?

Ans. It comprises:

1. Koilonychia
2. Iron deficiency anemia
3. Dysphagia due to esophageal webs.

It is common in middle-aged females and is considered as a precancerous condition.

Q 8. What is sideroblastic anemia? What are its causes?

Ans. A red cell containing iron is called *siderocyte*. A developing erythroblast with one or two iron granules is called *sideroblast*. Iron granules free in cytoplasm of RBCs are normal, but when they *form a ring round the nucleus* in red cells, then they are considered abnormal and called *ring sideroblasts*.

- The anemia in which ring sideroblasts are present is called *sideroblastic anemia*.
- It is due to nonutilisation of the iron in the bone marrow resulting in accumulation of iron as granules in developing red cells.
- Sideroblastic anemia may be *primary* (hereditary or congenital) or *secondary* (acquired). The **causes** are:

I. **Hereditary (congenital)**

II. **Acquired**

- Inflammatory conditions
- Malignancies
- Megaloblastic anemias
- Hypothyroidism
- Drug-induced
- Lead poisoning
- Pyridoxine deficiency.

Q 9. What are causes of megaloblastic anemia?

Ans. It occurs due either to folate or vitamin B_{12} deficiency or both. The **causes** are:

1. **Nutritional,** e.g. inadequate intake, alcoholism.
2. **Increased demands of folic acid,** e.g. pregnancy, lactation.
3. **Following hemolysis**
4. **Malabsorption syndrome:**
   - Ileal disease
   - Gastrectomy
   - Blind loop syndrome
5. **Drug-induced,** e.g. anticonvulsants, methotrexate, oral contraceptive, pyrimethamine.
6. **Parasitic infestation,** e.g. *Diphylobothrium latum*.

Q 10. What are the causes of hemolytic anemia?

Ans. Read hemolytic jaundice.

Q 11. What are the causes of aplastic anemia?

Ans. Following are the causes:

I. **Primary**—red cell aplasia.

II. **Secondary**

i. *Drugs*
   - Dose related, e.g. methotrexate, busulfan, nitrosourea
   - Idiosyncratic, e.g. chloramphenicol, sulpha drugs, phenylbutazone, gold salts.

ii. *Toxic chemicals,* e.g. insecticides, arsenicals, benzene derivatives

iii. *Infections,* e.g. viral hepatitis, AIDS, other viral infections

iv. *Miscellaneous,* e.g. irradiation, pregnancy, paroxysmal nocturnal hemoglobinuria.

Q 12. What are the causes of reticulocytosis and reticulopenia?

Ans. **Reticulocyte** is a young red cell with basophilic cytoplasm (polychromasia). It matures into an adult RBC within 3 days. The normal reticulocyte count is 0.5–2% in adults and 2–6% in infants. An absolute increase in reticulocyte count is called *reticulocytosis*. The **causes** are:

1. Hemolytic anemia
2. Accelerated erythropoiesis
3. Polycythemia rubra vera.

Reticulocytopenia means low reticulocyte count (<0.5%), is seen in aplastic anemia and *megaloblastic anemia*.

Q 13. What is corrected reticulocyte count? What is reticulocyte production index?

Ans. Reticulocyte count corrected for anemia is called *corrected reticulocyte count*. It is calculated as reticulocyte count multiplied by hemoglobin of patient divided by normal hemoglobin, e.g. if reticulocyte count is 9% and Hb is 7.5 g/dl then corrected reticulocyte count = $9 \times 7.5 \div 15 = 4.5$.

Reticulocyte production index is calculated by dividing corrected reticulocyte count by reticulocyte maturation time which varies from 1–3 depending on severity of anemia. For moderate anemia, a correction of 2 is used as follows:

Reticulocyte production index

$$= \frac{\text{corrected reticulocyte count}}{2} = \frac{4.5}{2} = 2.25$$

Q 14. What is significance of reticulocyte production index?

Ans. It implies bone marrow response to anemia. It is calculated by correcting the reticulocyte count first for degree of anemia (see above) secondly for maturation time. A normal cut off limit is 2.5.

- Index <2.5 indicates hypoproliferative anemia due to maturation defect.
- Index >2.5 indicates invariably hemolytic anemia.

Q 15. Name the chronic systemic diseases associated with anemia.

Ans. Following are the systemic diseases:

- Chronic infections, e.g. tuberculosis, SABE, osteomyelitis, lung suppuration
- Collagen vascular disorders, e.g. SLE
- Rheumatoid arthritis
- Malignancy anywhere in the body
- Chronic renal failure
- Endocrinal disorders, e.g. Addison's disease, myxedema, thyrotoxicosis, panhypopituitarism
- Cirrhosis of the liver especially alcoholic.

Q 16. What is morphological classification of anemia?

Ans. Morphological classification refers to average size and hemoglobin concentration of RBCs.

I. **Microcytic hypochromic** (reduced MCV, MCH and MCHC)
   - Iron deficiency anemia
   - Sideroblastic anemia
   - Thalassemia
   - Anemia of chronic infection.

II. **Normocytic normochromic** (MCV, MCH and MCHC normal)
   - Hemolytic anemia
   - Aplastic anemia.

III. **Macrocytic** (MCV is high. MCH and MCHC relative low): Folate and vitamin B_{12} deficiency (read the causes of megaloblastic anemia).

IV. **Dimorphic anemia** (microcytic as well as macrocytic)
   - Nutritional deficiency
   - Pregnancy
   - Malabsorption syndrome
   - Hookworm infestation.

Q 17. What is functional classification of anemia?

Ans. Functional classification: Anemia is classified (Fig. 1.19C) into:

i. Functional defect in RBC production (low reticulocyte production index <2.5)

ii. Decreased red cell survival (high reticulocyte index >2.5)

Q 18. What are diagnostic clues to hookworm infestation?

Ans. The **clues** are:

- Occupation (e.g. workers in tea-garden, farmers, coal-miners)
- History of walking bare-footed
- Presence of ground itch in interdigital spaces
- Pain abdomen (epigastrium simulating peptic ulcer)
- History of pica
- Diarrhea or steatorrhea
- Iron deficiency or dimorphic anemia
- Prevalence of hookworm disease in that area.

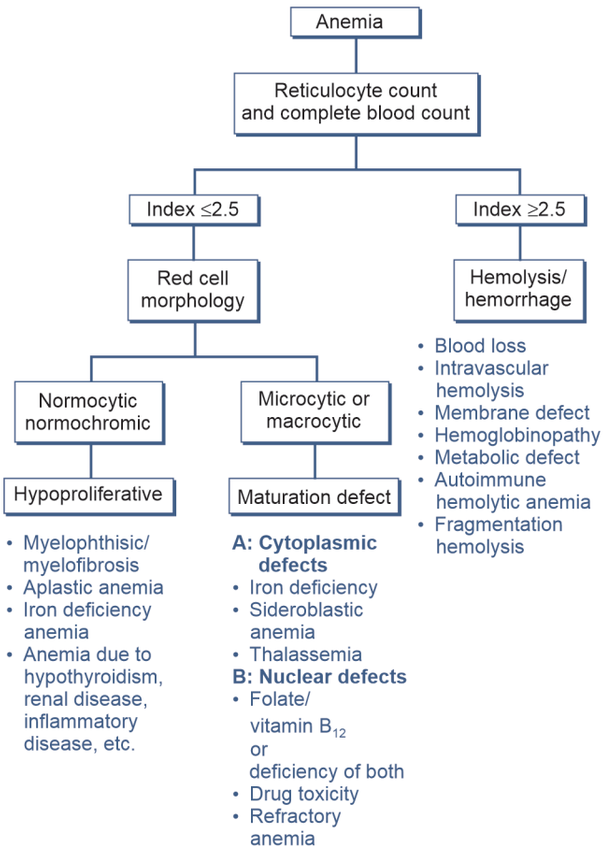


Fig. 1.19C: Classification of anemia based on reticulocyte production index

Q 19. How will you investigate a patient with anemia?

Ans. Investigations are done to confirm anemia and to find out the cause of anemia:

A. **Tests to Confirm Anemia**

- Hemoglobin and red cell count
- *Peripheral blood film for type of anemia and to find out any abnormality of the shape of RBCs and presence of malarial parasite or any other abnormal cells.* Reticulocytosis indicates accelerated erythropoiesis.
- *Bone marrow examination: It provides assessment of cellularity, details of developing RBCs, assessment of iron store, presence of marrow infiltration by parasites, fungi and secondary carcinoma.*

It gives valuable information regarding reticulocyte count, reticulocyte production index and myeloid/erythroid ratio to classify the anemia. A reticulocyte production index <2.5 and M:E ratio of 2 or 3:1 indicates hypoproliferative anemia while reticulocyte production index >2.5 and M:E ratio 1:1 indicates hemolytic disease.

In addition, bone marrow gives information regarding iron stores and can demonstrate the cause of anemia such as parasites.

B. **Specific Tests**

Anemia with low reticulocyte count index (<2.5)

I. ***For iron deficiency anemia (microcytic hypochromic)***
- Serum iron is low (normal 50–150 mg/dl)
- Iron binding capacity is raised (normal 300–360 mg/dl)
- Serum ferritin low (normal about 100 pg/dl in males and about 30 pg/dl in females)

Transferrin saturation low (normal 25–50%)
- Stool for occult blood
- Upper GI endoscopy
- Colonoscopy, barium studies
- Prothrombin time and INR
- Hemoglobin for electrophoresis.

II. ***For megaloblastic anemia***
- Plasma LDH markedly elevated
- Serum iron elevated
- Serum ferritin elevated
- Serum bilirubin—unconjugated hyperbilirubinemia
- Antiparietal cell antibodies and an abnormal vitamin B_{12} absorption studies (Schilling test) may be observed in vitamin B_{12} deficiency anemia or pernicious anemia.
- Serum folate levels/red cell folate levels.
- Upper GI endoscopy.

C. **Anemia with high reticulocyte count index (>2.5)**

Hemolytic anemias
- PBF for morphology of the RBCs (spherocytes, ovalocytes, elliptocytes, sickle cells) and for malarial parasite
- Hemoglobin electrophoresis for thalassemia (HbF >2%)
- Coombs' test (direct and indirect)—may be abnormal
- Osmotic fragility test may be positive
- Serum bilirubin shows unconjugated hyperbilirubinemia
- Red cell survival studies may reveal decreased survival
- Sickling test positive in sickle cell anemia.

Q 20. What are the causes of refractory anemia?

Ans. The anemia that does not respond to appropriate treatment given for optimal period is called *refractory anemia*. The causes are:
1. Aplastic anemia
2. Thalassemia
3. Sideroblastic anemia (pyridoxine responsive)
4. Refractory anemia due to myelodysplastic syndrome
5. Anemia due to leukemia, e.g. erythroleukemia or aleukemic leukemia.

CASE 20: LEUKEMIA

A patient (Fig. 1.20A) presented with fever, dyspnea and bleeding from the nose. There was history of a big mass in the left hypochondrium with dragging pain. Another patient (Fig. 1.20B) presenting with bleeding from the gums, excoriation of mouth, fever, breathlessness and pallor. There was also history of mass abdomen and pain abdomen.

Clinical Presentations

- ***Patients with acute leukemia*** usually children or adolescents present with acute onset of symptoms and signs of bone marrow failure, i.e. anemia (pallor, lethargy, dyspnea, palpitations, etc.), thrombocytopenia (bleeding from gums, epistaxis, petechiae and spontaneous bruising) and neutropenia (infections leading to fever, excoriation of mouth and respiratory infection). They may also present with hepatosplenomegaly and/or lymphadenopathy.
- ***Patients with chronic leukemia*** usually middle aged or old persons present with ***insidious onset of symptoms*** of ***anemia, bone pain, infections (fever)*** and ***bleeding tendencies***. These cases especially with chronic myeloid leukemia present with ***mass abdomen*** while that of chronic lymphoid leukemia with ***lymphadenopathy*** and ***splenomegaly***. A significant number of cases are discovered incidentally.

N.B.: Hepatosplenomegaly with anemia is a classic feature of CML. A mass abdomen with dragging pain is a presenting feature.

Points to be Noted in History

- Onset and progression of symptoms
- History of fever, sore throat, ulceration in the mouth
- History of bleeding from any site, e.g. gum, nose, urine, sputum, skin
- History of weakness of any part of the body, convulsions
- History of visual impairment or loss
- History of breathlessness, fatigue or pain abdomen.

General Physical Examination

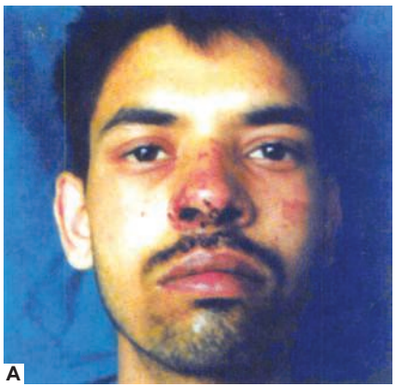
- **Face:** Expression, puffiness
- **Oral cavity,** e.g. gum bleeding, anemia or excoriation or aphthous ulceration
- **Neck** examination for PVP, lymphadenopathy, thyroid enlargement
- **Pulse, BP, temperature and respiration**
- **Hands** for koilonychia or platynychia, clubbing, sub-lingual hematoma or bleeding
- **Skin** for bleeding spots or ecchymotic patches
- Elicit *sternal tenderness*
- **Edema** feet.

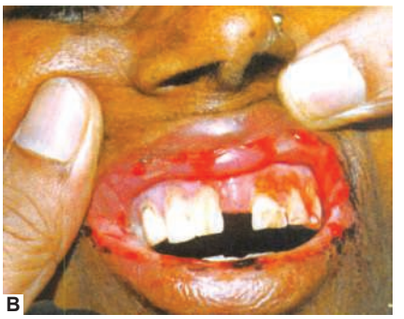
Systemic Examination

Examination of Abdomen

Inspection

- A mass (bulge) in the left hypochondrium





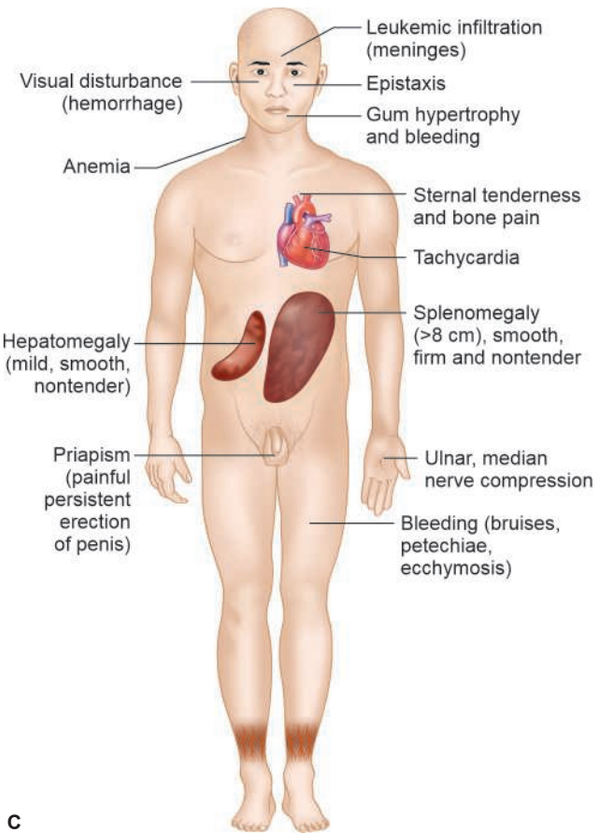


Fig. 1.20A to C: A. Chronic myeloid leukemia. A. Patient presented with epistaxis; **B.** Patient presented with gum bleeding; **C.** Clinical manifestations of CML (diagram)

- Shape and position of the umbilicus may be normal or distorted by the mass if it is huge
- Hernial sites normal.

Palpation

- A palpable mass in left and right hypochondrium. Described its characteristics
- Any tenderness of abdomen.

Percussion

- Percuss over the mass. There will be dullness over splenic and liver mass
- Normal abdominal resonance
- Define the upper border of liver to confirm liver enlargement.

Auscultation

- Auscultate the bowel sounds
- Auscultate over the mass for any bruit, rub, etc.

Other Systems

CVS Examination

- Look for anemia
- Auscultate for sounds, murmurs or friction rub
- Looks for signs of CHF.

Nervous System

Look for entrapment neuropathy, e.g. carpel tunnel syndrome or peripheral neuropathy.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis of the patients in picture?

Ans. Both the patients are adults and presented with bleeding from nose (A) and gums (B) with a mass in left abdomen (both patients), the *diagnosis* of chronic myeloid leukemia is most likely.

Q 2. What is your differential diagnosis?

Ans. Read the differential diagnosis of hepatosplenomegaly with anemia (Case 23)

Q 3. What are points in favour of your diagnosis?

Ans. 1. An adult patient with insidious onset of symptoms and signs
2. Presence of anemia
3. Sternal tenderness
4. Massive splenomegaly and mild hepatomegaly.

Q 4. How do you define leukemia? What is subleukemic or aleukemic leukemia?

Ans. The *leukemias* are a group of white cell disorders characterised by malignant transformation of blood white cells primarily in the bone marrow resulting in increased number of primitive white cells (blasts cells) in the bone marrow which ultimately spill into peripheral blood raising the total leukocyte count in peripheral blood.

Subleukemic or aleukemic leukemia is defined as the presence of immature cells in the bone marrow with little or no spilling into peripheral blood, hence, the WBC count is not high; may be normal or even reduced. The *diagnosis* is confirmed on bone marrow examination.

Q 5. What are differences between acute and chronic leukemias?

Ans. Depending on the clinical behaviour of leukemia, it has been classified into *acute* and *chronic*.

- In acute leukemias, the history is short and life expectancy without treatment is short.
- In chronic leukemias, the patient is unwell for months and survives for years.

The differences between acute and chronic leukemias are summarised in Table 1.65.

Table 1.65: Differentiation between acute and chronic leukemias

Acute	*Chronic*
Common in children and adolescents	Common in adults and old age
Acute onset	Slow insidious onset
Presentation is bone marrow failure, i.e. anemia, thrombocytopenia and leukopenia with their systemic effects	Presentation is extramedullary hematopoiesis, e.g. hepatosplenomegaly
Cell count varies in thousands, usually does not cross a lakh	Cell count varies in lakh
Predominant cell type is blast cells	Predominant cell type is cytic cells (myelocytic, premyelocytic, metamyelocytic)
Blast cells usually exceed 30% in the marrow	Blast cells are usually less than 10%
Prognosis is bad, usually months to a year	Prognosis is good usually few years

Q 6. How do you classify leukemias?

Ans. The leukemia on the basis of cell types are classified into *myeloid* and *lymphoid* and on the basis of natural history into acute and chronic as described above. The subclassification of leukemia is depicted in Table 1.66.

Q 7. What are symptoms and signs of leukemia?

Ans. Clinical symptoms (*see* Fig. 1.20C) are:

I. **Symptoms due to anemia**
   - Weakness
   - Dyspnea
   - Pallor
   - Tachycardia.

II. **Symptoms due to hypermetabolism**
   - Weight loss
   - Lassitude
   - Anorexia
   - Night sweats.

III. **Symptoms due to hyperplasia of bone marrow or infiltration of marrow by leukemic cells**
   - Bone pain
   - Sternal or iliac tenderness.

Table 1.66: Subclassification of leukemia

1. **Acute lymphoblastic**
× Common type (pre B)
× T cell
× B cell
× Undifferentiated
2. **Acute myeloid (FAB* classification)**
× M0 = Undifferentiated
× M1 = Minimal differentiation
× M2 = Differentiated
× M3 = Promyelocytic
× M4 = Myelomonocytic
× M5 = Monocytic
× M6 = Erythrocytic
× M7 = Megakaryocyte
3. **Chronic lymphocytic/lymphoid**
× B cell—common
× T cell—rare
4. **Chronic myeloid**
× Ph' positive
× Ph' negative, BCR-ABL positive
× Ph' negative
× Eosinophilic leukemia

FAB*: French, American, British
Ph': Philadelphia chromosome
BCR: Break point cluster region
ABL oncogene: Abelson oncogene

IV. **Symptoms due to infection**
- Fever
- Perspiration.

V. **Bleeding tendencies**
- Easy bruising, ecchymosis
- Epistaxis
- Menorrhagia
- Hematomas.

VI. **Symptoms of hyperuricemia produced by drug treatment**
- Asymptomatic
- Uric acid stones
- Precipitation of an attack of gout
- Uric acid nephropathy.

Q 8. How will you arrive at the diagnosis of CML?

Ans. CML is diagnosed on the clinical findings and confirmed on investigations.

Clinical findings in CML

1. Adult patient
2. Gradual onset of dragging pain and mass in the left hypochondrium
3. Progressive anemia; anorexia, abdominal fullness, marked weight loss
4. Moderate hepatomegaly with huge splenomegaly (>8 cm below the costal margin)
5. Sternal tenderness.

Confirmation of CML

- Peripheral blood and bone marrow examination
- Philadelphia chromosome, if present, clinches die diagnosis
- Low leukocyte alkaline phosphatase score
- RNA analysis for presence of BCR-ABL oncogene.

Q 9. What are the causes of bleeding gums?

Ans.
1. Leukemias, e.g. acute (myelomonocytic common) and chronic (CML)
2. Bleeding disorders, e.g. thrombocytopenia scurvy
3. Dilantin toxicity (hypertrophy-cum-gum bleeding)
4. Gingival disorders
5. Local trauma.

Q 10. What are the causes of sternal tenderness?

Ans. Sternal tenderness is usually due to expansion of the bone marrow due to its proliferation, hence, can be present in all those conditions which cause bone marrow proliferation, i.e.
- Acute leukemia (AML and ALL)
- CML
- Severe anemia especially acute hemolytic anemia or crisis
- Multiple myeloma
- Following sternal puncture. This is easily diagnosed by the presence of either sternal puncture mark or attached cotton seal or benzene stain over sternum.

Q 11. What is genetics of CML?

Ans. The fusion of C-ABL (normally present on chromosome 9) with BCR sequences on chromosome 22 is pathognomonic of chronic phase of CML called the Philadelphia chromosome.

The p53 gene is the culprit in CML with blast transformation and there are structural alterations of RBI of N-ras in few case (<10%) of myeloid blast crisis.

Q 12. What do you understand by the term 'myeloid metaplasia'?

Ans. *Myeloid metaplasia* also called extramedullary hematopoiesis means formation of blood at sites other than bone marrow, i.e. in the liver and spleen. It is commonly associated with bone marrow fibrosis (*agnogenic myeloid metaplasia*).

Q 13. What is myelodysplastic syndrome (MDS)? What are conditions included in it?

Ans. *Myelodysplasia (MDS)* describes a group of acquired bone marrow disorders that are due to defect in the stem cells. They are characterided by increasing bone marrow failure with qualitative or quantitative abnormalities of all three myeloid cell lines (red cells, WBCs and platelets).

WHO and FAB classified myelodysplasia into 3 categories (Table 1.67).

Q 14. What are complications of CML?

Ans. Common complications of CML are as follows:
1. Blastic crisis or blastic transformation of CML
2. Hemorrhage or bleeding

Table 1.67: Classification of myelodysplasia by WHO and FAB

Category	*Peripheral blast (1%)*	*Bone marrow (1%)*
1a (Refractory anemia)	<1	Blasts <5, ring sideroblasts <15
2a (Refractory anemia with sideroblasts)	<1	Blast <5, ring sideroblasts >15
3a (Refractory anemia with excess blasts I)	1–4	Blasts 5–10
3b (Refractory anemia with excess blasts II)	5–19	Blasts 11–19

3. Recurrent infections (respiratory infection common)
4. Hyperuricemia (due to disease as well as treatment)
5. Leukemic infiltration in cranial nerves (compression neuropathy), pleura (pleural effusion), bones (paraplegia)
6. Priapism—persistent painful erection of penis
7. Infarction or rupture of the spleen. Presence of splenic rub indicates infarction; while tender spleen can occur both in infarction and rupture.

Conversion of CML to acute leukemia indicates blastic crisis.

Q 15. What is blastic crisis?

Ans. It refers to transformation of chronic stable phase of chronic leukemia into acute unstable phase characterised by *progressive anemia*, *onset of severe bleeding* (e.g. *petechiae*, *bruises*, *epistaxis*, *GI bleed*) and *on examination*, one would find:

- Sternal tenderness
- Appearance of lymphadenopathy (due to transformation to ALL).

The **diagnosis** is confirmed by peripheral blood examination which shows >30% blast cells (usually in CML, blast cells are <10%).

Table 1.68: Two common types of acute leukemia—similarities and dissimilarities

Features	*AML*	*ALL*
Age	Adults (15–40 years)	Children (<15 years)
Incidence	Constitutes 20% of childhood leukemia	Constitute 80% of childhood leukemia
Symptoms	Fever, tiredness, bleeding manifestations, mouth ulceration and recurrent infections	Same as AML. Bone pain and tenderness common
Physical findings	Hepatosplenomegaly (+)	Hepatosplenomegaly (+ + +)
	Lymphadenopathy (+)	Lymphadenopathy (+ +)
	Gum hypertrophy (+)	Gum hypertrophy (+ +)
	Bone tenderness (+)	Bone tenderness (+ +)
	Chloroma (common), i.e. localised tumor masses in orbit, skin and other tissue	Chloroma—rare
	Anemia (+ +)	Anemia (+ + +)
	Leukemic meningitis (uncommon)	Leukemic meningitis (common)
	Sternal tenderness (+ +)	Sternal tenderness (+ +)
Laboratory findings	Low to high WBC count with predominant myeloblasts (>30%)	Low to high WBC count with predominant lymphoblasts
Cytochemical	Myeloperoxidase positive	PAS positive
Stain	Sudan black positive	—
Remissions	Remission rate is low, duration of remission short	Remission rate high and duration of remission prolonged

Signs used (+) means present (+ +) to (+ + +) means a marked feature

Table 1.69: Similarities and dissimilarities between CIVIL and CLL

Features	*CML*	*CLL*
Age	Peak age 55 years	Peak age 65 years
Onset	Insidious	Very insidious
Symptoms and signs	Hepatosplenomegaly marked	Hepatosplenomegaly mild
	Anemia early	Anemia develops late
	Lymphadenopathy uncommon	Lymphadenopathy is common presentation
	Sternal tenderness present	Sternal tenderness absent
	Blast crisis (common)	Blast crisis (uncommon)
Laboratory findings	Very high WBC count with predominant myelocytes and metamyelocytes	WBC count high, predominant cells are lymphocytes
	Philadelphia chromosome positive	Philadelphia chromosome negative
Response to treatment	Good	Excellent
Prognosis	Good	Excellent

N.B.: Blastic crisis in CML is seen in patients with long duration of disease being treated with myelosuppressive drugs.

Q 16. What are differences between acute myeloid and acute lymphoid leukemias?

Ans. The ALL is common in children while AML is common in adults. The contrasting features of two types of leukemias are summarised in Table 1.68.

Q 17. What are similarities between CML and CLL? How they differ from each other?

Ans. Table 1.69 differentiates between CML and CLL.

Q 18. Which lymphomas can convert to leukemias?

Ans.
- Small cell lymphoma to CLL
- Burkitt's lymphoma to B cell ALL
- Lymphoblastic lymphoma to T cell ALL

Q 19. What is significance of Philadelphia chromosome?

Ans. The significances are:
- The Philadelphia chromosome (Ph') results from reciprocal translocation between the parts of long arms of chromosomes 9 and 22.
- Found in 90% cases of CML. Rest 10% are Philadelphia chromosome negative. It is considered as diagnostic tool for CML.
- Philadelphia chromosome positive cases have better prognosis than Philadelphia chromosome negative cases.
- It is found in myeloid and erythroid series of blood cells in bone marrow. It is never seen in lymphocytes.
- It can differentiate AML from blastic crisis in CML.
- Philadelphia chromosome is positive throughout the course of the disease during treatment, however, Philadelphia positive cells decrease with alpha-interferon and imatinib mesylate therapy.

Q 20. How will you investigate a case with CML?

Ans. Investigations are as follows:

1. **Blood examination**
   - Hemoglobin and RBC count. They are low
   - WBC count high (1–5 lakh/mm^3). Differential count shows 20–30% myelocytes, 20–25% metamyelocytes, 2–3% promyelocytes and rest are polymorphs. Myeloblasts (< 10%) may be seen. There may be increase in basophils and eosinophils in early disease.
   - Platelet count—normal to increased in early stages but decreased in late stages.
2. **Bone marrow examination.** It is not must for diagnosis as presence of immature cells (>30%) in the peripheral blood are sufficient for diagnosis. It shows increased myelocyte series of cells with increased myeloid and erythroid ratio (20:1). Bone marrow is hypercellular. Myeloblasts >30% in the bone marrow in CML indicates blastic crisis.
3. **Chromosomal study for Philadelphia chromosome.** It is positive in 90% cases
4. **RNA analysis** for BCR-ABL oncogene
5. **Leukocyte alkaline phosphatase** score is diminished
6. **Other tests**
   - High uric acid and LDH level
   - High serum vitamin B_{12} level.

Q 21. What is busulphan lung?

Ans. Interstitial lung fibrosis seen during therapy with busulphan is called *busulphan lung*.

CASE 21: LYMPHADENOPATHY

A 30-year-old male patient (Fig. 1.21) presented with multiple swelling in the neck with low grade fever, fatigue and malaise for the last 8 months. On examination, there was lobulated mass in the cervical region.

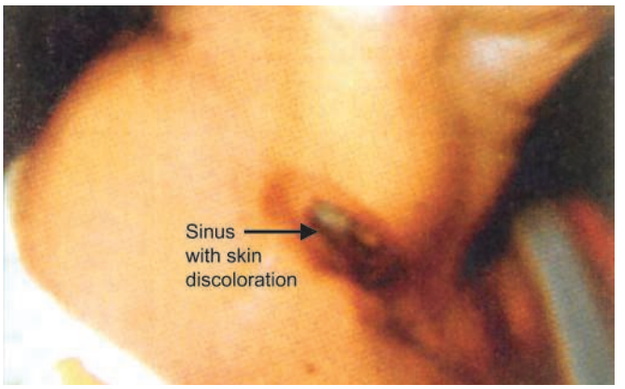


Fig. 1.21: A patient with cervical lymphadenopathy presented with mass in the neck which has irregular surface, is firm in consistency, adherent to overlying skin with a sinus and skin discoloration

Clinical Presentations of Lymphadenopathy

1. **Asymptomatic.** Lymphadenopathy may be an incidental finding in patients being examined for various reasons.
2. **When symptomatic,** the symptoms may vary according to size, site and cause of involvement. They may present with:
   - *Multiple swellings* at one site or at different sites, e.g. neck, axillae and groins.
   - *Mediastinal lymph node enlargement* may present as superior mediastinal compression syndrome or superior vena caval obstruction syndrome.
   - *Para-aortic abdominal lymph node enlargement* produces pain abdomen and mass abdomen.
3. *Patients may present with PUO (fever),* night sweats, weight loss or pain in the nodes.
4. *Patients may present with the symptoms and signs of basic disease*, e.g. leukemia, lymphoma, acute infections, etc. and lymphadenopathy is a part and parcel of the clinical spectrum.

History

Points to be Noted in History

- Site(s), duration and extent
- Any history of swelling in the axilla or groin
- Any history of pain abdomen or mass abdomen (e.g. spleen and/or liver)
- Any history of fever, night sweats, fatigue, malaise and weight loss
- Any history of cough, dyspnea or hoarseness of voice (for hilar lymphadenopathy)
- Any history of injury or infection of neck or extremity
- **Past history** of fever, tuberculosis, malignancy or injury/infection (HIV)
- **Personal history** including occupation.

General Physical Examination

Examine

- **Face** for puffiness or edema.
- **Mouth** for anemia or evidence of infection, petechiae and pharyngitis (glandular fever).
- **Skin** for evidence of bleeding or infection.
- **Neck**. Examine the various groups of cervical lymph nodes and describe the *number*, *consistency*, *tenderness*, *matting*, *adherence to underlying structures or overlying skin*. Note the *temperature* over the mass. Look for *JVP* and *thyroid*. Examine the neck for *preauricular*, *postauricular*, *submental*, etc. (*Read Clinical Methods in Medicine* by Prof SN Chugh).
  - ★ Examine *axilla* and *inguinal region* in addition to all other sites of lymph node.
- Look for *engorgement of neck/chest veins, suffusion of the face and cyanosis* (e.g. superior mediastinal compression).
- *Pulse*, *BP*, *respiration* and *temperature*
- Look for *anemia*, *jaundice*, *edema*, etc.

Systemic Examinations

I. Examination of Abdomen

- Inspect the abdomen for any swelling or protuberance
- Palpate the abdomen for liver, spleen or lymph node enlargement
- Look for the presence of ascites.

II. Examination of Respiratory System

- Inspect the chest for any retraction or deformity
- Palpate the trachea for any deviation
- Look for any evidence of mediastinal shift due to lung collapse
- *Look for signs of superior mediastinal compression*, e.g. periorbital edema, chemosis, conjunctival suffusion, prominence of neck veins and veins over the chest, absent venous pulsation in the neck.

III. Examination of Hematopoietic System

- Look for any purpuric spots or ecchymotic patches
- Elicit sternal tenderness
- Look for any evidence of infection
- Ocular fundus examination.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis of the patient in picture?

Ans. The presence of a lobulated irregular mass in cervical region with irregular surface, firm in consistency, not mobile, fixed to the skin with formation of a sinus and skin pigmentation indicate a lymph node mass due to tuberculosis, e.g. ***tubercular lymphadenitis with scrofuloderma***.

Q 2. What is differential diagnosis?

Ans. The following conditions come into differential diagnosis of cervical lymphadenopathy:

- Tubercular lymphadenitis, HIV infections
- Infectious mononucleosis
- Hodgkin's and non-Hodgkin's lymphoma, leukemia (ALL)
- Lung carcinoma
- Pyogenic lymphadenitis: Infection in the draining area, i.e. face, neck
- Sarcoidosis.

Q 3. How do you define lymphadenopathy? What is meant by significant lymphadenopathy?

Ans. *Lymphadenopathy* literally means enlargement of lymph nodes which may be significant or insignificant.

Significant lymphadenopathy means enlargement that needs further evaluation. Lymph nodes enlargement ≥1 cm in size anywhere in the body is considered as significant except the groin where ≥2 cm size of the lymph node is considered significant. *Insignificant enlargement* means nonspecific, small lymph nodes usually <0.5 cm in diameter, may be palpable due to past infection.

Q 4. What are common causes of generalised lymphadenopathy?

Ans. The common causes are:

- Tuberculosis
- Infectious mononucleosis
- Toxoplasmosis
- AIDS and other viral infections
- Collagen vascular disorders, e.g. SLE, mixed connective tissue disorders
- Lipid storage disorders, e.g. Gaucher's disease
- Leukemias, e.g. acute and chronic lymphocytic leukemias
- Lymphomas (Hodgkin's and non-Hodgkin's).

Q 5. What is differential diagnosis of a case with regional adenopathy?

Ans. The site of regional lymphadenopathy may provide useful clue to the cause (Table 1.70).

Q 6. How will you proceed to examine a case of lymphadenopathy?

Ans. Points to be noted in lymphadenopathy are:

- Site
- Size and shape
- Consistency or texture (soft, firm, hard, rubbery
- Tenderness (present or absent)
- Fixation (mobile or fixed to the underlying or overlying structures)
- Matted or discrete
- Local temperature is raised or not (hot or cold)
- Change in colour of the skin-scrofuloderma
- Margins-defined or ill-defined
- Associated features
- Associated splenomegaly or hepatosplenomegaly.

Q 7. What are the causes of painful tender lymph nodes?

Ans. The causes are:

1. **Acute inflammation or infection**
   - Viral—infectious mononucleosis
   - Bacterial—pyogenic infections, tuberculosis, brucellosis, plague, diphtheria, leprosy
   - Parasitic—toxoplasmosis
   - Fungal infections.
2. **Immunological causes**
   - SLE and other collagen vascular disorders
   - Rheumatoid arthritis.
3. **Neoplastic**
   - Acute leukemia (lymphoblastic)
   - Metastases in the lymph node.

Table 1.70: Site of involvement of lymph node as a clue to the diagnosis

Site	*Cause(s)*
Occipital adenopathy	Scalp infection
Preauricular adenopathy	Conjunctival infection
Left supraclavicular lymph node (Virchow's gland)	Metastasis from gastric or gastrointestinal cancer
Supraclavicular nodes enlargement	× Tuberculosis, sarcoidosis, toxoplasmosis × Metastases from lung, breast, testis or ovary
Axillary lymphadenopathy	× Injuries of upper limb × Localized infection of ipsilateral upper extremity × Malignancies, e.g. melanoma, lymphoma and breast carcinoma
Inguinal lymphadenopathy	× Infections or trauma of lower extremity, plague × Sexually transmitted diseases, e.g. lymphogranuloma venereum, primary syphilis, genital herpes or chancroid × Lymphomas and metastases from rectum and genitalia
Thoracic lymph nodes (hilar lymphadenopathy)	× Tuberculosis, sarcoidosis, fungal infection × Lymphoma, malignancy lung with metastases in lymph node
Abdominal lymphadenopathy (retroperitoneal, para-aortic)	× Tuberculosis (mesenteric lymphadenitis) × Lymphoma × Metastases from the abdominal viscera

Tenderness or pain in lymphadenopathy is due to stretching of the capsule as a result of rapid or sudden enlargement of lymph node due to any cause.

Q 8. What is the cause of egg-shelled calcification in hilar lymph nodes?

Ans. Silicosis

Q 9. What do you know of Sister Joseph's nodule?

Ans. It refers to a nodule around umbilicus seen in gastric adenocarcinoma, represents either a metastatic deposit or an enlarged anterior abdominal wall lymph node.

Q 10. What are the causes of fixation of the lymph nodes to surrounding structures?

Ans. The **causes** are:

- Tuberculosis
- Malignancy or metastases in the lymph nodes.

Q 11. What are the causes of lymphadenopathy with splenomegaly?

Ans. The **causes** are:

- Infectious mononucleosis
- Lymphoma
- Acute or chronic leukemia especially lymphatic
- Sarcoidosis
- Collagen vascular disorders, e.g. SLE, RA
- Toxoplasmosis
- Cat-scratch disease
- Disseminated or miliary tuberculosis.

Q 12. What are non-Hodgkin's lymphomas?

Ans. They are heterogenous group of malignant disorder of lymphoid tissue involving chiefly the B cells and to some extent T cells. They vary in their presentation and natural history varying from slow indolent course to a rapidly progessive disease.

Q 13. How do you classify non-Hodgkin's lymphoma?

Ans. Previous classification of non-Hodgkin's lymphoma into low grade (slow, indolent and favourable prognosis) and high grade (aggressive, unfavourable) has been replaced by WHO (2001) as follows:

I. **B cell lymphoma**
   - Precursor B cell lymphoma
   - Mature B cell lymphoma.

II. **T/NK cell lymphoma**
   - Precursor T cell lymphoma
   - Mature T/NK cell lymphoma.

The main two groups are further subdivided to include aggressive forms also.

Q 14. What is mode of presentation of Hodgkin's disease?

Ans.
- Usually as a *painless lymph node enlargement* in young age
- Other presenting symptoms include systemic features such as *pyrexia*, *drenching night sweats*, *weight loss*, *pain in the affected lymph nodes* after ingestion of alcohol and generalised itching.

Q 15. How do you stage Hodgkin's disease?

Ans.
Stage I : One lymph node site involved
Stage II : More than 2 lymph nodes sites involved on one side of the diaphragm
Stage III : Lymph nodes involved on both sides of the diaphragm
Stage IV : Disseminated disease with extranodal involvement (e.g. bone marrow, liver)

- **A** means absence of systemic symptoms
- **B** means presence of systemic symptoms, e.g. fever, sweating, weakness and weight loss.

Q 16. What do you understand by the term Hodgkin's disease?

Ans. It is abnormal proliferation of lymphoid tissue (neoplasm of lymphoid tissue), characterised by development of lymphadenopathy at single or multiple sites. The pathological hallmark is *Reed-Sternberg cells* derived from germinal centre B cells, rarely peripheral T cells.

Q 17. What are histological subtypes of Hodgkin's disease?

Ans. The 4 subtypes are:

1. Lymphocyte predominance
2. Nodular sclerosis
3. Mixed cellularity
4. Lymphocyte depletion.

Q 18. How would you treat Hodgkin's lymphoma?

Ans.
- Localised disease (stages IA, IIA) is treated by radiotherapy.
- Disseminated disease (IIIB and IV stages) is treated with combination chemotherapy (e.g. ABVD and MOPP regimen).
- Stages II B and III A are nowadays treated with combination chemotherapy.

Q 19. How will you investigate a case with lymphadenopathy?

Ans. The investigations are done to find out the cause. They are planned depending on the site and type of involvement.

1. **Complete hemogram.** Presence of anemia (low hemoglobin) with lymphadenopathy indicates chronic infections, chronic disorders (e.g. rheumatoid arthritis, or Felty syndrome, SLE) or malignant disease (e.g. leukemias, lymphomas, metastasis). Anemia in these conditions is normocytic and normochromic.

   Complete blood count can provide useful data for diagnosis of acute or chronic leukemia (leukocytosis with immature cells), infectious mononucleosis (leukopenia), lymphoma, pyogenic infections (leukocytosis) or immune cytopenias in illness like SLE.

   Raised ESR suggests tuberculosis, rheumatoid arthritis, SLE, acute infections.

2. **Serological tests**
   - To demonstrate antibodies specific to EBV, CMV, HLV and other viruses, *Toxoplasma gondii*, Brucella
   - VDRL test for syphilis
   - Antinuclear antibodies, LE cell phenomenon and anti-DNA antibodies for SLE and other collagen vascular disorders
   - Rheumatoid factor for rheumatoid arthritis.
3. **Blood culture** for causative organism in acute infections.
4. **Chest X-ray.** It will reveal hilar or mediastinal lymph node enlargement, if any. Unilateral hilar lymph node enlargement usually suggests malignancy lung or tuberculosis; bilateral enlargement indicates sarcoidosis, histoplasmosis or lymphoma.

The chest X-ray will also confirm the involvement of lung in acute infections, tuberculosis, and primary or metastatic lung tumors.

5. **Imaging techniques** (ultrasound, color Doppler ultrasonography, CT scan, MRI) have been employed to differentiate benign from malignant lymph nodes especially in head and neck cancer. These techniques especially USG have been used to demonstrate the ratio of long (L) axis to short (S) axis in cervical nodes. An L/S ratio of <2.0 is used to distinguish between benign and malignant lymph nodes in head and neck cancer and has sensitivity and specificity of 95%. This ratio has greater sensitivity and specificity than palpation or measurement of either the long or short axis alone.

   Ultrasonography or CT scan of abdomen will also reveal lymph node enlargement in the chest and abdomen (mesenteric, para-aortic) which are not palpable on per abdomen examination. These imaging techniques are used for staging lymphomas and to detect enlargement of spleen before it becomes palpable.
6. **Lymph node biopsy.** The indications for lymph node biopsy are:
   - If history and physical findings suggest a malignancy, i.e. a solitary, hard, nontender cervical node in an older patient who is chronic smoker.
   - Supraclavicular lymphadenopathy
   - Generalised or solitary lymphadenopathy with splenomegaly suggestive of lymphoma.
   - A young patient with peripheral lymphadenopathy (lymph node size >2 cm in diameter with abnormal chest X-ray).

Generally, any lymph node >2 cm in diameter should be biopsied for etiological diagnosis.

Fine needle aspiration should not be performed as the first diagnostic procedure. Most diagnoses require more tissue than obtained on FNAC.

CASE 22: SPLENOMEGALY

A female patient (Fig. 1.22A) presented with a mass in the left hypochondrium and associated dragging pain. There was no history of fever, hematemesis or bleeding from any site. She gave history of weakness and exertional dyspnea. No history of jaundice or drug intake or prolonged cough in the past. A mass was palpable in the left hypochondrium.

Clinical Presentations of Splenomegaly

- *Splenomegaly* may be asymptomatic and without any disease.
- *Pain and dragging sensation in the left upper quadrant* is a common presentation with chronic splenomegaly. Massive splenomegaly can produce early satiety.
- *Acute pain in left upper quadrant* may result due to acute splenomegaly with stretching of the capsule or infarction (vascular occlusion of splenic vessels in subacute bacterial endocarditis, sickle cell crisis in children) or inflammation (perisplenitis) of the spleen.
- *Rupture of the spleen* either from trauma or infiltrative disease means rupture of the capsule with intraperitoneal bleeding, may result in shock, hypotension and death. The rupture itself may be painless. The disease associated with rupture of spleen include; *chronic leukemias, myelofibrosis, congestive splenomegaly.*

History

Points to be Noted

- History of abdominal distension
- History of fever, sore throat, bleeding from nose, mouth, rectum, etc.
- History of piles and/or hematemesis, jaundice
- History of palpitation, dyspnea, orthopnea and PND
- Any history of weight loss, fatigue, bone pain, night sweats (CML)
- Is the area endemic for malaria or kala-azar?
- Family history of Gaucher's disease
- *Past history of jaundice, hematemesis, RHD, tuberculosis, malignancy.*

General Physical Examination

Examine

- *Face* for puffiness or edema
- *Mouth* for any evidence of infection, ulceration or excoriation or thrush
- *Tongue and mucous membranes*—look for anemia
- *Neck* for lymphadenopathy, JVP, thyroid enlargement
- *Pulse, BP, respiration* and *temperature*
- *Hands* for clubbing, splinter hemorrhage, Roth's spots, gangrene
- *Feet* for edema
- Normally, the spleen is neither palpable nor becomes palpable unless enlarged by two and half times, hence, spleen may be enlarged but not palpable. Therefore, percussion of 9th, 10th and 11th space (*Traube's area*) is a useful diagnostic technique.

Systemic Examinations

I. Examination of Abdomen

- ***Look for any swelling or protuberance of abdomen*** especially in left hypochondriac region.
- ***Palpate the abdomen*** for enlargement of spleen, liver and lymph nodes. In case spleen or liver is enlarged, note the details of characteristics of liver or splenic mass.
- **Rule of palpation for spleen** (Fig. 1.22B)**:** Start low while examining the spleen and be gentle during palpation. Even if you are certain it is spleen, you must follow the rules of palpation of spleen to rule out renal mass. Do not forget to do a bimanual palpation (spleen is bimanually palpable and kidney is ballottable). Feel for the splenic notch and auscultate for the splenic rub.
- **Percussion over the mass**. In a case with splenomegaly percuss for Traube's area for dullness. In case of hepatomegaly, define the upper border of liver dullness on percussion and record the liver span by measurement.
- **Auscultate over the mass** for any rub, bruit, etc.

II. Examination of Respiratory System

- *Examine for signs of hilar lymphadenopathy (e.g. superior mediastinal syndrome—read short case discussion on it)*

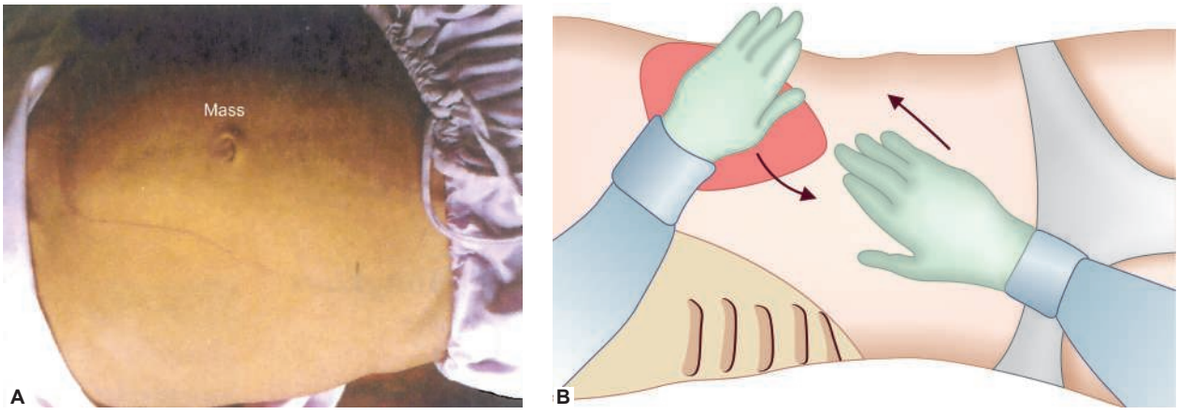


Fig. 1.22A and B: A. A patient with massive (>8 cm) splenomegaly producing left hypochondriac protrusion; **B.** Method of palpation for splenomegaly (diagram)

- Look for signs of LHF (orthopnea, cyanosis, crackles at the bases of lungs).

III. Examination of CVS

- Inspect the precordium for any precordial bulge or cardiac enlargement
- Palpate the apex for any evidence of derivation/shift or thrill
- Auscultate the heart for sounds, murmurs or rub and for evidence of LVF or pericardial disease especially pericardial effusion or rheumatic valvular disease.

IV. Examination of Blood

- Look for signs of hemorrhage or bleeding into the skin or organ
- Elicit sternal tenderness.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. Massive splenomegaly due to chronic myeloid leukemia.

Q 2. What are the points in favour of your diagnosis?

Ans. 1. History of fever, bone pains, night sweats, dyspnea
2. Presence of anemia and sternal tenderness
3. Massive (>8 cm) non-tender splenomegaly.

Q 3. How do you define splenomegaly?

Ans. *Splenomegaly* literally means enlargement of spleen.

- Palpable spleen means its enlargement 2 to 3 times than normal.
- Normal spleen measures 12 7 cm on ultrasonography, radionuclide scan and CT scan.
- Spleen is palpable in 1–3% normal individuals without any cause. Its incidence in normal population in New Guinea has been reported to be very high (up to 60%).
- Spleen is said to be enlarged if its span on USG is >14 cm.

Q 4. What is differential diagnosis of massive splenomegaly (>8 cm)?

Ans. The following conditions must be considered:

- Chronic malaria
- Kala-azar
- Chronic myeloid leukemia/hairy cell leukemia myelofibrosis/myelosclerosis
- Gaucher's disease.

N.B.: Read the characteristics of these disorders as well as that of spleen in case discussion of hepatosplenomegaly.

Q 5. Which bedside investigation would you carry out to confirm the diagnosis?

Ans. Peripheral blood film examination for total leucocyte count and immature cells. Immature cells >30% will clinch the diagnosis.

Q 6. Name the conditions producing moderate splenomegaly.

Ans. Read Table 1.71.

Q 7. What are the causes of mild splenomegaly (e.g. spleen is just palpable)?

Ans. Read the Table 1.71.

Q 8. What are the causes of palpable spleen without enlargement?

Ans. Normally, spleen may be palpable without being enlarged in:

- Some children below 10 years of age
- Thin lean persons
- COPD (spleen is pushed down by hyperinflated lung
- Visceroptosis (drooping of viscera including spleen).

Q 9. What are the causes of splenomegaly with fever?

Ans. Spleen enlarges within a few days to a few weeks of fever. **Causes** are:

- Bacterial endocarditis
- Acute malaria
- Kala-azar
- Tuberculosis
- Infectious mononucleosis
- Histoplasmosis
- Typhoid fever
- Acute leukemia

Table 1.71: Causes of various grades of splenomegaly

Mild (<3 cm)	*Moderate (3–8 cm)*	*Massive (>8 cm)*
× Congestive heart failure	× Cirrhosis of the liver with portal hypertension	× Chronic malaria and kala-azar
× Bacterial endocarditis	× Lymphomas	× Chronic myeloid leukemia (CML)
× Typhoid fever	× Hemolytic anemia	× Myelofibrosis/myelosclerosis
× SLE	× Infectious mononucleosis	× Chronic lymphatic leukemia (CLL)
× Acute malaria (chronic malaria produces massive splenomegaly)	× Amyloidosis	× Hairy cell leukemia
× Rheumatoid arthritis, sarcoidosis	× Chronic lymphatic leukemia	× Gaucher's disease in children
× Glandular fever (infectious mononucleosis)	× Hairy cell leukemia	
× Idiopathic thrombocytopenic purpura	× Splenic abscess or cyst	
× Polycythemia	× Idiopathic thrombocytopenic purpura	

- Lymphoma
- SLE
- Hemolytic crisis.

Q 10. What are the causes of splenomegaly with Anemia?

Ans. The **causes** are:
- Bacterial endocarditis
- Hemolytic anemia
- Cirrhotic portal hypertension with repeated hematemesis
- Myeloproliferative disorders
- Malaria
- Felty's syndrome
- SLE
- Rheumatoid arthritis.

Q 11. What are the causes of splenomegaly with jaundice?

Ans. Jaundice may be hemolytic or hepatic. **Causes** are:
- Cirrhosis of the liver
- Acute viral hepatitis (uncommon)
- Acute malaria (*P. falciparum*) due to hemolysis
- Hepatic vein thrombosis (Budd-Chiari syndrome)
- Hemolytic anemia
- Lymphoma
- Miliary tuberculosis.

Q 12. What are the common causes of fever, lymphadenopathy, splenomegaly with or without rash?

Ans. The **conditions** are:
- Infectious mononucleosis
- Sarcoidosis
- Acute leukemia or blast crisis in chronic leukemia
- SLE
- Lymphoma
- Felty's syndrome.

Q 13. What are the causes of splenomegaly with ascites?

Ans. The **causes** are:
- Portal hypertension
- Budd-Chiari syndrome
- Lymphoma
- CML
- Constrictive pericarditis.

Q 14. What are the causes of splenic rub? Where do you hear it? What does it indicate?

Ans. **Splenic rub** can be heard over the enlarged spleen with stethoscope in conditions associated with splenic infarction (*perisplenitis*) due to vascular occlusion of spleen. The patient complains of acute left upper quadrantic pain abdomen which may radiate to tip of left shoulder. The spleen is enlarged and tender. The **causes** are:
- Subacute bacterial endocarditis
- Chronic myeloid leukemia
- Sickle cell anemia
- Following splenic puncture for diagnosis of kala-azar.

Splenic rub is heard over the spleen or left lower chest during respiration.

Q 15. What is hypersplenism? What are its causes?

Ans. *Hypersplenism* refers to overactivity of the splenic function, has nothing to do with the size of the spleen. It is characterized by a tetrad consisting of:
- Splenomegaly of any size
- Cytopenias/pancytopenias (anemia, leukopenia and/or thrombocytopenia)
- Normal or hypercellular marrow
- Reversibility following splenectomy.

Causes of hypersplenism are
- Lymphoma
- Cirrhosis of the liver
- Myeloproliferative disorders
- Connective tissue disorders.

Q 16. What are causes of hyposplenism or asplenia?

Ans. It refers to virtual absence of spleen (asplenia) or malfunctioning spleen (hyposplenism).
Causes are:
- Associated with dextrocardia
- Sickle cell disease leading to multiple infarcts
- Celiac disease
- Fanconi's anemia (aplastic anemia with hypoplasia of spleen, kidney, thymus, etc.)
- Surgical removal of the spleen
- Splenic irradiation for autoimmune or neoplastic disease.

Q 17. How will you investigate a patient with splenomegaly?

Ans. The investigations to be done are:
- **Hemoglobin and RBCs count.** Hemoglobin is low in thalassemia major, SLE, cirrhotic portal hypertension and increased in polycythemia rubra vera.
- **WBC count.** Granulocyte counts may be normal, decreased (Felty's syndrome, congestive splenomegaly, aleukemic leukemia) or increased (infections, or inflammatory disease, myeloproliferative disorders).
- **Other investigations** are same as discussed under hepatosplenomegaly (read them there).

Q 18. What are indications of splenectomy (removal of spleen)?

Ans. **Indications** are:
1. For correction of cytopenia in immune-mediated destruction of one or more cellular blood elements, e.g. in immune thrombocytopenia
2. For sickle cell crises (splenic sequestration) in young children
3. Hereditary spherocytosis
4. For correction (reversibility) of cytopenias in patients with hypersplenism

5. For disease control in patients with splenic rupture
6. More often splenectomy is performed in stage III and stage IV of Hodgkin's disease
7. For symptom control in patients with painful massive splenomegaly in CML unresponsive to chemotherapy.

Q 19. What are the clinical manifestations of splenectomy?

Ans.
- The immediate manifestation within 2–3 weeks is ***leukocytosis and thrombocytosis***.
- **Marked variations in size and shape of RBCs** (anisocytosis, poikilocytosis)
- **Presence of Howell-Jolly bodies** (nuclear remnants), **Heinz bodies** (denatured Hb), **basophilic stippling** and an occasional **nucleated** RBC in the peripheral blood.

Q 20. What will be the consequences of splenectomy?

Ans. The **consequences** will be:

1. The most serious consequence of splenectomy is *predisposition to bacterial infections*, particularly with *S. pneumoniae, H. influenzae* and some gram-negative enteric organisms. They should be immunized against these organisms. The vaccination recommended are given in the box below.
2. The splenectomized patients are more *susceptible to a parasitic disease—babesiosis*, hence, they should avoid visit to areas where the parasite—Babesia is endemic.

Vaccination before and after splenectomy

The Advisory Committee on Immunization Practices recommends that pneumococcal vaccine should be administered to all patients before elective splenectomy and a repeat dose of vaccination 5 years later.

The vaccination against *N. meningitidis* should also be given to patients in whom elective splenectomy is planned.

Q 21. What is abscopal effect?

Ans. Tumor regression or regression of systemic illness following splenectomy or splenic irradiation in patients with CML and prolymphocytic leukemia is known as abscopal effect.

Q 22. What is Traube's area? What is its significance?

Ans. Normal Traube's area is bounded above by the lung resonance, below by the costal margins; on the right by left border of the liver and on the left by the normal splenic dullness. It lies in left lower chest behind 9th, 10th and 11th ribs.
- Normally, it is resonant because it is occupied by stomach (tympanic note)
- It becomes dull in:
  - Left side pleural effusion
  - Splenomegaly
  - Distended stomach with fluid or solid growth.

COMMONLY ASKED QUESTIONS

Q 23. What are differences between a splenic and left renal mass?

Ans. Read *Clinical Methods* by Prof SN Chugh.

Q 24. How will you palpate spleen in the presence of ascites?

Ans. For method of palpation of spleen (Fig. 1.22B), read Clinical Methods. However, in the presence of ascites, spleen is palpated by dipping method.

Q 25. What are characteristics of a splenic mass?

Ans. Read *Clinical Methods in Medicine*.

Q 26. What are other causes of mass in left hypochondrium?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

CASE 23: HEPATOSPLENOMEGALY

The patient (not in picture) presented with gradual onset of fever, malaise, weakness. There was history of masses in the abdomen with dyspnea, pallor. Patient gave history of taking antimalarial drug following which the fever subsided.

Clinical Presentations of Hepatosplenomegaly

These patients usually present either with dull ache or pain in right and left hypochondrium, but most of the time they may complain of masses in the abdomen (Fig. 1.23).

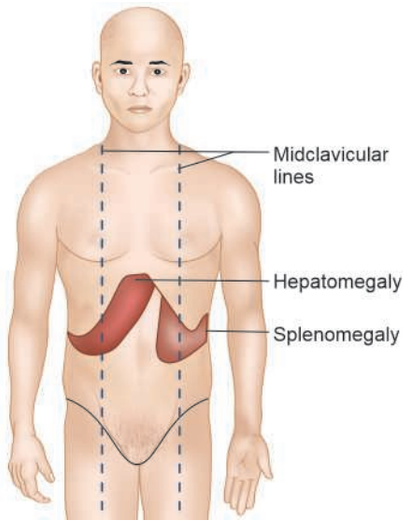


Fig. 1.23: Hepatosplenomegaly—a diagram

History

Points to be Noted

- History of fever or sore throat, jaundice, bleeding from any site
- History of palpitation, breathlessness, orthopnea, PND
- Any history of infection, mouth ulcerations, mouth thrush, excoriation, etc.
- History of pallor, fever, dark urine.

General Physical Examination

Look at

- ***Face*** for puffiness, edema
- ***Mouth*** for ulceration, excoriation or thrush
- ***Tongue*** for anemia. Look other sites for anemia
- ***Neck*** for lymph node enlargement, PVP and thyroid enlargement
- ***Pulse***, ***BP***, ***temperature*** and ***respiration***
- ***Hands*** for koilonychia, platynychia, splinter hemorrhage, clubbing
- ***Feet*** for edema.

Systemic Examination

I. Abdomen

- Look for any swelling or bulge
- Palpate the masses in the abdomen and describe their characteristics
- Percuss for Traube's area for splenic dullness and define the upper border of the liver for its enlargement and liver span measurement
- Auscultate over the mass(es) for any bruit or rub.

II. CVS Examination

- Examine the heart for any enlargement, murmur, sounds or rub
- Look for the signs of valvular heart disease, LVF, SABE and pericardial disease especially pericardial effusion.

III. Examination of Blood

- Look for any hemorrhage into the skin or joint or organ
- Examine ocular fundi for hemorrhage.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. Hepatosplenomegaly

Q 2. What are the causes of hepatosplenomegaly?

Ans. The **causes** are:

1. **Infections,** e.g. malaria, kala-azar, typhoid, acute miliary or disseminated tuberculosis, viral hepatitis (occasional) and brucellosis
2. **Blood disorders,** e.g. hemolytic anemia, chronic myeloid leukemia, lymphoma, polycythemia rubra vera, chronic lymphatic leukemia, acute leukemias
3. **Extramedullary erythropoiesis,** e.g. myelofibrosis, myelosclerosis
4. **Diseases of liver,** e.g. cirrhosis, Budd-Chiari syndrome
5. **Congestive hepatosplenomegaly,** e.g. pericardial effusion, constrictive pericarditis and congestive cardiac failure (cardiomyopathy)
6. **Infiltrative disorders,** e.g. amyloidosis
7. **Miscellaneous,** e.g. sarcoidosis.

Q 3. What is the differential diagnosis of hepatosplenomegaly in an adult?

Ans. The conditions that come into differential diagnosis are discussed below.

Chronic Malaria

The characteristic features are:

- Patient belongs to an endemic zone
- Fever with chills and rigors. Fever may come on alternate days periodically
- Anemia and mild jaundice may be present if hemolysis occurs
- Massive splenomegaly with moderate hepatomegaly, firm to hard and nontender
- Diagnosis is confirmed by demonstration of the parasite in the peripheral blood.

Chronic Kala-azar

- Patient belongs to an endemic area
- Double rise or peak in temperature (biphasic pattern) in 24 hours may be present
- Patient is well despite symptoms and signs
- The skin is dry and pigmented
- Hepatosplenomegaly in which spleen is massively enlarged while liver enlargement is moderate. Both are firm and nontender.
- The diagnosis is confirmed by demonstration of LD bodies in buffy coat preparations of blood or in the bone marrow smear or lymph node, liver, or spleen aspirates (splenic puncture).

Thalassemia (Cooky's Anemia)

- A heredofamilial disorder of hemoglobin (hemoglobinopathy) hence, die patient is usually a child or young person with positive family history.
- Stunted growth and mongoloid facies
- Moderate hepatosplenomegaly, nontender, soft to firm
- Severe anemia and mild jaundice (hemolysis)
- Anemia is microcytic hypochromic
- Leg ulcers
- Diagnosis is confirmed by radiological study of skull and presence of abnormal hemoglobin (HbF >2%) on electrophoresis.

Hemolytic Anemia

- Gradual onset of anemia
- Mild jaundice
- Dark coloured urine and stool during an episode of hemolysis
- Moderate nontender hepatosplenomegaly
- Positive tests for hemolysis will confirm the diagnosis.

Chronic Myeloid Leukemia

- Patient is middle-aged or old-aged person with slow onset of symptoms.
- The presenting symptoms are dragging pain in left hypochondrium due to massive splenomegaly and profound weakness, weight loss and sweating.
- Moderate anemia.
- Hepatosplenomegaly due to extramedullary erythropoiesis. The spleen is massively enlarged (>8 cm), firm to hard and occasionally a splenic rub may be present if a splenic infarct occurs. The liver is moderately enlarged.
- Sternal tenderness is present.
- Diagnosis is confirmed by presence of anemia, high WBC count (in lakh) with immature WBCs (myelocytes, metamyelocytes and promyelocytes with few myeloblasts (<10%).

Lymphoma

- Painless progressive enlargement of cervical, axillary and inguinal lymph nodes, discrete, firm, but rubbery in consistency in Hodgkin's lymphoma
- Fever, weight loss, weakness, pruritus with drenching night sweats may occur
- Moderate hepatosplenomegaly
- Moderate anemia
- Eosinophilia present
- Lymph node biopsy is diagnostic.

Cirrhosis (Postnecrotic) of Liver

- Symptoms and signs of chronic liver disease, e.g. weakness, malaise, muscle wasting.
- Past history of jaundice, e.g. viral hepatitis.
- Features of portal hypertension, e.g. hematemesis, melena, splenomegaly, fetor hepaticus, caput medusae or distended veins on the abdomen with ascites.
- Moderate hepatosplenomegaly, firm, nontender.
- Diagnosis is made by esophageal varices, splenoportal venography and liver biopsy
- Presence of other stigmatas of cirrhosis (read case discussion on cirrhosis of the liver).

Budd-Chiari Syndrome (Hepatic Vein Thrombosis)

- Gradual onset of symptoms.
- The triad of signs and symptoms includes: gross intractable ascites, jaundice and massive tender hepatomegaly.
- Splenomegaly will occur along with hepatomegaly in patients who develop portal hypertension. Other signs of portal hypertension will also appear.
- Peripheral edema is present if there is inferior vena cava obstruction
- The diagnosis is confirmed on (i) *Doppler ultrasound* (obliteration of hepatic veins, reversed flow or associated portal vein thrombosis), (ii) *CT scan* showing enlargement of caudate lobe, (iii) *hepatic venography* showing obstruction of hepatic veins, and (iv) *liver biopsy* demonstrates centrilobular congestion with fibrosis.

Enteric Fever

- History of fever which rises in step-ladder pattern, headache, diarrhea or constipation, epistaxis, cough, rose spots over skin and relative bradycardia.
- The tongue is red (angry-looking).
- Mild to moderate hepatosplenomegaly which is soft and tender, appears on 7 to 10th of fever.
- Diagnosis is confirmed by blood culture and rising titers of antibodies on widal test.

Myelofibrosis/Myelosclerosis

- It may be primary or secondary to toxins, malignant infiltration of bone marrow, lymphoma or irradiation.
- Massive splenomegaly with moderate hepatomegaly due to extramedullary hematopoiesis. Splenic rub may be present occasionally.
- Leucoerythroblastic blood picture with high platelet count.

- Ground glass appearance of bones on X-ray
- Bone marrow examination may yield a 'dry tap', hence, trephine biopsy is needed to confirm the diagnosis.

Miliary Tuberculosis

- Gradual onset of symptoms with fever, anorexia, weight loss and night sweats
- Cough, breathlessness, headache, hemoptysis may be present
- Tachycardia, tachypnea with few chest signs such as fine crackles
- Mild to moderate hepatosplenomegaly
- Signs of meningitis may be present. CSF shows changes of meningitis
- Fundus examination may reveal choroid tubercles (25% cases)
- Leukocytosis is absent
- Mantoux test is negative
- Chest X-ray shows miliary mottling shadows widely distributed in both the lungs
- Sputum examination may or may not be positive.

Amyloidosis

- It is secondary to suppurative lung disease (lung abscess, bronchiectasis), Crohn's disease, multiple myeloma, rheumatoid arthritis, leprosy
- Macroglossia may be present
- Mild to moderate hepatosplenomegaly
- Evidence of renal involvement, i.e. massive proteinuria (nephrotic syndrome)
- Other associated involvement includes malabsorption, lymphadenopathy, peripheral neuropathy, cardiomyopathy
- The diagnosis is confirmed on liver, gingival or rectal biopsy.

COMMONLY ASKED QUESTIONS ARE 4–9

Q 4. What are the causes of fever with hepatosplenomegaly?

Ans. The presence of fever indicates infection or inflammation, hence, may be associated with leukocytosis or leukopenia. The **causes** are:

- *Parasitic infections*, e.g. malaria, kala-azar
- *Bacterial infection*, e.g. enteric fever, brucellosis, miliary tuberculosis
- *Viral infection*, e.g. acute lupoid hepatitis
- *Acute leukemia* and *lymphoma*
- *Hemolytic crisis*.

Q 5. What are the causes of hepatosplenomegaly with lymphadenopathy?

Ans. The liver, spleen and lymph nodes constitute the lymphoreticular system, hence, the disorders involving this system will produce their enlargement such as:

1. Acute leukemia especially ALL in children
2. Lymphoma (Hodgkin's and non-Hodgkin's)
3. Miliary tuberculosis
4. Sarcoidosis
5. AIDS
6. Infectious mononucleosis
7. Collagen vascular disorders, e.g. SLE.

Q 6. What are the causes of hepatosplenomegaly with jaundice?

Ans. Jaundice in presence of hepatosplenomegaly occurs either due to decompensation of liver or infection of the liver or due to hemolysis. The **causes** are:

1. Cirrhosis of the liver with decompensation
2. Budd-Chiari syndrome (hepatic vein thrombosis)
3. Lupoid hepatitis
4. Malaria (falciparum infection producing hemolysis)
5. Lymphoma (especially non-Hodgkin's)
6. Miliary tuberculosis.

Q 7. What are conditions that produce hepatosplenomegaly with ascites?

Ans. Ascites in the presence of hepatosplenomegaly may be a sign of portal hypertension or hepatocellular failure or may be due to malignant infiltration of the peritoneum. The **causes** are:

1. Malignancy of liver with portal hypertension
2. Cirrhosis of the liver with portal hypertension
3. Budd-Chiari syndrome with portal hypertension
4. Chronic myeloid leukemia
5. Lymphoma (non-Hodgkin's)
6. Subacute or lupoid hepatitis with or without hepatocellular failure.

Q 8. What are the causes of congestive hepatosplenomegaly?

Ans. The **conditions** are:

- Congestive heart failure
- Pericardial effusion/constrictive pericarditis
- Budd-Chiari syndrome
- Extramedullary erythropoiesis, e.g. chronic myeloid leukemia, myeloid metaplasia.

Q 9. How will you investigate a case of hepatosplenomegaly?

Ans. The **investigations** to be done are:

1. **TLC and DLC.** Leukocytosis indicates pyogenic infections, polycythemia and leukemia while leukopenia occurs in malaria, enteric fever, kala-azar. Pancytopenia indicates hypersplenism.
2. **Peripheral blood film** for MP, kala-azar (LD bodies) and hemolytic anemia (abnormal type of cells) or other types of anemia. Reticulocytosis indicates hemolytic anemia. Presence of premature WBCs indicate leukemia (acute or chronic).
3. **Blood culture** for enteric.
4. **Special tests**
   - Paul-Bunnell test for infectious mononucleosis
   - Widal test for typhoid and Brucella

- Serum bilirubin for jaundice
- Aldehyde test for kala-azar
- Tests for hemolysis, e.g. osmotic fragility, Coombs' test.

5. **Radiology**
   - ***Chest X-ray for***
     - Miliary tuberculosis (miliary mottling)
     - Lymphoma and sarcoidosis (mediastinal widening due to mediastinal lymphadenopathy)
   - ***X-ray bones***
     - Skull ('hair on end' appearance in thalassemia)
     - Long bones, e.g. expansion of lower ends of the bone in Gaucher's disease. Increased density of the bones in myelofibrosis or myelosclerosis.
6. **USG of abdomen**
   - To confirm hepatosplenomegaly
   - To detect the presence of ascites, portal hypertension (portal vein diameter >14 mm) and dilated venous collaterals.
   - To detect echogenic pattern of the liver (heterogenous pattern indicates cirrhosis).
7. **Biopsy**
   - Lymph node biopsy for tuberculosis, sarcoidosis and lymphoma
   - Liver biopsy for cirrhosis of the liver and amyloidosis
   - Bone marrow biopsy (trephine) for myelofibrosis
   - Bone marrow aspiration for leukemia, lymphoma, Gaucher's disease and, hypersplenism (pancytopenia with hypercellular marrow), splenic aspirate for kala-azar.
8. **Skin tests**
   - Mantoux test for tuberculosis
   - Kveim test for sarcoidosis (not done nowadays).
9. **CT scan of abdomen**
   - To detect lymph node enlargement
   - To confirm the findings on USG
   - To stage the lymphoma.

CASE 24: THYROTOXICOSIS

The young female (Fig. 1.24) presented with palpitation, drenching sweats and a neck swelling. There was history of off and on loose motions and she had lost 3 kg weight past 1 month.

Examination of the patient revealed—tachycardia, rapid collapsing pulse, exophthalmos, staring look, lid lag and lid retraction. The thyroid was enlarged with smooth texture. A bruit was heard over the thyroid.

Clinical Presentations of Thyrotoxicosis

- *Patients usually present with goiter* (swelling in the neck) and symptoms of thyrotoxicosis. These are cases of Graves' disease and nodular goiter (Fig. 1.24).

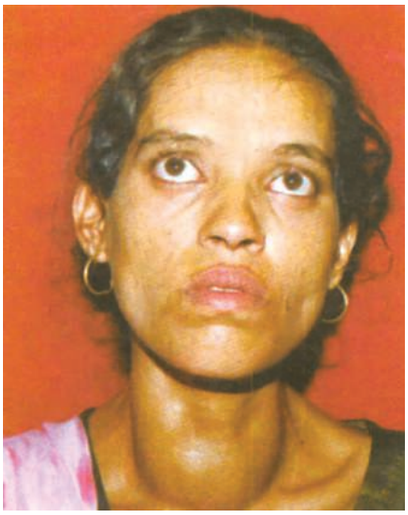


Fig. 1.24: Graves' disease

- *Patients may present with unexplained weight loss* inspite of good appetite, without any diarrhea or malabsorption. These are usually cases of occult thyrotoxicosis.
- *Patients may present with arrhythmias (atrial fibrillation)* especially old patients.
- *The young patients present with symptoms of sympathetic overactivity*, i.e. palpitations, nervousness, sweating, insomnia, tremulousness, weakness, menstrual irregularity (in females).
- *Patients may present with psychiatric manifestations*, e.g. irritability, anger, hyperactivity, depression.

Note: Patients present with variety of ways because thyrotoxicosis disturbs the general metabolism in such a way that every system is affected and patient may present with symptoms related to any system.

History

Points to be Noted

- Record the chief complaints in chronological order and describe their details
- Ask for any restlessness, irritability, behaviour change, hyperexcitability
- Ask for weight loss, increased appetite, nausea, vomiting, diarrhea
- Ask for palpitation, breathlessness, heat intolerance
- Ask for menstrual irregularity, loss of libido, gynecomastia, hair loss, etc.
- Ask for proximal muscle weakness or periodic paralysis.

General Physical Examination

- Look at the *face* for perspiration, staring look, exophthalmos, loss of frowning or wrinkling
- *Look for eye signs* of thyrotoxicosis, e.g. lid lag, lid retraction, exophthalmos, ophthalmoplegia, loss of accommodation
- *Examine neck for thyroid enlargement*. Describe the size, shape, measurement, palpate thyroid for smooth texture or nodularity and auscultate for bruit. Examine the neck veins for JVP
- *Record the pulse* (AF), *BP* (wide pulse pressure), *temperature* and *respiration*
- Look at the hands for *tremors*, *clubbing*, *moistness*, *perspiration*, *warmth*, *palmar erythema*. Shake hands with the patient to note sweaty palms
- Examine *feet for edema* and *legs for pretibial myxedema*.

Systemic Examinations

I. CVS Examination

- Inspect the apex beat and look for cardiac enlargement
- Palpate the apex beat, define its location and other characters
- Percuss the heart for cardiomegaly
- Auscultate the heart for third heart sound, murmur(s) or any other abnormal sound or rub.

II. Respiratory System

Examine for crackles and rales for LVF.

III. Nervous System

- Higher function testing for psychosis
- Abnormal movements, e.g. tremors, choreoathetosis
- Examine for peripheral neuropathy, proximal myopathy, etc.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis of the patient in Fig. 1.24?

Ans. The young female has symptoms and signs suggestive of thyrotoxicosis with diffuse thyroid enlargement. The probable diagnosis is **Graves' disease**.

Q 2. How do you define thyrotoxicosis?

Ans. *Thyrotoxicosis* implies a state of hyperthyroidism in which the thyroid hormone is toxic to the tissues producing clinical features; while *hyperthyroidism* simply implies excessive thyroid function. However, both are not synonymous, yet are used interchangeably.

Q 3. What is Graves' disease?

Ans. It is an autoimmune disorder characterised by *hyperthyroidism, diffuse goiter, ophthalmopathy and dermopathy (pretibial myxedema) and thyroid acropachy (clubbing of fingers)*. A thyroid scan and antithyroid antibodies (TPO, TRAb) are diagnostic.

Q 4. What is the differential diagnosis of thyrotoxicosis?

Ans. The two common conditions causing thyrotoxicosis are compared in Table 1.72.

Table 1.72: Differential diagnosis of thyrotoxicosis

Feature	*Graves' disease*	*Toxic multinodular goiter*
Age	Young age	Old age
Sex	Common in females	Common in females
Goiter	Diffuse, firm, smooth. Bruit is heard commonly	Nodular, firm to hard, irregular surface. No bruit
Eye signs	Common	Uncommon
Dermopathy (pretibial myxoedema)	May occur	Does not occur
Thyroid bruit	Common	Uncommon
Severity of thyrotoxicosis	Moderate to severe	Mild to moderate
Atrial fibrillation	Uncommon	Common
Compressive symptoms	Uncommon	Common
Cause	Autoimmune, may be associated with other autoimmune diseases	Autonomous
Treatment of choice	Drug therapy	Surgery or radioactive iodine

Q 5. What are the causes of thyrotoxicosis?

Ans. Causes of thyrotoxicosis are described in Table 1.73.

Q 6. What are symptoms and signs of thyrotoxicosis?

Ans. See the Table 1.74. The symptoms and signs are due to sympathetic stimulation induced by excess of thyroid hormones.

Table 1.73: Causes of thyrotoxicosis

Common (>95%)	*Less common (3–5%)*	*Rare (<1%)*
Graves' disease	Thyroiditis, e.g. subacute (de Quervain's and postpartum)	Pituitary or ectopic TSH by a tumor
Multinodular goiter	Drug-induced (e.g. amiodarone, radioactive contrast media or iodine prophylaxis program)	Thyroid carcinoma
Autonomously functioning solitary thyroid nodule	Factitious (self-induced)	
	Struma ovarii	

Table 1.74: Symptoms and signs of Graves' disease or hyperthyroidism

1. **Goiter** (e.g. diffuse or rarely nodular)
2. **Gastrointestinal**
   - Weight loss in spite of good appetite, vomiting, diarrhea or steatorrhea
3. **Cardiovascular**
   - High resting pulse rate or tachycardia, good volume pulse with wide pulse pressure (>60 mm Hg)
   - Exertional dyspnea, systolic hypertension
   - Arrhythmias (atrial fibrillation is common)
   - Precipitation of angina in a patient, with ischemic heart disease or cardiac failure
4. **Neuromuscular**
   - Nervousness, irritability, restlessness, psychosis
   - Tremors of hands
   - Proximal myopathy, exaggerated tendon reflexes
5. **Dermatological**
   - Perspiration (moist hands, increased sweating or hyperhydrosis). Warm and vasodilated peripheries
   - Clubbing of fingers (rare), loss of hair
   - Pretibial myxedema, thyroid acropachy
   - Redness of palms (palmar erythema)
6. **Reproductive**
   - Menstrual irregularity (amenorrhea is common)
   - Abortions, infertility, loss of libido or impotence
7. **Ophthalmological**
   - Lid lag or lid retraction, staring look
   - Wide palpebral fissure, exophthalmos
   - Diplopia or ophthalmoplegia, excessive watering of eyes
8. **Miscellaneous**
   - Heat intolerance, excessive thirst
   - Outburst of anger, fatigability or apathy

Q 7. How do you classify the eye changes in Graves' disease?

Ans. Many scoring systems have been used to gauge the extent and severity of orbital changes in Graves' disease. As a mnemonic, the NOSPECS scheme is used to class the eye signs as follows:

0 = **N**o sign or symptom
1 = **O**nly sign (lid lag or retraction), no symptoms
2 = **S**oft tissue involvement (pretibial myxedema)
3 = **P**roptosis (>22 mm)
4 = **E**xtraocular muscle involvement (diplopia)
5 = **C**orneal involvement
6 = **S**ight loss.

Q 8. How would you assess proptosis?

Ans. It is assessed by Hertel's exophthalmometer (>20 mm is considered as an exophthalmos).

Q 9. What is pretibial myxedema?

Ans. Pretibial myxedema is a late manifestation of Graves' disease.

The name justifies the site of skin changes, i.e. over the anterior and lateral aspects of the lower leg in front of tibia. The typical skin change is noninflamed, indurated, pink or purple colour plaque giving an 'orange-skin' appearance. Nodular involvement can uncommonly occur.

Q 10. What are various types of pretibial myxedema?

Ans. 1. Nonpitting edema accompanied by hyperkeratosis pigmentation and pinkish, brownish red or yellow discolouration.
2. Plaque form consisting of raised, discrete or confluent plaques.
3. Nodular form characterised by formation of nodules.

Q 11. How will you investigate a case of thyrotoxicosis?

Ans. The investigations to be performed are:

1. **Measurement of radioactive iodine uptake.** It is increased.
2. **Thyroid hormones**. The total or free T3 and T4 are increased while TSH is decreased in primary thyrotoxicosis (Graves' disease or MNG); while all the three are increased in secondary (pituitary or ectopic) thyrotoxicosis.
3. **Ultrasound of thyroid** will demonstrate either the diffuse (Graves' disease) or multinodular goiter.
4. **Thyroid scan.** A radionuclide scan of thyroid either by ^{131}I or ^{99m}Tc will demonstrate functioning thyroid tissue. It will show diffuse increased uptake in Graves' disease but increased or decreased uptake in multinodular goiter. A **hot nodule** means increased uptake while **cold nodule** indicates decreased uptake. Thyroid scan will also detect an ectopic thyroid tissue in the neck or chest.
5. **Antithyroid antibodies.** Antithyroid antibodies are detected in Graves' disease and Hashimoto's thyroiditis. TRAb antibodies and TPO antibodies are raised in Graves' disease.
6. **Needle biopsy** of the diyroid is done in MNG to detect underlying malignancy.
7. **Other tests** such as ECG for tachycardias and arrhythmias.
   - CT scan or MRI, TSH suppression tests for pituitary origin of thyrotoxicosis.
8. **Other biochemical abnormalities** are: (i) Raised bilirubin and transferases, (ii) Raised calcium and glycosuria or impaired glucose tolerance. These are due to other autoimmune diseases associated with it.

Q 12. What are the causes of low TSH?

Ans.
- Subclinical hyperthyroidism
- Overt hyperthyroidism
- First trimester of pregnancy
- Medications, e.g. dopamine, steroids
- Nonthyroidal illness with low free T4.

Q 13. Name the other autoimmune diseases associated with thyrotoxicosis.

Ans. These are:
- Diabetes mellitus
- Hyperparathyroidism
- Chronic active hepatitis
- Autoimmune hemolytic anemia.

Q 14. What is subclinical hyperthyroidism?

Ans. In this condition, the serum T3 and T4 are either normal or lie in the upper limit of their respective reference range and the serum TSH is undetectable. This combination is found in patients with nodular goiter. These patients are at increased risk of atrial fibrillation and osteoporosis, hence, the consensus view is to treat such cases with ^{131}I. As these cases can transform to overt hyperthyroidism, therefore, annual review is mandatory.

Q 15. What is thyroiditis (hyperthyroidism with reduced iodine uptake)?

Ans. In patients with hyperthyroidism, the radioactive iodine uptake (RAIU) is usually high but a low or negligible uptake of iodine indicates thyroiditis (subacute or postpartum). If a RAIU test is not routinely performed in patients with hyperthyroidism, such cases are likely to be missed and inappropriate treatment may be given.

1. **Subacute (de Quervain's) thyroiditis.** It is a viral-induced (*coxsackie, mumps, adenovirus*) thyroiditis in which there is release of colloid and thyroid hormones into circulation leading to hyperthyroidism.

   It is characterised by *fever*, *pain in the region of thyroid gland* which may radiate to angle of the jaw and the ears, made worse by swallowing, coughing and movements of neck. The thyroid gland is enlarged and tender. It is seen in young females 20–40 years.

   The thyroid hormone levels are high for 4–6 weeks but RAIU is low indicating transient hyperthyroidism which is followed by asymptomatic hypothyroidism and finally erythyroid state is achieved with hill recovery

within 3–6 months. No treatment is required except steroids and beta blockers for initial period of hyperthyroidism.

2. **Postpartum thyroiditis.** It is subacute autoimmune thyroiditis occurring during postpartum period or within 6 months of delivery. These women exhibit biochemical disturbances of thyroid function reflecting hyperthyroidism, hypothyroidism and hyperthyroidism followed by hypothyroidism lasting for a few weeks. These patients have antithyroid peroxidase (TPO) antibodies in the serum in early pregnancy. Thyroid biopsy shows lymphocytic thyroiditis. These patients are asymptomatic. Thyroid scan shows low iodine uptake.

   Postpartum thyroiditis tends to recur after subsequent pregnancies, hence may ultimately lead to permanent hypothyroidism. No treatment is needed except beta blockers during early period of hyperthyroidism.

Q 16. What are the causes of hyperthyroidism with reduced iodine uptake?

Ans.
- Thyroiditis (de Quervain's and postpartum)
- Malignancy thyroid
- Struma ovarii.

COMMONLY ASKED QUESTIONS (17–27)

Q 17. What are the complications of hyperthyroidism?

Ans. They are:

1. *Precipitation of angina* in a patient with IHD and CHF and digitalis toxicity in patients with valvular heart disease receiving digitalis.
2. *Cardiac arrhythmias* (atrial fibrillation is the most common)
3. *Thyrotoxic myopathy* (proximal muscle weakness)
4. *Thyrotoxic hypokalemic periodic paralysis*
5. *Thyrotoxic crisis/thyroid storm*
6. *Malabsorption syndrome*.

Q 18. What are the eye signs of thyrotoxicosis?

Ans. The various eye signs are:
- ***von Graefe's sign:*** Upper lid lag
- ***Joffroy's sign:*** Absence of wrinkling on forehead when asked to look upwards with face inclined downward.
- ***Gilford's sign:*** Non-retraction of upper lid manually.
- ***Loclur's sign:*** Stare look.
- Naffziger's sign: Protrusion from superciliary phase.
- ***Dalrymple's sign:*** Visible upper sclera.
- ***Mobius' sign:*** Failure to converge eyeballs.
- ***Stellwags' sign:*** Stare look, infrequent blinking, widening of palpebral fissure.

N.B.: Read the signs and their methods of demonstration in *Clinical Methods in Medicine* by Pror SN Chugh.

Q 19. Name the treatment modalities available for Graves' disease.

Ans.
- Drug treatment
- Subtotal thyroidectomy
- Radioactive iodine therapy.

Q 20. Which drugs are used in thyrotoxicosis?

Ans.
- Carbimazole
- Methimazole
- Propylthiouracil.

Q 21. Which drug is safest in pregnancy?

Ans. Propylthiouracil.

Q 22. What are disadvantages of drug treatment in thyrotoxicosis?

Ans.
- High rate of relapse once treatment is withdrawn
- Troublesome hypersensitivity reaction
- Rarely life-threatening agranulocytosis and hepatitis may occur.

Q 23. What are indications of radioiodine therapy in thyrotoxicosis?

Ans.
- Graves' disease with large goiter and relapse on treatment
- Multinodular goiter
- Toxic adenoma
- Ablation therapy in those with severe manifestations such as heart failure, AF or psychosis.

Q 24. What are contraindications of radioiodine in thyrotoxicosis?

Ans.
- Breastfeeding and pregnancy
- Allergy to iodine.

Q 25. Does thyrotoxicosis affect bone?

Ans. Yes, it causes osteoporosis.

Q 26. What is the effect of iodine on thyroid status?

Ans. It may cause transient hypothyroidism (*Wolff-Chaikoff effect*) or hyperthyroidism (*Jod-Basedow effect*).

Q 27. What are indications of subtotal thyroidectomy?

Ans.
- Large goiter
- Patient's preference
- Drug noncompliance
- Disease relapse on drug withdrawal.

CASE 25: HYPOTHYROIDISM

The young girl (12 years) (Fig. 1.25A) presented with puffiness of face, weight gain, hoarseness of voice, protuberant abdomen, laziness, and lethargy. She has dropped schooling at the age of 10. She has delayed milestones and has mental insufficiency according to the parents. The another patient 35 years female (Fig. 1.25B) presented with recent weight gain, constipation, cold intolerance and puffiness of face with hoarseness of voice.

Examination revealed mental insufficiency (IQ 50%) in patient (Fig. 1.25A), otherwise both the patients have coarse facial features, thick lips, puffiness of face, thick dry rough skin, bradycardia, hoarseness and nonpitting pedal edema. The patient (Fig. 1.25B) has hypertension (BP 150/100 mmHg).

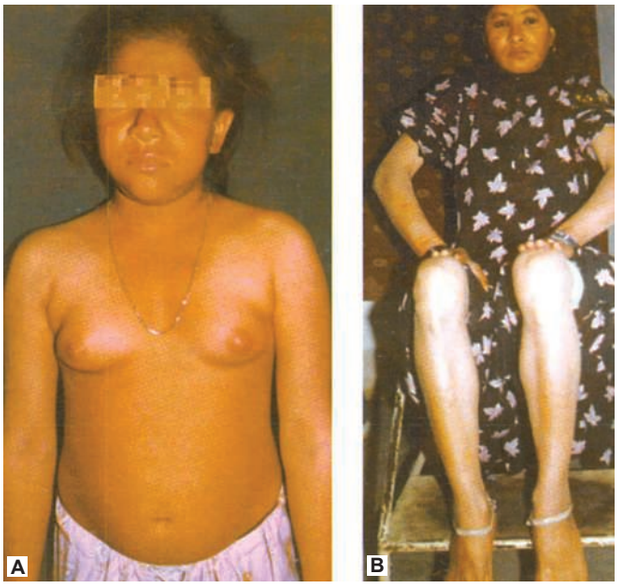


Fig. 1.25A and B: Hypothyroidism. **A.** Cretinism (infantile onset of hypothyroidism); **B.** Adult hypothyroidism

Clinical Presentations of Hypothyroidism

1. *Infants (<1 year) present with mental retardation*, pot belly, large protruding tongue (macroglossia), flat nose, dry skin, sparse hair and delayed milestones of development. Other features of hypothyroidism are present. The condition is called *cretinism*. This may persist in childhood.
2. *The adolescents with hypothyroidism (juvenile hypothyroidism)* present with short stature, retarded growth, poor performance at school, delayed puberty and sexual maturation. Other features of adult hypothyroidism are present.
3. *The adult patients present usually with myxedema* in which features of hypothyroidism are associated with myxomatous changes in skin (dry, toad-like skin, puffiness of face, hands and feet), larynx (hoarseness of voice or slurred speech), and ear (leading to deafness). They may complain of carpal tunnel syndrome (entrapment neuropathy).
4. *Majority of the women with mild hypothyroidism present with increase in weight*, menstrual irregularity, mental feature (depression) or slowness of activity and generalised ache and pains.

History

Points to be Noted

- Onset of symptoms and their progression
- History of recent weight gain, change in appearance and voice, malaise, tiredness and slowness of activity
- History of cold intolerance, change in mood or behaviour disturbance, deafness
- History of arthralgia, myalgia, dryness of skin, decreased sweating
- History of menstrual irregularity, poor libido, sterlity
- History of anorexia, constipation
- History of delayed milestones, slow mentation or mental insufficiency in a child
- History of infertility, depression, muscle cramps, dementia
- History of radioiodine therapy for Graves disease or medications (e.g. lithium, amiodarone, contrast agents, iodine containing expectorants
- **Family history** of thyroid disorder, DM, Addison's disease, etc.

General Physical Examination (GPE)

- **Face.** Note puffiness or periorbital edema, coarse thick facial appearance, rounded face, peaches and cream complexion (Fig. 1.25)
- **Eyes** for xanthelasma, loss of outer third of eyebrows
- **Tongue.** Large protruding (macroglossia)
- **Lips** thick
- **Neck** examination for JVP, thyroid enlargement and lymph node, scar of thyroidectomy
- **Pulse**, **BP**, **temperature**, and **respiration**
- **Skin.** Note the texture, dryness, coarse (toad-like)
- **Hair.** The hair are sparse, thin, brittle in hypothyroidism
- **Hands.** Dry cold hands, thick skin, creases of palm prominent, carpal tunnel syndrome
- **Feet.** Note dryness and nonpitting edema.

Systemic Examinations

I. CVS Examination

Examine the heart for evidence of CHF and pericardial effusion.

II. Examination of Abdomen

For paralytic ileus and any organ enlargement.

III. Nervous System

- Higher function for mental insufficiency
- 8th cranial nerve exam for deafness
- Motor system for myopathy (proximal), myotonia and for delayed reflexes
- Sensory system for peripheral neuropathy, carpal tunnel syndrome

IV. Respiratory System

Chest wall is thick with decreased and slow movements.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. The patient 1 (12-yr F) has features suggestive of juvenile hypothyroidism (cretinism). Read the features in next question. The patient 2, adult female has all features suggestive of myxedema (adult hypothyroidism).

Q 2. What are the clinical features of hypothyroidism in these cases?

Ans. The clinical features of hypothyroidism are tabulated (Table 1.75). Most of the clinical features were present.

Q 3. What are cardiovascular manifestations in hypothyroidism?

Ans. Read Table 1.75

Q 4. What are neurological manifestations in hypothyroidism?

Ans. Read Table 1.75

Table 1.75: Symptoms and signs of adult hypothyroidism

General features	Tiredness, weight gain, cold intolerance, hoarseness of voice and lethargy are common. Somnolence and goiter are less common. Non-pitting edema over feet and legs common. 'Peaches and cream' complexion may occur
Cardiovascular	Slow pulse rate or bradycardia, hypertension and xanthelasma are common pericardial effusion, precipitation of angina and cardiac failure less common
Neuromuscular	Aches and pains, delayed relaxation of anide jerks, muscle stiffness are common carpal tunnel syndrome, deafness, psychosis, depression, myotonia and proximal myopathy are less common, myxedema madness and myxedema coma are rare. Hoffmann's syndrome (muscle aches with myotomia) is also rare
Hematological	Anemia may be present
Dermatological	Dry thick skin (toad skin), sparse hair including loss of hair on lateral third of eyebrow, nonpitting edema are common. Hypothermia is common. Vitiligo and alopecia are rare
Reproductive	Menorrhagia, infertility (common), galactorrhea and impotence (less common)
Gastrointestinal	Constipation (common) and adynamic ileus (less common)

Q 5. What is hypothyroidism?

Ans. Hypothyroidism is a clinical condition reflecting hypofunctioning of thyroid gland, characterised by low levels of circulating thyroid hormones. It is called primary when the cause of it lies in the thyroid gland itself. It becomes secondary when hypothyroidism occurs due to disease of anterior pituitary or hypothalamus.

Goitrous hypothyroidism means enlargement of thyroid gland associated with hypothyroidism.

Subclinical hypothyroidism means biochemical evidence of hypothyroidism (low to normal T3 and T4 but raised TSH) without any symptoms of hypothyroidism (asymptomatic hypothyroidism). The cause of subclinical hypothyroidism are same as described under transient hypothyroidism. It may persist for many years. Treatment with replacement therapy with small dose of thyroxine is indicated.

Transient hypothyroidism refers to a state of reversible thyroid function, often observed during die first 6 months of:

1. Subtotal thyroidectomy or ^{131}I treatment of Graves' disease
2. Post-thyrotoxic phase of subacute thyroiditis
3. Postpartum thyroiditis
4. In some neonates, transplacental passage of TSH receptors-binding antibodies (TRAbs) from the mother with Graves' disease or autoimmuune thyroid disease may cause transient hypothyroidism.

Congenital hypothyroidism is asymptomatic state detected during routine screening of TSH levels in spot blood samples obtained 5–7 days after birth. It results either from *thyroid agenesis*, *ectopic hypoplastic glands* or from dyshormonogenesis. Early detection and early treatment with replacement thyroxine therapy is mandatory to prevent irreversible brain damage.

Q 6. What are the causes of hypothyroidism?

Ans. These are:

1. **Spontaneous atrophic or idiopathic hypothyroidism.**
2. **Goitrous hypothyroidism**
   - Hashimoto's thyroiditis
   - Iodine deficiency
   - Drug-induced (PAS, phenylbutazone, lithium, iodides)
   - Dyshormonogenesis.
3. **Postablative**
   - Following surgery
   - Following ^{131}I.
4. **Transient during thyroiditis**
   - Subacute
   - Postpartum.
5. **Maternally transmitted** (iodides, antithyroid drugs, TRABs antibodies).

Q 7. What is thyroid status in Hashimoto's thyroiditis?

Ans. Read Table 1.76. Usually there is hypothyroidism in Hashimoto's thyroiditis.

Q 8. How would you differentiate simple diffuse goiter from Hashimoto's thyroiditis?

Ans. Read Table 1.76.

Table 1.76: Differentiation between two common diffuse goiters

Features	*Simple diffuse goiter*	*Goiter due to Hashimoto thyroiditis*
Age	Common in young girls (15–25 years) or during pregnancy	Common in young females (20–50 years)
Thyroid enlargement	Mild, tends to be noticed by friends and relatives	Large, visible from distance
Goiter	Soft, nontender	Firm, tender
Prevalence	Endemic or sporadic	Sporadic
Symptoms	Asymptomatic or there is a tight sensation in neck Patient seeks medical attention from asthetic point of view	Pain radiating to jaw or neck, increased during swallowing, coughing and neck movements
Cause	Suboptimal dietary iodine intake and minor degrees of dyshormonogenesis	Autoimmune disease, may be associated with other autoimmune conditions
Thyroid status	Normal	25% cases are hypothyroid at presentation, others become later on. Initially, there may be transient thyrotoxicosis
Thyroid antibodies (TPO antibodies)	Negative	Positive (95% cases)

Q 9. What is best clinical parameter of hypothyroidism?

Ans. Delayed ankle jerks.

Q 10. How would you record delayed ankle jerks?

Ans. Photomotogram.

Q 11. What is the cause of delayed relaxation of jerks in hypothyroidism?

Ans. The exact cause is unknown. It is probably due to decreased muscle metabolism

Q 12. What is Pendred's syndrome?

Ans. It is a genetically determined syndrome (autosomal inheritance) consisting of a combination of dyshormonogenetic goiter, mental retardation and nerve deafness. The dyshormogenesis is due to deficiency of intrathyroidial peroxidase enzyme.

Q 13. What is the relation between iodine and hypothyroidism?

Ans. Both iodine deficiency and iodine excess can produce hypothyroidism.

Iodine when taken for prolonged period (iodine excess) in the form of expectorants containing potassium iodide or use of amiodarone (contains a significant amount of iodine) may cause *goitrous hypothyroidism* by inhibiting the release of thyroid hormones. This is common in patients with underlying autoimmune thyroiditis.

Iodine deficiency in certain parts of the world especially Himalayas, produces endemic goiter (>70% of the population is affected). Most of the patients usually are euthyroid and have normal or raised TSH levels. In general, more severe is the iodine deficiency, the greater is the incidence of hypothyroidism.

Q 14. How will you diagnose hypothyroidism?

Ans. The diagnosis is made on the basis of:

1. Clinical manifestations
2. Investigations

The investigations are done to confirm the diagnosis, to differentiate between primary and secondary hypothyroidism, for follow-up of treatment and to monitor the response. The TSH levels are used to monitor the response to treatment (Table 1.77).

Table 1.77: Thyroid hormone levels in various forms of hypothyroidism

Hormone	*Primary*	*Secondary*	*Subclinical*
T3	Low	Low	Normal (lower limit of normal)
T4	Low	Low	Normal (lower limit of normal)
TSH	High	Low	Slightly high

Q 15. What are other laboratory changes in hypothyroidism?

Ans.
- **Serum cholesterol** is high (hypercholesterolemia)
- **ECG** may show bradycardia, low voltage graph and ST-T changes
- **Blood examination** may reveal anemia (usually normocytic or macrocytic)
- **Thyroid peroxidase antibodies** (TPO) help to find out the cause of hypothyroidism. Their presence indicate autoimmune thyroiditis as the cause of hypothyroidism
- **X-ray chest.** It may be normal or may show cardiomegaly due to pericardial effusion—common in primary rather than secondary hypothyroidism
- **Hyperprolactinemia**
- **Hyponatremia.**

Q 16. What is best laboratory indicator in hypothyroidism?

Ans. Elevated TSH level.

Q 17. What are the causes of raised TSH?

Ans.
- Subclinical hypothyroidism
- Overt hypothyroidism
- Medications such as lithium and amiodarone
- Recovery from hypothyroxinemia of nonthyroidal disorders.

Q 18. What do you understand by subclinical hypothyroidism?

Ans. This is a condition characterised by low normal serum thyroxine levels with elevated serum TSH >10 mIU.

Q 19. How would you treat hypothyroidism?

Ans. Oral thyroxine replacement is given for lifelong. Therapeutic dose varies from 100 to 200 pg/day taken as single dose empty stomach and adjustments are made once in 3 weeks. The dose is adjusted depending on the clinical response and suppression of TSH levels.

Lack of response indicates poor compliance, an underlying psychiatric abnormalities or an associated autoimmune disease (e.g. Addison's disease).

Q 20. What precaution would you take while prescribing thyroxine in elderly?

Ans. Rapid T4 replacement in elderly may precipitate angina and myocardial infarction, hence, starting dose of thyroxine in elderly should be low (25–50 μg/day).

Q 21. What are the complications of myxedema?

Ans. Complications arise as a result of infiltration of myxomatous tissue in various other structures, especially in primary myxedema.

1. **CVS,** e.g. pericardial effusion, restrictive cardiomyopathy, conduction disturbances
2. **Respiratory.** Cor pulmonale, type 2 respiratory failure
3. **Myxedematous** madness and myxedema coma
4. **Entrapment neuropathy** (carpal tunnel syndrome).

CASE 26: DIABETES MELLITUS (TYPE 1 AND TYPE 2)

I. An 18-year-old male (Fig. 1.26A) presented with diabetic ketoacidosis as an emergency. On recovery he gave history of polyuria, polydipsia, polyphagia and weakness.
II. A 45-year-old female (Fig. 1.26B) presented with history of polyuria, polydipsia and puffiness of face and edema feet. She admitted a past history of diabetes for the last 5 years taking antidiabetic medication. Her BP was 160/100 mmHg in right arm in lying down position.

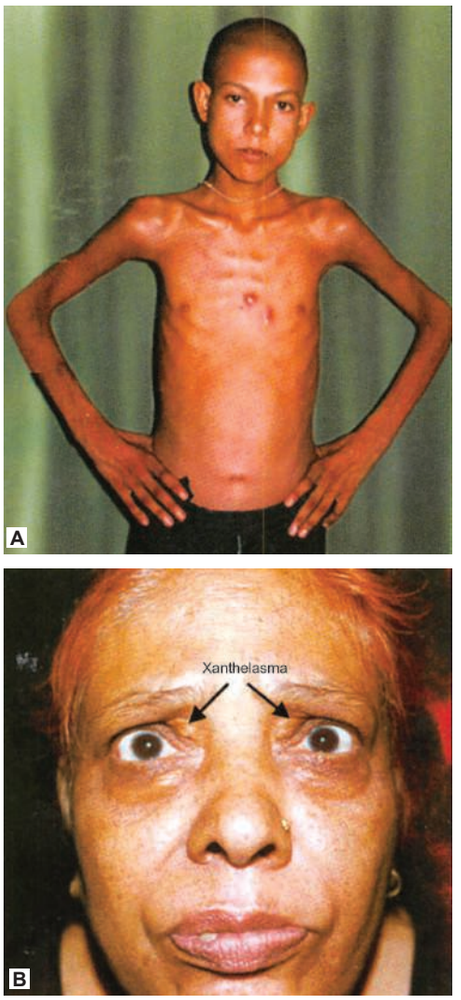


Fig. 1.26A and B: A. Type 1 diabetes; **B.** Type 2 diabetes

Clinical Presentations of Diabetes Mellitus

1. **Asymptomatic diabetes.** The diabetes is detected on investigations.
2. **Type 1 diabetics** (acute presentation)
   - Type 1 diabetics present with a symptom triad of polyuria, polydipsia and polyphagia along with weakness and marked weight loss.
3. **Subacute presentation:** The clinical onset may be over several months; occurs commonly in older patients who complain of thirst, polyuria, weight loss, lack of energy, visual disturbance, changes in eye-refraction and pruritus vulvae (in females).
4. **Type 1 diabetics may also present with complications** such as ketoacidosis, diabetic neuropathy and/or nephropathy.
5. **Type 2 diabetics present** in different speciality with different complaints (Table 1.78).

History

Points to be Noted

- Onset of symptoms and their course
- Ask any history of fever, cough, expectoration, hemoptysis, pain chest, night sweats, fatigue, etc.
- Ask for history of dysuria, pyuria, increased frequency, burning micturition
- History of chronic diarrhea, vomiting, gastric distention
- History of breathlessness, orthopnea, PND, etc.
- Ask for edema feet or legs
- History of menstrual irregularity, sterility, vaginal discharge, etc.
- History of paresthesias, loss of sensations, motor deficit (monoplegia, paraplegia, etc.), facial asymmetry, deafness, mental features, disturbance in consciousness
- Ask for symptoms of hypoglycemia such as profuse sweating, palpitation, air hunger, nausea and convulsions, etc.
- History of visual disturbance or visual loss or decreased vision.

General Physical Examination

- Body habitus/fat distribution
- Dry mouth/dehydration (dry tongue)
- Air hunger
- Skin and mucosal sepsis, candidiasis
- Skin pigmentation, vitiligo, dermopathy
- Weight loss (insulin deficiency)
- Obesity—may be abdominal (insulin resistance)
- White spots on shoes (glycosuria)
- Deep sighing respiration (Kussmaul breathing)
- Eyes for xanthelasma (Fig. 1.26B), evidence of infection
- Ear for infection and deafness
- Neck examination for JVP, lymph nodes enlargement and carotid pulsations
- Record pulse, BP, temperature and respiration.

Examination of Insulin Injection Sites if Patient is Taking Insulin

Main areas to be inspected are:
i. Anterior abdominal wall
ii. Upper thighs/buttocks
iii. Upper outer arms

Main abnormalities to be noted are:
1. Lumps (lipodystrophy)
2. Subcutaneous fat deposition (lipohypertrophy)
3. Subcutaneous fat loss (lipoatrophy as pits; associated with injection of unpurified animal insulins—now rare)
4. Erythema, infection (rare).

Examination of the Hands

- **Limited joint mobility (sometimes called cheiroarthropathy)** may be present. This is the inability to extend (150 to 180) the metacarpophalangeal or interphalangeal joints of at least one finger bilaterally. The effect can be demonstrated in the prayer's sign. causes painless stiffness in the hands, and it occasionally affects the wrists and shoulders.
- **Dupuytren's contracture** is common in diabetes and may include nodules or thickening of the skin and knuckle pads.
- **Carpal tunnel syndrome** is common in diabetes and presents with wrist pain radiating to the hand.
- **Trigger finger** (flexor tenosynovitis) may be present in people with diabetes.
- **Muscle-wasting/sensory changes** may be present as features of a peripheral sensorimotor neuropathy, although this is more common in the lower limbs.

Examination of the Feet

- **Look for evidence of callus formation on weight-bearing areas, clawing of the toes** (a feature of neuropathy), loss of the plantar arch, discolouration of the skin (ischemia), **localised infection** and the **presence of ulcers**.
- **Deformity of the feet** may be present, especially in **Charcot neuroarthropathy**.
- **Fungal infection** may affect skin between toes, and nails.

Examination of Legs

- *Muscle wasting, sensory abnormality*
- *Granuloma annulare, lipoid dystrophica diabeticorum*
- *Hair loss*
- *Tendon reflexes lost.*

Systemic Examinations

I. Nervous System

- Test higher mental functions
- Cranial nerve examination.

Visual acuity

- Distance vision using Snellen chart at 6 metres
- Near vision using standard reading chart
- Impaired visual acuity may indicate the presence of diabetic eye disease, and serial decline may suggest development or progression in severity.

Lens opacification

- Look for the red reflex using the ophthalmoscope held 30 cm from the eye
- The presence of lens opacities or cataract should be noted.

Fundus examination

The pupils must be dilated with a mydriatic (e.g. tropicamide) and examined in a dark clear room for retinopathy.

Sensations; test the following

- *Light touch*
- *Vibration sense:* Use of 128 Hz tuning fork over big toe/malleoli
- *Pin-prick:* Use pin for superficial pain.
- *Deep pain:* Pressure over Achilles tendon, calf tenderness on squeezing
- *Proprioception: Test position sense* at big toe
- Test for distal *anesthesia/hypoesthesia* in glove-stocking distribution.

Reflexes

- Test plantar and ankle reflexes
- Test other reflexes also.

II. Cardiovascular System

- **Pulses.** Palpate all the peripheral pulses. Capillary refill should be tested
- **Examine the heart for cardiomegaly.** Auscultate the heart for any murmur or rub or an abnormal sound.

III. Respiratory System

Examine for any evidence of *tuberculosis, pneumonia, pleural effusion* or *empyema*.

IV. Examination of Abdomen

- *Palpate* for *liver*, *spleen* or *kidney enlargement*
- *Palpate* for any *other mass*.

V. Genitourinary System

- *Examine the penis for evidence of infection* or *discharge* per urethra. *Examine scrotum* and *epididymis* for tenderness or swelling
- *Examine vulva* and *vagina* for evidence of infection and discharge. *Perform per vaginal examination* also.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. Type 1 DM with ketoacidosis in Case No. 1
Type 2 DM with nephropathy in Case No. 2

Q 2. What are the points in favor of your diagnosis?

Ans. **Case No. 1**

- Young adult (20 years)
- History of polyuria, polydipsia and polyphagia
- Presence of ketoacidosis (acetone smell, Kussmaul breathing).

Case No. 2

- Middle-aged female (46 F)
- Obesity
- Polyuria, polydipsia and polyphagia
- Xanthelasma
- Puffiness of face, edema and hypertension indicate nephropathy.

Q 3. What bedside test would you like to perform to confirm the diagnosis?

Ans.

- *Urine exam for sugar, proteins and ketone bodies*
- *Bedside blood sugar* by glucometer, if possible.

Q 4. How do you define diabetes mellitus and impaired glucose tolerance (IGT)?

Ans. A clinical syndrome of hyperglycemia with or without glycosuria either due to lack of insulin (type 1) or insufficiency of insulin with insulin resistance (type 2) is termed diabetes mellitus.

Impaired glucose tolerance (IGT): It is defined as an abnormal response to 75 g of oral glucose on glucose tolerance test. Fasting blood sugar <126 mg and postprandial glucose between 180 and 200 mg indicate IGT.

Q 5. What is gestational diabetes mellitus (GDM)?

Ans. Glucose tolerance is impaired during pregnancy, results as a result of insulin resistance related to metabolic changes of late pregnancy, increases insulin requirement and may lead to impaired glucose tolerance and GDM. GDM occurs in about 4% women during pregnancy which reverts to normal glucose tolerance in postpartum, but diere is risk of developing permanent DM later in life.

Q 6. What is classical triad of type 1 DM?

Ans. *Polyuria*, *polydipsia* and *polyphagia* is clinical triad and hallmark of Type 1 DM.

Q 7. What is the clinical presentation of type 2 diabetes?

Ans. See Table 1.78.

Table 1.78: Clinical presentation of type 2 DM (NIDDM)

These patients present to different specialities or superspecialities with following features which arise as a result of complications. The organs/systems involvement and their presenting features are as follows:

Organ/system affected	*Clinical presentation*
Eye	Recurrent styes, chalazion, anterior uveitis (hypopyon), frequent change of glasses due to error of refraction, visual impairment due to premature development of cataract or retinopathy
Urinary tract	Urinary tract infections, acute pyelitis or pyelonephritis, nephrotic syndrome
GI tract	Chronic diarrhea, malabsorption, gastroparesis (dilatation of stomach)
Genital tract	Females present with pruritus vulvae, vaginal discharge, menstrual irregularities, recurrent abortions, infertility, etc.
Cardio-vascular	Ischemic heart disease, hypertension peripheral vascular disease (cold extremities, absent peripheral pulses, gangrene or diabetic foot)
Nervous	Peripheral neuritis (tingling sensations in the extremities with numbness) symptoms of autonomic neuropathy (Table 1.93), cerebral ischemic episodes and strokes.
Skin	Multiple boils, carbuncles, abscesses, non-healing wounds, mucocutaneous candidiasis
Respiratory	Pneumonias, lung abscess, tuberculosis, etc.

Q 8. How do you classify diabetes?

Ans. The broad categories of DM are type 1 and type 2. Type 1 is divided into A and B. A means immunological destruction of pancreas leading to insulin deficiency (autoimmune type) while B is nonautoimmune idiopathic (Table 1.79).

Table 1.79: Classification of DM based on etiology

I. **Type 1 diabetes mellitus** (beta cell destruction with absolute insulin deficiency)
   - A. Immune-mediated
   - B. Unknown mechanism (idiopathic)

II. **Type 2 DM** (either due to insulin resistance with relative insulin deficiency or insulin secretion defect with insulin resistance)

III. **Other specific types of diabetes**
   - A. Genetic defect of beta cell function leading to gene B mutation)
     - MODY I (hepatocyte nuclear transcription factor (HNF-4-alpha)
     - MODY 2 (glucokinase). MODY3 (HNF-1-alpha) MODY4 (insulin promotor factor, MODY5 (HNF-1-beta), MODY 6(Neuro DI)
     - Proinsulin or insulin conversion
   - B. Genetic defect in insulin action
     - Type 1 insulin resistant
     - Lipodystrophy syndromes
   - C. Pancreatic diabetes (pancreatitis, hemochromatosis, cystic fibrosis)
   - D. Endocrinopathies (acromegaly, Cushing's syndrome, thyrotoxicosis, pheochromocytoma)
   - E. Drug and chemical induced
   - F. Other genetic syndromes, e.g. Down's and Klinefelter's syndrome, DIDMOAD (diabetes insipidus, DM, optic atrophy and deafness), Turner's syndrome, hereditary ataxia, Huntington's chorea, Laurence-Moon-Biedl and dystrophic myotonia

IV. **Gestational diabetes mellitus (GDM)**

Type 2 DM is heterogenous group of disorders characterised by variable degree of insulin resistance, impaired glucose secretion and increased glucose production. Type 2 DM is preceded by impaired fasting glycemia or impaired glucose tolerance called *prediabetic states*.

Q 9. What are prediabetic states?

Ans.
- Impaired fasting glucose (IFG)
- Impaired glucose tolerance (IGT)

Both are prediabetic states.

Q 10. What is pathogenesis of type 1 diabetes?

Ans. It is considered as an autoimmune disorder. The various criteria of autoimmunity are given in Box 1.1. Genetic susceptibility is a major determinant while environmental factors act as a trigger to initiate autoimmune destruction of beta cells of the pancreas. The genetic predisposition is HLA linked class II genes. Immunological response results in production of antibodies against beta cells which cause autoimmune destruction.

Box 1.1: Points in favour of autoimmunity

- HLA linkage
- Its association with other autoimmune disorders
- Lymphocytic infiltration of beta cells pancreas
- Circulating anti-insulin antibodies

Recurrence of beta cells destruction in pancreas

Q 11. What is pathogenesis of clinical features of type 1 diabetes and ketoacidosis?

Ans. 1. Lack of insulin stimulates counter-regulatory hormone release, e.g. glucagon, GH and catecholamines in addition to stimulation of catabolism of nutrients producing neoglucogenesis, glycogenolysis and liposis and subsequently ketoacidosis.
2. Lack of insulin results in hyperglycemia due to increased hepatic output of glucose and poor peripheral utilisation of glucose.
3. The resultant glycosuria, osmotic diuresis and salt and water loss produced result in various clinical features of type 1 diabetes. Diabetic ketoacidosis is an acute metabolic complication.

Q 12. What are the differences between type 1 and type 2 DM?

Ans. Table 1.80 deals with general clinical characteristics of type 1 and type 2 DM.

Table 1.80: Differentiating clinical characteristics of type 1 and type 2 DM

Features	*(Type 1) (Fig. 1.26A)*	*(Type 2) (Fig. 1.26B)*
1. Gene locus	Chromosome 6	Chromosome 11
2. Age of onset	<30 years	>30 years
3. Onset of symptoms	Rapid	Slow
4. Body weight	Thin, lean	Normal weight or obese
5. Duration of symptoms	Weeks	Months or years
6. Presenting features	Polyuria, polydipsia, polyphagia	Present with different complications
7. Ketonuria	Present (ketone-prone)	Absent (ketone-resistant)
8. Complications at the time of diagnosis	Absent	Present (10–20%)
9. Family history	Negative	Positive
10. Plasma insulin	Low or absent	Normal to high
11. Choice of treatment	Insulin	Oral hypoglycemics
12. Mortality if untreated	High	Low

Q 13. How do you diagnose DM?

Ans. Table 1.81 describes criteria for diagnosing diabetes mellitus and prediabetic states.

Table 1.81: American Diabetic Association (1997) criteria endorsed by WHO (1998) for diagnosis of diabetes or other related conditions

Condition	*Venous plasma glucose concentration in mg% (mmol/L)*	
	Fasting	Postprandial (2 hr GTT)
Normal	<110 (6.1)	<140 (7.3)
Diabetes	>126	>200
	Or	
	Symptoms of diabetes plus random blood sugar >200 mg% (11.1 mmol/L)	
Impaired fasting glycemia	110–126 (6.1–7.0)	<140 (7.8)
Impaired glucose tolerance	<126(7.0)	>140 but <200 (7.8–11.1)

Note: 2 hours GTT means following 75 g glucose load. Venous blood glucose concentration is lower than capillary blood. Whole blood glucose is lower than plasma because RBC contains little glucose.

Q 14. What are characteristics of hyperosmolar nonketotic diabetic coma?

Ans. It is common in elderly people with type 2 diabetes with several weeks history of polyuria, weight loss and diminished oral intake followed by confusion and coma.

The *physical examination* reveals marked dehydration, hypotension, tachycardia and altered mental status. The GI symptoms and Kussmaul acidotic breathing are notably absent.

The biochemical characteristics of this coma include:

- Hyperglycemia (blood glucose >600 mg%)
- Hyperosmolality (>350 mOsm/L). Normal osmolality 280–290 mOsm/L
- *Absent or minimal ketone body in the blood or urine.* Acidosis is also absent
- Pre-renal azotemia.

Q 15. What are factors which push a controlled patient of diabetes into uncontrolled state or coma?

Ans.
- Acute concurrent illness
- Infection, sepsis
- Acute catastrophic event, e.g. MI, stroke
- Hemodialysis or any other procedure
- Surgery.

Q 16. Name the various types of coma in DM.

Ans. These are:
1. *Diabetic ketotic coma* (common in type 1 diabetics)
2. *Hyperosmolar hyperglycemic, nonketotic coma* (common in type 2 diabetics)
3. *Hypoglycemic coma* (common in both type 1 and type 2 diabetics)
4. *Lactic acidosis coma.*

Q 17. What are chronic or late complications of DM?

Ans. Chronic complications can be divided into vascular and nonvascular (Table 1.82); the vascular complications are further divided into microvascular and macrovascular.

Q 18. What are pathogenic mechanisms for complications of DM?

Ans. The pathogenic mechanisms are:
- *Activation of polyol pathway*
- *Formation of advanced glycation end products (AGEs)* leading to endothelial dysfunction
- *Activation of protein kinase-C*—second messanger system
- *Oxidative stress.*

Q 19. What are various neurological complications in DM? How do you manage them?

Ans. These may be somatic or autonomic (Table 1.84).

Table 1.82: Chronic or long-term complications of DM

I. **Vascular**

A. Microvascular

i. Eye disease
- Retinopathy (see Table 1.83)
- Macular edema

ii. Neuropathy, e.g. sensory, motor, mixed, autonomic (see Table 1.84)

iii. Nephropathy

B. Macrovascular
- Coronary artery disease
- Peripheral vascular disease
- Cerebrovascular disease
- Diabetic foot
- Hypertension

II. **Others/nonvascular**
- Gastrointestinal, e.g. gastroparesis, diarrhea
- Genitourinary (nephropathy (Fig. 1.26C)/sexual dysfunction)
- Dermatological, e.g. lipoid dystrophica diabeticorum
- Infections/pressure sore (Fig. 1.26D)
- Cataracts
- Glaucoma

Table 1.83: Fundoscopic findings in diabetic retinopathy
- Increase in capillary permeability
- Microaneurysms (earlier to appear as dark spots/dots)
- Retinal hemorrhage (blot hemorrhage)
- Hard and soft exudates (cotton wool exudates)
- Neovascularization (new vessels formation)
- Preretinal hemorrhage
- Vitreous hemorrhage
- Retinitis proliferans, fibrosis and retinal detachment

Q 20. What are the autonomic disturbances in diabetes?

Ans. Read the Table 1.84.

Q 21. What is glycosylated hemoglobin? What is its significance?

Ans. The hemoglobin (Hb) gets glycosylated due to attachment of glucose molecule with β-chain of hemoglobin.
- *Glycosylated Hb* is related to prevailing glucose concentration, hence, hyperglycemia and its excursions lead to increased glycosylation.

Table 1.84: Classification, clinical features and steps of management of diabetic neuropathy

Classification	*Symptoms and signs*	*Treatment*
1. **Somatic**		
a. Symmetric sensory and distal (large fiber, small fiber, mixed type)	• Tingling or burning sensation in the extremities (hands and feet), nocturnal pain in limbs, numbness and coldness of extremities • Glove and stocking type of anesthesia • Loss of tendon reflexes and muscle wasting • Disorganisation of joints (Charcot's joints) • Abnormal gait (wide based, thumping gait) • Nerve conduction velocity delayed in distal parts	• To maintain near or near normal metabolic control on long-term basis with insulin • Insulin is better for control than OHA • Symptomatic relief of pain in extremities is achieved by anti-depressants (imipramine or amitriptyline) or by anti-epileptic (dilantin or carbamazepine or gabapentine or valproate)
b. Asymmetric, motor, proximal (diabetic amyotrophy)	• Lower motor neuron paralysis with wasting of muscles • Hyper- or hypoesthesia may be present on anterior aspect of thighs • Lower limbs are commonly involved than upper limbs • Tendon reflexes are lost on affected side • Lumbosacral area is site of involvement	• Aldolase reductase inhibitors may be useful, if available • Optimal control will not only delay die progress of neuropathy but metabolic complications may even be reversed
Mononeuropathy		
• Mononeuritis or cranial polyneuritis	• 3RD and 6TH cranial nerves involvement common producing diplopia and loss of eye movements	
• Mononeuritis multiplex (entrapment of ulnar, median and popliteal nerves)	• Carpal tunnel syndrome with ulnar and median nerve involvement (wrist drop) • Foot drop; due to sciatic or popliteal nerve involvement	
2. **Autonomic (visceral)**		
a. Cardiovascular	• Vertigo, giddiness and blurring of vision due to postural hypotension, resting tachycardia and fixed heart rate	• Support the limbs by stockings • Fludrocortisone therapy to raise BP • Monitor Na^+, K^+ and BP
b. Gastrointestinal	• Nausea, vomiting, abdominal distension, nocturnal diarrhea, constipation due to colonic atony, gastroparesis, dysphagia due to esophageal atony	• For gastroparesis use metoclopramide • Itopride or mosapride (prokinetic) 5–15 mg/day • For diarrhea, tetracycline • 250 mg after every 6 hours
c. Genitourinary	• Loss of libido, impotence, urinary incontinence, difficulty in micturition (atony of bladder)	• Penile prosthesis (silicon rods) • Injection of papaverine into corpora cavernosa • Avoid beta-blockers, methyldopa, other anti-hypertensives
d. Pseudomotor plus vasomotor	• Abnormal or gustatory sweating, anhydrosis, fissuring of feet, cold extremities, dependent edema	• Propantheline 15 mg tid may relieve gustatory sweating
e. Eye (pupils)	• Constriction of pupils, absent or delayed light	

- *Glycosylated Hb* is expressed as percentage of normal hemoglobin (4–6% depending on the technique of measurement).
- Its value >6.5% indicates diabetes
- It is parameter of long-term control (i.e. past 6 weeks) of DM because it is an index of average blood glucose concentration over the life of die hemoglobin molecule (e.g. approx 6 weeks).
- Its higher values reflect various grades uncontrolled DM.
- The WHO target value of glycosylated Hb (HbAlc) for control of diabetes is <7%.

Q 22. What is diabetic retinopathy? What are ocular fundi changes in DM?

Ans. The involvement of retina (basement membrane, blood vessels) in diabetes is called *diabetic retinopathy*. It is an important cause of blindness among diabetics. The fundosocopic findings are given in Table 1.83.

The dot (microaneurysms) and blot (leakage of blood into deeper layer) hemorrhages are the characteristic findings of background retinopathy in DM.

Q 23. What is the earliest sign of diabetic retinopathy?

Ans. An increase in capillary permeability evidenced by leakage of dye into the vitreous humor after fluorescein injection.

Q 24. What are the clinical stages and time course of diabetic nephropathy?

Ans. The clinical stages and their time course is as follows:

1. **Stage of microalbuminuria** (incipient nephropathy). It takes 5 years for its appearance
2. **Overt proteinuria** (non-nephrotic range). They take 5–10 years for development
3. **Nephrotic syndrome** (Fig. 1.26C). It takes 5–10 years for development

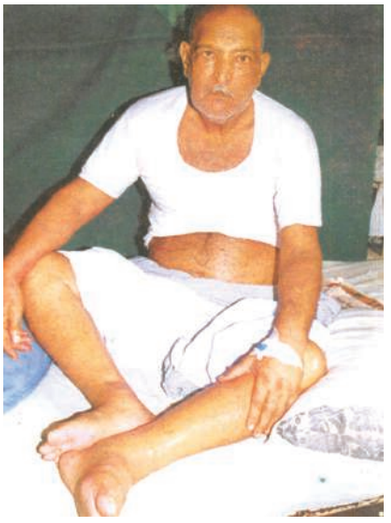


Fig. 1.26C: Nephrotic syndrome in a patient with diabetes of >10 years duration. Note the gross edema and puffiness of face

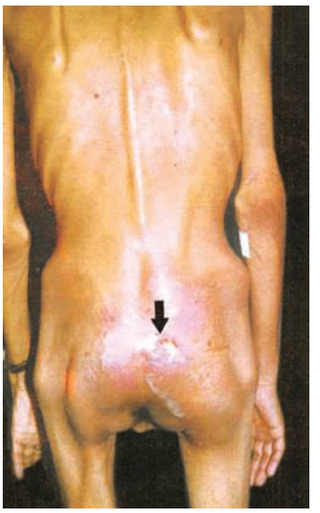


Fig. 1.26D: Pressure sore. The wound is infected

4. **Renal failure/insufficiency:** It takes 10–15 years for their development
5. **End stage renal disease (ESRD):** It takes 10–15 years for their development.

Q 25. Why dose of insulin decreases in diabetic nephropathy?

Ans. It is due to:

- Excretion of insulin binding antibodies with albumin in urine
- Decreased degradation of insulin
- CRF tends to impair neoglucogenesis.

Q 26. What are GI complications of DM?

Ans. Gastrointestinal complications in DM are:

- *Candidiasis or fungal infections of oral cavity* (an opportunistic infection)
- *Diabetic esophageal hypomotility* and *gastroparesis*
- Chronic gastritis
- Diabetic enteropathy
- Pancreatitis (chronic) causing steatorrhea
- Hepatomegaly (fatty infiltration)
- Acalculous cholecystitis.

Q 27. Name the various microvascular complications of diabetes.

Ans. Read the Table 1.82.

Q 28. What is microalbuminuria? What is its significance?

Ans. Microalbuminuria is defined as:

i. Loss of <300 mg of albumin in urine over 24 hours
ii. Albumin excretion rate in urine is 20 µg/min

- It indicates early diabetic nephropathy, a stage from which nephropathy can be reversed with tight metabolic control.

Q 29. What is diabetic foot? What are its types?

Ans. The clinical features of diabetic foot (Fig. 1.26E) are given in Table 1.85. Diabetic foot results as a result of:

1. Neuropathy
2. Vasculopathy
3. Infections.

Diabetic foot is either neuropathic or ischemic or both.

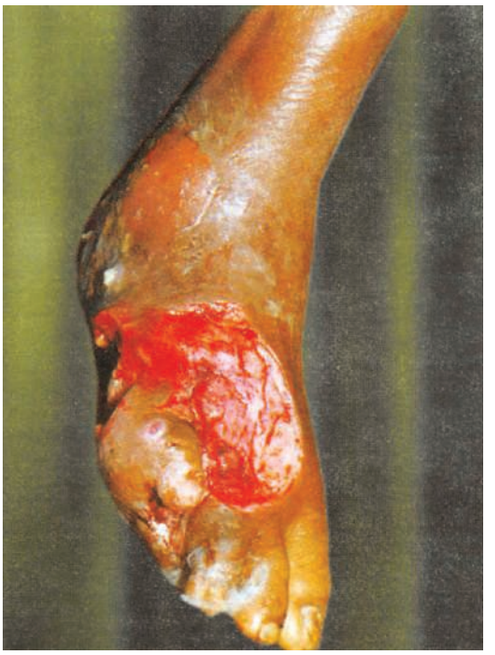


Fig. 1.26E: Diabetic foot

Table 1.85: Features of diabetic foot

Neuropathy	*Vasculopathy*
× Paresthesia	× Claudication
× Numbness	× Rest pain
× Pain × Loss of sensations	× Loss of dorsalis pedis and or posterior tibial pulsations
× Decreased tendon Jeeks	
Structural damage	× Feet are cold to touch
× Ulcer on the foor × Sepsis, abscess	× Skin is shining and atrophic with sparse hair
× Loss of the arch of foot	
× Osteomyelitis	
× Digital gangrene (loss of peripheral pulses)	
× Charcot joint	

Q 30. What is diabetic vasculopathy (ischemic foot)?

Ans. It refers to occlusive vascular disease involving both microangiopathy and atherosclerosis of large and medium sized arteries.

Q 31. How would you manage diabetic foot?

Ans.
- Debridément of necrotic tissue and antiseptic dressing daily.
- Control of hyperglycemia with insulin.
- Antibiotics for infection.
- Removal of weight bearing and friction from ulcerated area, e.g. avoid crutches, use appropriate footwear.
- Patient education. Avoid smoking and alcohol, inspect foot daily for blisters. Do not walk barefooted. Avoid tight shoes, cut toenails across.
- Chiropody.
- Surgical and orthopedic consultation.

Q 32. What is pathogenesis of neovascularisation?

Ans. It is due to production of following factors by ischemic retina
- Angiogenic factors
- Vascular endothelial growth factor.

Q 33. How will you manage a case of type 2 DM?

Ans. The essential steps in the management of type 2 diabetes are represented in Fig. 1.26F.

Q 34. How will you classify oral hypoglycemics?

Ans. Read Unit IV—commonly used drugs.

Q 35. What do you understand by the term insulin sensitizers? Name them. What are their advantages?

Ans. Insulin sensitizers are the drugs which lower the blood sugar in type 2 DM by sensitizing the insulin receptors to insulin hence, overcome insulin resistance and hyperinsulinemia in type 2 DM. They are:
- Biguanides, e.g. *metformin*
- Thiazolidinedione derivatives, e.g. rosiglitazone, pioglitazone.

Advantages are
- Hypoglycemia is rare as compared to insulin secretogogues, e.g. sulphonylureas
- They lower the blood lipid
- They lower the mortality and morbidity
- They can be used to lower blood sugar in patients with impaired glucose tolerance (IGT).

Warning: The insulin sensitizers need the presence of insulin for their action, hence, cannot be used in type 1 diabetes mellitus.

Q 36. What are key points (Do's and Don'ts) in the management of type 2 DM?

Ans. The Do's and Don'ts are tabulated (Table 1.86) and illustrated in Fig. 1.26G.

Q 37. How will you investigate a case with DM?

Ans. The various investigations done are:
1. **Blood**
   - *TLC, DLC, ESR* for an evidence of infection
   - *Sugar* (fasting and PP) for diagnosis and monitoring of diabetes
   - *HbA1c* (glycosylated Hb) for long-term management of diabetes
   - *Serum lipids* for hyperlipidemia—a common finding in DM.
2. **Urine examination** for specific gravity, pus cells, RBCs, proteins, sugar, casts and culture and sensitivity.

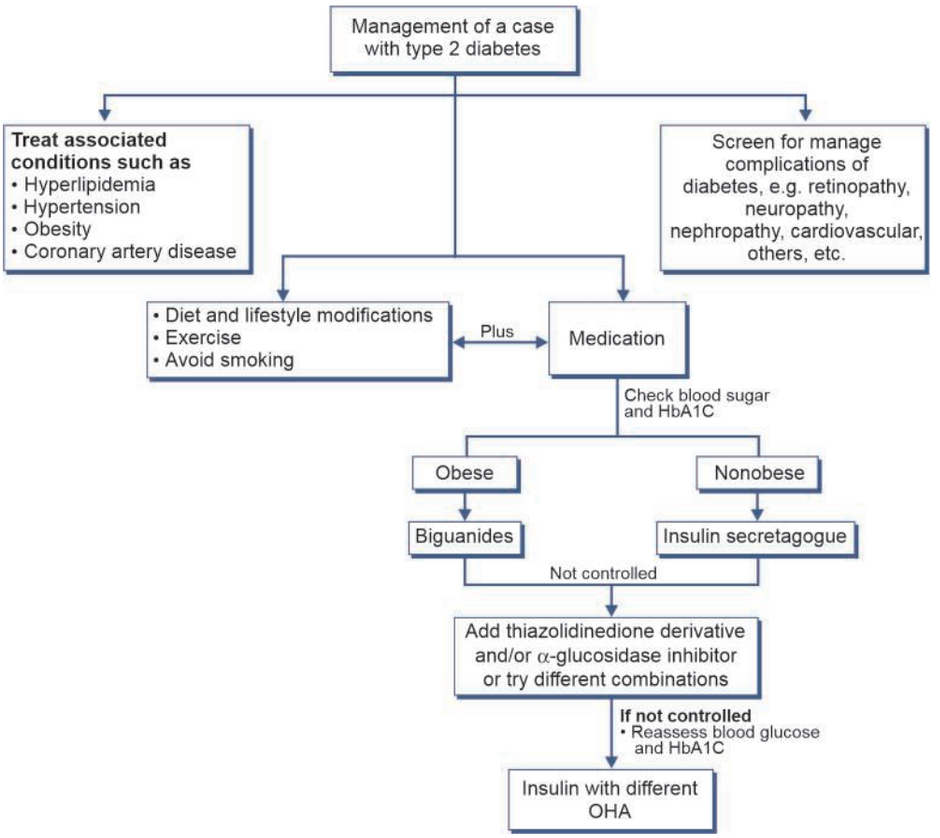


Fig. 1.26F: Management of type 2 diabetes mellitus

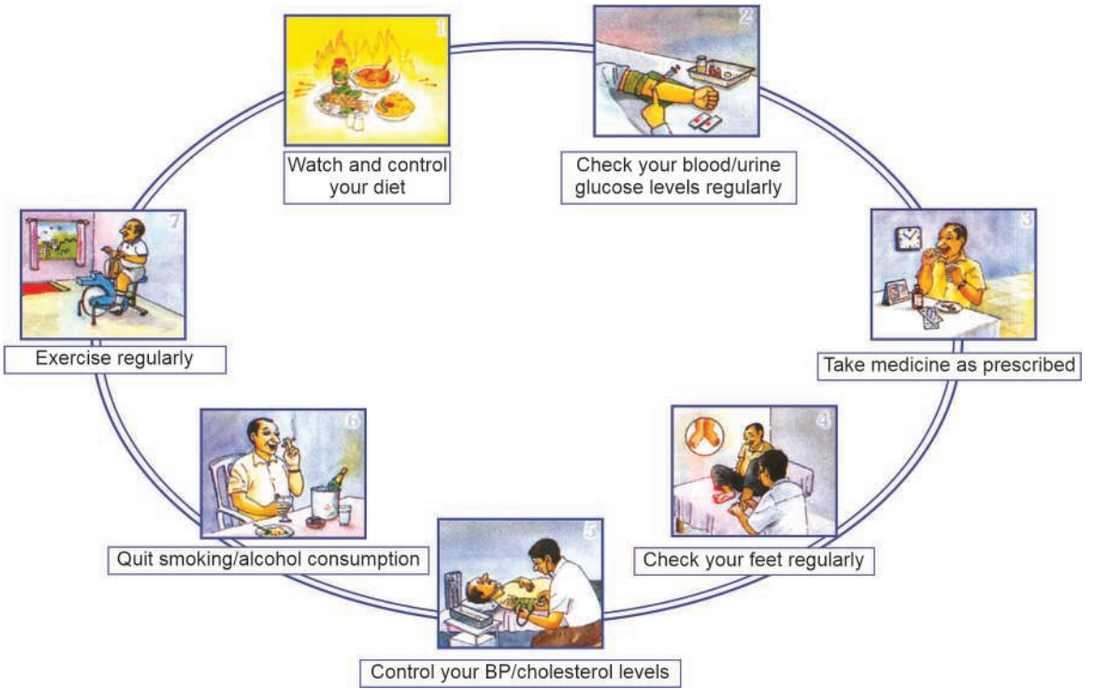


Fig. 1.26G: Key points in the management of type 2 diabetes mellitus

Table 1.86: Do's and Don'ts in the management of type 2 DM

	Do's	*Don'ts*
Diet	× Eat a balanced diet, eat fiber rich foods × Consume small, frequent meals	× Avoid consumption of sweetened beverages fried foods, alcohol, red meat, honey, jaggery sugar, and bakery products. Do not skip your meal.
Exercise	× Exercise should be low to moderate in intensity. Consult your doctor before starting any exercise. Remember to walk and exercise daily. Keep sugar or something sweet, e.g. candy, to avoid low blood sugar levels	× Do not exercise if your blood sugar values are low or high and diabetes is not under control × Do not exercise on an empty stomach
Foot	× Keep your feet clean, warm and dry. Change daily clean, soft socks and wear well fitting shoes × Examine your shoes daily for cracks, pebbles, nails and other irregularities	× Do not use alcohol based solution. It makes your feet dry × Never walk barefooted × Never apply heat of any kind to your feet × Do not cut corns or calluses yourself
Eye	× Consult your doctor if you have pain in your eyes. Have an yearly eye examination done by your doctor	× Do not neglect any infection in your eyes

*Adapted from 2004 clinical practice recommendations by ADA

3. **ECG** for diagnosis of silent myocardial infarction or hypertension.
4. **Chest X-ray** for pulmonary tuberculosis, fungal infections, cardiomegaly
5. **Fundus examination** for diabeteic retinopathy.
6. **Other investigations** are specifically performed depending on the system involved.

Q 38. What are parameters used for control of DM?

Ans. Parameters of control are:

i. *Urine sugar* (negative or just positive)
ii. *Blood sugar*, e.g. F. <126 mg% PP <200 mg%
iii. *Serum lipids*
   - HDL: Male >40 mg/dl and Female >60 mg/dl
   - LDL <100 mg/dl
   - Triglycerides <150 mg/dl
iv. HbA1C (glycosylated Hb)
   - <7% with a check once in 3 months.

Q 39. What is hypoglycemia?

Ans. It is defined as blood glucose level less than lower limit of normal, i.e. <7.0 mg%. Hypoglycemia is classified traditionally into (i) *postprandial* (occurs in response to meals) and (ii) *fasting*. *Fasting hypoglycemia* usually occurs in the presence of disease while *postprandial* occurs in the absence of a recognisable disease (Table 1.87). The factors responsible for hypoglycemia are given in Table 1.88.

Q 40. What is Whipple triad?

1. Symptoms and signs suggestive of hypoglycemia
2. Documentation of hypoglycemia
3. Reversal of hypoglycemia with administration of glucose.

Table 1.87: Classification of hypoglycemia

1. **Postprandial hypoglycemia**
   - × Alimentary, e.g. dumping syndrome (following gastric surgery) due to hyperinsulinemia and idiopathic (true or pseudohypoglycemia)
   - × Galactosemia and hereditary fructose intolerance (common causes of hypoglycemia in children)

2. **Fasting hypoglycemia**

i. Hyperinsulinism
   - × Insulinoma (pancreatic beta-islet cell tumor)
   - × Nonpancreatic tumor secreting insulin-like growth factor I
   - × Excessive exogenous insulin
   - × Drugs, e.g. sulphonylurea, quinine, salicylates, propranolol, pentamidine

ii. Endocrinal causes
   - × Hypopituitarism. Addison's disease.
   - × Glucagon and catecholamines deficiency

iii. Liver diseases
   - × Severe hepatitis
   - × Cirrhosis of the liver

iv. Renal disease: Renal failure

v. Enzymatic defects
   - × G6PD
   - × Liver phosphorylase
   - × Pyruvate carboxylase
   - × Glycogen synthetase

vi. Substrate deficiency
   - × Malnutrition
   - × Pregnancy

Table 1.88: Factors responsbile for hypoglycemia in diabetes

The **factors** are:

1. Intake of too little food or no food but insulin is taken as regular
2. Unaccustomed exercise is attempted but preceding dose of insulin is not reduced
3. Alcohol intake
4. Poorly designed insulin regimen. There is mismatch between insulin administration and food habits
5. Defective counter-regulatory mechanisms such as release of glucagon and catecholamines in diabetes. They are anti-insulin in action.
6. Impaired gastric emptying. This produces mismatch between intake of food and insulin action
7. Malabsorption of food
8. Factitious (self-induced) hypoglycemia
9. An unrecognised low renal threshold for glucose. Attempts to render the urine sugar-free will inevitably produces hypoglycemia
10. Renal failure. The kidneys are important sites for the clearance of insulin which tends to accumulate if renal failure is present.

Q 41. What are the symptoms and signs of hypoglycemia?

Ans. Symptoms and signs of hypoglycemia occur due to effects of low levels of glucose per se as well as stimulation of sympathetic system. These are given in Table 1.89.

There is a great degree of variation among individuals in awareness of symptoms of hypoglycemia in diabetes.

- Some patients may feel symptoms when blood sugar is <70 mg% while others may not appreciate the symptoms even when blood glucose level is less than 55 mg%.
- Hypoglycemia is reversible with administration of glucose, symptoms and signs may disappear rapidly if it is insulin induced but may take sometime if induced by oral hypoglycemics.

Table 1.89: Symptoms and signs of hypoglycemia

- **CVS:** Palpitation, tachycardia, anxiety, cardiac arrhythmias
- **CNS:** Tremors, confusion, headache, tiredness, difficulty in concentration, incordination, slurred speech, drowsiness, convulsions, plantars, extensors, coma
- **GI tract:** Nausea, vomiting
- **Skin:** Sweating, hypothermia

Q 42. What are the causes of fasting hypoglycemia?

Ans. Read Table 1.87.

Q 43. What are causes of postprandial hyperglycemia?

Ans. Read Table 1.87.

CASE 27: AORTIC STENOSIS (AS)

The patient (not shown) presents with history of exertional dyspnea and off and on chest pain and syncope. There was history of pain in right hypochondrium and edema legs and feet. The auscultatory findings of the patient are depicted in Fig. 1.27A.

Clinical Presentations of AS

1. ***Asymptomatic.*** It may be asymptomatic, detected on examination as an incidental finding. ***Congenital or mild. AS remains asymptomatic*** throughout life.
2. ***Patients of moderate or severe AS*** may complain of ***palpitation, dyspnea, anginal pain,*** etc.
3. Patients with ***severe AS*** may also complain of ***syncope*** or ***giddiness*** and ***vertigo***.

History

Points to be Noted

- Age of onset of symptoms
- Exertional dyspnea
- Angina pectoris
- Cough, hemoptysis, dyspnea, orthopnea, PND due to left heart failure

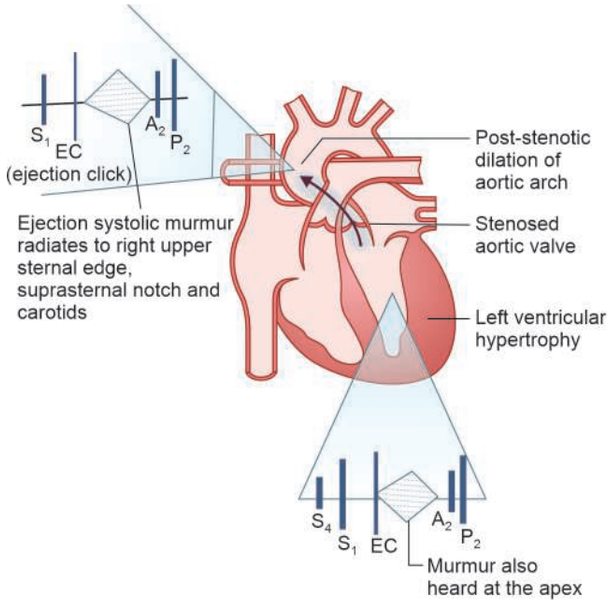


Fig. 1.27A: Aortic stenosis. Auscultatory findings and hemodynamic consequences

- Exertional syncope due to low cardiac output
- Sudden death.

General Physical Examination

- **Pulse** is low volume, anacrotic, slow rising in moderate to severe stenosis, normal in mild stenosis
- **Pulse pressure** is low
- **Jugular venous pressure** is raised if right heart failure develops. Prominent 'a' wave may be seen
- **Ankle edema** may be present if heart failure develops.

Systemic Examination

Inspection

Apex beat may be normally placed or displaced down beyond left 5th intercostal space outside the mid clavicular line due to left ventricular hypertrophy/enlargement. It is forceful and sustained (heaving).

Palpation

- *Apex beat* may be normally placed or displaced downwards and outwards due to left ventricular hypertrophy. It is forceful and sustained (heaving)
- *Left ventricular thrust* may be palpable
- *P2* may become palpable if pulmonary hypertension develops
- *Systolic thrill* over the aortic area and carotids.

Percussion

Cardiac dullness is within normal limits.

Auscultation

- *A mid-systolic ejection murmur* which is diamond-shaped (crescendo-decrescendo) often with thrill best heard at right 2nd space (A1 area) or left 3rd space (A2 area), is radiated to carotid vessels and downwards to apex.
- *Murmur* is best heard in sitting position with patient bending forward
- *An ejection click (EC)* is heard in valvular aortic stenosis (Fig. 1.27A).
- *Second heart sound (S_2)* is short and feeble, normal or paradoxically split.
- *An atrial sound (S4)* may be heard
- **Other systems examination**
  1. *Respiratory system:* Basal rales at both the bases of the lungs
  2. *Abdomen*
     - Hepatomegaly may be present
     - No ascites, no splenomegaly.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your probable diagnosis?

Ans. The patient has pure aortic stenosis either rheumatic or congenital in origin. It is moderate in severity with CHF with sinus rhythm without SABE

Q 2. What are points in favour of your diagnosis?

Ans. 1. **History of exertional dyspnea, syncope, chest discomfort**
2. *Signs of CHF*, e.g. raised JVP, cyanosis, edema and tender hepatomegaly
3. Displaced apex beat (down and out) with heaving character
4. *Signs of pulmonary hypertension*, e.g. loud P2 with narrow splitting
5. *An ejection click and ejection systolic murmur* over A1 and A2, best heard in sitting position and leaning forward. It radiates to carotid. A2 is soft
6. *Systolic thrill* over aorta and carotids.

Q 3. What is aortic stenosis? What are its types?

Ans. Aortic stenosis is defined as narrowing of the aortic orifice due to valve or wall involvement leading to left ventricular outflow obstruction (pressure overload).

Types and Forms

1. **Valvular aortic stenosis (bicuspid aortic valve).** It is the commonest type of congenital aortic stenosis.
2. **Congenital subvalvular AS.** This congenital anomaly is called idiopathic hypertrophic subaortic stenosis (IHSS).
3. **Supravalvular AS.** This uncommon congenital anomaly is commonly seen in William's syndrome (Table 1.90).

Table 1.90: William's syndrome

- ***Elfin facies***, e.g. broad forehead, pointed chin, upturned nose, hypertelorism, peg-shaped incisors, low set ears
- Supravalvular aortic stenosis
- Mental retardation
- Hypercalcemia

Q 4. What are causes of aortic stenosis?

Ans. The likely etiology varies with the age of the patient (Table 1.91).

Table 1.91: Causes of aortic stenosis

1. **Infants, children, adolescents**
- Congenital aortic stenosis (valvular)
- Congenital subvalvular aortic stenosis
- Congenital supravalvular aortic stenosis
2. **Young adults and middle-aged persons**
- Calcification and fibrosis of congenitally bicuspid aortic valve
- Rheumatic aortic stenosis
3. **Old age**
- Senile degenerative aortic stenosis
- Calcification of bicuspid valve
- Rheumatic aortic stenosis

Q 5. What are important features of aortic stenosis?

Ans. Common features of AS are:

- *Dyspnea*, *angina* and *syncope* on exertion
- *Slow rising sustained low volume pulse* called anacrotic pulse, occurs in severe stenosis, pulse is normal in mild AS
- *Low systolic pressure* with low pulse pressure (<20 mmHg)
- Apex beat down and out or may be normal with heaving in character
- Cardiomegaly
- *Ejection click* and *ejection systolic murmur* and a thrill in aortic area conducted to carotids. The same murmur is also heard at apex
- *Basal crackles and rales*. Signs of pulmonary congestion may be present (LVF).

Q 6. What does second heart sound tell us in AS?

Ans.
- A soft and muffled S2 indicates valvular stenosis
- A single S2 indicates fibrosed/fused cusps or fenestrated valve
- Reverse splitting of S2 indicates mechanical or electrical prolongation of ventricular systole.
- A normal S2 rules out the possibility of critical aortic stenosis.

Q 7. How will you investigate a patient with AS?

Ans. Following investigations are done:

1. **Electrocardiogram (ECG)** may show left atrial and left ventricular hypertrophy with strain, i.e. ST-T wave changes due to myocardial ischemia may be present. Heart blocks and bundle branch block in calcific aortic stenosis may occur sometimes.
2. **Chest X-ray.** It may be normal. Sometimes, heart is enlarged due to a left ventricular hypertrophy. Poststenotic dilatation of aorta may be seen in some cases. Lateral view may show calcification of aortic valve.

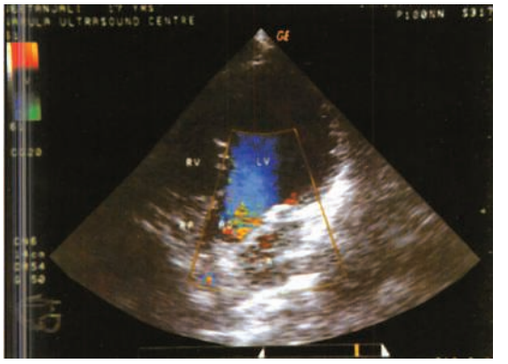


Fig. 1.27B: Aortic stenosis. Colour Doppler echocardiogram showing aortic stenosis with gradient of 50 mm across the valve

3. **Echocardiography** (Fig. 1.27B). It will show left ventricular enlargement and hypertrophy, severity of AS, calcification of valve and decreased left ventricular function.
4. **Doppler echocardiography:** Demonstrates the systolic gradient across the valve, detects presence and absence of aortic regurgitation.

Q 8. How would you grade AS on electrocardiography?

Ans. It is graded as mild (valve area >1.5 cm), moderate (valve area 1–1.5 cm^2) and severe (valve area <1 cm^2).

Q 9. How will you differentiate valvular AS from IHSS?

Ans. 1. **Valvular AS** (its important features have already been listed)

2. **Subvalvular aortic stenosis (idiopathic hypertrophic subaortic stenosis—IHSS).** The features are:
   - Dyspnea, angina pectoris, fatigue and syncope
   - Double apical impulse (apex beat)
   - A rapidly rising carotid arterial pulse
   - Pulsus bisferiens (double upstroke)
   - A harsh, diamond-shape ejection systolic murmur without ejection click is best heard at lower left sternal border as well as at the apex. It does not radiate to neck vessels. It becomes louder with Valsalva maneuver.
   - Early diastolic murmur of aortic regurgitation may also be heard in some patients.
   - No post-stenotic dilatation
   - Second heart sound is normal, single.

Q 10. What are the complications of AS?

Ans. Common complications are as follows:
- Left ventricular failure
- Hemolytic anemia
- Systemic embolization
- Congestive cardiac failure
- Infective endocarditis
- Arrhythmias (ventricular) and conduction disturbances (heart blocks)
- Precipitation of angina
- Sudden death. It is more common in hypertrophic cardiomyopathy (HOCM).

Q 11. How will you differentiate between aortic stenosis and pulmonary stenosis?

Ans. Differences between AS and PS are dealt with in Table 1.92.

Table 1.92: Differentiation between aortic stenosis and pulmonary stenosis (PS)

Features	*AS*	*PS*
Pulse	Small amplitude anacrotic, parvus et tardus,	Normal
BP	Low systolic	Normal
Apex beat	Heaving	Normal
Second heart sound	A_2 soft	P_2 soft
Splitting of S_2	Reverse	Wide
Location of systolic murmur	Aortic area, conducted to carotids	Pulmonary area, no conduction
Relation to respiration	No change	Increases on inspiration
Associated ventricular hypertrophy	LVH	RVH

Q 12. What are characteristics of severe aortic stenosis?

Ans. Aortic stenosis is said to be severe when:
- Pulse character is slowly rising plateau
- Pulse pressure is narrow
- Signs of LVF present
- S2 is soft, single or paradoxically split
- Presence of S4
- Systolic thrill and late peaking of ejection systolic murmur
- Cardiac catheterization reveals transvalvular gradient >60 mmHg.

Q 13. What are causes of systolic murmur in aortic and pulmonary area?

Ans. The murmurs in this area are **ejection** or **mid-systolic**.

The causes of ejection systolic murmur (ESM) are given in Table 1.93.

Table 1.93: Systolic murmurs at base of the heart

Aortic area (A1 and A2) (right 2nd and left 3rd space)
- AS
- Systemic hypertension
- Coarctation of the aorta
- Aneurysm of the ascending aorta
- Atherosclerosis of the aorta (old age)
- Functional flow murmur in AR

Pulmonary area (left 2nd interspace)
- Pulmonary stenosis
- Pulmonary hypertension
- Cor pulmonale (acute or chronic)
- Flow murmur in hyperkinetic states, e.g. anemia, thyrotoxicosis, fever, pregnancy
- Congenital heart diseases, e.g. ASD, VSD, Fallot's tetralogy
- Innocent (benign) murmur

Q 14. What are benign (innocent) murmurs?

Ans. These murmurs are flow murmurs without organic cause, commonly seen in children due to: **Hyperkinetic circulatory state** in children especially during exercise, crying or fever.
- **Increased resistance of the pulmonary vascular bed**

Characteristics
- Usually systolic localized to pulmonary outflow tract
- There is no associated thrill
- Best heard in supine position, may disappear in upright position
- Heart sounds are normal.

Q 15. What is a hemic murmur?

Ans. It is an ejection systolic murmur heard at the pulmonary area due to rapid blood flow in a patient with severe anemia. It is due to hyperkinetic circulatory state combined with dilatation of pulmonary artery and its vasculature.

Note: Hemic murmurs are also functional ejection systolic murmur similar to hear in various hyperkinetic states.

Q 16. What are functional flow murmurs?

Ans. These murmurs occur in the absence of organic heart disease, are due to turbulence produced by rapid flow of blood across a normal valve (flow murmurs). These may be systolic and diastolic (Table 1.94).

- These murmurs are not loud, are localised in nature, and usually not associated with thrill.
- They are hemodynamically insignificant, do not produce cardiomegaly.
- They are also called flow or hernic murmurs.

Table 1.94: Functional murmurs

Systolic
× Systolic murmur across pulmonary valve in left to right shunt, e.g. ASD, VSD
× Functional systolic murmur in aortic area in patients with severe AR
Diastolic
× Grahm-Steell murmur (early diastolic) due to pulmonary regurgitation in pulmonary hypertension
× Apical mid-diastolic murmur (Austin-Flint murmur) in severe AR.

Q 17. How would you manage this condition?

Ans.
1. **Mild asymptomatic AS with valvular gradint <50 mmHg needs observation only.**
2. Moderate AS with symptoms needs medical management of LVF with salt restriction, diuretics and vasodilators. Digoxin should not be used. These patients need valve replacement.

Q 18. What are indications of valve replacement?

Ans.
1. **Symptomatic AS with valvular gradient >50 mmHg.** It is an absolute indication.
2. Asymptomatic patients with severe AS (gradient >50 mmHg. LVH, left ventricular systolic dysfunction and valve area <0.6 cm^2).
3. Asymptomatic moderate AS in patients who are undergoing mitral or aortic root surgery or coronary artery bypass surgery.

Q 19. Which valve would you prefer for replacement?

Ans. Mechanical prosthetic valve in young age and tissue valve (bioprosthetic value) in old age.

CASE 28: AORTIC REGURGITATION (AR)

A patient (not shown) presented with palpitation, dyspnea and off and on chest pain. The auscultatory findings are depicted in Fig. 1.28. The patient had mild edema feet.

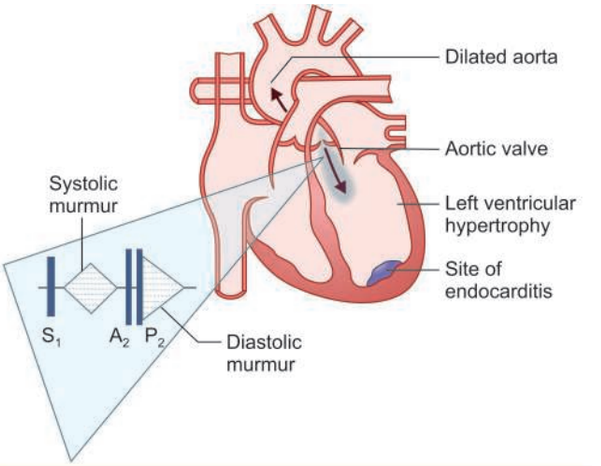


Fig. 1.28: Aortic regurgitation

Clinical Presentations of AR

I. Mild to Moderate AR

- Often asymptomatic
- Palpitation—pounding of heart is a common symptom
- Symptoms of left heart failure appear but late.

II. Severe AR

- Symptoms of heart failure, i.e. dyspnea, orthopnea, PND are present at onset
- Angina pectoris is frequent complaint
- Arrhythmias are uncommon.

History

Points to be Noted

- Onset of symptoms and their course
- Ask the history of cough, dyspnea, orthopnea, PND
- Ask for history of hemoptysis, anginal pain, headache
- History of fever
- History of edema feet and legs
- History of loss of function of any part, i.e. paralysis
- **Past history** of sore throat, skin infection or arthralgia (fleeting) or joint pain (arthritis).

General Physical Examination

- *Face* for appearance, i.e. dyspneic or orthopneic, ill-look. Note puffiness
- *Look for Argyll-Robertson pupils* of syphilis
- *Mouth*. Look for anemia or bleeding or evidence of infection, high-arch palate
- *Neck* examination for arterial pulsation. JVP and lymph nodes
- *Pulse, BP, respiration* and *temperature*
- Note the following other *peripheral signs* in case of AR
  - i. ***Collapsing or good volume pulse*** (wide pulse pressure)
  - ii. ***Bounding peripheral pulses***
  - iii. ***Dancing carotids*** (Corrigan's sign)
  - iv. ***Capillary pulsations*** in nail beds (***Quincke's sign***)
  - v. ***Pistol shots*** sound and ***Duroziez's sign***/murmur (to and fro systolic and diastolic murmur) produced by compression of femoral by stethoscope
  - vi. *Head nodding* with carotid pulse—*de Musset's sign*
  - vii. *Hill's sign* (BP in lower limbs > upper limbs)
    - ★ Cyanosis (peripheral, central or both) may be present
    - ★ Pitting ankle edema may be present
    - ★ Tender hepatomegaly if right heart failure present
    - ★ Look for stigmatas of Marfan's syndrome.
    - ★ Look for joint deformity for rheumatoid arthritis and ankylosing spondylitis.

All these peripheral signs may not be evident in mild AR. In our case, they were present indicating severe AR.

Examination of CVS

Inspection

- Apex beat is displaced down and outside the midclavicular line and is forceful
- Left ventricular thrust
- Pulsations in suprasternal notch and epigastrium are usually seen.

Palpation

- Apex beat is forceful and sustained
- No thrill is palpable
- Tender hepatomegaly if right heart failure present.

Percussion

Cardiac dullness is within normal limits.

Auscultation

- An *early diastolic murmur* is best heard in A2 area (3rd left intercostal space) or A1 area (2nd right intercostal space) in sitting position with patient leaning forward and during held expiration
- An *ejection systolic murmur* in the same area. It is due to increased stroke volume. It may also radiate to neck vessels
- Ejection click suggests bicuspid aortic valve.
- *Austin flint* (soil, mid-diastolic) murmur at apex in severe AR
- Second heart sound is soft and feeble
- Loud pulmonary component in second left space indicates pulmonary hypertension
- Signs of left heart failure (fine end-inspiratory rales at bases of lungs)
- A 3rd heart sound at apex is present in severe AR.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your provisional diagnosis?

Ans. In view of clinical features and auscultatory findings, the provisional diagnosis is aortic regurgitation with congestive cardiac failure without evidence of endocarditis or thromboembolic complication. The cause of AR is to be found out.

Q 2. Is it severe or moderate AR?

Ans. The presence of all the signs of wide pulse pressure indicates severe AR in this patient. However, the signs of severity are described in Table 1.95.

Q 3. How do you define AR?

Ans. When blood is pushed by left ventricle into the aorta during systole, a part of it regurgitates back into same ventricle during diastole due to inadequate closure of the aortic valve, called *aortic regurgitation*. It leads to volume overload of the left ventricle resulting in its hypertrophy and enlargement.

Q 4. What are causes of chronic AR?

Ans. The **causes** are:

I. **Congenital**
Bicuspid valve

II. **Acquired**
- Rheumatic heart disease
- Infective endocarditis (acute regurgitation)
- Trauma leading to valve rupture
- Atherosclerosis, hypertension
- Marfan's syndrome (aortic dilatation)
- Syphilitic aortitis
- Ankylosing spondylitis, rheumatoid arthritis
- Dissecting aneurysm of ascending aorta.

Q 5. What are causes of acute AR?

Ans. Causes of acute AR
- Acute bacterial endocarditis
- Rupture of sinus of Valsalva
- Failure of prosthetic valve
- Trauma to the chest
- Acute dissection of the aorta.

Q 6. What are clinical features of acute AR?

Ans. The clinical features of acute AR will be:
- An acutely ill patient with severe breathlessness, chest discomfort
- Acute left ventricular failure (LVF)
- Peripheral signs of AR will be absent.

Q 7. Differential diagnosis of AR.

Ans. The common conditions causing AR are:
1. Rheumatic AR
2. Syphilitic AR
3. Marfan's syndrome with AR
4. Atherosclerotic AR.

Q 8. What are differences between AR and PR (pulmonary regurgitation)?

Ans. These are summarized in Table 1.96.

Q 9. What are the characteristics of rheumatic AR?

Ans. Read Table 1.97

Table 1.96: Differentiation between AR and PR

Feature	*AR*	*PR*
Peripheral signs of wide pulse pressure	Present	Absent
Apex beat	Hyperdynamic	Normal
Site of early diastolic murmur	Best heard in aortic area	Best heart in pulmonary area
Relation of murmur to respiration	None	Increases with inspiration
Ventricular enlargement	LVH	RVH

Table 1.95: Signs of aortic regurgitation (AR) and its seventy.

Sign of severe AR	*Signs of moderate AR*
All signs of moderare AR	*Peripheral signs**
Wider pulse pressure (normal 20–40 mm). Wider the pulse pressure, severe is AR	Collapsing or good volume pulse (wide pulse pressure) bounding peripheral pulses
Soft second heart sound	Dancing carotids (*Corrigan's sign*)
Signs of left heart failure	Capillary pulsations in nail beds (*Quincke's sign*)
Duration of the decrescendo diastolic murmur; longer the murmur, sever is AR	Pistol shot sound and Duroziez's sign/murmur
Hill's sign (normal difference in BP of LL and UL is <20 mmHg). Larger the difference, severe is AR	Head nodding with carotid pulse—de Musset's sign
A difference of 20–40 mm indicates moderate AR and >60 mm difference suggests severe AR	*Hill's sign* (BP in lower limbs >upper limbs)
Presence of third heart sound. It indicates severe AR	Cyanosis (peripheral, central or both) may be present
Austin-Flint murmur—a low pitched, soft mid-diastolic murmur caused by vibration of the anterior mitral cusp by die regurgitant jet and is heart at the apex. It indicates severe AR	Fundus examination will reveal capillary pulsations
	Pitting ankle edema may be present
	Tender hepatomegaly if right heart failure present

*All these peripheral signs may not be evident in mild AR because these indicate wide pulse pressure due to significant aortic run-off into the heart

Table 1.97: Differential diagnosis of AR

Rheumatic AR	*Syphilitic AR*	*Aortic dilatation (Marfan's syndrome)*
Young age group History of rheumatic fever in the past	Older age group History of sexual exposure	Young age Eunuchoidism (lower segment > upper segment, arachnodactyly)
Other valves may be involved	Usually an isolated lesion	Mitral valve may be involved (floppy mitral valve syndrome)
Diastolic thrill absent	Thrill may be present	Aortic pulsation in suprasternal notch. No thrill
A_2 diminished or absent	A_2 may be loud (tambour-like)	A_2 normal
Murmur best heard in left 3rd space (A_2 area)	Murmur best heard in right second or 3rd space along right sternal border	Murmur heard in second right and third left intercostal space
Peripheral signs present	Peripheral signs are marked, Austin-Flint murmur may be present	Peripheral signs are usually absent

Table 1.98: Differential diagnosis of MDM in AR

Feature	*Severe AR (Austin-Flint murmur)*	*AR with MS*
Peripheral signs of AR	Florid	Masked
Character of murmur	Soft	Rough and rumble
First heart sound (S_1)	Normal	Loud
Opening snap (OS)	Absent	Present
LA enlargement	Absent	Present
Calcification of mitral valve	Absent	May be present
Echocardiogram	Normal	Suggestive of MS

Q 10. How will you decide whether MDM in mitral area is due to severe AR or due to associated MS?

Ans. The mid-diastolic murmur in AR may be confused with MDM of MS though both lesions may coexist.

The differentiation is given in Table 1.98.

Q 11. What are the causes of mid-diastolic murmur in AR? How would you differentiate them?

Ans. **Causes** are:

1. Severe AR
2. AR with MS.

For differentiation, read Table 1.98

Q 12. How will you investigate a patient with AR?

Ans. Following investigations are done:

1. **Chest X-ray (PA view) may show**
   - Cardiomegaly (LV enlargement—boot-shaped heart)
   - Dilatation of ascending aorta, valvular calcification.
   - Aortic knuckle prominent.
2. **ECG may show**
   - LVH and left atrial hypertrophy in moderate to severe AR
   - ST segment depression and T wave inversion due to left ventricular strain.
3. **Echocardiogram.** It detects:
   - Left ventricular enlargement, hyperdynamic left ventricle and assessment of severity of AR
   - Fluttering of anterior mitral leaflet in severe AR
   - Aortic root dilatation and valve morphology
   - Vegetations may be detected in a case with endocarditis
   - Assessment of LV (dimension, size systolic function).
4. **Colour Doppler flow studies** detect the reflux through aortic valve and its magnitude
5. **Radionuclide imaging** in asymptomatic patients where echocardiographic images are of poor quality
6. **Cardiac catheterization** is necessary when coronary artery disease is suspected
7. **MRI and spiral CT** scan for assessment of aortic root size.

Q 13. What are complications of AR?

Ans. Following are common complications:

- Acute LVF
- Infective endocarditis
- CHF
- Cardiac arrhythmias
- Heart blocks (calcific aortic valve)
- Precipitation of angina.

Q 14. What are the causes of an ejection systolic murmur in aortic area? How would you differentiate them?

Ans. **Causes** are:

1. Severe AR
2. AR with AS
3. Isolated AS.

The differences between severe AR or AR with AS are compared in Table 1.99.

Q 15. How will you decide the dominance of a lesion in combined AS and AR?

Ans. The features of dominant AS or AR in combined aortic lesion are given in Table 1.100.

Q 16. How would you treat AR?

Ans. Mild asymptomatic disease does not require treatment

- **Moderate to severe disease** is treated by salt restriction, diuretics, digitalis and vasodilators (ACE inhibitors). Surgery is the final answer.
- **Severe AR** needs surgery (valve reconstruction or replacement) in addition to medical management.

Table 1.99: Differential diagnosis of an ejection systolic murmur (ESM) in AR

Feature	*Severe AR*	*AR with AS*
Signs of wide pulse pressure (water-hammer pulse, Corrigan's sign, dancing carotids, and pistol shot sounds, etc.)	Present	Absent
Systolic BP	High systolic	Normal or low systolic
Ejection click	Absent	Present
Radiation of murmur	Usually localised, may radiate to neck vessels	Widely radiated to neck vessels as well as to apex
Systolic thrill	Absent	Present

Q 17. What are indications of surgery in AR?

Ans. 1. *Severe AR with concomitant angina*
2. *Severe AR with heart failure and reduced ejection fraction (e.g. between 30 and 50%).*
3. Aortic root dilatations, i.e. aortic root diameter is >55 mm.

Q 18. Which valve would you prefer for replacement in AR?

Ans.
- *If patient is young, mechanical prosthetic valve* would be preferred as they are more durable.
- *Bioprosthetic (tissue valve) valve is used in elderly* because they are prone to degeneration and calcification may need re-operation after 7–10 years.

Table 1.100: Dominant aortic stenosis vs aortic regurgitation in combined AS and AR

Features	*Dominant AS*	*Dominant AR*
I. **Symptoms**		
× *Exertional angina* × *Dyspnea on effort* × *Fatigue* × *Syncope* × *Palpitation*	All are marked	Chest pain, dyspnea, palpitation common
II. **Signs**		
× *Pulse*	Low volume Pulsus bisferiens (tidal wave prominent than percussion wave)	High volume collapsing pulse Pulsus bisferiens (percussion wave prominent than tidal wave)
× *BP*	× Low systolic BP × Low pulse pressure	× High systolic BP × Wide pulse pressure
× *Peripheral signs of AR*	Masked	Marked
× *Apex beat*	Heaving	Hyperdynamic
× *Thrill*	Systolic	No thrill
× S_3	Absent	Present
× S_4	May be present	Absent
× *Ejection click*	Present	Absent
× *Diastolic murmur*	Short early diastolic	Prominent early diastolic
× *Systolic murmur*	Marked, radiating to neck vessels	Present, does not radiate to neck vessels

CASE 29: MITRAL STENOSIS (MS)

The patient (not shown) presented with off and on cough and expectoration with dyspnea and PND for the last 4–5 years. There was history of pain abdomen, edema feet and hemoptysis off and on. His auscultatory findings are depicted in Fig. 1.29. Loud 1st heart sound, opening snap and a rough rumbling mid-diastolic murmur were present in this case.

Clinical Presentations of MS

1. *The patients of mild MS may be asymptomatic* and a presystolic murmur may be an evidence which increases on exercise.
2. *Patients of mild to moderate MS present with symptoms of low cardiac output*, e.g. syncope, fatigue, weakness. They may have exertional dyspnea only.
3. *Patients of moderate to severe MS present with symptoms and signs of left heart failure* followed by right heart failure and congestive cardiac failure.
4. *These cases of MS of any severity may present with features of embolization* (e.g. hemiplegia, recurrent hemoptysis, gangrene of peripheral parts) due to thrombus either in left atrium or peripheral venous system; the formation of which is triggered by either a transient arrhythmias (e.g. AT) or LVF or CHF.

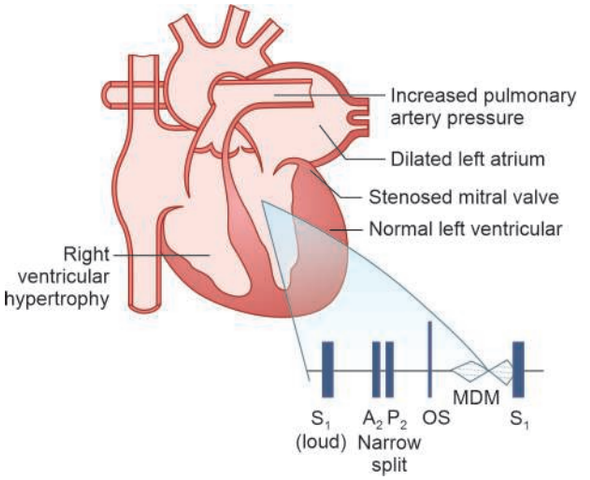


Fig. 1.29: Mitral stenosis. Hemodynamic effects and auscultatory findings in MS. Roll the patient to the left to hear MDM (low pitched mid-diastolic rumbling murmur, which is best heard with the bell of stethoscope

History

Points to be Noted

- History of exertional dyspnea, orthopnea, PND
- Any history of pain chest, hemoptysis, hoarseness of voice
- History of dizziness, vertigo or syncope
- History of fever, joint pain or urinary disturbance
- History of pain abdomen, edema feet or legs, distension of abdomen
- History of any paralysis (motor or sensory deficit)
- History of missing of heartbeat.

Past history

- History of sore throat, joint pain, rash or abnormal movement or skin infection
- History of recurrent chest pain or hemoptysis.

Physical Signs

- *Mitral facies*: A characteristic bilateral, cyanotic or dusky pink hue (malar flush) on cheeks
- *Low volume pulse*, which may be irregularly irregular if atrial fibrillation is present
- *Low pulse pressure*
- *Raised jugular venous pressure* and 'a' wave on jugular venous pulse will be absent in atrial fibrillation
- *Cold extremities*: Extremities are usually warm but may be cold in severe mitral stenosis or due to embolization
- *Pitting ankle edema.*

Note: Always look for the signs of bacterial endocarditis (Read Case 31) or acute rheumatic activity in a case of MS, if complicated.

I. Examination of Heart (CVS)

Inspection

- Apex beat is normally situated or apex beat is displaced outwards but not downwards
- Pulsation of pulmonary artery may be visible in 2nd left intercostal space
- Epigastric pulsations may be visible due to right ventricular hypertrophy
- Left parasternal lift may be visible.

Palpation

- Apex beat is palpable and tapping in character
- An apical diastolic thrill may be palpable in left lateral position
- 1st heart sound at apex (mitral area) may become palpable, best demonstrated in left lateral position
- Parasternal heave is usually present
- Second sound (pulmonary component) may become palpable at left 2nd intercostal space
- Right ventricular pulsations may be palpable in epigastrium.

Percussion

- Left border of heart corresponds with apex beat
- 2nd and 3rd left intercostal spaces may become dull due to pulmonary hypertension.

Auscultation

1. **Mitral area (apex)**
   - Heart beats may be irregular due to atrial fibrillation
   - *First heart sound is loud and banging*, short and snappy
   - *A mid-diastolic murmur*, best heard in left lateral position with the bell of stethoscope. It is rough and rumble. It is accentuated during late diastole called 'presystolic accentuation'. A presystolic murmur without mid-diastolic murmur is an early sign of mitral stenosis, and in mild mitral stenosis this may be the only finding.

- *Opening snap (OS)* is present. It is snapping sound heard after 2nd heart sound. Its proximity to S2 determines the severity of mitral stenosis. Nearer die opening snap to 2nd heart sound, more severe is the mitral stenosis. It is absent if valve becomes calcified.

2. **Pulmonary area** (left 2nd intercostal space)
   - Loud 2nd heart sound due to pulmonary arterial hypertension
   - There may be an ejection systolic or an early diastolic murmur (*Graham-Steell murmur*) due to pulmonary regurgitation
   - *Splitting of 2nd heart sound* becomes *narrow.*
3. **Tricuspid area (lower left parasternal border)**
   There may be a pansystolic murmur due to functional tricuspid regurgitation which may develop in cases with severe mitral stenosis.
4. **Aortic area** (right 2nd intercostal space)
   Normal 2nd heart sound heard. No abnormality detected in this area.

II. Examination of other Systems

a. **Examination of lungs:** There may be fine crepitations (end-inspiratory crackles) at both the bases of lungs due to LHF. There may be hydrothorax (pleural effusion).

b. **Examination of abdomen:** Liver is enlarged, soft and tender. Ascites may be present. Spleen gets enlarged in presence of subacute bacterial endocarditis.

c. **Examination of nervous system**
   - Monoplegia/hemiplegia due to embolism
   - Sydenham's chorea
   - Optic fundi for Roth's spots.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis?

Ans. In view of symptoms and physical signs described in this case, the patient appears to have RHD with MS, sinus rhythm (say AF if present), CHF without infective endocarditis or acute rheumatic activity.

Note: In cardiac cases, one has to tell the basic cardiac disease (e.g. valvular, hypertensive, cardiomyopathy, congenital, thyrotoxicosis, etc.) first followed by sequence of the heart disease (e.g. with or without pulmonary hypertension and with/without LHF or CHF and then its complication/sequela (e.g. normal sinus rhythm/abnormal rhythm, presence/absence of SABE and/or acute rheumatic activity).

Q 2. What are points that favour your diagnosis of MS? How would you explain them?

Ans. Points in favor of mitral stenosis are:

1. **History** of cough, dyspnea, orthopnea and PND. Hemoptysis was present
2. **Palpable apex beat.** Apex beat is palpable and tapping in character (tapping character is due to palpable first heart sound)
3. **Loud first heart sound (S_1).**
4. **Mid-diastolic murmur (MOM) with presystolic accentuation.**
   - The murmur is rough, rumbling, low-pitched, low frequency, of variable duration
   - Best heard at the apex in left lateral position with bell of the stethoscope
   - There is presystolic accentuation of the murmur.
5. **Opening snap (OS)**
   - This is a snappy, sound produced due to sudden forceful opening of the mitral valve during diastole due to elevated left atrial pressure.
   - It is heard in expiration with diaphragm of stethoscope at or just medial to cardiac apex.
   - This sound follows aortic component of second heart sound (A_2).

Q 3. What are common clinical features of MS?

Ans. The common features of MS and their pathogenesis is described in Box 1.2.

Q 4. What are the common causes of mitral stenosis?

Ans. The causes are:

1. **Rheumatic:** MS is invariably rheumatic in origin.
2. **Congenital,** e.g. parachute mitral valve where all chordae tendineae are inserted into a single papillary muscle.
3. **Rarely carcinoid syndrome, SLE, endomyocardial fibrosis, Hurler's syndrome, RA (rheumatoid arthritis) and calcification of mitral annulus and leaflets.**

Box 1.2: Clinical manifestations of MS

1. **Symptoms due to low cardiac output, e.g.**
   - Fatigue
   - Tiredness
   - Weakness
   - Lethargy
2. **Symptoms of pulmonary congestion (left heart failure), e.g.**
   - Dyspnea
   - Orthopnea
   - Paroxysmal nocturnal dyspnea (PND)
   - Hemoptysis
3. **Symptoms of right heart failure, e.g.**
   - Puffiness of face and edema of legs
   - Pain in right hypochondrium due to hepatomegaly
4. **Symptoms due to embolization, e.g.**
   - Right-sided embolization leads to hemoptysis and pain chest
   - Left-sided or systemic embolization leads to hemiplegia, acute pain abdomen (infarction of viscera), loss of peripheral pulses or gangrene, etc.
5. **Symptoms related to arrhythmias, e.g.**
   - Palpitation
   - Missing of beat(s)

Q 5. What is normal cross-sectional area of mitral valve? When do symptoms and signs of MS appears? What is critical MS?

Ans. The normal mitral valve orifice is 4–6 cm^2 (average 5 cm^2) in diastole in adults. Narrowing of the mitral valve is called *mitral stenosis*. The symptoms arise when valve orifice is reduced to half of its original size (2.0 cm^2 approx).

- Mitral stenosis is severe when orifice is 1 cm^2 or less and said to be *critical*.

Q 6. What is functional MS?

Ans. **Functional mitral stenosis** refers to functional obstruction to inflow of blood from left atrium to left ventricle, is due to rapid flow through a normal valve

Causes

(i) Hyperdynamic circulation (VSD, ASD, PDA, thyrotoxicosis, anemia, etc.)

(ii) In severe mitral regurgitation.

Q 7. What is significance of OS?

Ans.

- The presence of OS indicates organic MS
- The OS indicates that mitral valve is still pliable (i.e. not calcified). It disappears if valve is calcified
- It also decides the severity of MS. Diminishing A2-OS gap (gap between second heart sound and OS) indicates increasing severity of the MS
- It disappears following valvotomy.

Q 8. What conditions simulate MS?

Ans.

1. Atrial myxoma—read features of atrial myxoma further in this case
2. Ball valve thrombus in left atrium
3. Cor triatriatum—a rare congenital heart condition.

N.B.: These conditions constitute the differential diagnosis of MS.

Q 9. What are the causes of loud S1?

Ans. Following are causes:

1. Mitral stenosis
2. Tricuspid stenosis
3. In tachycardia. S1 is loud due to short P-R.
4. Hyperkinetic circulation (exercise, anemia, thyrotoxicosis, fever, pregnancy, etc.)
5. **Short P-R interval.** P-R interval influences the heart rate, short P-R causes loud S1 while long P-R causes muffling of S1.
6. Children or young adults (physiological).

Q 10. What are the causes of muffling of S1 in MS?

Ans. Causes of muffling S, in MS are:

1. MR or AR
2. Mitral valve calcification
3. Acute rheumatic carditis
4. Myocardial infarction
5. Dilated heart
6. Obesity, emphysema, pericardial effusion.

Q 11. What are causes of mid-diastolic murmur (MDM) at the apex?

Ans. In addition to MS, the other conditions/diseases that lead to mid-diastolic murmur are:

1. **Active rheumatic carditis (valvulitis).** It produces a soft mid-diastolic (Carey-Coombs') murmur without loud S1, opening snap and diastolic thrill. It is due to edema of valve cusps.
2. **Severe aortic regurgitation (Austin-Flint murmur).** The murmur has following characteristics:
   - It is neither associated with loud S1 nor presystolic accentuation
   - Opening snap is absent
   - No thrill
   - The patient has florid signs of severe AR (read aortic regurgitation).
3. **Functional mid-diastolic murmur** (increased flow through a normal valve). This is seen in left to right shunts (VSD, ASD, PDA) or in hyperdynamic circulation.
4. **Severe mitral regurgitation.** A soft mid-diastolic murmur with a pansystolic murmur and S3 indicates severe MR.
5. **Left atrial myxoma.** The characteristic features of atrial myxoma are:
   - Tumor plop—a sound produced by striking of myxoma against the valve.
   - Disappearance or change in the intensity and character of the murmur during lying down. The murmur is best heard in sitting position.
   - No associated thrill or opening snap.
6. **Tricuspid stenosis.** The murmur has similar characteristics as in MS, but is best heard at left sternal edge.
7. **Ball valve thrombus.**

Q 12. What does presystolic murmur or presystolic accentuation in MS indicate?

Ans. Presystolic murmur *vs* presystolic accentuation of MDM in MS is as follows:

- The presystolic murmur is due to forceful atrial contractions against the stenotic mitral valve.
  1. The isolated presystolic murmur indicates mild MS
  2. Presystolic accentuation of the mid-diastolic murmur indicates severe mitral stenosis.

Note: Presystolic accentuation of MDM disappears in AF and big atrial thrombus.

Q 13. What are the causes of opening snap?

Ans. Following are the causes:

- Mitral stenosis
- Tricuspid stenosis
- Left to right shunt (VSD, ASD, PDA)
- Sometimes in severe MR.

Q 14. What is Lutembacher's syndrome?

Ans. It comprises:

- Atrial septal defect ASD)
- MS (rheumatic in origin)

Q 15. How do you decide the severity of mitral stenosis?

Ans. The auscultatory findings that determine the severity of MS are:

- Lower volume pulse and low pulse pressure
- Cold peripheral extremities
- Longer duration of the mid-diastolic murmur with the pre-systolic accentuation.
- Proximity of the OS to second heart sound.

More near is the OS to the aortic component of second heart sound, more severe is the MS.

Q 16. What is Ortner's syndrome?

Ans. It is hoarseness of voice due to compression of recurrent largyngeal nerve by enlarged left atrium in MS.

Q 17. What is juvenile mitral stenosis?

Ans. In the west, MS is seen usually in 4th or 5th decade, but in India, it develops early and may be seen in children commonly. The criteria for juvenile MS are:

- Occurs below 18 years of age
- It is usually severe (pin-point mitral valve)
- Atrial fibrillation is uncommon.
- Calcification of valve uncommon
- Needs immediate surgical correction.

Q 18. What are signs of pulmonary arterial hypertension?

Ans. Signs are:

1. Prominent 'a' wave in neck veins
2. Pulmonary arterial pulsation in pulmonary area and parasternal heave
3. P_2 may be palpable
4. On auscultation, P_2 may be loud, narrowly split and there is *Graham-Steell murmur*
5. Pulmonary ejection click and on ejection systolic murmur.

Q 19. How will you investigate a case with MS?

Ans. The investigations are as follows:

1. **ECG:** It may show left atrial hypertrophy (P mitrale), right ventricular hypertrophy and atrial fibrillation.
2. **Chest X-ray:** Mitralised heart; left atrium is conspicuously prominent on left border of heart which is straightened. There is double atrial shadow. Signs of pulmonary congestion present. Pulmonary conus is prominent.
3. **Echocardiogram shows**
   - Thickened immobile mitral cusps
   - Reduced rate of diastolic filling (EF slope is flattened)
   - Reduced valve orifice area
   - Left atrial thrombus, if present.
4. **Cardiac catheterization**
   Pressure gradient between LA and LV.

Q 20. What are the complications of mitral stenosis?

Ans. Common complications are as follows:

1. **Acute pulmonary edema (left heart failure)**
2. **Pulmonary hypertension and right heart failure**
3. **Arrhythmias, e.**g. atrial fibrillation, atrial flutter, VPCs
4. **Left atrial thrombus** with systemic embolization leading to stroke.
5. **Recurrent massive hemoptysis** leading to hemosiderosis
6. **Infective endocarditis—rare.** It is common in mitral regurgitation than stenosis
7. **Recurrent pulmonary infections due to chronic passive venous lung congestion**
8. **Compression produced by enlarged left atrium**
   - ***Ortner's syndrome.*** Hoarseness of voice due to compression of recurrent laryngeal nerve.
   - ***Dysphagia*** (compression of esophagus)
   - ***Collapse of the lung*** due to pressure on left bronchus
9. A big thrombus fits like a ball into mitral valve.
10. Interlobar effusion (*phantom tumor*) or hydrothorax (*pleural effusion*).

Q 21. What are clinical signs of acute pulmonary edema?

Ans. Read mitral regurgitation.

Q 22. What are the causes of pulmonary edema?

Ans. It may be cardiogenic or noncardiogenic (Table 1.101)

Table 1.101: Causes of pulmonary edema

I. Cardiogenic
× Left heart failure due to any cause
× Acute MI
× Cardiac arrhythmias
× Acute pulmonary thromboembolism
II. Noncardiogenic
1. Inhalation of toxic and irritant gases (phosgene, phosphine (PH_3), hyperbaric O_2)
2. High altitude pulmonary edema
3. Drowning or near drowning
4. Aspiration of gastric contents or corrosive poisoning
5. Aluminium phosphide poisoning (insecticide, pesticide)
6. Acute hemorrhagic pancreatitis
7. Narcotic overdose
8. Snake bite
9. Sudden removal of air (pneumothorax) or fluid (pleural effusion) from thoracic cavity
10. Fluid overload
11. Chronic renal failure (CRF), Goodpasture's syndrome

Q 23. How would manage the patient?

Ans. The patient is managed as follows:

- If the patient is in acute LVF, then it is an emergency requiring *parenteral diuretics*,

bronchodilators, *vasodilators* along with *oral digoxin* (0.5 mg stat) or IV digoxin (not preferred nowadays). In addition, patient needs prop up position and O_2 inhalation.

- **Mild stenosis** is treated with salt restriction and diuretics.
- **Moderate to severe MS** needs, propped up position, O_2 inhalation, oral digoxin and diuretics. Vasodilators are needed to reduce afterload. As patient improves, he/she is prepared for surgery.
- **Treatment of atrial fibrillation** if present, by digitalis or calcium channel blocker, beta blocker. Anticoagulant is also needed to prevent thromboembolism.
- **Prophylaxis against bacterial endocarditis** by penicillin, benzathine penicillin 12.5 lakh units/every 3–4 weeks for 5 years or up to 25 years of age depending on the age of onset of MS.
- **Surgery.**

Q 24. What are indications for surgery?

Ans.
- Severe or significant symptomatic MS with pliable valve
- Patient with recurrent hemoptysis and pulmonary hypertension
- Recurrent thromboembolism despite anticoagulation.

Q 25. Name the surgical procedures for MS.

Ans.
1. **Closed commissurotomy:** Closed mitral valvotomy by mechanical dilators or valvuloplasty by balloon dilatation of the mitral valve.
2. **Open commissurotomy:** It requires cardiopulmonary bypass and allows surgical repair of valve under direct vision.
3. **Valve replacement:** It is done when valve is fibrosed, disorganized, calcified or when there is associated mitral regurgitation.

Q 26. What are complications of surgery?

Ans.
- Mitral regurgitation may occur
- Risk of thromboembolic event
- Restenosis.

CASE 30: MITRAL REGURGITATION (MR)

The patient (not shown) presented with complaints of palpitation, dyspnea, PND and chest discomfort. There was history of cough with no hemoptysis. Patient had history of pain abdomen and edema feet.

Examination revealed normal pulse, BP and raised JVP. Apex beat was down and outside the midclavicular line in 5th intercostal space, forceful and diffuse. Left parasternal heave present. A systolic thrill present at apex. The auscultatory findings included soft and muffled SI, a pansystolic murmur, a third heart sound (Fig. 1.30).

Clinical Presentations of MR

- ***The patient may be entirely asymptomatic***, murmur is often detected in medical board examination more often in young females without any apparent disability
- ***These patients may present with symptoms of left heart failure (cough, dyspnea, PND, hemoptysis, etc.)***
- These patients in addition to above symptoms may present with ***complications***, e.g. ***hemiplegia, gangrene of finger, toes***
- ***Acute mitral regurgitation may present as acute LHF*** in a patient with acute MI due to rupture of papillary muscle or chordae tendineae.

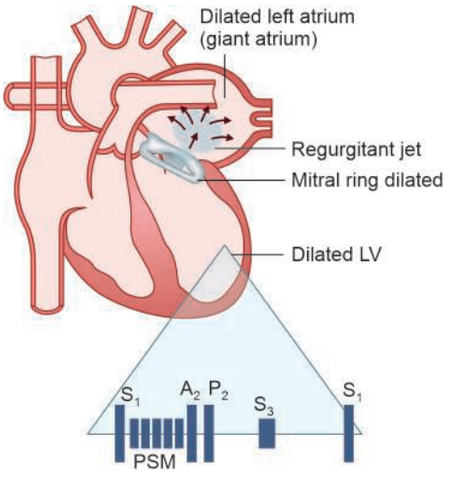


Fig. 1.30: Mitral regurgitation. Hemodynamic effects and auscultatory findings

History

Points to be Asked/Noted

Ask for the following:

- History of repeated chest infections, e.g. fever, cough, sputum
- Exertional dyspnea, nocturnal dyspnea, palpitation
- Symptoms of acute pulmonary edema, e.g. cough, frothy sputum, dyspnea at rest and hemoptysis
- Fatigue, weakness, tiredness due to reduced cardiac output
- Puffiness of face, edema or leg swelling, ascites due to right heart failure
- History of trauma to chest or cardiac surgery, MI, connective tissue disease, infective endocarditis.

Past History

- Ask for history of sore throat, skin infection, rheumatic fever (joint pain)
- History of recurrent chest infections, fever, paralysis.

General Physical Examination

- ***Pulse*** may be good volume or normal volume or jerky. It is usually regular but becomes irregular in presence of atrial fibrillation or ventricular ectopics
- ***Pulse pressure*** may be wide or normal.

  Note: BP, temperature and respiration
- ***Cyanosis*** (peripheral or central or both) may be present
- ***Raised jugular venous pressure*** with prominent 'a' wave in severe pulmonary hypertension and 'v' wave if TR develops
- ***Pitting pedal edema***
- ***Look for signs of bacterial endocarditis***, e.g. fever, splinter hemorrhage, Janeway's lesion, palmar erythema, clubbing of fingers, painful fingertips or gangrenous finger(s), cold extremities, red colouration of urine
- ***Look for signs of acute rheumatic activity***, e.g. arthritis, fever, erythema marginatum, subcutaneous nodules, etc.
- *Note for the presence of features of Marfan's syndrome*, e.g. tall stature arachnodactyly, high-arched palate, ectopia lentis.

Systemic Examinations

I. Cardiovascular System

Inspection

- Apex beat is displaced down beyond 5th intercostal space outside the midclavicular line and is diffuse but forceful
- Pulmonary artery pulsations in 2nd left intercostal space may be seen
- Left parasternal heave may be visible.

Palpation

- Left parasternal heave may be palpable
- Displaced down and out forceful apex beat
- Systolic thrill at apex may be palpable
- P2 may be palpable in pulmonary area in pulmonary hypertension.

Percussion

Left border of heart corresponds to apex beat, i.e. dullness does not extend beyond apex beat.

Auscultation

- *First heart sound soft or muffled* and buried in the pansystolic murmur
- *Pansystolic murmur at apex*, high-pitched soft and radiates to left axilla, heard with diaphragm of the stethoscope in expiration
- *Third heart sound (S3)* may be present, is caused by rapid flow of blood causing tensing of papillary muscle, chordae tendineae and valve leaflets
- *P2 may be loud and narrowly split*. Ejection systolic and/or diastolic murmur (Graham-Steell) at 2nd left space. These are signs of pulmonary arterial hypertension.

II. Examination of other Systems

1. **Respiratory system**
   - Tachypnea may be present
   - Crackles and rales at bases of lungs.
2. **Abdominal examination**
   - Mild tender hepatomegaly
   - No ascites, no splenomegaly.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is the clinical diagnosis in this case?

Ans. The symptoms and signs suggest the diagnosis of mitral regurgitation (MR) with CHF with normal sinus rhythm without SABE and acute rheumatic activity in this case.

Q 2. What are points in favour of your diagnosis?

Ans.
1. **History of dyspnea,** orthopnea and PND.
2. **Signs of MR,** i.e. down and out apex beat, parasternal heave, a pansystolic murmur radiating to axilla, muffled S1 and a S3.
3. **Signs of pulmonary hypertension,** e.g. loud P2, narrow split S2.
4. **Signs of CHF, e.g.** raised JVP, tender hepatomegaly and edema feet.

Q 3. Could it be mitral valve prolapse (MVP)?

Ans. No, there is no click and murmur is holosystolic instead of mid and late systolic.

Q 4. What is prevalence of MVP in general population?

Ans. About 9–10%. More common in young females (15–35 years).

Q 5. What is mechanism of click in MVP?

Ans. It is due to sudden tensing of mitral valve apparatus as the leaflet prolapse into the left atrium during systole.

Q 6. How do you define mitral regurgitation? What are its hemodynamic consequences?

Ans. Regurgitation of blood through the mitral valve during systole is called *mitral regurgitation*.

Hemodynamic consequences

1. Dilatation of left atrium (*giant atrium*). It occurs first of all.
2. Dilatation of left ventricle due to volume overload leading to subsequent LVF.
3. The back flow of blood from overloaded left atrium produces lung congestion, pulmonary edema and subsequent pulmonary arterial hypertension.
4. Ultimately pulmonary arterial hypertension leads to right ventricular hypertrophy, then congestive heart failure.

Q 7. What are the causes of mitral regurgitation?

Ans. The causes are rheumatic (less common) and non-rheumatic (common, read Table 1.102).

Table 1.102: Causes of mitral regurgitation

1. **Rheumatic (less common)**
× Rheumatic heart disease, acute rheumatic fever
2. **Non-rheumatic (common)**
× Mitral valve prolapse
× Myocarditis
× Acute MI (due to papillary muscle dysfunction or rupture of chordae tendineae producing acute mitral regurgitation)
× Infective endocarditis
× Dilated cardiomyopathy
× Trauma during valvotomy
× Marfan's syndrome
× SLE (Libman-Sack's endocarditis)
× Rarely congenital
3. **Left ventricular dilatation (Wolverine dilatation) secondary to:**
× Aortic valve disease, e.g. AS, AR or both
× Systemic hypertension
Remember: Isolated mitral regurgitation is commonly nonrheumatic in origin.

Q 8. What are the frequencies with which various valves get affected by rheumatic heart disease?

Ans.
- Mitral valve disease (80%). MS is the commonest lesion followed by combined MS and MR
- Aortic valve (50%)
- Combined mitral and aortic valve lesion (20%)
- Tricuspid valve involvement (10%)
- Pulmonary valve involvement rare (<1%).

Q 9. What are congenital causes of MR?

Ans.
1. Ostium primum atrial septal defect (cleft mitral valve)
2. Endocardial cushion defect (partial atrioventricular canal).

Q 10. Where are clinical characteristic features of severe MR?

Ans. Clinical characteristic features of severe MR are:
1. A good volume pulse with wide pulse pressure
2. Raised JVP with prominent 'a' wave
3. Bilateral pitting pedal edema
4. *Apex beat is hyperdynamic* and goes down and out. A *systolic thrill* may be palpable.
5. Left parasternal heave
6. **On auscultation**
   - The S1 is generally muffled, soft or buried within pansystolic murmur
   - A pansystolic murmur radiating to left axilla
   - S3 or S4 may be audible
   - A short-soft diastolic murmur may be heard in severe MR.

Q 11. How would you grade systolic murmurs?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 12. What is pansystolic murmur and what are its causes?

Ans. **Definition:** A pansystolic or holosystolic murmur starts with the first heart sound (S1) and continues throughout the systole and embraces S2. It has uniform intensity hence called *holosystolic*.

Causes

1. **MR due to any cause (read the causes in** Table 1.118.
2. **TR:** The pansystolic murmur is best audible in the tricuspid area (left parasternal), increases in intensity with inspiration (Carvallo's sign).
3. **Ventricular septal defect (malade Roger):** The murmur is rough, pansystolic, best heard across the chest (on both sides of sternum). Very often, there is an associated thrill.
4. **Dilated cardiomyopathy** sometimes *myocarditis*
5. **Functional pancystolic murmur (left ventricular dilatation):** These murmurs are usually soft, mostly midsystolic, may be pansystolic.
6. **Papillary muscle dysfunction.**

Q 13. What does mid-diastolic murmur in MR indicate?

Ans. It indicates:

1. MR with MS
2. Severe MR with functional MS.

Q 14. What are causes of acute MR?

Ans. Causes of acute MR are:

1. Rupture of papillary muscle or chordae tendineae in MI.
2. Acute bacterial endocarditis with rupture/perforation of valve cusps or chordae tendineae.
3. Traumatic rupture of chordae tendineae.
4. Myxomatous degeneration of the valve.

Q 15. What are the characteristics of mitral valve prolapse syndrome (Barlow's syndrome, mid-systolic click-murmur syndrome, floppy mitral valve syndrome)?

Ans. The characteristic features are:

1. It is characterised by myxomatous degeneration of the mitral leaflets resulting in redundant mitral leaflets.
2. It is commonly seen in young females (20–35 years).
   - It is asymptomatic and mid-systolic murmur or the click or both may be the only evidence. Valsalva maneuver and standing increase the murmur while squatting decreases it.
3. There is prolapse of one of mitral cusp into LA, during systole.
4. β-blockers are indicated for symptom relief and prophylaxis.

Q 16. When does the murmur of MR radiates to neck (or base of heart) instead of axilla?

Ans. Rarely involvement of posterior mitral leaflet in mitral valve prolapse syndrome or ruptured chordae tendineae, reflects the murmur towards the base of heart.

Q 17. What are the causes of mitral valve prolapse?

Ans. Following are causes:

1. Marfan's syndrome
2. Ehlers-Danlos syndrome
3. SLE
4. Straight-back syndrome (a thoracic cage abnormality)
5. As a sequel of acute rheumatic fever
6. Ischemic heart disease
7. Cardiomyopathy.

Q 18. What is Cooing or 'Seagull' murmur?

Ans. When a patient of MR either develops SABE or rupture of chordae tendineae in MI, a systolic murmur appears that has either a cooing or musical or seagull quality—here the chordae tendineae act like strings of a musical instrument.

Q 19. What is effect of Valsalva maneuver on MR?

Ans. The systolic murmur of MR is increased by isometric strain (handgrip) but is reduced during the Valsalva maneuver.

Q 20. What are clinical signs of congestive heart failure?

Ans. Following are signs of congestive heart failure:

1. Extremities may be cold or pale.
2. Tachycardia and tachypnea.
3. Profuse sweating or perspiration.
4. Central cyanosis, raised JVP, pitting edema.
5. Low volume pulse or pulsus alternans.
6. Cheyne-Stokes breathing.
7. Third heart sound (S3). Ventricular gallop rhythm means triple rhythm (S1, S2, S3 sounds) with tachycardia—is so named because it resembles with the sound produced by galloping of a horse).
8. Fine basal pulmonary rales/crackles.
9. Expiratory wheezing.
10. Hydrothorax or pleural effusion may be present
11. Oliguria and nocturia may be present
12. Cardiomegaly with other signs of basic heart disease.

Q 21. What are the causes of right heart failure?

Ans. Following are the causes:

1. **Pulmonary valve disease**
   - Pulmonary stenosis
   - Pulmonary hypertension due to any cause
   - Acute cor pulmonale (pulmonary thromboembolism)
   - Chronic cor pulmonale.
2. **Tricuspid diseases**
   - Tricuspid stenosis
   - Tricuspid regurgitation (dilated cardiomyopathy).
3. **Depressed myocardial contractility**
   - Right ventricular infarction
   - Right ventricular dysplasia (right ventricular cardiomyopathy)
   - Myocarditis.

4. **Secondary to left heart failure.** The left ventricular failure ultimately may lead to right ventricular failure.

Q 22. What are the complications of MR?

Ans. Complications of MR are:

1. Acute LVF (acute pulmonary edema).
2. Infective endocarditis.
3. CHF and deep vein thrombosis.
4. Arrhythmias, e.g. ventricular ectopics, atrial fibrillation common. Atrial fibrillation is due to giant left atrium.
5. Giant left atrium may produce pressure symptoms, e.g. hoarseness, dysphagia.
6. Thromboembolism.
7. Atypical chest pain.

Q 23. How will you investigate a patient with MR?

Ans. Investigations required are as follows:

1. **Chest X-ray.** It may show:
   - Cardiac shadow is enlarged and occupies >50% of transthoracic diameter.
   - The left atrium may be massively enlarged and forms the right border of the heart.
   - The left ventricle is also enlarged producing *boot-shaped heart*.
   - There may be pulmonary venous congestion (e.g. upper lobar veins prominent producing increased bronchovascular marking or there may be diffuse haze from hilum to periphery—pulmonary edema), interstitial edema (*Kerley's B lines*) and sometimes interlobar fissure effusion or hydrothorax.
   - Mitral valve calcification may occur, seen in penetrating films.
2. **ECG.** It may show:
   - Right atrial, left atrial or biatrial hypertrophy
   - LV or biventricular hypertrophy
   - AF
   - Inferior or posterior wall ischemia/infarction if CAD is the cause.
3. **Echocardiogram and Doppler imaging.** The 2D-echocardiogram is useful for assessing the cause of MR displacement of one or both cusps into left atrium during systole in AVP and for estimating the LV function and ejection fractions. Left atrium are left ventricle enlarged. Vegetations may be seen in infective endocarditis. The echocardiogram M-mode shows characteristic feature of MVPS (incomplete coaptation of anterior and posterior leaflets during mid and late systole).
4. **Colour Doppler flow study** is most accurate diagnostic technique for detection and quantification of MR. It shows a characteristic regurgitant jet.

Q 24. What are the causes of LVH? What are its ECG characteristics?

Ans. Read *Practical Electrocardiography* by Prof SN Chugh.

Q 25. How will you decide clinically the dominance of mitral valve lesion in a patient with combined mitral valve disease (MS and MR)?

Ans. The dominance is decided by features described in Table 1.103.

Q 26. How will you treat a patient with MR?

Ans. 1. **Medical treatment**
   - Asymptomatic disease does not require treatment except penicillin prophylaxis such as mitral valve prolapse
   - Salt restriction
   - Digitalis and diuretics

Table 1.103: Features of dominant MS or MR in combined valvular lesion

Feature	*Dominant MS*	*Dominant MR*
1. **Clinical presentations**	Dyspnea on exertion, orthopnea and PND. Palpitation is uncommon occurs if AF present	Palpitations common, followed by dyspnea, orthopnea and PND
2. **Symptoms**		
× Hemoptysis and PND	Marked	Mild
× Symptoms of CHF		
× Systemic embolization		
× Lung congestion		
3. **Signs**		
× Pulse	Low volume	Normal volume
× BP	Low systolic	Within normal limits
× Apex	Tapping, not displaced	Heaving and displaced down and out
× Left parasternal heave	Grade III	Grade I
× First heart sound	Short, loud and snappy	Soft or muffled
× Opening snap	Present	Absent
× Third heart sound (S3)	Absent	Present
× Murmur and thrill	× Rough and rumbling diastolic murmur with thrill	× Soft pansystolic murmur radiating to axilla with a systolic thrill
	× Pansystolic murmur present, does not radiate to axilla	× Soft mid-diastolic murmur
4. **Chest X-ray**	Mitralized heart	Cardiomegaly with giant left atrium forming right heart border
5. **ECG**	RVH with left axis deviation	LVH with right axis deviation

- Bronchodilatation if there is severe bronchospasm
- Vasodilators (ACE-inhibitors) to reduce the regurgitant flow in severe cases.
- *Prophylaxis.* Penicillin prophylaxis is must.

2. **Surgical treatment is valve replacement.**

Q 27. What is indication of surgery in MR?

Ans. Moderate to severe symptomatic disease with good left ventricular function.

Q 28. What does 3rd heart sound in MR indicate?

Ans. The presence of 3rd heart sound in MR indicates rapid ventricular filling due to free flow of blood through mitral valve.

- It signifies moderate to severe MR
- It indicates dominance of MR over MS in combined mitral valve lesion.

Q 29. How will you treat digitalis toxicity?

Ans. The steps of treatment are:

- Stop digoxin
- Stop diuretic
- Give potassium
- Give phenytoin for digitalis-induced arrhythmia
- Give digitalis Fab antibody.

Q 30. How would you differentiate MR from TR?

Ans.

Feature	*Mitral regurgitation*	*Tricuspid regurgitation*
Pulse	Good volume Jerky or normal volume	Normal pulse
JVP	Raised with prominent 'a' wave	Raised with 'VY' collapse
Palpation	Left ventricular heave	Left parasternal heave
Auscultation	× Pansystolic murmur	× Pansystolic murmur at apex at left parasternal edge or epigastrium
	× Murmur radiates to axilla	× Murmur may be heard in epigastrium and right sternal border
	× Intensity increases with expiration	× Intensify increases with inspiration
	× 3rd heart sound present	× 4th heart sound present
Other features	× Liver may be enlarged without pulsation	× Liver enlarged with pulsations (pulsatile liver)
	× Lungs congested with crackles	× Lungs may or may not be congested, depend on its cause—isolated or associated

Q 31. What are signs of digitalis toxicity?

Ans. The signs are as follows:

1. **GI manifestations, e.**g. anorexia, nausea, vomiting. These are earliest to appear.
2. **Cardiac arrhythmias and conduction disturbances**
   i. Premature ventricular complexes (VPCs) usually ventricular bigeminy or multiforme.
   ii. Nonparoxysmal atrial tachycardia with block
   iii. Varying degrees of AV block
   iv. Ventricular tachycardia; bidirectional ventricular tachycardia is mainly due to digitalis.
3. **Miscellaneous effects**
   - Weight loss
   - Cardiac cachexia
   - Gynecomastia
   - Yellow vision (xanthopsia).
   - Mental features, e.g. agitation

Q 32. Mention recent Jones criteria for acute rheumatic fever.

Ans. Table 1.104 explains the Jones criteria for acute rheumatic fever.

Table 1.104: Jones diagnostic criteria for acute rheumatic fever

1. **Major**
   - × Carditis
   - × Polyarthritis
   - × Chorea
   - × Erythema marginatum
   - × Subcutaneous nodules
2. **Minor**
   - × Fever
   - × Arthralgia
   - × Previous rheumatic fever
   - × Raised ESR or C-reactive protein
   - × Leukocytosis
   - × First degree or second degree AV block
   - × Echocardiographic evidence of endocarditis

The diagnosis is *definite* if:

- × Two or more major manifestations are present
- × One major and two or more minor manifestations

Plus

- × Supporting evidence of preceding streptococcal infection, recent scarlet fever, raised ASO titers or other streptococcal antibody titer, positive throat culture, or echocardiographic evidence of carditis

Q 33. What are various types of prosthetic valves?

Ans. I. **Mechanical valves**

- Ball and cage (*Starr-Edwards*)
- Tilting disc valve (*Bjork-Shirley and St Jude*).

II. **Tissue (biological valves)**

- *Xenografts* (porcine valves and pericardial valves derived from animal tissue)
- *Homograft* human *cadaveric* aortic or pulmonary valve).

Q 34. What are indications of valve replacement?

Ans.

- Severe calcified mitral stenosis
- Calcific aortic stenosis
- Severe mitral regurgitation
- Severe aortic regurgitation.

Q 35. What kind of valve would you use to replace mitral valve and why?

Ans. Mechanical valve because of durability. Anticoagulant is to be used to protect them.

Q 36. Why mechanical valves are preferred over bioprosthesis?

Ans. Mechanical valves are preferred because of two reasons:

- Lower rate of reoperation
- Lower chances of anticoagulant related bleeding.

Q 37. Which bioprosthesis is commonly used?

Ans. Porcine heart valve.

Q 38. What are complications of porcine heart valve?

Ans.

- Degeneration with time
- Calcification.

Q 39. What are the complications of mechanical valves?

Ans.

i. High incidence of hemolysis leading to anemia
ii. Thromboembolism
iii. Bleeding due to anticoagulants use
iv. Endocarditis
v. Valve dysfunction, e.g. valve leak, valve dehiscence and valve obstruction by thrombus or clogging
vi. Structural dysfunction, e.g. fracture, cuspal tear and calcification.
vii. Nonstructural dysfunction, e.g. perivalvular leak, suture entrapment.

Q 40. Which patients should receive bioprosthetic valve?

Ans.

1. Those unable to take anticoagulants.
2. Those not expected to live longer than predicted lifespan of prosthesis (7–10 years).
3. Patients over the age of 70 years who require an aortic valve replacement as the rate of degeneration is slow in these patients.

Q 41. How would you recognise that patient had prosthetic valve?

Ans.

i. Mid-sternal vertical thoracotomy scar
ii. Metallic heart sounds in mitral area (mitral valve replaced) or aortic area (aortic valve replaced).

Q 42. In women of childbearing age, which valve would you prefer?

Ans. Until recently bioprosthetic valves were being preferred to avoid risk of anticoagulation on the fetus and spontaneous abortion. Nowadays, mechanical valves are preferred because studies have now shown low risk of warfarin and spontaneous abortion in women.

Q 43. Which valve would you use in presence of AF?

Ans. Mechanical valve as these patients need anticoagulation treatment.

CASE 31: INFECTIVE ENDOCARDITIS

The patient (not in picture) presented with palpitation, cough, breathlessness and chest discomfort. There was history of PND and edema of feet off and on for the last few years. He was taking treatment and edema and breathlessness relieved. Now he complained of fever with chills, rigors and diaphoresis. He developed gangrene of the fingers (Fig. 1.31A) suddenly.

Clinical Presentations of Infective Endocarditis

1. **Acute endocarditis** caused by more virulent organisms mostly *Staphylococcus aureus* involves normal heart valves or cardiac structures, produces acute febrile illness with fever, chills, diaphoresis and acute onset of regurgitant murmur due to damage to valves and cardiac structures, with septic embolization to various viscera and peripheral structures.
2. **Subacute infective endocarditis caused by less virulent organisms such as bacteria, i.e. (***Streptococci, Pneumococci, Staphylococci, fastidious gram-negative coccobacilli, HACEK group—Haemophilus, Actinobacillus, Corynebacterium, Eikenella and Kingella***), fungi (***Candida***) or rickettsia (cause insidious onset of fever with chills and rigors) is characterised by changing or new cardiac murmurs, precipitation of CHF and embolization to viscera and peripheral vessels in a patient who is already suffering from either a congenital heart disease or acquired rheumatic heart disease or has undergone cardiac surgery or has prosthetic valve.**

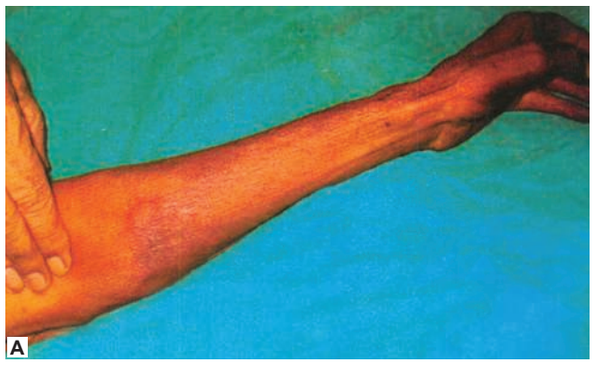
History

Points to be Noted

- Onset, duration of symptoms.
- History of fever, sore throat
- Dyspnea, palpitation, cough, chest discomfort due to basic heart disease, i.e. valvular or congenital lesion
- Fever with chills, diaphoresis
- Symptoms of complications such as CHF or systemic embolization, e.g. cold extremity, hemiplegia, hematuria
- Visual disturbance or visual loss
- History of procedure or dental extraction in a patient with underlying congenital or acquired valvular heart disease
- History of recent cardiac surgery
- History of IV drug misuse
- History of sepsis, skin infection
- Ask about **past history** of rheumatic or congenital heart disease.

General Physical Examination

- General look-toxic (present). Patient is febrile
- Weight loss
- The skin may show purpuric spot, ecchymosis, Janeway lesion
- Neck for JVP and lymphadenopathy
- *Extremities.*
  - Clubbing of fingers
  - Janeway lesion
  - Digital gangrene
  - Petechiae
  - Splinter hemorrhage
  - Osler's nodes
  - Coldness of extremities
  - Painful fingertips
- **Eyes** for subconjunctival hemorrhage, Roth's spots
  - Look for anemia, cyanosis, jaundice, edema
  - **Examine vitals**, e.g. pulse, BP, respiration and temperature
  - **Palpate all the peripheral pulses.** Pulsation in left brachial artery absent in this case (Fig. 1.31A).



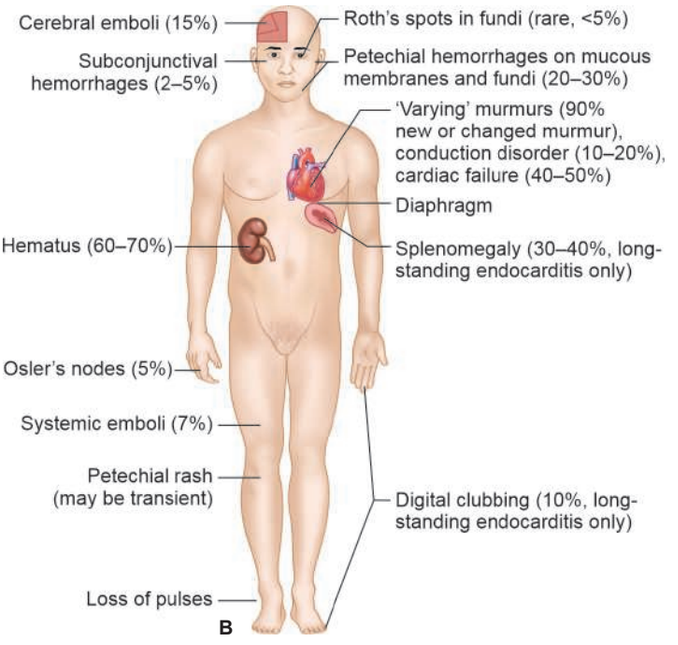


Fig. 1.31A and B: Infective endocarditis. **A.** Gangrenous fingers, hand and forearm on left side due to embolic occlusion of brachial artery on Doppler study. The patient had cold extremities with absent brachial and radial pulses on left side; **B.** Clinical features of endocarditis (diagram). **Note: Brachial/pulsation absent on left side and radial**

Systemic Examinations

1. CVS

- *Inspection.* Look for signs of LHF and basic heart disease.
- *Palpation.* Look for signs of LHF and basic heart disease.
- *Percussion* for cardiac dullness.
- *Auscultation.* Auscultate for any murmur, change in previous murmur and appearance of new murmur in addition to findings of heart disease.

2. Other Systems

- *Nervous system* for motor or sensory deficit due to embolization (stroke). Examine ocular fundi
- *Respiratory system* for pulmonary embolism, infection, LVF
- *Kidneys* for pain and tenderness in renal area or hematuria
- Abdomen palpate for *splenomegaly* and hepatomegaly.

Remember: In patients with infective endocarditis. Always look for signs of heart failure. Auscultate for any murmur, change in murmur and appearance of new murmur in addition to basic findings of underlying disease.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. In view of history suggestive of some heart disease with CHF combined with embolic occlusion of brachial artery with gangrenous fingers, the **provisional diagnosis** is infective endocarditis due to underlying cardiac disorder which will be apparent on physical signs and on investigations.

Q 2. Name the conditions that produce clinical feature similar to endocarditis.

Ans.
- Atrial myxoma
- Sickle cell disease
- SLE
- Nonbacterial endocarditis.

Q 3. How you do define endocarditis? What are common causative organisms?

Ans. *Infective endocarditis* is microbial infection of a heart valve (native, prosthetic), the lining of a cardiac chamber, or blood vessels or a congenital septal defect or a congenital anomaly. The causative organism is either a bacterium (*S. viridans, S. aureus, S. faecalis*) or a fungus or a rickettsia (*Q fever endocarditis*).

I. Acute endocarditis is usually bacterial in origin, has rapid onset, fulminant course causing destruction of cardiac structures, perforation of valve cusps and hematogenously seeds the extracardiac sites, and if untreated, progresses to death within weeks.

II. Subacute endocarditis follows an indolent course, causes structural cardiac damage slowly and rarely causes metastatic infection, and is gradually progressive unless complicated by a major embolic event or rupture of mycotic aneurysm.

Q 4. What are symptoms and signs of endocarditis? What is their pathogenesis?

Ans. The symptoms and signs (Table 1.105) are due to:
- Infection and fluctuating toxemia
- Embolization
- Immune-complex mechanism
- Anemia.

Table 1.105: The symptoms and signs of infective endocarditis

Organ	*Symptoms and signs (Fig. 1.31B)*
General	Fever, nausea, anorexia, sweating, weakness
	Temperature is raised, weight loss is present
Heart	Dyspnea, palpitations, cough, pain chest
	× Tachycardia
	× Changing or appearance of new murmurs
	× Conduction defects
	× CHF
	× Muffling of heart sounds
Lung	Hemoptysis, chest pain
	Pleuritic rub due to embolic pulmonary infarct may be present
CNS	Headache, toxic encephlopathy, meningitis
	Monoplegia or hemiplegia due to embolization
Blood vessels	Coldness of extremities
	× Loss of peripheral pulses due to embolization
	× Digital gangrene
	× Clubbing of the fingers
	× Splinter hemorrhages
	× Osler's nodes (painful tender swellings at fingertips) Janeway's lesion (large nontender maculopapular eruptions in palm and sole)
Skin	× Petechial hemorrhage
	× Purpuric spots
	× Eyes, i.e. redness of eyes, visual disturbance
	× Subconjunctival hemorrhage (blindness)
	× Roth's spots
Kidneys	× Hematuria
	× Renal angle tender
	× Acute flank pain, pain in splenic area
	× Splenomegaly
	× Splenic infarct (rub)
Blood	Pallor, lassitude, fatigue
	Anemia

Q 5. What are complications of endocarditis?

Ans. Common complications are:
1. **Heart failure.** Endocarditis may precipitate or aggravate the heart failure.
2. **Embolization** to any organ producing an infarct.
3. **Neurological complications.** *Embolic stroke* is the most common neurological complication.

Intracranial hemorrhage may occur due to ruptured mycotic aneurysm.

4. **Septicemia, meningitis and brain abscess can occur.**
5. **Valve destruction, e.**g. acute regurgitation.
6. **Local extension, e.**g. myocarditis (abscess) and purulent pericarditis.
7. **Glomerulonephritis (immune-complex).**

Q 6. What are clinical features of acute bacterial endocarditis?

Ans. Clinical features are as follows:

1. Fever and toxemia (chills, rigors)
2. Often involves the normal heart valves and has rapid downhill course.
3. **Staphylococcus** is the commonest pathogen
4. Right-sided involvement is common because it is common in IV drug users. Pneumonia is common.
5. Clubbing is not a feature.
6. Cardiac and renal failure develop rapidly.
7. Perforation of cusps (aortic, mitral) may occur leading to acute valvular regurgitation.

Q 7. When do you suspect infective endocarditis in a patient with heart lesion?

Ans. Diagnosis of infective endocarditis is suspected: In each and every patient of rheumatic valvular heart disease or a congenital heart disease developing fever, tachycardia, worsening dyspnea or congestive heart failure or an embolic episode, e.g. monoplegia/hemiplegia, hematuria, etc.

Q 8. Name the predisposing factors for endocarditis.

Ans. Predisposing factors are:

1. **Valvular heart disease.** Mitral and aortic valvular lesion predispose to infective endocarditis.
2. **Congenital heart disease.** The VSD, PDA and bicuspid aortic valve are common predisposing lesions.

Remember: The ASD does not lead to endocarditis.

3. **Prosthetic valve.**
4. **Immunocompromised state** either due to disease (diabetes, malignancy) or due to drugs (steroids and immunosuppressive drugs).
5. **Intravenous drug abusers.**
6. **Prior heart surgery** (valvotomy, balloon dilatation and valve replacement).

Q 9. How will you investigate a patient suspected of endocarditis?

Ans. Investigations required are as follows:

1. **Blood examination.** There may be anemia (normocytic normochromic) leukocytosis and raised ESR and high C-reactive protein levels.
2. **Urine examination reveals mild albuminuria and microscopic hematuria.** Gross hematuria is rare.
3. **Immune-complex titer and rheumatoid factor titers may be elevated.**
4. **Blood culture.** Isolation of the microorganism from blood cultures is crucial not only for diagnosis but also for determination of antimicrobial sensitivity and planning the management. In the absence of prior antibiotic therapy; a total of 3 blood culture sets, ideally with the first separated from the last by at least 1 hour from different sites should be obtained from different venipuncture sites over 24 hours. If the cultures remain negative after 48 to 72 hours; two or three additional blood cultures, including a lysis-centrifugation culture, should be obtained, and the laboratory should be asked to pursue fastidious microorganisms by prolonging the incubation time and performing special subcultures.
5. **Echocardiogram.** Vegetations may be identified on valves or congenital defects. **Transesophageal echocardiography** offers the greatest sensitivity for detection of vegetations.
6. **Serological tests.** Polymerase chain reaction can be used to identify some organisms that are difficult to recover from the blood culture.

Q 10. What are the diagnostic criteria for endocarditis?

Ans. The diagnosis of infective endocarditis is established with certainty only if culture from the vegetations is positive. Nevertheless, a highly sensitive and specific diagnostic criteria—*Duke's criteria* have been developed (Table 1.106).

Table 1.106: The Duke's criteria for the clinical diagnosis of infective endocarditis

Infective endocarditis is definite if following criteria using specific definitions listed below are met:

I. Two major criteria
II. One major and three minor criteria
III. Five minor criteria

Major criteria

1. *Positive blood culture* (viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*)
   - i. Typical microorganism for infective endocarditis from two separate blood cultures
   - ii. Persistently positive blood culture, i.e.
     - Blood cultures drawn >12 hours apart
     - All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart
     - Single positive blood culture for *Coxiella burnetii* or phase 1 IgG antibody titer of >1:800
2. Evidence of endocardial involvement on echocardiogram, i.e. vegetation, an abscess over the valve.

Minor criteria

1. Predisposing heart condition or injection drug use
2. *Fever* = 38°C (=100.4°F)
3. *Vascular phenomena:* Major arterial emboli, intracardial hemorrhage, conjunctival hemorrhage, Janeway lesions
4. *Immunologic phenomena*: Glomerulonephritis, Osler's nodes, Roth's spots
5. Microbiologic evidence: Positive blood culture but not meeting major criterion

Abbreviation; HACEK: Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella.

Q 11. What precautions would you take to prevent bacterial endocarditis in a patient with valvular heart disease?

Ans. *Antibiotic prophylaxis* before conducting a procedure in a patient with rheumatic heart disease, congenital heart diseases and prosthetic heart valve.

Q 12. How would you treat a patient suspected to have endocarditis?

Ans. Until culture report becomes available, IV benzylpenicillin and gentamicin will be given on empirical basis. In severely ill patients cloxacillin would be added to the regimen.

Q 13. What is marantic endocarditis?

Ans. **Marantic or Libman-Sacks endocarditis** is seen in SLE. It is a postmortem diagnosis. It is rarely detected clinically.

CASE 32: COR PULMONALE

A 60-year-old male (Fig. 1.32A) presented with cough, breathlessness, progressive in nature for the last 7 years. He has been taking treatment and getting relief on and off. Now for the last 1 month, he complains of increase in breathlessness, cough and edema of legs and feet. Examination revealed emphysematous chest (barrel-shaped) with hyperresonant note on percussion. Auscultation revealed vesicular breathing with prolonged expiration, crackles and rhonchi on both sides.

Clinical Presentation of Cor Pulmonale

- ***Patients suffering from chronic lung disease*** (obstructive or suppurative or interstitial) present with signs of right ventricular failure (*distended neck veins*, *cyanosis*, *tender hepatomegaly* and *pitting edema*).
- ***A patient with chronic chest deformity,*** e.g. ***kyphoscoliosis*** may present with symptoms of *progressive dyspnea*, *worsening cough* over the last few years. They may complain of *pain abdomen* and *edema feet* due to right heart failure.

History

Points to be Noted

Ask about

- Age, sex, onset and duration of symptoms
- Cough, its frequency, seasonal relation, nocturnal, etc.
- Sputum production, quantity, colour, smell, consistency and history of hemoptysis
- Any recent change in the symptoms. History of recent fever, sore throat or loose motions
- History of swelling feet, abdomen (hepatomegaly)
- Ask for any aggravating or relieving factors
- Take full drug history, drug being taken and their effect.

Past history

- Cough or expectoration in the past
- History of allergy or rhinitis or asthma in the past.

Personal history

History of smoking, alcoholism, exposure to dust or fumes.

Occupational history.

General Physical Examination

- Patient is adult male.
- Patient is orthopneic, sitting with hands on cardiac table and legs dangling/hanging from the bed to relieve breathlessness. This is typical posture and opted by patient with CHF and cor pulmonale.
- Cyanosis present
- Neck veins distended. JVP raised. There may be v and y collapse due to TR (present in this case).
- Pulse and respiratory rate increased
- Warm extremities, clubbing of fingers and edema feet may be present (present in this case)
- Pursed lip breathing may be present (present in this case)
- Action of extra-respiratory muscles, i.e. there may be hyperactivity.

Systemic Examinations

I. Examination of Respiratory System

- Inspection
- Palpation
- Percussion

} There will be evidence of COPD or other chronic lung disease

- Auscultation—reveals vesicular breathing with prolonged expiration. Crackles and rhonchi were scattered all over the chest.

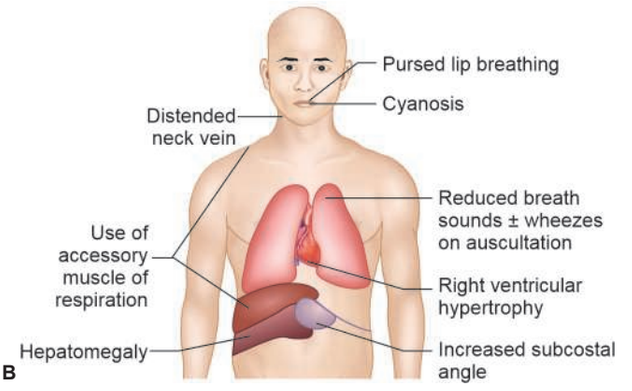


Fig. 1.32A and B: **A.** Chronic cor pulmonale. The patient has signs of COPD. Note the pursed lip breathing, cyanotic spells. The patient has edema and raised JVP. Note the common position adopted by patient with COPD and acute exacerbation with cor pulmonale to get relief from breathlessness; **B.** Clinical signs of chronic cor pulmonale (diagram)

2. Examination of CVS

Inspection

- Apex beat may be normally placed or centrally placed or displaced outwards but not downwards or may not be visible
- No other visible pulsation.

Palpation

- Apex beat may or may not be palpable (not palpable in this case)
- Parasternal heave present
- Right ventricular pulsations palpable in epigastrium.

Percussion

Cardiac dullness may be masked or just limited to center due to overdistended (cardiac dullness was masked).

Auscultation

- Heart sounds normal
- Second heart sound narrowly split
- There may be an ejection systolic murmur in P2 area and a pansystolic murmur in tricuspid area.

3. Abdominal Examination

- Liver is enlarged, soft, tender and may be pulsatile if TR present (liver was enlarged and tender in this case)
- There may be signs of ascites (fluid thrill and shifting dullness present).

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. The symptoms and signs suggest COPD with pulmonary hypertension with chronic cor pulmonale and congestive heart failure.

Q 2. What is differential diagnosis in your case?

Ans. When all the signs of CHF such as raised JVP, cyanosis, dyspnea/tachypnea, ascites and edema are present then following conditions will constitute the differential diagnosis.

1. **Valvular heart disease:** The presence of cardiomegaly, presence of precordial pulsations, murmurs and thrill and added heart sounds make the diagnosis clear.
2. **Cardiomyopathies:** The cardiomegaly with or without murmurs when there is no cause to explain cardiomegaly constitute myocardial disease. Signs of pulmonary disease will be absent.
3. **Primary pulmonary hypertension:** In this condition, symptoms and signs of lung disease will be absent. These patients usually present with progressive dyspnea commonly in females, occurs due to repeated pulmonary embolisation. All signs of pulmonary hypertension (loud P2, narrow split S2 and Graham-Steell murmur, signs of TR) are present with RV failure.
4. **Constrictive pericarditis:** The precordial chest pain, distended neck veins with raised JVP and prominent χ descent with muffled heart sounds, enlarged cardiac shadow on X-ray chest suggest the diagnosis of pericardial disease.
5. **Cor pulmonale secondary to pulmonary disease:** Features of cor pulmonale has been described as separate question.

Q 3. How do you define cor pulmonale?

Ans. **Chronic cor pulmonale** is defined as right ventricular hypertrophy or dilatation secondary to the disease of the lung parenchyma, pulmonary vasculature, thoracic cage and ventilatory control.

Q 4. What are positive features in favour of your diagnosis?

Ans. Sir, *first of all* history is suggestive of COPD, i.e. history of cough for most of the days in a week for 3 months in a year for 2 consecutive years.

Secondly symptoms such as breathlessness, cough, sputum production, hemoptysis and signs such as pursed lip breathing, cyanosis, action of extra respiratory muscles, excavation of suprasternal and supraclavicular fossae, barrel-shaped chest or change in AP and transverse thoracic diameter ratio, decreased respirating movement, diminished expansion and recession of intercostal spaces, reduced vocal fremitus, hyperresonant note on percussion with pushing down of liver dullness to 7th intercostal space suggest COPD. On auscultation, harsh vesicular breathing with prolonged expiration, crackles and rhonchi favour obstruction to the respiratory passage.

Findings of distended neck veins with pulsations and raised JVP, enlarged liver, edema of legs and feet indicate right venticular failure, therefore, after combining the two conditions the diagnosis becomes COPD with cor pulmonale with congestive heart failure:

Q 5. What are the other conditions that produce right heart failure (RHF)?

Ans.

1. *Severe pulmonary stenosis* **(congenital)**
2. *Pulmonary hypertension* due to any cause (valvular heart disease, cor pulmonale, pulmonary vascular disease, etc.).
3. *Eisenmenger's syndrome*, i.e. reversal of left to right shunt (VSD, ASD, PDA) due to development of pulmonary hypertension.
4. Secondary to left heart failure due to any cause.
5. Dilated cardiomyopathy.
6. *Constrictive pericarditis* or chronic or acute *myocarditis*.

Q 6. What are the causes of chronic cor pulmonale?

Ans. The causes are described in Table 1.107.

Table 1.107: Causes of cor pulmonale

I.	**Parenchymal lung disease**
1.	COPD
2.	Hypertrophic emphysema
3.	Diffuse interstitial lung disease
4.	Pneumoconiosis
II.	**Occlusion of pulmonary vascular bed**
1.	Pulmonary thromboembolism (recurrent, medium-sized vessel embolization)
2.	Primary pulmonary hypertension
III.	**Diseases of thoracic cage affecting lung function, i.e. produce chronic hypoventilation**
1.	Obesity (Pickwickian syndrome)
2.	Sleep apnea (rare)
3.	Chest wall dysfunction, e.g. kyphoscoliosis, ankylosing spondylitis
4.	Idiopathic

Q 7. What are clinical signs of pulmonary hypertension (pH)?

Ans. ***Clinical signs of pulmonary arterial hypertension (PH)***

The physical signs which are:

A. **General physical**
- Pulse-low volume
- Neck veins—distended. JVP raised and 'a' wave prominent

B. **Signs on chest examination**
- ***Inspection***
  - Epigastric pulsations due to RV hypertrophy
  - Pulmonary artery pulsations in 2nd left interspace may not be visible due to hyperinflated lungs covering the artery
- ***Palpation***
  - Apex beat may not be visible
  - P2 is palpable
  - Left parasternal heave may be present due to RVH.
- ***Percussion***
  - Cardiac dullness will be masked due to hyperinflated lungs or limited to center (heart is pushed centrally by the overdistended lungs).
- ***Auscultation***
  - Loud P_2—an ejection click in left second intercostal may be present
  - Ejection systolic murmur
  - Close or narrow splitting of S_2
  - Graham-Steell murmur
  - Right-sided S_3.

Q 8. Does definition of cor pulmonale include right heart failure? What are its signs?

Ans. Right heart failure is not included in die definition of chronic cor pulmonale. It is a complication of cor pulmonale.

Q 9. How do you classify pulmonary arterial hypertension?

Ans. See Table 1.108.

Table 1.108: Classification of pulmonary hypertension

I.	**Primary pulmonary hypertension**
	Idiopathic
II.	**Secondary pulmonary hypertension (PH)**
1.	Passive or reactive PH (from left-sided heart lesions) such as MS, MR, AS and AR
2.	Hyperkinetic PH (left to right shunt), e.g. ASD, VSD, PDA
3.	Vasoconstrictive (hypoxic) PH
4.	Obstructive PH (reduction in vascular bed), e.g. pulmonary thromboembolism
5.	Obliterative PH, e.g. Pulmonary angiitis/vasculitis

Q 10. What is normal pulmonary arterial pressure? What is pressure in pulmonary hypertension?

Ans. Normal pulmonary arterial pressure 18–25/6–10 mmHg. In pulmonary hypertension:
- Pulmonary artery systolic pressure is >30 mmHg
- Mean pulmonary artery wedge pressure is >20 mmHg.

Q 11. What are causes of TR? Name its two characteristics?

Ans. The causes of TR are:
1. Right ventricular dilatation secondary to pulmonary hypertension
2. Rheumatic heart disease
3. Right-sided endocarditis in drug abusers
4. Right ventricular infarction
5. Carcinoid syndrome.

The two ***characteristic signs*** of TR are:
1. A **pansystolic murmur** in tricuspid area (right parasternal area/epigastrium) is heard which increases with inspiration.
2. Pulsatile liver and positive.
3. Hepatojugular reflux.

Q 12. How will you investigate a patient with cor pulmonale?

Ans. Investigations required are as follows:
1. **Chest X-ray.** It will show:
   - Cardiomegaly
   - Pulmonary conus is prominent
   - Hilar bronchovascular markings prominent with pruning of the peripheral pulmonary vessels
   - Signs of COPD (emphysema) on X-ray will be evident (read radiology section).
2. **ECG.** It will show
   - Low voltage graph
   - Right axis deviation, clockwise rotation
   - Right atrial hypertrophy (P-pulmonale)
   - Right ventricular hypertrophy (R>S or R:S >1 in lead VI but both complexes being small)
   - SI, SII, and SIII syndrome
   - ST-T wave changes
   - Arrhythmias (MAT—multifocal atrial tachycardia is common).

3. **Echocardiography.** It will show increased right atrial and right ventricular wall thickness and enlargement of cavity. Interventricular septum is displaced leftward. Colour Doppler may reveal functional TR.
4. **MRI** useful to measure RV mass, wall thickness, and ejection fraction.
5. **Ventilation and perfusion scan are helpful in confirming the diagnosis of chronic pulmonary vascular disease.**

Q 13. What are the complications of cor pulmonale?

Ans. Following are complications:

1. Right heart failure
2. Secondary polycythemia
3. Deep vein thrombosis
4. Cardiac arrhythmias (multifocal atrial tachycardia, ventricular arrhythmias).

Q 14. Is cor pulmonale high output failure? What are other causes of high output failure?

Ans. Initially, cor pulmonale is high output failure when hypoxia dominates leading to wide pulse pressure, later on due to involvement of myocardium, it becomes low output failure. **Other causes** of high output failure are:

i. Aortic regurgitation
ii. Severe anemia (Hb <4 g%)
iii. Severe thyrotoxicosis
iv. Arteriovenous fistula
v. Paget's disease
vi. Cirrhosis of the liver
vii. Beriberi heart disease.

Q 15. What is treatment of cor pulmonale?

Ans.
- **General measures**, i.e. back rest or prop up position, salt restriction and O_2 inhalation. Long-term domiciliary O_2 therapy is helpful in patients with severe COPD as it reduces pulmonary artery pressure and lowers pulmonary vascular resistance.
- **Antibiotics:** Acute respiratory infection is common precipitant of RV failure. Broad spectrum antibiotic may be used initially followed by antibiotic on the basis of sputum culture and sensitivity.
- **Bronchodilators** are used to relieve obstruction and to improve oxygenation.
- **Diuretics** are used to relieve edema.
- **Vasodilators** may be used to reduce preload.
- **Digitalis** should be used cautiously as it may induce arrhythmias in hypoxic myocardium.
- **Phlebotomies** to be done to reduce hematocrit, if there is polycythemia.

Q 16. What are the signs of acute cor pulmonale?

Ans.
1. Sudden onset of dyspnea, cough, hemoptysis
2. Tachypnea, tachycardia
3. Evidence of DVT or any other cause for thromboembolism
4. Signs of RHF, e.g. distended neck, raised JVP, prominent 'V' waves, a pansystolic murmur (may or may not be present), hepatomegaly and edema (may or may not be present)
5. Signs of pulmonary hypertension
   - Loud P2
   - Narrow splitting of second heart sound
   - Grahm-Steell murmur.

Q 17. Which diuretic is preferred in cor pulmonale?

Ans. You can use any diuretic but loop diuretics should be used with caution as it may cause metabolic alkalosis and thereby blunt the respiratory drive. Thiazides are better than loop diuretics.

Q 18. What is indication of beta blocker in heart failure due to cor pulmonale?

Ans. They should be avoided.

Q 19. What are precipitants for cor pulmonale?

Ans. The precipitants of cor pulmonale are:
- Acute respiratory infection
- Thyrotoxicosis
- Salt intake
- Mental stress
- Arrhythmias
- Noncompliance to treatment
- Pulmonary embolism
- Anemia.

Q 20. What is primary pulmonary hypertension (PPH)?

Ans. When the cause of elevated pulmonary vascular resistance responsible for cor pulmonale cannot be defined, the condition is referred to as primary pulmonary hypertension.

CASE 33: CHEST PAIN

The patient (Fig. 1.33A and B) 55-year-old male presented with chest pain on exertion, relieved on rest. No radiation of pain. No associated symptoms. Examination was normal.

Presenting Symptoms of Anginal Chest Pain

- **Patients with chest pain present with typical anginal symptoms**, or atypical anginal symptoms, e.g. angina equivalents, gastroesophageal reflux disease (GERD)
- They may present with *musculoskeletal disease* where pain is related to movements
- Patient with *neurosis* have cardiac symptoms (*cardiac neurosis*).

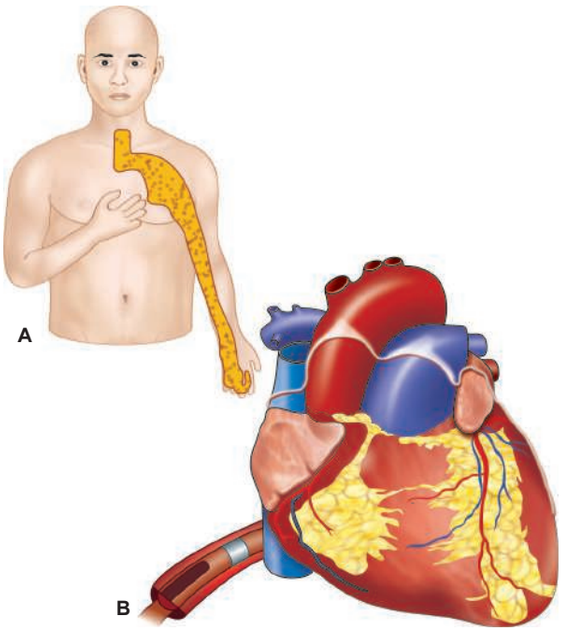


Fig. 1.33A and B: Chest pain. **A.** Patient with ischemic chest pain (diagram); **B.** Evidence of coronary thrombosis

History

Points to be Asked

- Age and onset of chest pain.
- Have you ever had such type of pain or discomfort in the chest before?
- How would you describe the pain (burning, heaviness or tightness, stabbing, pressure)?
- Do you get this pain chest during walking at normal pace or does it come when you walk fast or in a hurry?
- Does the pain get relieved by rest or by nitroglycerine?
- Is this pain localised or radiate to some other sites?
- Can you pinpoint the pain with your finger?
- Does the food has any relation with pain?
- Are there any associated symptoms of retching, nausea, vomiting, sweating, syncope, palpitation, dyspnea.
- Ask about **risk factors** such as smoking, diabetes, HT, alcohol, oral contraceptive.
- Is there any **family history of ischemic heart disease?** Did the patient has MI in the past?
- Is there any **aggravating** or **relieving factor** blown?

General Physical Examination

- **Facial appearance**, e.g. depressed or normal
- **Pulse** (rate and rhythm) and BP (all the four limbs). Feel all other pulses (carotids, femoral)
- **Eyes** for xanthelasma, fundus examination for evidence of hypertension
- **Neck** for thyroid enlargement and JVP
- **Skin** for xanthomas
- **Hands** for nicotine staining (smoking)
- **Look for signs of any cardiac** or **extracardiac disease**
- Look for **anemia**.

Systemic Examinations

I. CVS Examination

Inspection

No abnormality detected

Palpation

- Apex beat normal
- Chest expansion/movement normal
- Tenderness over chest present.

Percussion

Percussion note/cardiac dulness (normal/abnormal).

Auscultation

Auscultate for the presence of a pansystolic murmur of papillary muscle dysfunction or a pericardial rub or a fourth heart sound.

II. Respiratory System

Examine respiratory system for any consolidation or evidence of pulmonary infarction or COPD.

III. Abdomen Examination

- For any evidence of mass
- For aortic pulsations.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis and why?

Ans. In view of middle-aged male having central chest pain, constricting/squeezing in quality with no radiation, occurs on exertion, relieved by rest, my provisional diagnosis is acute coronary syndrome, or angina pectoris.

Q 2. What is differential diagnosis?

Ans. As the pain chest is central in location, it could be due to cardiovascular, gastrointestinal and musculoskeletal cause (Table 1.109)

Q 3. What are differences between cardiac and noncardiac chest pain?

Ans. Read Clinical Methods by Prof SN Chugh.

Q 4. What is mechanism of angina pectoris?

Ans.
- It is caused by increased myocardial oxygen demand triggered by physical activity.
- Coronary vasospasm is the other mechanism which causes transient decrease in O_2 supply.
- Nonocclusive intracoronary thrombi cause unstable angina pectoris.

Q 5. How would you grade angina?

Ans. The **Canadian Cardiovascular Society** has graded angina into four functional classes.

Class I: Angina occurs on strenous or prolonged exertion.

Class II: Angina with slight limitation of ordinary normal activity.

Class III: Angina with marked limitation of ordinary activity.

Class IV: Angina at rest with inability to perform any physical activity.

Q 6. What is Prinzemetal's angina?

Ans. It is a variant angina that occurs at rest, frequency at night and coronary vasospasm is the underlying cause. It is characterised by transient elevation of ST segment (>4 mm) during pain which resolves with relief of pain.

Q 7. What are the risk factors for acute coronary syndrome?

Ans. Risk factors are:
- Genetic predisposition
- Advancing age and male sex
- Smoking
- Alcohol
- Diabetes
- Hypertension
- Hyperlipidemia
- Lack of exercise (sedentary lifestyle)
- Deficiency of antioxidant vitamins
- Homocysteinemia (homocysteinuria)
- Oral contraceptive
- High levels of fibrinogen and factor VIII.

Q 8. What do you understand by the term acute coronary syndrome?

Ans. Acute coronary syndrome refers to coronary events that occur due to atherosclerosis. It includes *unstable angina/non-ST elevation myocardial infarction* and *ST elevation myocardial infarction (STEMI)*.

Table 1.109: Differential diagnosis of central chest pain

Cause	*Site*	*Quality/Severity/Timing*	*Aggravating/relieving factors*
Angina pectoris	Retrosternal or across the chest, radiating to left arm, neck, shoulder, lower jaw, upper abdomen	Squeezing/pressing/tightness in chest, moderate in intensity lasting for a few minutes (1–3 min)	× Exertion, cold, heavy meal and psychological upset exacerbate it × Rest, nitroglycerine relieve it
Myocardial infarction	Same as above	Same as above. Pain is more severe and prolonged, associated with diaphoresis	× No aggravating or relieving factor × Underlying risk factor may be evident
Pericarditis	Central limited to precordium may radiate to shoulder or back	Sharp, cutting (knife-like) pain, often severe and persistent	× Breathing, change in posture, coughing lying may exacerbate it × Sitting and forward blenolling relieve it
Aortic dissecting aneurysm	Anterior chest wall radiating to back between scapula	Tearing pain severe and persistent	× Hypertension aggravate it × No relieving factor × Associated feature, e.g. syncope, aortic diastolic murmur help in the diagnosis
		GASTROINTESTINAL CAUSES	
Reflex esophagitis / gastrointestinal reflux disease/diffuse esophageal spasms	Retrosternal, may radiate to back	Burning/squeezing, mild to moderate in intensity	× Large meals, bending, emotional upset, spicy food aggravate it × Lying down and antacid relieve it × Heart burn and acid taste in mouth are common accompaniments
		MUSCULOSKELETAL CAUSES	
Myalgia	Often below the left breast	Stabbing or dull ache of fleeting nature, severity variable	× Movement of the chest, aggravate it × There is local tenderness
Tietze syndrome	Pain along the left costal margins	Sticking/stabbing, variable severity	-do- × There may be tenderness of costochondral junctions (2nd to 4th ribs)
		PSYCHOGENIC	
Cardiac neurosis	Precordial, below the left breast or whole of anterior crest	Stabbing, variable intensity, fleeting in nature	× Stress and effort precipitate it × Mental rest and anxiolytic relieve it × Anxious look, palpitations hyperventilation, frequent sighs are common associated symptoms

Q 9. What is microvascular angina (cardiac syndrome X)?

Ans. It refers to classic anginal symptoms with ST depression on stress ECG testing and a normal coronary angiogram in the absence of any demostrable cardiac abnormality.

Q 10. What is prevalence of angina?

Ans. The prevalence of angina is approx 2% with an incidence of new cases each year approximately 1 per 1000.

Q 11. What are common clinical patterns of angina?

Ans.
- **Classical or exertional angina pectoris.**
- **Decubitus angina** (angina on lying down) indicates angina with impaired LV function.
- **Nocturnal angina** (critical coronary artery disease and vasospasm are the causes)
- **Variant (Prinzmetal's) angina** (rest angina without any provocation).
- **Unstable angina** (angina of recent onset <1 month, worsening angina or angina at rest).

Q 12. What are anginal equivalents?

Ans. These are symptoms of myocardial ischemia other than angina, carry same significance as angina. These include *dyspnea*, *fatigue* and *faintness*. They are more common in elderly and in diabetic patients.

Q 13. What do you understand by the term unstable angina?

Ans. It refers to more severe and frequent angina superimposed on chronic stable angina, angina at rest or minimal exertion or new onset angina <1 month which is brought about by minimal exertion.

Q 14. What is postprandial angina? What is its mechanism and significance? What is its treatment?

Ans. Angina following meals is called *postprandial angina*. It results from the carbohydrate content of the meal. It indicates severe coronary artery disease and could occur as a result of intramyocardial stealing of blood from stenotic territories to normal territories.

Q 15. How would you investigate a case of angina?

Ans.
- **Hemoglobin** for anemia (anemia aggravates angina).
- **Resting ECG** (LV hypertrophy, ST-T changes, prior Q-wave MI).
- **Exercise ECG** for ST change (horizontal or downsloping ST segment depression >1 mm staying for 60–80 ms or ST elevation) or an arrhythmia or production of symptoms.
- **Rest echocardiogram** for any evidence of asymptomatic aortic stenosis or hypertrophic cardiomyopathy.
- **Exercise myocardial perfusion imaging/** exercise echocardiography in patients having abnormal ECG at rest.
- **Coronary angiography** for coronary anatomy for any abnormality (atherosclerotic occlusion) or nonatherosclerotic causes (e.g. vasospasm, coronary anomaly/dissection/vasculopathy).

Q 16. How would you treat a patient with chronic stable angina?

Ans. Treatment is denoted by Mnemonic **ABCDE**
- **A**spirin
- **B**eta blocker and **B**lood pressure control
- **C**igarette smoking abstinence and **C**holesterol reduction
- **D**iet and **D**iabetes control
- **E**ducation and **E**xercise.

Q 17. What is the prognostic significance of stress testing in evaluation of chest pain?

Ans. Stress testing determines high-risk and low-risk population of patients with chest pain suggestive of ischemic heart disease.

I. **Low-risk group:** These are patients who can complete 1 minute of exercise using Bruce protocol without any change in ST segment and can achieve a maximum heart rate >160/min without discomfort. These were found to have good prognosis (1 year survival in 99% and 4 years in 93%) and cardiac catheterisation and CABG can be deferred.

II. **High-risk group:** These are patients who were forced to stop exercise in stage I and stage II (under 6 minutes). Survival rate was reduced to 85% at one year and 63% at 4 years.

Q 18. What are glycoprotein II/IIIb inhibitors?

Ans. Glycoprotein II/IIIb inhibitors are antithrombotic agents useful for preventing thrombotic complications in patients with STEMI undergoing PCI.

Q 19. Name the cardiac markers. What is their significance?

Ans. Cardiac markers are:
- CPK-MB
- Troponins I and T
- Myoglobin

Troponins are useful for early diagnosis before enzymes rise.

Q 20. What is Tietze syndrome?

Ans. Read Table 1.109.

Q 21. What is gastroesophageal reflux disease? What are its causes?

Ans. Gastroesophageal reflux disease is defined as reflux of gastric contents into the esophagus

resulting in inflammation of esophagus (reflux esophagitis caused by H^+ ion, pepsin and bile salts). The causes are:

- Old age and smoking
- Fat, chocolate, coffee, spicy food and alcohol
- Hiatus hernia
- Gastric stasis (e.g. gastroparesis in diabetes, due to anticholinergics and systemic sclerosis)
- Raised intra-abdominal pressure (e.g. pregnancy, ascites, straining at stool/urination)
- Obesity and sedentary habits.

Q 22. What are angina precipitants?

Ans. Angina precipitants are:

- Physical exertion
- Heavy meals
- Recumbency (angina decubitus)
- Emotional disturbance
- Cold exposure
- Vivid dreams (nocturnal angina)
- Thyrotoxicosis
- Asymptomatic aortic valve disease
- Drugs, e.g. beta-adrenergic stimulants
- Tachycardia and tachyarrhythmias.

CASE 34: DILATED CARDIOMYOPATHY

The patient presented with history of breathlessness on exertion for the last 3 years (Fig. 1.34). It was progressive in nature and interfered with normal activities. Now for the last 2 months, patient develops dyspnea on minimal exertion and there is history of orthopnea and PND off and on. For the last 15 days patient is having swollen legs and distended abdomen. On symptomatic enquiry, there is history of palpitations, headache, weakness and fatigue. Examination revealed raised JVP, hepatomegaly, ascites and edema. There was cardiomegaly with pansystolic murmur heard over whole of the precordium with 'vy' collapse. A soft 3rd heart sound was also heard. There were end-inspiratory crackles at both bases of the lungs.

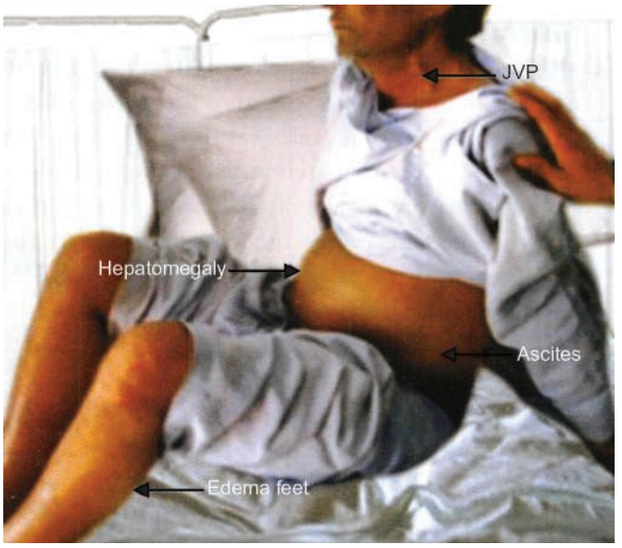


Fig. 1.34: A patient of rheumatic heart disease with mitral stenosis and mitral regurgitation showing signs of congestive heart failure

Clinical Presentation of Dilated Cardiomyopathy

- Patients suffering from dilated cardiomyopathy present with *palpitation*, *dyspnea* and *CHF*.
- Patients of alcoholism may present with *cirrhosis*, *neuropathy* and *cardiomyopathy*.
- Patients of *postpartum cardiomyopathy* present with symptoms and signs of CHF within 6 months following delivery.

History

Points to be Noted

Ask about

- Onset and progression of symptoms
- Cough, its frequency, nocturnal, etc.
- Sputum production, quantity, colour, smell, consistency and history of hemoptysis.
- Any recent change in the symptoms. History of recent fever, sore throat or loose motions
- History of swelling feet, abdomen (hepatomegaly)
- Ask for any aggravating or relieving factors
- Take full drug history, drug being taken and their effect.

Past history

- History of delivery or abortion
- History of diabetes.

Personal history

History of smoking, alcoholism.

Family history

EXAMINATION

General Physical Examination

- Patient is orthopneic, lying in prop up position
- Cyanosis present
- Neck veins distended. JVP raised. There may be and y collapse due to TR (present in this case)
- Pulse and respiratory rate increased
- Cold extremities and edema feet may be present (present in this case)
- Record BP, pulse and temperature.

Systemic Examination

Examination of CVS

Inspection

- Apex beat may be normally placed or centrally placed or displaced outwards and downwards
- No other visible pulsation all over the precordium.

Palpation

- Apex beat may be palpable outside the midclavicular line (palpable in this case)
- Parasternal heave present
- Right ventricular pulsations palpable in epigastrium (present in this case).

Percussion

Cardiac dullness area increased due to dilated heart. Dullness corresponds with apex beat.

Auscultation

- Heart sounds normal/feeble
- Second heart sound normally split
- There may be an ejection systolic murmur in P2 area and a pansystolic murmur in tricuspid and mitral areas.

Abdominal Examination

- Liver is enlarged, soft, tender and may be pulsatile if TR present (liver was enlarged and pulsatile in this case)
- There may be signs of ascites (fluid thrill and shifting dullness present).

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. In view of clinical findings, patient has features of congestive heart failure probably due to dilated cardiomyopathy (primary).

Q 2. What are the points in favour of your diagnosis?

Ans.
1. History of dyspnea, progressive in nature, orthopnea and PND.
2. A middle-aged female patient.
3. *Signs of congestive heart failure* without signs of pulmonary hypertension, e.g. raised JVP, tender hepatomegaly, ascites and pitting edema. There were end inspiratory crackles in the lungs.
4. *Signs of cardiomegaly*, e.g. dilated heart with heaving apex beat which is down and out.
5. *Exclusion of other causes of heart failure* such as valvular, hypertensive, thyrotoxic and ischemic heart disease.
6. *The features suggestive of mitral and tricuspid regurgitation* (*pansystolic murmur in both the areas*) indicates dilated cardiomyopathy as simultaneous occurrence of both regurgitant lesions commonly occur in dilated cardiomyopathy.

Q 3. Could it be rheumatic mitral regurgitation leading to tricuspid regurgitation?

Ans. No. There are no signs of pulmonary hypertension (loud P2, narrow splitting of 2nd heart sound, Graham-Steell murmur or an ejection systolic murmur).

Q 4. What are the signs of tricuspid regurgitation in this patient?

Ans.
- Raised JVP with 'vy' collapse
- Signs of RVH, e.g. left parasternal heave and pulsations in the epigastrium
- Liver is enlarged and pulsatile
- There is pansystolic murmur heard at left parasternal border and also heard at right sternal edge and epigastrium which increases on inspiration.

Q 5. What is your differential diagnosis?

Ans. Following myocardial diseases come into the differential diagnosis of idiopathic dilated cardiomyopathy:
- **Peripartum cardiomyopathy** in female (there will be history of delivery followed by signs and symptoms of CHF within 6 months).
- **Alcoholic cardiomyopathy** (history of alcoholism, stigmatas of alcoholism and other associated diseases, e.g. cirrhosis or neuropathy).
- **Neuromuscular disease associated cardiomyopathy, e.g. Friedrich's ataxia, Duchenne's muscular dystrophy, myotonic dystrophy, etc. (features of disease, neurological diseases will be present)**
- **Myocarditis viral.**
- **Diabetic cardiomyopathy** (history of long duration of diabetes with other complications).

Q 6. What are clinical types of cardiomyopathy?

Ans. WHO classified cardiomyopathy clinically into three main groups:

i. **Dilated cardiomyopathy** characterised by ventricular enlargement, CHF, inpaired systolic function, arrhythmias and embolization.

ii. **Restrictive cardiomyopathy** characterized by restriction to left and/or right ventricular filling. It resembles constrictive pericarditis.

iii. **Hypertrophic cardiomyopathy** characterised by left ventricular free wall hypertrophy along with septal hypertrophy without any dilatation of the ventricular cavity.

Q 7. Name few common causes of dilated cardiomyopathy.

Ans. The common causes are:
- **Primary** (unknown cause)
- **Secondary** due to:
  - Alcohol-induced cardiomyopathy
  - Peripartum cardiomyopathy
  - Ischemic cardiomyopathy
  - Metabolic cardiomyopathy, e.g. thyrotoxic, diabetic
  - *Viral:* Chronic myocarditis, Chagas disease
  - Drug-induced, e.g. doxorubicin, cocaine, cyclophosphamide.

Q 8. What is peripartum cardiomyopathy?

Ans. It develops during the last trimester or within 6 months after delivery, hence, the patient usually a multiparous woman over the age of 30 years develops symptoms and signs of CHF either 1 month before or immediately after delivery. The investigations revealed a dilated heart with depressed ejection fraction.

Q 9. How would you investigate such a case?

Ans.

i. **ECG.** It will often show sinus tachycardia or atrial fibrillation, ventricular arrhythmias, left atrial enlargement, nonspecific ST-T changes and sometimes conduction defects and low voltage graph.

ii. **Chest X-ray** will show cardiomegaly. There will be pulmonary venous congestion and interstitial/alveolar edema (Kerley's lines).

iii. **Echocardiogram.** It will show ventricular dilatation with normal or thinned walls. The ejection fraction is markedly reduced.

iv. **Radionuclide ventriculography,** usually, not required, may confirm ventricular dilatation and thinning/thickening of the walls.

v. **Brain natriuretic peptide** levels are elevated.

vi. **Cardiac catheterisation and coronary angiography:** They are often performed to exclude ischemic heart disease (ischemic cardiomyopathy).

vii. **Transvenous endomyocardial biopsy.**

Q 10. How would you treat?

Ans. Treatment is symptomatic with:

- Salt restriction, diuretics, digitalis and ACE inhibitors
- Aiticoagulation for systemic embolization
- Antiarrhythmics in case of arrhythmias
- Sophisticated therapy such as biventricular pacing (resynchronization therapy for intraventricular conduction delay, bundle branch blocks) and insertion of implantable cardioverter-defibrillator (ICD) for symptomatic ventricular arrhythmias
- Avoid alcohol and NSAIDs.

CASE 35: HEMIPLEGIA

A young female (18 years, Fig. 1.35) having rheumatic heart disease presented with cough and breathlessness on exertion for the last 4 years. She was well on treatment. There was no history of orthopnea, PND, hemoptysis or pain chest. Now for the last 2 days, she is complaining of weakness of right half of the body with deviation of face. After recovery, she was able to walk and the picture was taken to show the gait. Examination revealed signs of UMN paralysis on right side.

Fig. 1.35: A young female with hemiplegia walking with circumducting gait. She has recovered recently from stroke

Clinical Presentation of Hemiplegia

- Patient usually complain of *weakness of one half of the body with asymmetry of face*. There may be complaints of sensory and speech disturbance.
- In addition to weakness, patient may complain of symptoms of the underlying disorder if it is the cause, i.e. *hypertension, diabetes, TIA*, rheumatic heart disease (valvular lesion Fig. 1.34), cardiomyopathy, etc.

History

Points to be Noted

- Age and sex
- Note the date and time of onset of stroke
- Mode of onset, e.g. sudden or gradual
- Evaluation of paralysis, i.e. whether it was transient (TIA), or stationary (stroke-in-evolution or complete stroke)
- Any known precipitating factor(s)
- Progress or course of paralysis, e.g. improving, stationary or deteriorating or waxing and waning
- Any associated motor and sensory symptoms
- Any disturbance of consciousness/convulsion, visual disturbance, speech disturbance
- Symptoms of raised intracranial tension.

Past History

- History of similar episodes in the past which recovered completely (TLA)
- History of head injury or epilepsy
- History of HT, diabetes, RHD, meningitis, tuberculosis, migraine, exposure to sexually transmitted diseases
- Intake of oral contraceptive.

Family history, e.g. HT, DM, epilepsy, migraine and similar illness in other family members.

Personal history. History of overweight or obesity, smoking, alcoholism.

EXAMINATION

1. **General physical**
   - Is patient conscious or cooperative?
   - Posture of the patient
   - *Neck examination* for pulsations, lymph node, thyroid
   - *Vitals*, e.g. pulse, BP and temperature
   - *Edema*
   - Any obvious deformity.
2. **Nervous system** (*read proper nervous system examination*)
   - Higher functions
   - Cranial nerves (UMN or LMN paralysis of 7th nerve), fundus for papilledema
   - Neck rigidity absent
   - **Motor system examination**
     - There will be UMNs signs on the side of the body involved (i.e. opposite to the CNS lesion) if lesion is above the cervical cord
     - Gait will be spastic
     - Cerebellar and autonomic functions normal
     - Speech involved if dominant hemisphere is the site of lesion
     - Sensory system may show hemianesthesia or may be normal.
3. **Other systems examination**
   - CVS
   - Respiratory
   - GI tract and genitourinary
   - Lymphoreticular system.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. In view of the presentation of weakness of right half of the body, the patient appears to be a case of young CVA (left) with right-sided hemiplegia. The cause of stroke is cerebral embolism.

Q 2. What are the points in favour of diagnosis?

Ans.
1. Patient is a case of RHD with MS and AF.
2. Sudden onset of hemiplegia without convulsion and speech disturbance.
3. 7th supranuclear palsy on right side and hemiplegia on right-side (uncrossed hemiplegia).
4. UMN signs (exaggerated reflexes increased tone and plantar extensor response) present in right upper and lower limbs.

Q 3. What do you think the cause of hemiplegia in this case and why?

Ans. Embolic stroke. Points in favour are:
- Catastrophic onset
- Underlying RHD with MS
- Atrial fibrillation present
- Complete uncrossed hemiplegia
- More or less complete recovery.

Q 4. What is your complete diagnosis in this case?

Ans.
- The clinical diagnosis is CVA left side with hemiplegia right side
- Site of the lesion is internal capsule
- Neurological deficit is pyramidal tract only
- Etiology is embolic stroke due to underlying RHD with MS and atrial fibrillation.

Q 5. What is hemiplegia? What are its various types?

Ans. *Hemiplegia* is defined as complete loss of motor functions (paralysis) on one half of the body; whereas partial loss of motor function is designated as *hemiparesis*. It is usually due to UMN lesion at any level from the cerebrum to spinal cord. The tracts involved are ascending and descending motor tracts especially the pyramidal tracts.

Terminology used for hemiplegia

1. **Complete hemiplegia:** It is said to be complete if UMN 7th nerve palsy accompanies the hemiplegia.
2. **Incomplete hemiplegia:** It is hemiplegia without 7th nerve involvement.
3. **Crossed hemiplegia.** It refers to ipsilateral LMN paralysis of one of the cranial nerves with contralateral (opposite side) hemiplegia. It signifies the brainstem as the site of the lesion.
4. **Uncrossed hemiplegia.** It refers to UMN 7th nerve palsy on the side of hemiplegia (i.e. both being opposite to cerebral lesion). For example, if UMN 7th nerve palsy and hemiplegia are on the left side, the cerebral lesion is on the right side.
5. **Dense hemiplegia.** The complete loss of voluntary functions (weakness) of equal magnitude in both upper and lower limbs on the side of the body involved constitutes dense hemiplegia. This signifies an internal capsular lesion as corticospinal fibres are condensed there.
6. **Pure motor hemiplegia.** Isolated unilateral involvement of corticospinal tract gives rise to pure motor hemiplegia. A lacunar (small vessel) infarct of posterior limb of the internal capsule produces pure motor hemiplegia.
7. **Stuttering hemiplegia.** Transient speech disturbance (aphasia, dysarthria) with hemiplegia indicates stuttering hemiplegia, is due to progressive occlusion of internal carotid artery) (stroke-in-evolution). It ultimately results in complete stroke.
8. **Transient ischemic attack or transient hemiplegia.** It is sudden transient loss of motor function (paralysis) on one side of the body which recover completely within 24 hours.
9. **Homolateral hemiplegia.** It means hemiplegia occurring on the same side of the lesion, is seen in unilateral cervical spinal cord lesion (Brown-Séquard's syndrome).

Q 6. What are the causes of hemiplegia?

Ans. Read Table 1.110.

Table 1.110: Important causes of hemiplegia

1. Transient ischemic attack (TIA)
2. CVA (cerebrovascular accident), e.g. thrombosis, embolism and hemorrhage
3. Subdural hematoma
4. Brain tumor
5. Cerebral trauma
6. Encephalitis, meningitis
7. Multiple sclerosis
8. Functional, e.g. astasia-abasia (hysterical)

Q 7. What do you mean by stroke?

Ans. A stroke is defined as a neurological deficit occurring as a result of CVA (atherosclerosis, thrombosis, embolism and hemorrhage) and lasting for more that 24 hours. Stroke in clinical practice is used for hemiplegia.

Q 8. What is TIA and what is RIND? What is completed stroke?

Ans.
1. **TIA.** It means transient hemiplegia or neurological deficit occurring as a result of ischemia which recovers within 24 hours.
2. **Stroke-in-evolution.** The neurological deficit worsens gradually or in a stepwise pattern over hours or days.
3. **Completed stroke.** Neurological deficit is complete at the onset and persists for days to weeks and often permanently.

4. **Reversible ischemic neurological deficit (RIND).** It means neurological deficit persisting for more than 24 hours but recovers totally within a week.

Q 9. How would you classify stroke?

Ans. Based on Bomford clinical classification; stroke is divided into:

1. **Total anterior circulation syndrome**
   i. Hemiplegia (motor deficit of face, arm and leg)
   ii. Homonymous hemianopia
   iii. Higher cortical dysfunction (aphasia, memory, neglect).
2. **Posterior circulation syndrome**
   One or more of the following features present:
   i. Bilateral motor or sensory signs not secondary to brainstem compression by a large supratentorial lesion
   ii. Cerebellar signs (ataxic hemiparesis)
   iii. Unequivocal diplopia with or without external ocular muscle palsy
   iv. Crossed sign, e.g. left facial and right limb weakness
   v. Hemianopia alone or with any of the four features described above.

Q 10. How will you localise the lesion in a case with hemiplegia?

Ans. The site or the level of lesion can be deduced from associated neurological signs.

1. **Cortical or subcortical (corona radiata) lesion.** The **characteristic features** of cortical/subcortical lesion are:
   i. Contralateral hemiplegia of uncrossed type.
   ii. Convulsions (Jacksonian) may occur.
   iii. Speech disturbance (aphasia) if dominant hemisphere is involved. The dominant hemisphere is decided from handedness of a person. If a person is right-handed, the left hemisphere is dominant and contains the speech area.
   iv. Cortical type of sensory loss (astereognosis, loss of sense of position, tactile localisation, and two-point discrimination).
   v. Anosognosia, visual field defect.
   vi. Supranuclear 7th nerve palsy.
2. **Internal capsular lesions**
   i. Contralateral hemiplegia of uncrossed type
   ii. Contralateral hemianesthesia
   iii. Dense hemiplegia—complete paralysis of face, upper and lower limbs
   iv. UMN paralysis of 7th nerve
   v. No convulsion, no speech, taste or visual disturbance.
3. **Midbrain lesion**
   i. Contralateral hemiplegia of crossed type
   ii. The 3rd nerve nuclear paralysis with contralateral hemiplegia constitutes Weber's syndrome
   iii. Contralateral hemianesthesia and analgesia
4. **Pontine lesion**
   i. Contralateral hemiplegia of crossed type
   ii. Contralateral hemianesthesia and analgesia
   iii. Ipsilateral 6th or 7th cranial nerve paralysis (LMN type) with contralateral hemiplegia is called *Millard-Gubler syndrome*
   iv. Constriction of pupil (*Horner's syndrome*) on the same side of the lesion due to involvement of sympathetic fibres
   v. Ataxic hemiplegia with or without dysarthria indicates a lacunar infarct.
5. **Medulla oblongata lesion**
   i. Paralysis of one of the lower cranial nerve (9th, 10th, 11th, 12th) on the side of lesion.
   ii. UMN hemiplegia on the opposite side
   iii. Facial numbness (Vth nerve involvement) may or may not be present.

Q 11. What is hysterical hemiplegia?

Ans. In hysterical hemiplegia, the patient drags the affected leg along the ground behind the body and does not circumduct the leg or use it to support the body weight. At times, hemiplegic leg is pushed ahead of the patient and used mainly for support. The arm on the affected side remains limp and is kept by the side of the body and does not develop flexed posture commonly seen in hemiplegia from organic causes (Fig. 1.35). The characteristic signs of hysterical hemiplegia are:

1. **Hysterical gait**
2. **Normal tone of the limbs**
3. **The tendon reflexes** are normal on both the sides
4. **Plantars** are flexor or down-going
5. **Hoover's sign and Babinski's combined leg flexion tests** are helpful in distinguishing hysterical from organic hemiplegia.

'To elicit *Hoover's sign*, the supine patient is asked to raise one leg from the bed against resistance. In a normal individual the back of heel of contralateral leg presses firmly down, and the same is true for organic hemiplegia when attempts are made to lift the paralysed leg. The hysterical patient will press down the supposedly paralysed limb more strongly under these circumstances which can be appreciated by placing a hand below the normal heel.

In *Babinski's combined leg flexion* test, the patient with organic hemiplegia is asked to sit upon the bed from lying down position without using his/her arms; in doing this, the paralysed leg flexes (if power is good) at the hip and heel is lifted from the bed, while the heel of the normal leg is pressed into the bed which is appreciated by putting the hand below the heel. This sign is absent in hysterical hemiplegia'.

Q 12. How would you decide vascular lesion in hemiplegia?

Ans. The three common cerebrovascular lesions that can produce hemiplegia are compared in Table 1.111.

Table 1.111: Differential diagnosis of cerebrovascular accidents with hemiplegia

Features	*Cerebral thrombosis*	*Cerebral embolism*	*Cerebral hemorrhage*
Onset	Sudden, may be slow (stroke-in-evolution)	Abrupt like bolt from the blue	Sudden, catastrophic
Premonitory symptoms	May be present in the form of TIA	Absent	May be present in the form of speech disturbance or attacks of weakness in a limb
Consciousness	Preserved or there may be slight confusion	Preserved, sometimes patient may be dazed or drowsy	Usually semiconscious or unconscious
Headache	Absent but occurs if cerebral edema develops	Absent	Severe, persistent
Neck stiffness	Absent	Absent	Present if bleed leaks into subarachnoid space
Neurological deficit	Slowly developing	Maximum at the onset, followed by initiation of recovery	Rapidly developing and progressive
Precipitating or predisposing conditions	Hypertension, diabetes, dyslipidemia, hypothyroidism, hypercoagulable states (pregnancy, puerperium, oral contraceptives), dehydration or shock	Evidence of source of embolization, i.e. heart disease (ischemic, rheumatic), aneurysm (arterial, ventricular), thrombosis (atherosclerosis, atrial)	Precipitated by stress, exertion, physical act, sudden rise in BP. Atheromatous arteries, aneurysm of arteries or AV malformations predispose to hemorrhage
Symptoms and signs of raised intracranial tension	Absent	Absent	May be present if bleed leaks into subarachnoid space
Recovery	Slow, may be partial or complete	Rapid, recovery is the rule	Slow, if patient recovers. Residual damage persists

Q 13. What are the characteristic features of hemiplegia due to a brain tumor? What are false localising signs?

Ans. They are given in Table 1.112.

Table 1.112: Hemiplegia due to brain tumor

1. Slow onset and slow progression
2. **Focal symptoms:** Jacksonian fits (focal epilepsy), aphasia, hemiplegia or monoplegia
3. **Symptoms and signs of raised intracranial tension,** e.g.
   - Headache, vomiting, papilledema
   - Bradycardia, slight rise in BP, rise in respiratory rate
   - Mental features—confusion, disorientation, emotional apathy, depression, somnolence, urinary and fecal incontinence
   - Epileptic seizures
   - *False localising signs*
     - Unilateral 6th nerve palsy (diplopia with lateral deviation of the eye), sometimes it may be bilateral
     - Bilateral plantar extensor response
     - Bilateral grasp reflexes
     - Cerebellar signs
     - Fixed dilated pupils

Q 14. What are features of hemiplegia due to chronic subdural hematoma?

Ans. The features of hemiplegia in chronic subdural hematoma are:

i. There may be history of injury or fall. Patient may have underlying liver disease, bleeding diathesis or may be on anticoagulants.

ii. Slow or chronic onset with fluctuating headache, slow thinking, confusion, drowsiness, personality changes, seizures, etc.

iii. There may be lucid interval (weeks, months or more than a year) between the onset of injury and symptoms.

iv. Hemiplegia is uncrossed, due to compression effect on pyramidal tracts.

Q 15. List the predisposing factors for CVA (hemiplegia).

Ans. The following are the risk factors for accelerated atherogenesis predisposing to cerebral thrombosis (CVA). These must be taken into account in the past/present history (Table 1.113).

Table 1.113: Risk factors in CVA

- Systemic hypertension
- Heart disease, e.g. ischemic, rheumatic with atrial fibrillation, cardiomyopathy
- Diabetes
- TIA
- Hyperlipidemia (familial or nonfamilial), atherosclerosis
- Homocysteinemia and homocysteinuria
- Deficiency of proteins C and S
- Strong family history
- Smoking
- Obesity
- Oral contraceptives
- Hyperviscosity syndrome, e.g. polycythemia, antiphospholipid syndrome
- Increasing age (old age)

Q 16. What are causes of recurrent CVA/hemiplegia?

Ans. **Causes** are:

- TIA (transient ischemia attack) is common cause
- Postepilepsy—Todd's paralysis
- Hypertensive encephalopathy
- Migrainous hemiplegia (vasospastic hemiplegia)
- Hysterical hemiplegia.

Q 17. What are the causes of stroke in young?

Ans. **Causes** are:

1. **Cerebral embolism** from a cardiac source, commonly rheumatic valvular disease
2. **Subarachnoid hemorrhage** (rupture of Berry aneurysm or AV malformations or anticoagulant therapy)
3. Hyperviscosity syndrome, e.g. polycythemia, postpartum state, oral contraceptive
4. Arteritis, e.g. tubercular
5. Demyelinating disease, e.g. multiple sclerosis
6. Head injury
7. Inflammatory disease, e.g. meningitis, encephalitis
8. Procoagulant states, e.g. protein C and S deficiency, homocysteinemia, antiphospholipid syndrome.

Q 18. What are bladder and bowel disturbances in the hemiplegia?

Ans. Unilateral involvement of bladder usually does not produce much symptoms, hence, in hemiplegia, there can be either no disturbance or there is hesitancy or precipitancy.

Q 19. What is lacunar syndrome? What is small vessel infarct?

Ans. The term lacunar syndrome or infarction implies atherothrombotic or lipohyalinotic occlusion of a small vessel (<300 μm) in the brain; most of such infarcts being small are not picked up on CT scan. Now, it has been replaced by another term called *small vessel infarct or stroke* which denotes occlusion of a small penetrating artery and >50% of these infarcts are picked up on CT scan. Small vessal stroke accounts for >20% of stroke.

Q 20. Name the various lacunar syndromes.

Ans.

1. Pure motor hemiparesis
2. Pure sensory hemiparesis
3. Ataxic hemiparesis
4. Dysarthria and clumsy hand or arm syndrome
5. Aphasic hemiparesis syndrome.

Q 21. How would you manage a case of TIA?

Ans.

1. Evaluate clinical risk profile and institute lifestyle modifications, i.e.
   - Stop smoking and alcohol
   - Dietary management
   - Exercise as advised by the doctor
   - Weight control
   - Maintain the BP and sugar control in diabetes
   - Antiplatelets, e.g. aspirin or aspirin plus clopidogrel or dipyridamole.
2. **Statins:** Several trials have confirmed that statin drugs reduce the risk of TIA and stroke even in patients without elevated LDL or low HDL. Therefore, all patients of TIA must receive one of statins.
3. **Control of hypertension** by angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. Lowering of blood pressure to levels below those traditionally defining hypertension with these drugs reduce the risk of stroke further, hence they also can be included in medical regimen of TIA.

Q 22. How will you investigate a patient with hemiplegia?

Ans. Investigations are done for diagnosis, to find out the underlying cause and risk factors. They are given in Table 1.114.

Table 1.114: Investigations for a patient with hemiplegia

1. Blood count, clotting and thrombophilia screen
2. Blood biochemistry, e.g. sugar, lipids
3. ECG
4. Radiology
   - Chest X-ray
   - USG
   - Doppler studies (carotid)
   - MRI brain

CASE 36: PARAPLEGIA

A patient (not shown) presented with weakness of both lower limbs which was slowly progressive with difficulty in passing urine. There was history of numbness of both the lower limbs below the umbilicus. There was no history of fever or trauma preceding this illness. The physical signs of the patient are represented in Fig. 1.36.

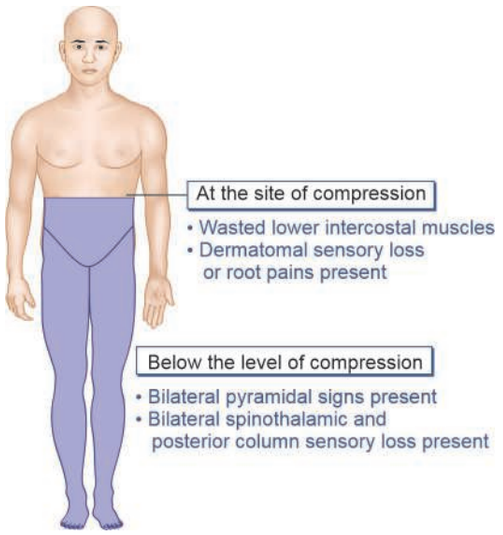


Fig. 1.36: Compression paraplegia with transverse thoracic spinal cord lesion with definite level. There are UMN signs below the site of compression. There is bilateral loss of all sensory modalities below the level of compression

Clinical Presentations of Paraplegia

- Weakness of both lower limbs
- Numbness of both lower limbs
- Difficulty in passing urine and stool.

History

Points to be Noted

- Note date and time of onset of paralysis
- Mode of onset (sudden or gradual)
- Precipitating factors, e.g. fever, spinal trauma, vaccination
- Progress of paralysis, e.g. increasing, stationary, progressive, waxing or waning type
- Sensory symptoms, e.g. root pain, sensation of pins and needles, numbness, history of a constriction band around the waist
- Motor symptoms including inability or difficulty in walking.

Past History

Ask for

- History of fever, tuberculosis, exposure to STD
- History of similar episodes in the past
- History of spinal trauma
- History of diabetes, HT
- History of alcoholism
- Pain in back.

Family History

- Diabetes, HT
- History of paraplegia in other members of the family
- Tuberculosis.

Unilateral Compression

(Brown-Séquard syndrome) The signs are:

i. Ipsilateral in the side compression) pyramidal signs
ii. Contralateral (opposite to the side involved) spinothalamic sensory loss of pain, touch and temperature.

EXAMINATION

I. **General physical:** Note the following:
   - Consciousness or cooperative, posture
   - Neck for lymphadenopathy
   - Vitals, e.g. pulse, BP and temperature
   - Skin, e.g. pigmentation, neurofibroma.

II. **Nervous system. Examine**
   - Higher functions
   - Neck rigidity
   - Cranial nerves
   - Cerebellar functions
   - Motor system including gait
   - Sensory system.

III. **Examination of spine**
   Kyphosis, scoliosis, gibbus, tenderness and spina bifida (a tuff of hair).

IV. **Other systems**
   - *Respiratory system examination* for tuberculosis, bronchogenic carcinoma and lymphoma
   - *CVS*—as discussed in hemiplegia
   - *GI tract* for hepatosplenomegaly, ascites
   - *Lymphoreticular system* for sternal tenderness, hemorrhagic spots and lymphadenopathy.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your clinical diagnosis?

Ans. Presence of UMN signs in both lower limbs with localised LMN signs over the lower part of chest, suggest the provisional diagnosis of compression (spastic) paraplegia.

Q 2. Where is the site of lesion? What are points in favour of your diagnosis?

Ans. Site of lesion is upper thoracic region between T2 and T5. The points in favour are:

1. Presence of normal upper limb reflexes which indicate intactness of all cervical segments and first thoracic.

2. Loss of abdominal reflexes indicate lesion above T6.
3. Weakness of intercostal muscles of T4, T5 and a dermatomal sensory loss points the lesion at this site. However, there was no bony deformity of spine at this level.

Q 3. What is net neurological deficit in your case?

Ans.
- Bilateral pyramidal tract involvement
- Bilateral sensory involvement of all modalities (spinodialamic and posterior column involvement)
- Sphincter involvement (autonomic involvement).

Q 4. What does paraplegia mean?

Ans. It refers to complete loss of motor functions (paralysis) of both lower limbs. Partial weakness is designated as *paraparesis*.

Q 5. What is the type of lesion in your case?

Ans. Extramedullary spinal cord compression. The points in favour are:
1. Slowly progressive paraplegia, symmetric involvement.
2. History of root pain and dermatological sensory loss.
3. Brisk lower limb reflexes sensory loss of all modalities below the level of compression.
4. Bowel and bladder involvement.
5. There is no sacral sparing.

Q 6. Why do you say compression paraplegia in your case?

Ans. It is a case of compression paraplegia because:
1. There is evidence of LMN paralysis and dermatomal sensory loss (weakness of intercostal muscles and loss of sensation at T_4–T_6).
2. UMN signs are present below the level of compression (spasticity, exaggerated reflexes and plantar extensors).

N.B.: To decide the site of lesion, Read Table 1.116.

Q 7. What is cerebral paraplegia? Name one or two causes?

Ans. The lower limbs and bladder (micturition centre) are represented in paracentral lobule (about upper one inch of cerebral cortex), hence, lesion of this area produces paraplegia with bladder disturbance (retention of urine) and cortical type of sensory loss. There may be associated headache, vomiting and convulsions or Jacksonian fits. The two important causes are:
1. Superior sagittal sinus thrombosis
2. Parasagittal meningioma.

Q 8. What is spastic paraplegia?

Ans. The involvement of spinal cord and cerebrum produces spastic (UMN) paraplegia. Spastic paraplegia is of two types:
1. Paraplegia-in-extension
2. Paraplegia-in-flexion

The differences between paraplegia-in-extension and paraplegia-in-flexion are summarised in Table 1.115.

Q 9. What is flaccid paraplegia? List 5 common causes.

Ans. Flaccid paralysis means lower motor neuron type of paralysis resulting from the diseases involving anterior horn cells, radicals, peripheral nerves and muscles.

Five important causes are:
1. Poliomyelitis
2. Polyradiculoneuropathy (Guillain-Barré syndrome)
3. Myopathies, polyneuropathies
4. Cauda equina syndrome
5. Periodic paralysis (electrolytic disturbance).

Q 10. What are five important causes of spastic paraplegia?

Ans.
1. Pott's disease
2. Spinal cord tumor

Table 1.115: Distinction between paraplegia-in-extension and paraplegia-in-flexion

Feature	*Paraplegia-in-extension*	*Paraplegia-in-flexion*
Posture	Lower limbs adopt an extension posture and extensor muscles are spastic. Extensor spasms occur	Lower limbs adopt flexed posture Intermittent flexor spasms occur in which there is flexion of both lower limbs
Neurological deficit	Only pyramidal tracts involved	Both pyramidal and extrapyramidal tracts are involved
Positions of limbs	Hip extended and adducted, knee extended and feet plantar-flexed	Thigh and knee flexed, feet dorsiflexed
Tone	Clasp-knife spasticity in extensor groups of muscles	Rigidity in flexor groups of muscles
Tendon jerks	Exaggerated	Diminished
Plantar response	Extensor	Extensor but evokes flexor spasms
Incontinence of bowel and bladder	Absent	Present
Mass reflex*	Absent	Present

N.B.: **Mass reflex* is an enlarged area of hyperexcitability of reflex activity. Just stroking the skin of either lower limbs or lower abdominal wall, produces the reflex evacuation of the bladder and bowel with reflex flexor spasms of the lower limbs and lower trunk muscles.

3. Spinal arachnoiditis
4. Traumatic injury to spinal cord.
5. Multiple sclerosis.

Q 11. What is neuronal (spinal) shock?

Ans. It refers to depression or loss of reflex activity (absent tendon reflexes) in acute lesion of spinal cord. It is transient, may last for a few days followed by recovery. This explains the loss of deep tendon reflexes in acute onset UMN lesion of the cord.

Q 12. What are common causes of hypertonia?

Ans.
- UMN lesion
- Tetanus
- Strychnine poisoning
- Hysterical
- Voluntary in noncooperative patients
- Extrapyramidal lesion except chorea
- Myotonia
- Catatonia
- Decerebrate rigidity.

Q 13. How will you calculate the level of spinal segments in relation to vertebra in a case with compression paraplegia?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

N.B: If spinal segment involved is known then vertebral level can be calculated as detailed above.

Q 14. What is hemisection of spinal cord?

Ans. **Brown-Séquard syndrome**. It is hemisection of spinal cord, commonly due to gunshot injury.
It consists of:
- Contralateral loss of pain and temperature with ipsilateral loss of posterior column sensations
- Monoplegia or hemiplegia on the same side of the lesion below the site of involvement
- UMNs signs below the level of lesion, i.e. exaggerated tendon jerks and plantar extensors. Superficial reflexes are lost
- A band of hyperesthesia or a zone of anesthesia at the level of compression.
- Segmental signs, i.e. muscle atrophy, redicular pain and loss of a reflex on the side involved.

Q 15. What are the two common causes of Brown-Séquard syndrome?

Ans.
1. Syringomyelia
2. Cord tumor.

Q 16. How will you distinguish compressive from noncompressive myelopathy?

Ans. The absolute characteristic of compression of the cord is either
1. Motor loss (loss of tendon jerk, muscle wasting, fasciculations)
2. A sensory sign (hyperesthesia, analgesia) at the site of compression while no such phenomenon is seen in noncompressive myelopathy.

Q 17. What are the causes of paraplegia without sensory loss?

Ans. **Causes** are:
- Hereditary spastic paraplegia
- Lathyrism
- GB syndrome
- Amyotrophic lateral sclerosis
- Fluorosis.

Q 18. What are the causes of paraplegia with loss of deep tendon jerks?

Ans. In paraplegia, the tendon jerks are brisk. They can only become absent when either patient is in spinal shock or there is involvement of spinal roots (radiculitis) or peripheral nerves (peripheral neuropathy).

Q 19. What are the causes of quadriplegia?

Ans. Quadriplegia means weakness of all the four limbs. Therefore, cause may lie in the brain or spinal cord anywhere from the cortex to spinal level T1. The *causes* are:
1. Cerebral palsy
2. High cervical cord compression, e.g. cranio-vertebral anomaly, high spinal cord injury, etc.
3. Multiple sclerosis
4. Motor neuron disease
5. Acute anterior poliomyelitis
6. Guillain-Barré syndrome
7. Peripheral neuropathy
8. Myopathy or polymyositis.

Q 20. How will you localise of the lesion in compressive myelopathy?

Ans. Diagnostic clues to lesions at different sites are depicted in Table 1.116.

Note: Horner's syndrome may occur at any level of cervical cord compression.

Table 1.116: Lesions at different sites and their signs

Site of lesion (spinal segment)	*Symptoms and signs*
High cervical cord lesion e.g. at C_1–C_4	× UMN quadriplegia × There may be weakness of respiratory muscles or diaphragmatic palsy × There may be suboccipital pain radiating to neck and shoulder × Sensory loss over upper part of chest
Thoracic cord lesion	
× Deep tendon reflexes below the level of lesions are exaggerated × Abdominal reflexes are lost if lesions lie above T_6 × Upper abdominal reflexes are lost and umbilicus is turned downwards in lesion of T_7–T_9. While upper abdominal reflexes spared and umbilicus turned upwards in lesion of T_{10}–T_{12}.	
Lesion of L1 of spinal cord	
Paraplegia with loss of cremosteric reflex	
Cauda equina lesion	
Read Case Discussion 37	

Q 21. What are classical features of acute transverse myelitis?

Ans. Following are classical features:

- Acute onset of fever with flaccid paralysis. There may be neck or back pain
- Cause is mostly viral
- Bladder involvement is early
- Girdle constriction (constriction band) around the waist is common indicating mid-thoracic region as the common site of involvement
- Variable degree of sensory loss (complete or incomplete) below the level of the lesion. A zone of hyperesthesia may be present between the area of sensory loss and area of normal sensation
- There is loss of all tendon reflexes (areflexia) due to spinal shock. Abdominal reflexes are absent. Plantars are silent. As the spinal shock passes off, hyperreflexia returns with plantar extensor response.

Q 22. What is lathyrism?

Ans. It is a slowly evolving epidemic spastic paraplegia due to consumption of '*Khesari dal*' (*Lathyrus sativus*) for prolonged period. It occurs in areas where drought are commonly seen, e.g. UP, Bihar, Rajasthan and MP where poor people consume often a mixture of wheat, Bengal gram and Khesari dal—called '*birri*'. It may involve many families in a locality. The causative factor is BOAA—a neurotoxin. Initially, patients complain of nocturnal muscle cramps, stiffness of limbs and inability to walk. Ultimately due to increasing spasticity they pass through one-stick stage (scissor type gait), two-stick stage (patient uses two sticks to walk) and crawler stage (patient crawls on hands).

Q 23. How does tuberculosis cause paraplegia?

Ans. This is as follows:

Ans.

1. Compression of the cord by cold abscess (extradural compression)
2. Tubercular arachnoiditis
3. Tubercular endarteritis
4. Tubercular myelitis

Q 24. How will you investigate the case with paraplegia?

Ans. Investigations are:

1. **Routine blood tests** (TLC, DLC, ESR).
2. **Urine examination,** urine for culture and sensitivity.
3. **Blood biochemistry,** e.g. urea, creatinine, electrolytes.
4. **Chest X-ray** for tuberculosis or malignancy lung or lymphoma.
5. **CSF examination.** Features of *Froin's* syndrome below the level of compression will be evident if spinal tumor is the cause of spinal block:
   - Low CSF pressure
   - Xanthochromia
   - Increased protein
   - Normal cellular count
   - Positive Queckenstedt test (i.e. no rise in CSF pressure following compression of internal jugular vein).
6. **CT myelography or MRI** to determine the site and type of compression.

Q 25. What is albuminocytological dissociation?

Ans. It refers to increased protein content in CSF with no parallel rise in cell count, hence, the word dissociation is used. The causes are:

- GB syndrome
- Froin's syndrome (spinal block due to a spinal tumor)
- Acoustic neurofibroma
- Cauda equina syndrome.

Q 26. What are causes of xanthochromia (yellow colouration of CSF)?

Ans. Following are the causes:

- Old subarachnoid hemorrhage
- GB syndrome
- Froin's syndrome
- Acoustic neuroma
- Deep jaundice.

Q 27. What is tropical spastic paraplegia (HTLV-1 associated myelopathy)?

Ans. It is common in females (3rd, 4th decades) associated with HTLV-1 infection where the patient develops gradual onset of weakness of legs (paraplegia) which progresses and patient becomes confined to wheelchair within 10 years. This is UMN spastic paraplegia without sensory disturbance. Bladder disturbance and constipation are common. This is an example of noncompressive progressive myelopathy. The diagnosis is suggested by seropositivity for HTLV-1.

CASE 37: CAUDA EQUINA SYNDROME

The patient (Fig. 1.37) an electrician while at work fell down and developed sudden onset of weakness of both the lower legs without bladder and bowel dysfunction.

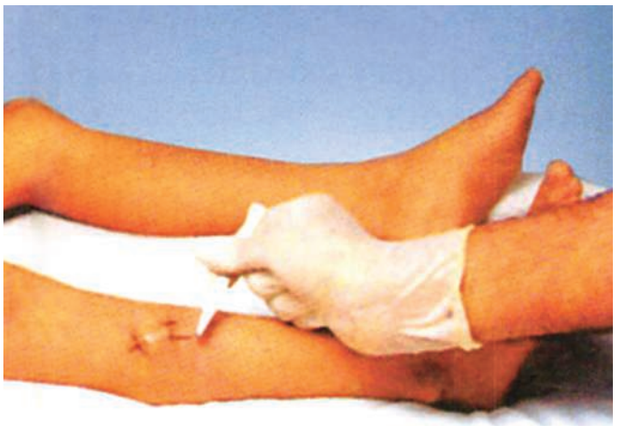


Fig. 1.37: Testing for sensations

Clinical Presentations of Cauda Equina Syndrome

- Patients present with paraplegia without sphincter involvement
- They may present with sensory loss over the buttocks
- They may present with muscle weakness and wasting.

History

Points to be Noted

- Onset and progression
- History of root pain involving to perineum and thighs
- History of trauma to spine (lower back)
- History of neurogenic claudication (pain in the calves during walking)
- Pain in anterior thigh
- Any trophic change
- History of leukemia or prostatic carcinoma
- History of disc prolapse.

EXAMINATION OF LOWER LIMBS

Motor System

- Thinning and atrophy of leg muscles
- There is wasting of quadriceps muscles and weakness of inverter of foot
- Nutrition of muscle is normal
- Tone is decreased in the muscles of foot and leg muscles
- Bilateral foot drop
- Bilateral ankle jerks and knee jerks are absent.

Sensory System

- Saddle distribution of sensory loss
- Sensory loss over the dorsum and sole of the foot, lateral aspect of the leg and a part of back of the leg
- Plantars are flexors (downgoing)
- Sphincters not involved in this case.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your probable diagnosis and why?

Ans. Sir, my provisional diagnosis is LMN type of paraplegia due to cauda equina syndrome.

The points in favour of the diagnosis are:

1. Sudden and symmetrical involvement of both lower limbs
2. History of root pain, radiating to the distribution of L3, L4, L5, S2–3 segments.
3. Saddle-shaped distribution of sensory loss
4. Flaccid paraparesis with loss of knee and ankle jerks
5. Plantars are flexors (downgoing)
6. Bowel and bladder function are spared.

Q 2. What is differential diagnosis?

Ans. All causes of acute onset LMN paraplegia will come into differential diagnosis such as:

1. Guillain-Barré syndrome
2. Diabetes mellitus producing symmetrical neuropathy and amyotrophy
3. Porphyria
4. Paraneoplastic conditions.

Q 3. What is the cause of cauda equina syndrome in your case?

Ans. As there is history of trauma to the spine, therefore, the cause in my case is traumatic compressive lesion, involving cauda equina.

Q 4. What are the causes of cauda equina syndrome?

Ans. i. Prolapse disc due to degeneration, tuberculosis, trauma, etc.
ii. Leukemic infiltration of the roots of cauda equina.
iii. Tumors of the cauda equina (e.g. ependymoma, neurofibroma).
iv. Secondaries in the spine causing compression of roots of cauda equina.

Q 5. Which vertebral level is the lesion in the cauda equina syndrome?

Ans. Spinal cord ends at the level of L_1, after that roots of cauda equina emerge. All the lumbar segments (L_2 to L_5) lie opposite to T_{10} to T_{12}. First lumbar vertebra overlies the sacral and coccygeal segments. Therefore, a lesion in the spinal cord at any level below the 10th thoracic vertebra

(below L_1 of spinal cord) can cause cauda equina syndrome.

Q 6. What is relationship of the spinal cord to the vertebra?

Ans. Read the examination of nervous system in *Clinical Methods in Medicine* by Prof SN Chugh.

Q 7. What are differences between cauda equina syndrome and conus medullaris lesion?

Ans. The conus medullaris is the terminal portion/point at which spinal cord ends and cauda equina (a bunch of roots) starts. Therefore, the main distinctions between the two is the plantars extensor and symmetrical LMN signs in conus medullaris; while plantar are flexor or not elicitable with asymmetric LMN paralysis in cauda equina syndrome (Table 1.117).

Table 1.117: Differentiating features between conus medullaris lesion and cauda equina syndrome

Conus medullaris lesion	*Cauda equina syndrome*
× Bilateral symmetrical involvement of both lower limbs	× Asymmetric involvement of both lower limbs
× No root pain	× Severe low back or root pain
× No limb weakness	× Asymmetric limb weakness
× Bilateral saddle anesthesia	× Asymmetric sensory loss
× The bulbocavernous (S_2–S_4) and anal reflexes (S_4–S_5) are absent	× Variable areflexia depending on the roots involved
× Bladder and bowel disturbance common	× They are relatively spared
× Plantars are extensor but not always	× Plantars are normal or not elicitable

Q 8. Name the conditions where ankle jerk is absent but knee jerk is preserved.

Ans.
- Peripheral neuropathy
- Tabes dorsalis
- Subacute combined degeneration.

Q 9. Name the conditions where knee jerk is absent but ankle jerk is present. Where is the site of lesion?

Ans. Absent knee jerk indicates LMN involvement of L2 to L4. Causes are:

i. Diabetic amyotrophy
ii. Proximal myopathy
iii. Disc prolapse compressing L2–L4 due to trauma or bone disease.
iv. Radiculitis involving L2–L4.

Q 10. What are root values of deep tendon jerks of lower limbs?

Ans. Read *Clinical Mediods in Medicine* by Prof SN Chugh.

Q 11. How would you elicit the different tendon jerks of lower limb?

Ans. Read *Clinical Methods in Medicine* and practise the various jerks in the class over the patients and in the hostel over your colleagues.

Q 12. What do you know about the term neurogenic claudication?

Ans. It implies that patient develops root pain and leg weakness usually a foot drop while walking which rapidly recovers on resting.

Q 13. What is sciatica syndrome?

Ans. It is characterised by low back pain that radiates along the sciatic nerve, occurs due to irritation of roots or nerve anywhere in the spinal canal, intervertebral foramina, in the pelvis or buttocks. Straight leg raising test is positive. There may be sensory or motor deficit with absent or depressed ankle jerk on the side involved. Causes include lateral protrusion of the disc, spinal tumors, or spondylolisthesis. Spinal canal stenosis can lead to bilateral sciatica with neurogenic claudication.

Q 14. How would you elicit straight leg raising test?

Ans. Read *Clinical Methods in Medicine* by Prof SN Chugh.

Q 15. What is spondylolisthesis?

Ans. It is anterior slippage of vertebral body, pedicles and superior articular facet leaving behind the posterior element: A 'Step' may be present on deep palpation of posterior elements of the segment above the spondylolisthetic joint.

Spondylolisthesis is associated with degenerative spine disease and spondylosis and occurs more frequently in women. It can be asymptomatic. Symptomatic disease produces back pain, root pain and sometimes cauda equina syndrome.

Q 16. What is spina bifida occulta?

Ans. It is a failure of closure of one or several vertebral arches posteriorly. The meninges and spinal cord are normal. A dimple or a tuff of hair or lipoma may overlie the defect. Most cases are asymptomatic and discovered incidently on X-rays spines during evaluation of back pain.

Q 17. How would you investigate a patient with cauda equina syndrome?

Ans.
1. **Routine laboratory investigations,** e.g. complete blood count, ESR, biochemistry profile and urinalysis.
2. **Plain X-ray films** of lumbosacral regions.
3. **CT myelography and MRI** are the radiological tests of choice for evaluation of cauda equina syndrome.
4. **EMG and nerve conduction velocities.** They are usually of uncertain values.

CASE 38: PERIPHERAL NEUROPATHY

The patient (Fig. 1.38A) presented with following complaints:
1. Sensations of pins and needles (tingling and numbness) in the distal parts of all the four limbs
2. Weakness of all the limbs especially distal parts
3. Thinning of legs.

Clinical Presentations of Peripheral Neuropathy

1. Distal paresthesias (pins and needles sensation) is the presenting symptom usually first affecting the feet and then the hands.
2. Loss of all types of sensations in a glove-stocking distribution (Fig. 1.38B). Patient may be unaware of injury or burn marks on the hands in smokers and on the feet in labourers.
3. Distal weakness of all the four limbs leading to bilateral foot drop and/or bilateral wrist drop areflexic paralysis of all the four limbs.
4. There may be autonomic disturbances in peripheral parts, i.e. postural edema, cold extremities, etc.

History

Points to be Noted

- Note the duration and onset of symptoms
- Initiation and distribution of sensory disturbance (i.e. glove-stocking anesthesia)
- Evolution of weakness (proximal or distal). Was there any difficulty in holding the things?
- Progression of symptoms, e.g. stationary, progressive, recovering or waxing and waning
- Is there any history of weakness of respiratory muscles or facial muscles? Difficulty in coughing or breathing?
- History of taking drugs (e.g. INH)
- Any precipitating factor or illness
- Bowel and bladder disturbance.

Past History

Ask for

- Alcoholism
- Headache, vomiting, convulsions
- Diplopia, dysphagia, nasal regurgitation
- History of fever, contact with a patient of tuberculosis, exposure to STD, vaccination
- History of systemic illness, i.e. diabetes, renal failure, chronic liver disease, diarrhea or malabsorption, etc.
- History of exposure to solvents, pesticides or heavy metals
- Past history of spinal trauma.

Family History

History of similar illness in other family members.

EXAMINATION

General Physical Examination

- Consciousness and behaviour
- Look for anemia, jaundice, edema
- Look for signs of vitamin deficiencies, i.e. tongue, eyes, mucous membranes
- Look for alcoholic stigmata, e.g. gynecomastia, testicular atrophy, muscle wasting, parotid enlargement, palmar erythema or flushing of face. Look at the skin for

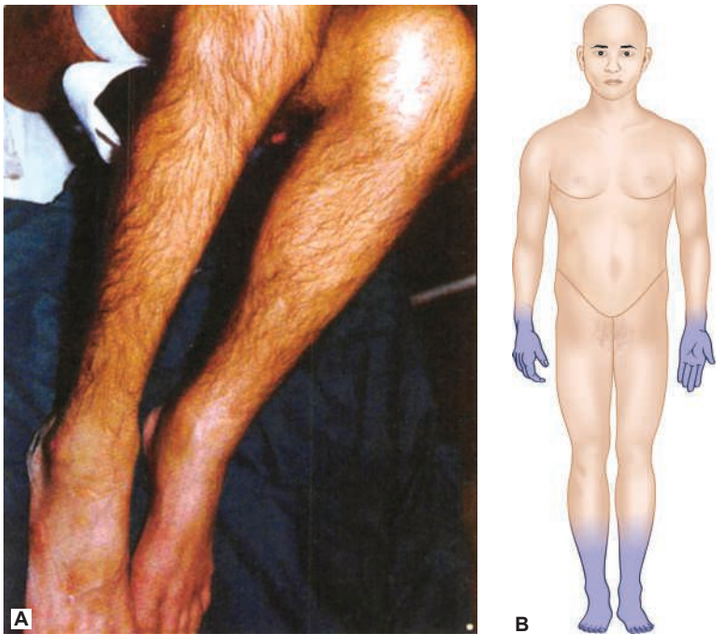


Fig. 1.38A and B: Peripheral neuropathy. **A.** A patient with bilateral foot drop due to peripheral neuropathy; **B.** Glove-stocking type of anesthesia (diagram)

hypopigmented or hyperpigmented patches, scar or burn mark
- Record pulse, BP and temperature.

Systemic Examination (Read CNS Examination)

- Higher functions
- Cranial nerves
- Neck rigidity.

Motor Function

- Look the posture (usually decubitus) and foot drop
- Note the nutrition, tone, power and coordination of the muscles
- Elicit the tendon jerks. Bilateral ankle jerks are usually absent.

Sensory System

- Test superficial and deep sensations including cortical sensations. They are lost in the peripheral parts
- Palpate the various long nerves (ulnar, radial, common peroneal). They may be palpable in diabetes, leprosy, hereditary polyneuropathy.

Other System Examination

1. CVS for sounds, bruits and murmurs
2. Respiratory system for evidence of tuberculosis, sarcoidosis, malignancy
3. GI tract for hepatosplenomegaly
4. Lymphoreticular system for lymph node enlargement.

COMMON QUESTIONS AND THEIR APPROPRIATE ANSWERS

Q 1. What is your probable diagnosis and why?

Ans. Sir, my provisional diagnosis is peripheral neuropathy, distal and symmetric. The points in favour of my diagnosis are:
- History of pins and needles in distal parts of all limbs.
- Loss of all types of sensations, i.e. superficial and deep (spinothalamic and posterior column) in peripheral parts of all the four limbs.
- Weakness of distal parts of all four limbs with hypotonia, loss of deep tendon jerks and superficial reflexes (plantar response) in the peripheral parts of all limbs.
- Presence of bilateral foot drop.
- Presence of trophic changes.

Q 2. What is differential diagnosis of polyneuropathy?

Ans. The differential diagnosis lies between its various causes. The characteristics of some common causes of neuropathies are discussed here.

1. **Guillain-Barré syndrome.** The characteristic features are given in Table 1.118.

Table 1.118: Diagnostic criteria for Guillain-Barré syndrome

Essential	*Supportive*
× Progressive weakness of 2 or more limbs due to neuropathy	× Relative symmetric weakness
× Areflexia (loss of reflexes)	× Mild sensory involvement
× Disease course <4 weeks	× Facial and other cranial nerve involvement
× Exclusion of other causes of LMN type of paraplegia or quadriplegia	× Absence of fever
	× Typical CSF changes (acellularity, rise in protein)
	× Electrophysiologic evidence of demyelination

2. **Diabetic peripheral neuropathy**
   - History of diabetes, i.e. type 1 (polyuria, polydipsia or polyphagia) or type 2 (impaired wound healing, infections, etc.)
   - History of intake of either insulin or OHA
   - Duration of diabetes is longer
   - A triad of retinopathy, neuropathy and nephropathy may occur but these complications can occur individually also
   - History of susceptibility to infection, weakness, impaired wound healing
   - The various types of neuropathy in diabetes have already been described.
3. **Leprosy**
   - Typical 'Leonine' facies
   - Typical hypopigmented and anesthetic skin lesions
   - Palpable peripheral nerves with peripheral neuropathy
   - Trophic changes
4. **Diphtheric neuropathy**
   - Common in children, but now rarely observed due to effective immunization against diphtheria
   - Palatal weakness followed by pupillary paralysis and sensorimotor neuropathy
   - Cranial nerves 3rd, 6th, 7th, 9th and 10th may be involved
   - The condition develops 2–6 weeks after the onset of disease
   - Myocarditis may occur in two-thirds of patients with diphtheria. It manifests on ECG as arrhythmias, conduction blocks, ST-T changes and CHF.
5. **Prophyric neuropathy**
   - Acute intermittent porphyria produces attacks of paroxysmal neuropathy simulating GB syndrome
   - This is associated with abdominal colic, confusion, autonomic disturbances and later coma
   - Alcohol and barbiturates precipitate the attacks.
6. **Arsenical neuropathy**
   - Rain-drop skin lesions with hyperkeratosis of palms and soles
   - People of known geographical area using deep tube well water are mainly affected

- Mees' line (white transverse ridges on nails) is diagnostic
- Presence of anemia with or without jaundice (hepatic involvement).

7. **Neoplastic neuropathy.** Polyneuropathy is sometimes seen as a nonmetastatic manifestation of a malignancy (paraneoplastic syndrome) which may be motor or sensorimotor.
8. **Hereditary neuropathy (Charcot-Marie-Tooth disease)**
   - An autosomal dominant/recessive/X-linked transmission. It occurs in first and second decades of life
   - Sensorimotor neuropathy characterised by distal muscle weakness and atrophy, impaired sensations, absent or hypoactive deep tendon reflexes
   - Pattern of involvement is feet and legs followed by hands and forearm
   - High-steppage gait with frequent falling due to bilateral foot drop
   - Foot deformity (pes cavus, high arch feet) and hand deformity due to atrophy of intrinsic muscles of the hands.

Q 3. Could your case be of Guillain-Barré syndrome?

Ans. Yes. The points in favour are:
- Short duration and acute onset of symptoms.
- Progressive weakness
- Areflexia with bilateral foot drop
- Peripheral neuropathy
- Bowel and bladder not involved.

Q 4. How would you confirm the diagnosis of Guillain-Barré syndrome?

Ans.
1. CSF examination for rise of proteins and albuminocytological dissociation
2. Immunoelectrophoresis of CSF proteins for rise in immunoglobulin
3. Nerve conduction velocities of peripheral nerve
4. Sural nerve biopsy and histopathology.

Q 5. What is the tone of muscles in your case?

Ans. There is hypotonia of all peripheral muscles (feet and hands) otherwise tone is preserved in other muscles. Bilateral foot drop in my case is an example of hypotonia.

Q 6. What are the causes of peripheral neuropathy?

Ans.
1. Diabetes mellitus
2. Alcoholic polyneuropathy (B_1, B_6, B_{12} def.)
3. Chronic renal failure
4. GB syndrome (acute inflammatory polyradiculoneuropathy)
5. Amyloidosis
6. Drug-induced (INH, NFT, vincristine)
7. Hereditary

Q 7. What are the causes of acute onset peripheral neuropathy?

Ans. **Causes** are:
- GB syndrome
- Diphtheria
- Diabetes mellitus
- Porphyria
- Drugs (TOCP, arsenic)
- Paraneoplastic syndrome.

Q 8. What are the causes of predominant motor neuropathy?

Ans. **Causes** are:
- GB syndrome (70%)
- Porphyria
- Connective tissue diseases, e.g. SLE, PAN
- Hereditary polyneuropathy
- Acute motor axonal neuropathy
- Delayed neurotoxicity due to organophosphates (TOCP, TCP)
- Diphtheria
- Lead intoxication
- Hypoglycemia
- High doses of dapsone.

Q 9. What are the causes of predominant sensory neuropathy?

Ans. **Causes** are:
1. Hereditary sensory neuropathy
2. Paraneoplastic syndrome
3. Leprosy
4. Vitamin B_1 and B_{12} deficiency
5. HIV
6. Chronic renal failure
7. Alcoholic polyneuropathy.

Q 10. What are the causes of palpable thickened peripheral nerves?

Ans.
1. Amyloidois
2. Guillain-Barré syndrome
3. Leprosy
4. Charcot-Marie-Tooth disease
5. Refsum syndrome (retinitis pigmentosa, deafness and cerebellar degeneration)
6. Dejerine-Sottas disease (hypertrophic peripheral neuropathy)
7. Diabetes.

Q 11. How do you classify neuropathy in diabetes mellitus?

Ans. Neuropathy is a microvascular complication of diabetes, occur commonly in type 2 than in type 1 diabetes. It may be symmetric or asymmetric, motor, sensory or mixed. Read case discussion on diabetes.

Q 12. What do you know about diabetic amyotrophy?

Ans. It is asymmetrical motor polyneuropathy characterised by asymmetric weakness and wasting of the proximal muscles of the lower limbs and sometime upper limbs, diminished or absent knee jerk and sensory loss in the thigh. It is usually accompanied by severe pain in the thigh, often awakening the patient at night. Patient usually recovers, hence, prognosis is good.

Q 13. What are the characteristic features of alcoholic neuropathy?

Ans.
1. It is nutritional neuropathy due to deficiency of B_1, B_6 and B_{12} induced by alcohol
2. It is predominantly sensory neuropathy
3. Other stigmatas of alcoholism may be present
4. Features of other alcohol-induced conditions e.g. hepatomegaly, cardiomyopathy.

Q 14. What are the causes of foot drop?

Ans. Paralysis of extensors of foot and peronei muscles produces foot drop. The common causes are:
1. Peripheral neuropathy (bilateral foot drop)
2. Common peroneal nerve palsy (unilateral foot drop)
3. PIVD (lesion involving L5) produces unilateral or bilateral foot drop
4. Motor neuron disease (bilateral foot drop)
5. Sciatic nerve lesion (unilateral foot drop)
6. Peroneal muscle atrophy (bilateral foot drop)

Q 15. What are the causes of wrist drop?

Ans. **Causes** are:
- Radial nerve palsy
- Lead neuropathy
- Other peripheral neuropathies.

Q 16. What is entrapment neuropathy? What are common entrapment neuropathies?

Ans. Entrapment means traping of the nerve in a tight anatomical compartment leading to compression of the nerve. The common entrapment neuropathies are:
1. Meralgia paresthetica (lateral cutaneous nerve trapped)
2. Carpal tunnel syndrome (median nerve trapped
3. Tarsal tunnel syndrome (posterior tibial nerve trapped)
4. Common peroneal nerve entrapment at head of fibula
5. Elbow tunnel syndrome (ulnar nerve trapped).

Q 17. How would you confirm your diagnosis?

Ans. By EMG and nerve conduction studies.

Q 18. Which drugs are effective for painful neuropathy in diabetes?

Ans.
- Tricyclic antidepressants
- Antiepileptics, e.g. phenytoin, carbamazepine, valproate, gabapentine/pregabalin
- Topical capsaicin.