STANDARD TREATMENT GUIDELINES
MEDICINE
(RESPIRATORY DISEASES)

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AIIMS

ACUTE RESPIRATORY DISTRESS SYNDROME

I. WHEN TO SUSPECT/ RECOGNIZE?

a) Introduction:

Acute respiratory distress syndrome (ARDS) is the most severe form of acute lung injury resulting in extensive bilateral pulmonary infiltrates, severe refractory arterial hypoxemia and stiff lungs. Of the numerous clinical conditions identified to cause ARDS, sepsis syndrome, polytrauma, obstetric complications, and surgery, among others appear to be the most common causes. The site of injury may be focused on either the vascular endothelium (eg. sepsis) or the alveolar epithelium (eg. aspiration of gastric contents). Injury to the endothelium results in increased capillary permeability and the influx of protein-rich fluid into the alveolar space. Injury to the alveolar lining cells also leads to pulmonary edema. In tropical countries, malaria, leptospirosis, tuberculosis (including miliary), enteric fever, and dengue haemorrhagic fever, organophosporus and paraquat poisoning; scorpion sting; inhalation of toxic fumes (e.g.chlorine); and heat stroke are important causes of ARDS. Other known risk factors are bacteremia, sepsis, trauma with or without pulmonary contusion, fractures, particularly multiple fractures and long bone fractures, burns, massive transfusion, pneumonia, aspiration, drowning, postperfusion injury after cardiopulmonary bypass and acute pancreatitis.

b) **Case definition** (for both situations of care):

Acute lung injury

Acute onset

$PaO_2/FIO_2 \leq 300$*

$SpO_2/FIO_2 \leq 315$*

Bilateral infiltrates on the chest radiograph

PCWP $\leq$ 18 mm Hg, or no clinical evidence of left atrial hypertension

Acute respiratory distress syndrome

Acute onset

$PaO_2/FIO_2 \leq 200$*

$SpO_2/FIO_2 \leq 235$

Bilateral infiltrates on the chest radiograph

PCWP $\leq$ 18 mm Hg, or no clinical evidence of left atrial hypertension

***** Irrespective of level of positive end-expiratory pressure

PaO_2 = partial pressure of oxygen in the patient's arterial blood; FIO_2 = fraction of inspired oxygen; SpO_2 = pulse oximetric measurement of oxygen saturation; PCWP = pulmonary capillary wedge pressure

The severity of hypoxemia is necessary to make the diagnosis of ARDS. The cardiogenic pulmonary edema must be excluded either by clinical criteria or by a pulmonary capillary wedge pressure (PCWP) lower than 18 mmHg in patients with a Swan-Ganz catheter in place.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

Global estimates suggest that ARDS occurs in 1.5 to 75 cases / 100,000 population. No systematic studies have been carried out till date to define the incidence of ARDS in India and reliable epidemiological data are not available.

III. DIFFERENTIAL DIAGNOSIS

1. Cardiogenic pulmonary oedema
2. Other considerations
    - 2.1 Pneumonia
    - 2.2 Diffuse alveolar haemorrhage
    - 2.3 Idiopathic acute eosinophilic pneumonia
    - 2.4 Cryptogenic organizing pneumonia
    - 2.5 Acute interstitial pneumonia (Hamman-Rich syndrome)
    - 2.6 Metastatic malignancy
    - 2.7 Near drowning
    - 2.8 Drug reaction
    - 2.9 Noncardiogenic pulmonary edema
        - Acute hypersensitivity pneumonitis
        - Transfusion-related acute lung injury (TRALI)
        - Leukemic infiltration
        - Fat embolism syndrome

IV. PREVENTION AND COUNSELING

No form of therapy is known to prevent the occurrence of ARDS.

OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

*Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited

a) **Clinical Diagnosis**

Symptoms

The onset of ARDS is acute. The acute, or exudative, phase is characterised by rapid onset of dyspnoea, dry cough, respiratory failure, disorientation and agitation that usually develop 24 to 72 hours after the inciting event. The patient may be febrile or hypothermic.

Signs

Tachypnoea, tachycardia, cyanosis, crepitations and rhonchi may be present. Arterial hypoxaemia that is refractory to high concentrations of supplemental oxygen therapy is a hall mark of ARDS. Chest auscultation may reveal bilateral rales and rales may be absent despite diffuse involvement. In intubated and mechanically ventilated patient decreased breath sounds over one lung may indicate a pneumothorax or endotracheal tube down the opposite main bronchus.

Careful physical examination to look for potential causes of sepsis including signs of lung consolidation or findings consistent with an acute abdomen, sites of intravascular lines, surgical wounds, drain sites, and decubitus ulcers for evidence of infection are needed. The cardiogenic pulmonary edema should be differentiated from ARDS, by carefully looking for signs of congestive heart failure or intravascular volume overload, including jugular venous distention, cardiac murmurs and gallops, hepatomegaly, and edema.

b) **Investigations**

1. **Pulse oximetry:** Pulse oximetry reveals SpO_2/FIO_2 ratio less than or equal to 235. Severe refractory hypoxaemia in spite of supplemental oxygen therapy is evident.
2. **Chest radiograph:** The radiographic changes become evident by about 12 hours after the clinical onset of respiratory failure. Initially, patchy, ill-defined opacities may become apparent throughout the lungs.
3. **Echocardiography:** Echocardiography is useful in differentiating ARDS from cardiogenic pulmonary oedema.
4. **Arterial blood gas (ABG) analysis**: ABG analysis usually reveals severe refractory hypoxemia, hypocapnia and alkalosis if the patient is breathing spontaneously. Hypercapnia usually does not occur unless chronic lung disease is co-existent.

c) Treatment:

Standard Operating procedure

a. In Patient

1. **General therapeutic measures**

1. SpO_2 monitoring by pulse oximetry
2. Ensure adequate circulation and blood pressure using volume infusion and/or vasopressors
3. Treatment of the aetiologcal cause of ARDS (e.g., appropriate antibiotic therapy for patients with sepsis syndrome)

2. **Supplemental oxygen therapy**

Initially, spontaneous ventilation using a face mask with a high flow gas delivery system can be used to deliver a FIO_2 of up to 0.5 to 0.6.

b. Out Patient

Not applicable. ARDS is managed in an intensive care (ICU) unit setting

d) **Referral criteria:**

1. Diagnosis not clear

2. Response to therapy not optimal. Hypoxaemia ($SpO_2 \leq 90$) persists in spite of supplemental oxygen therapy
3. Haemodynamic instability

***Situation 2: At Tertiary hospital where higher-end technology is available**

a) Clinical Diagnosis

As in situation V.1 a) above

b) Investigations

1. As in situation V.1b) above PLUS
2. **Computed tomography of the chest:** Early in the exudative phase, computed tomography (CT) of the chest reveals diffusely distributed non-uniform ground glass opacification or consolidation which may not conform to the gravity distribution. Later in the exudative phase, the consolidation becomes more homogeneous and gravity dependent. In the proliferative and fibrotic stages, there is a decrease in the overall lung density and the appearance of an interstitial reticular pattern. CT also facilitates identification of underlying pulmonary causes of ARDS (e.g., pneumonia and lung abscess) and complications of ARDS, such as, pneumothorax, pneumomediastinum and interstitial emphysema may also be evident.
3. **Swan-Ganz catheterization:** The pulmonary capillary wedge pressure (PCWP) is less than 18 mm Hg and the cardiac index is more than 2.1 L/min.
4. **Bronchoscopic procedures:** Bronchoscopic procedures are helpful to exclude infectious causes of ARDS.

c) Treatment:

Standard Operating procedure

a. In Patient

1. As in situation V.1c)a.1 above PLUS

2. General therapeutic measures

2.1. Haemodynamic stabilization. Pulmonary and systemic arterial lines are inserted for hemodynamic monitoring and rational fluid replacement therapy. Adequate circulation and blood pressure is ensured using volume infusion (crystalloids) and/or vasopressors, taking the CVP/PCWP as the guideline. The intravascular volume is maintained as low as possible while maintaining an adequate cardiac index, mean arterial pressure, at the same time ensuring adequate organ perfusion. In anaemic patients, transfusion of packed red cells can help improving oxygenation.

2.2. Adequate nutrition should be ensured through the use of enteral feeding.

2.3. Efforts should also be directed to prevent gastrointestinal bleeding and pulmonary thromboembolism

3. Supplemental oxygen therapy

3.1 Spontaneous breathing using a face mask with a high flow gas delivery system can be used to deliver a FIO_2 of up to 0.5 to 0.6. Continuous positive airway pressure (CPAP) may be added to improve PaO_2 without increasing FIO_2. If a FIO_2 of more than 0.6 and CPAP of more than 10 cm H_2O are needed to achieve PaO_2 of more than 60 mm Hg, tracheal intubation and assisted mechanical ventilation are required.

4. Ventilatory support

4.1 Aim of mechanical ventilation is to maintain gas exchange with minimal complications. Tidal volume should be set in the region of 6 ml/kg ("lung protective ventilation") rather than the conventional 10 to 12 ml/kg and the plateau pressure should be limited to 30 to 35 cm H_2O to prevent alveolar overdistension. PEEP and FIO2 settings are set as per ARDSnet protocol.

4.2 Other alternative approaches, such as, prone positioning of the patient, high frequency jet ventilation (HFJV), high frequency oscillatory ventilation (HFOV), and liquid ventilation among others can also been tried in selected patients. The relative merits of these alternative methods of mechanical ventilation must be critically weighed against the potential side effects in every setting.

5. Corticosteroids and ARDS

5.1 It is now conclusively established that corticosteroids have no useful role before the onset of ARDS or early in its course. When patients with ARDS have severe disease, and, do not show signs of improvement 7 to 14 days after the onset of ARDS (late ARDS), a one to two week trial with corticosteroids (prednisolone 2-4 mg/kg/day or equivalent) can be tried.

6. ARDS in the tropics

6.1 Infectious causes such as pulmonary and miliary tuberculosis, falciparum malaria, enteric fever, and leptospirosis are rare but treatable causes of ARDS. When recognized to be the aetiological cause of ARDS, appropriate specific treatment must be instituted for primary conditions.

b. Out Patient

Not applicable. ARDS is managed in an intensive care (ICU) unit setting

V. WHO DOES WHAT? and TIMELINES

a. ***Doctor*** Diagnosis and Management including counseling

b. ***Nurse*** Implementation of orders, monitoring of patients and counseling

c. Technician Investigations

Respiratory physiotherapist For administering supportive care to patients admitted in ICU

VI. FURTHER READING / REFERENCES

1. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994; 149:818-24.

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3. Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, deBoisblanc B, et al. National Heart, Lung, and Blood Institute acute respiratory

distress syndrome (ARDS) clinical trials network. Comparison of two fluid management
strategies in acute lung injury. N Engl J Med 2006;354: 2564-75.
4. Wheeler AP, Bernard GR, Thompson BT, Schoenfeld D, Wiedemann HP, deBoisblanc B, et al. National Heart, Lung, and Blood Institute acute respiratory distress syndrome (ARDS) clinical trials network. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. N Engl J Med 2006;354: 2213-24.

RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1. Physician with training in echocardiography 2. Nurse 3. Radiographer	1.Pulse oximetry 2.Chest X-ray 3.Echocardiography 4.ABG analysis	1.Oxygen 2. Antibiotics 3. Inhaled bronchodilators	1.Oxygen cylinder 2.Nasal prongs 3.MC mask 4.X-ray machine 5.Echocardiography machine 6.ABG analyzer
2	Above plus 1.Intensivist 2.ICU staff with pulmonary training 3.Respiratory physiotherapists 4.Radiologist 5.Microbiologist	Above plus 1.Computed tomography including CT pulmonary angiography 2.Bronchoscopy	Above plus 1.Parenteral and oral bronchodilators (theophylline, terbutaline) 2.Parenteral and oral steroids (hydrocortisone, prednisolone) 3.Central venous catheter 4.Swanz Ganz catheter	Above plus 1.CT machine 2.Microbiology laboratory service for infectious aetiology work-up 3.ICU 4.Noninvasive and invasive ventilators 5. HFOV (high frequency oscillatory ventilation) [if available] 6. Bronchoscope

BRONCHIAL ASTHMA

I. WHEN TO SUSPECT/ RECOGNIZE?

a) Introduction: Asthma is a common clinical problem encountered at all levels of health care. Asthma can be defined as a chronic inflammatory disorder of the airways. Different terms such as *allergic* or *asthmatic bronchitis*, *wheezy bronchitis*, *intrinsic and extrinsic asthma* are frequently employed in clinical practice. Asthma commonly begins in childhood and early youth, but may also start later in life at any age. Contrary to common belief, children do not necessarily 'grow out of asthma'. Almost two third of the asthmatic children continue to have symptoms in puberty/adulthood. About 5-10% children with 'mild' asthma may go on to develop severe asthma later in life.

b) Case definition (for both situations of care):
Asthma is characterized by recurrent episodes of cough, wheezing, breathlessness, and chest tightness that are often reversible, either spontaneously or with treatment.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

The prevalence rates are variable depending upon the definition and methodology employed. As per the results of the Indian Study on Epidemiology of Asthma, Respiratory symptoms and Chronic bronchitis (INSEARCH), the population prevalence in adults is about 2 percent or more. In children, the prevalence is likely to be higher, exceeding 5 percent. Both men and women are about equally affected.

III. DIFFERENTIAL DIAGNOSIS

Diagnosis of asthma is a two-step approach. The first important step is to suspect the diagnosis while the second step involves exclusion of other diagnoses and laboratory assessment to confirm the diagnosis and assess the severity stage of asthma. Documentation of reversibility and/or variability of forced expiratory flow, 1^{st} second (FEV1) or peak expiratory flow (PEF) is important to diagnose asthma and differentiate it from chronic obstructive pulmonary disease.

IV. PREVENTION AND COUNSELING

Exact cause of asthma is not known. Both environmental and genetic factors are important. A family history of asthma or atopy (allergy), presence of other atopic manifestations (e.g. allergic rhinitis, skin allergies) and airway hyper-responsiveness predispose an individual to develop asthma. However, asthma can develop in the absence of a family history. Asthma attacks are generally triggered by one or more of exposures/ risk-factors. Most patients may have more than one trigger.

Besides complying with the therapy for treatment and control of asthma, the common triggers (as below) should be identified and avoided:

Respiratory infections – usually viral
Allergens (Indoor/Outdoor)
Air pollution (Indoor/Outdoor) including smoke and fumes (biomass fuel)
Tobacco smoke (both active and passive)
Drugs – beta-blockers and non-steroidal anti-inflammatory drugs (NSAIDs)
Food additives and preservatives- food is normally not a trigger unless it is specifically proved to be so in an individual.

Since asthma is a lifelong problem, it is crucial that the patient and the family are educated about the disease and its management for a normal and healthy life.

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

*Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited

Diagnosis

e) The diagnosis is essentially based on history and physical findings of wheezing. FEV_1/FVC ratio less than 70% and reversibility more than 12% and 200 ml establishes the diagnosis.This should also be categorized in to mild, moderate and severe depending upon the symptoms and treatment requirement.

	Mild	Moderate	Severe
Symptoms disturbing sleep	< once per week	> once per week	Daily
Daytime symptoms	< Daily	Daily	Daily
Limitation of accustomed activities	Nil	Some limitation	Severe limitation
Use of rescue medication *	<1 unit per day	1-2 units per day	>2 units per day
FEV_1 or peak expiratory flow	Normal	60-80%	<60%

f) <u>Treatment:</u>

Basically in asthma four components are important in management; i) diagnosis, assessment and monitoring of severity ii) education for partnership of patient and doctor iii) identification and control of trigger factors and iv) pharmacologic management.

All these components of care are possible even at a place where resources are limited. Therefore primarily management of asthma does not vary due to resource constraint or lack of technology.

It is important to effectively manage asthma to help an individual to live a normal life, and avoid acute exacerbations as well as long-term complications. Currently available important anti-asthma drugs can be classified as controllers (required for maintenance treatment) and relievers (required for quick relief, rescue drugs). Inhaled corticosteroids constitute the cornerstone of maintenance therapy**.**

- **Controllers (Prophylactic, Preventive, Maintenance)**
  - Taken daily to keep asthma under control
  - Steroids, long-acting beta-2 agonists, sustained-release theophyllines, leukotriene receptor antagonists, and cromones
- **Relievers (Quick relief, Rescue)**
  - Rapid acting drugs that relieve bronchoconstriction
  - Short acting beta-2 agonists, anticholinergics, theophyllines, short-course oral steroids

The recommendations for use of drugs vary depending upon the stage of asthma. Mild asthma can be further divided into intermittent (symptoms for less than two days per week) and persistent (symptoms for more than two days per week) categories, and treatment given accordingly. Low dose inhaled steroids are

recommended. Alternatively, oral theophyllines can be used. Moderate asthma is treated with medium dose ICS + long acting beta-agonists (LABA) and/or leukotriene antagonists (LTRA). Alternate choices are: - medium dose ICS + LTRA / theophylline. Severe asthma is managed with high-dose ICS and/or oral steroids at the lowest dose + LABA + theophylline + LTRA.

Systemic corticosteroids on long-term basis must be avoided. A short-course of up to two weeks (0.5 mg/kg/day) is, however, often valuable for managing acute severe asthma.

In addition to daily controller therapy, reliever medications on as-needed basis may

be taken in all stages.

Asthma control requires frequent stepping up or down of therapy.

Patients with intermittent or seasonal symptoms can be managed with only reliever medications taken on an as-needed basis.

Management of acute severe asthma

Hour 1: 4 doses of inhaled salbutamol ± ipratropium, 100 mg hydrocortisone (IV) or oral prednisolone 60 mg, oxygen, adequate hydration

Hour 2: 4 more doses of inhaled salbutamol with ipratropium, IV aminophylline, subcutaneous terbutaline/adrenaline 0.3-0.5 mg (0.01 mg/kg for children) for 3 doses

Acute severe asthma not responding within 2 hours of treatment, or deteriorating:

REFER IMMEDIATELY

Expectorants and mucokinetic drugs do not have any significant role.

General principles of pharmacotherapy in patients with bronchial asthma

- Inhaled drugs should preferably be given using metered dose inhaler with spacer
- Education about proper inhalation technique is most essential for optimal results
- Long-acting beta-agonists (LABA) should always be combined with ICS
- Short-acting beta-agonists (SABA) should be used only as reliever medication
- Methylxanthines can be used as an alternative to inhaled steroids only in mild disease, or in acute severe asthma when standard treatment is not effective
- Anticholinergic drugs provide additive effect to SABA aerosol during exacerbations

Systemic glucocorticoids are important only in the treatment of mild to moderate

exacerbations of asthma.

g) **Referral criteria:**

- Diagnosis unclear or in doubt
- Atypical signs or symptoms
- Failure to respond to treatment over one month
- Other conditions complicating asthma or its diagnosis, necessitating additional work-up
- Severe persistent asthma
- Life-threatening asthma (cyanosis, mental obtundation)
- Patients requiring additional tests such allergy testing, induced sputum eosinophil, FeNO etc
- Patients requiring special treatment such as immunotherapy.

***Situation 2: At Super Specialty Facility in Metro location where higher-end technology is available**

d) Clinical Diagnosis:

Same as in Situation 1 (a)

e) Investigations: exhaled nitric oxide (FeNO), induced sputum eosinophils

f) Treatment:

Standard Operating procedure

a. **In Patient: ventilator care**
b. **Out Patient: same**
c. **Day Care: same**

VI. WHO DOES WHAT? and TIMELINES

a. ***Doctor:*** diagnosis, assessment of severity and prescription of medicines for the patient. Explaining action plan to deal with exacerbation.

b. ***Nurse:*** Educating patients about inhaler techniques and controlling trigger factors.

c. ***Technician:*** Proper spirometry and measurement of peak flow

VII. Further reading/ references

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	4. Physician 5. Nurse 6. Pulmonary function test technician 7. Radiographer	1. Chest radiograph 2. Pulmonary function test 3. Arterial blood gases	1. Inhaled bronchodilators (salbutamol, ipratropium) 2. Inhaled steroids (budesonide, beclamethasone) 3. ICS (fluticasone/budeson-ide)+ LABA (formoterol/salmete-rol) 4. Parenteral and oral bronchodilators (theophylline, terbutaline) 5. Parenteral and oral steroids (hydrocortisone, prednisolone) 6. Parenteral and oral antibiotics preferably macrolides	1. Oxygen cylinder 2. Nebulizers 3. Spirometer 4. Handheld spirometer (PEFR meter) 5. X-ray machine 6. ABG analyzer
2	Above plus 1. ICU staff with pulmonary training	Above plus 1. FeNO	Above plus 1. Higher generation antibiotics	Above plus 1. ICU set-up 2. Noninvasive and invasive ventilators 3. FeNO analyzer

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

I. WHEN TO SUSPECT/ RECOGNIZE?

c) Introduction:

COPD should be suspected in any person, particularly in middle life, with history of tobacco smoking and/or other risk factors, and presenting with:

- Cough, more during morning hours
- Frequent sputum production
- Breathlessness, mainly on exertion

On clinical examination features of hyperinflation, diminished vesicular breath sounds with prolonged expiration and rhonchi are found.

d) Case definition:

For both situations of care *(mentioned below*)*

COPD is a preventable and treatable disease condition characterised by airflow limitation, which is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases, primarily caused by tobacco smoking. Chronic cough and sputum production often precede the development of airflow limitation by many years. Although COPD affects lung, it also produces significant systemic consequences. The diagnosis must be substantiated by quality spirometry showing post bronchodilator $FEV_1/FVC < 0.7$ and $FEV_1 < 80\%$ of predicted.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

COPD is primarily a disease of the adults. The prevalence of COPD reported in different population based studies from India is highly variable (Table 1). The prevalence rates in male subjects of 2.12% to 9.4% in studies reported from North are generally higher than 1.4% to 4.08% reported from South

India. The respective range for female subjects varies from 1.33% to 4.9% from North and from 2.55% to 2.7% from South India. For epidemiological assessment, the rounded-off median prevalence rates were assessed as 5 percent for male and 2.7 percent for female subjects of over 30 years of age. The disease is distinctly more common in males. The male to female ratio varies from 1.32:1 to 2.6:1 in different studies with a median ratio of 1.6:1.COPD results from chronic inhalational exposure to various smokes, noxious particles and gases.

Table 1. Prevalence of COPD and its smoking association in various population studies from India.

	Population	**COPD prevalence (%)**			**Smoker: Non-smoker Ratio**
		Men	Women	M:F Ratio	
Wig (1964)	Rural Delhi	3.36	2.54	1.3	2.0
Sikand (1966)	Delhi	7.0	4.3	1.6	2.5
Viswanathan (1966)	Patna	2.12	1.33	1.6	
Bhattacharya (1975)	Rural U.P	6.67	4.48	1.6	
Radha (1977)	New Delhi	8.1	4.6	1.8	1.8
Thiruvengadam (1977)	Madras	1.9	1.2	1.6	10.2
Viswanathan (1977)	Delhi Rural	4.7	3.5	1.3	9.6
	Urban	8.0	4.3	1.9	4.0
Charan (1977)	Rural Punjab	2.28	1.63	1.4	
Malik (1986)	N.India Rural	9.4	4.9	1.9	5.5
	Urban	3.7	1.6	2.3	7.0
Jindal (1993)	N.India Rural	6.2	3.9	1.6	
	Urban	4.2	1.6	2.6	9.6
Ray (1995)	South India	4.08	2.55	1.6	1.6

III. DIFFERENTIAL DIAGNOSIS

Chronic bronchial asthma, bronchiectasis, tuberculosis, obliterative bronchiolitis, congestive cardiac failure, dilated cardiomyopathy, diffuse panbronchiolitis.

Asthma is a major differential diagnosis. In some patients with chronic asthma, a clear distinction from COPD is not possible using current imaging and physiological testing techniques. The following features sometimes help in differentiating the two conditions.

COPD	Asthma
• Onset in mid-life • Symptoms slowly progressive • Dyspnea during exercise • Usually irreversible airflow limitation • Long smoking history	• Onset early in life (often childhood) • Symptoms vary from day-to-day • Symptoms (especially cough) at night/early morning • Allergic rhinitis or conjunctivitis and/or atopic dermatitis also present • Family history of atopy or asthma • Predominantly reversible airflow limitation

IV. PREVENTION AND COUNSELING

a) Smoking cessation: Cessation of smoking is of fundamental importance to the successful management of all stages of COPD.
b) Adequate measures to control environmental pollutants and provision of occupational hygiene in dusty working environment.
c) Vaccines: COPD patients are particularly susceptible to influenza infection, thus annual influenza vaccination is recommended for all. Currently available vaccine pneumococcal vaccines (PPSV23) has not been shown to be effective particularly in high-risk patients. Trials are underway with pneumococcal conjugate vaccine [PCV-13 (CAPITA trail)] and further recommendations should wait till the outcomes of the trial are available.
d) Health education about COPD: It is not a curable disease rather it is a preventable and treatable disease.
e) Strict adherence to treatment i.e. use of inhaled bronchodilators, with or without other necessary pharmacologic treatment is essential.

f) Prompt recognition of features of an exacerbation is of paramount importance, therefore, patients should be educated about warning signs and symptoms.
g) Lifestyle modification and treatment of extrapulmonary manifestations such as coronary artery disease, osteoporosis, sarcopenia and anxiety/depression, and co-morbidities like type2 diabetes mellitus and metabolic syndrome.

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

*Situation 1: At Secondary Hospital/ Non-Metro situation: Optimal Standards of Treatment in Situations where technology and resources are limited

h) **Clinical Diagnosis**:

Patients usually present with:

- History of tobacco use.
- Cough with or without sputum production. Cough is particularly worse in the morning and sputum production is a frequent complaint in the early stages of COPD.
- Dyspnoea on exertion: progressive breathlessness in COPD is a persistent symptom with waxing and waning but there is never any time when patients are entirely asymptomatic. Onset of breathlessness is insidious with progressive course, and often a significant amount of ventilatory capacity has been lost before the patient presents to the physician.
- Many patients complain of intermittent wheezing. However, nocturnal wheezing is uncommon in COPD and suggests diagnosis of asthma or heart failure.

  On clinical examination: patients are frequently seen sitting leaning forward with their arms resting on a stationary object. Some patients also develop pursed lip breathing. Percussion of chest is not very helpful in COPD (might reveal features of hyperinflation of lungs). Auscultation

reveals diminished vesicular breath sounds with or without crackles and wheeze. Measurement of FET (forced expiratory time) is a valuable bedside technique to detect and assess airflow obstruction. An FET <5 seconds suggests that severe airflow limitation does not exist, whereas FET > 6 seconds indicates considerable airflow limitation. Many a times patients get disoriented, somnolent, or may complain of headache, which indirectly suggests CO_2 retention. Such a situation will require the application of non-invasive ventilation (NIV), if possible at the treating centre. Peripheral edema, raised JVP, and hepatomegaly are signs indicative of pulmonary hypertension and right ventricular failure (chronic cor pulmonale).

i) **<u>Investigations</u>**:

- Spirometry is essential to firmly establish the diagnosis. Post bronchodilator FEV_1/FVC <0.7 and post bronchodilator FEV_1<80%, 50% or 30% predicted are used for purpose of spirometric classification of COPD according to GOLD.

Stage	**FEV_1/FVC**	**FVC**
Mild COPD	≤0.7	≥80%
Moderate COPD	≤0.7	50% - 80%
Severe COPD	≤0.7	30% - 50%
Very severe COPD	≤0.7	<30% or <50% plus chronic respiratory failure or pulmonary hypertension

- Blood tests like haematocrit, chest radiograph (postero-anterior and lateral views) may be helpful in resource-poor settings.
- ECG and echocardiography (if available).
- 6-minute walk test.

j) Treatment:

The goals of COPD management include:

1. Relief of symptoms
2. Prevent disease progression
3. Improve exercise tolerance
4. Improve health status
5. Prevent and treat extrapulmonary manifestations
6. Prevent and treat complications
7. Prevent and treat exacerbations
8. Prevent or minimise side effects from treatment
9. Reduce mortality

Standard Operating procedure

a. In Patient

Patients would present to the hospital in an exacerbation which is defined as an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication.

Signs of severity of an exacerbation that would require hospitalisation include: use of accessory muscles of respiration, paradoxical chest wall movements, cyanosis, peripheral oedema, haemodynamic instability, and decreased mental alertness. A chest X-ray would help in identifying alternative diagnoses that could mimic an exacerbation, while an ECG would aid in the diagnosis of right heart hypertrophy, arrhythmias and ischaemic episodes. Blood tests including haemogram, sugar and renal functions should be performed. Blood sample for ABG measurement should be drawn, if facility exists.

Management of exacerbations:

- Administer controlled oxygen therapy

- Repeated administration of bronchodilators (β2 agonists and anticholinergics). Increased doses may be required in some patients.
- Add oral or intravenous glucocorticoids
- Consider adding an i.v. methylxanthine, if needed
- Consider antibiotics when signs of bacterial infection
- Monitor fluid balance and nutrition

b. Out Patient

Stable COPD can be managed with therapy at each stage of COPD as follows:

Mild COPD	**Moderate COPD**	**Severe COPD**	**Very Severe COPD**
FEV1/FVC<0.7 FEV1>= 80% PREDICTED	FEV1/FVC<0.7 50%<FEV1<80%	FEV1/FVC<0.7 30%<FEV1<50%	FEV1/FVC<0.7 FEV1<30% PREDICTED or FEV1<50% plus chronic respiratory failure
Active reduction of risk factor(s): Influenza vaccination Add short acting bronchodilator(when needed)			
Add regular treatment with one or more long acting bronchodilator(when needed); add rehabilitation			
Add inhalational corticosteroids (ICS) if repeated exacerbations			
Refer the patients to the specialist			

Antibiotics:

Antibiotics may be initiated in patients with altered sputum characteristics (increased volume and increased purulence) and increased dyspnoea. The choice should be based on local bacteria resistance patterns.

c) <u>Referral criteria:</u>

i. Marked increase in intensity of symptoms
ii. Severe COPD
iii. Appearance of cyanosis, edema
iv. Signs of respiratory failure
v. Significant co-morbidities
vi. Recurrent exacerbations
vii. New onset arrhythmias
viii. Diagnostic uncertainty
ix. Old age
x. Failure to control exacerbation

***Situation 2: At Super Specialty Facility in Metro location where higher-end technology is available**

g) Clinical Diagnosis:

Same as in Situation 1 (a)

h) Investigations:

- Same as in Situation 1 (b)
- Assessment of pulmonary haemodynamics
- CT-thorax and ventilation-perfusion scanning (especially for those being planned for lung surgery)
- Polysomnographic studies (if indicated)
- Cardiopulmonary exercise testing
- DEXA scan for osteoporosis [bone mineral density (BMD) and sarcopenia [fat free mass index (FFMI)]
- Psychiatric evaluation for anxiety/depression
- Alpha-1 antitrypsin deficiency screening (for those who develop COPD at a younger age and those with a strong family history of COPD).

i) Treatment:

Standard Operating procedure

a. In Patient

- Same as in Situation 1 (c)
- Noninvasive ventilation using BiPAP
- Mechanical (invasive) ventilation
- Surgical options including bullectomy and LVRS

Indications for mechanical ventilation:

1. Severe dyspnea, use of accessory muscles of respiration and paradoxical abdominal motion
2. Severe acidosis pH< 7.25, and/or hypercapnia $PaCO_2$> 60mmHg which does not respond to NIV
3. Somnolence, impaired mental status
4. Unable to tolerate NIV
5. Life-threatening hypoxemia
6. Respiratory rate > 35/min
7. Impending respiratory arrest

Diagnosis and management of cor pulmonale

The patient develops chronic cor pulmonale when there are alterations in the structure and function of the right ventricle caused by a primary disorder of the respiratory system. Invariably this would manifest as pulmonary hypertension on echocardiography.

Symptoms would include tachypnoea and increase in exertional dyspnoea. Patients with chronic cor pulmonale and right heart failure will present with distended neck veins with prominent 'V-y' pattern suggestive of tricuspid regurgitation, cyanosis, peripheral oedema, splitting of second heart sound with accentuation of pulmonary component, left parasternal heave, long systolic or pansystolic murmur with accentuation during inspiration in the lower left sterna border, occasionally presence of right ventricular third heart sound, right upper quadrant abdominal discomfort and pulsatile hepatomegaly.

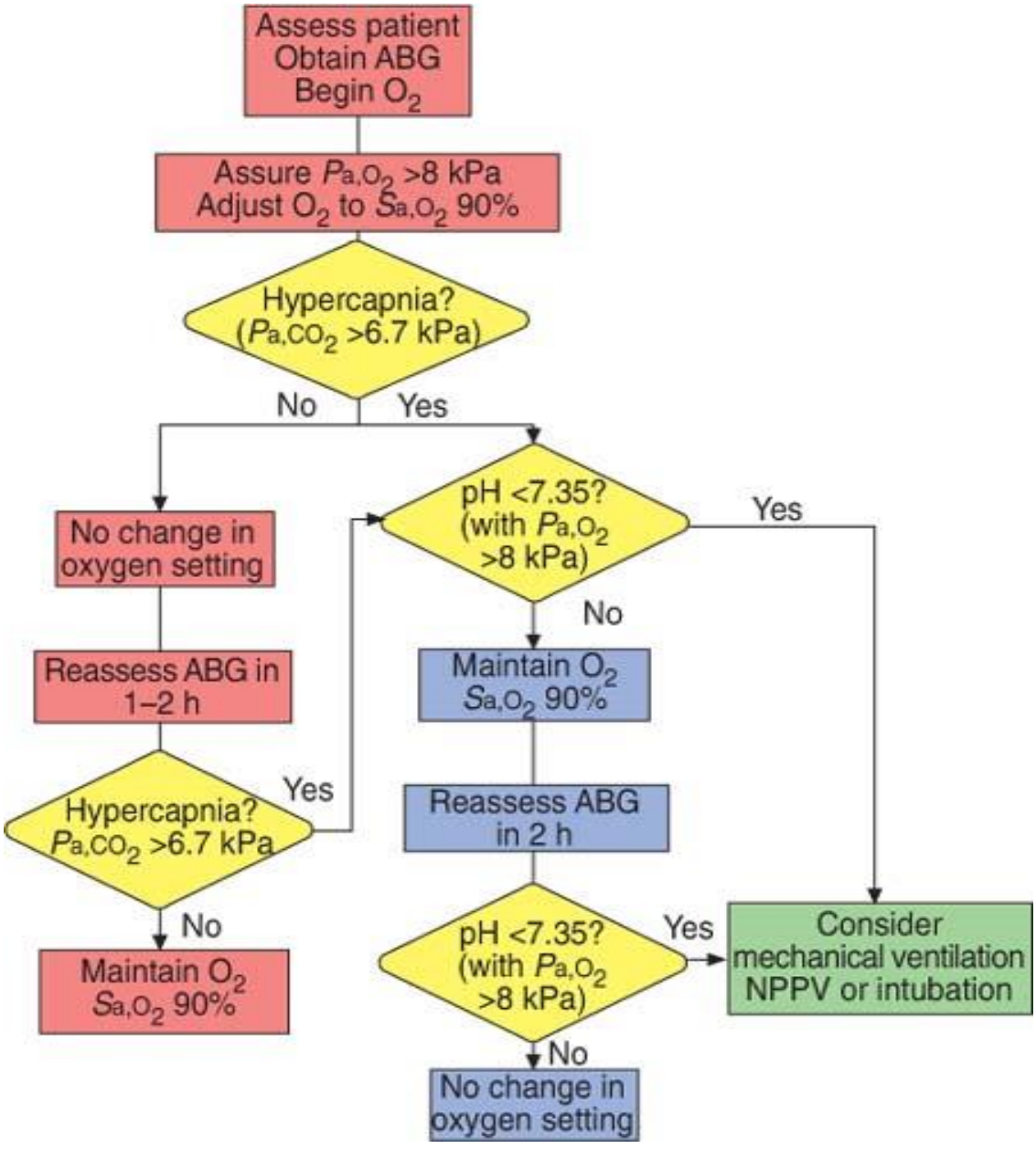
Medical therapy for chronic cor pulmonale is generally focused on treatment of the underlying pulmonary disease and improving oxygenation and right ventricular (RV) function by increasing RV contractility and decreasing pulmonary vasoconstriction.

In general, in patients with COPD, long-term oxygen therapy is recommended when the PaO_2 is less than 55 mm Hg or the O_2 saturation is less than 88%. However, in the presence of cor pulmonale or impaired mental or cognitive function, long-term oxygen therapy can be considered even if the PaO_2 is greater than 55 mm Hg or the O_2 saturation is greater than 88%. This must be documented in at least two consecutive ABGs done 3 weeks apart in stable state.

Pharmacotherapy includes salt restriction, diuretics, calcium channel blockers (indicated only if cardiac catheterization facilities available and vasoreactivity can be demonstrated), prostacyclin analogues (epoprostenol, treprostinil, and iloprost), endothelin-receptor antagonists (bosentan), PDE5 inhibitors (sildenafil and tadalafil).

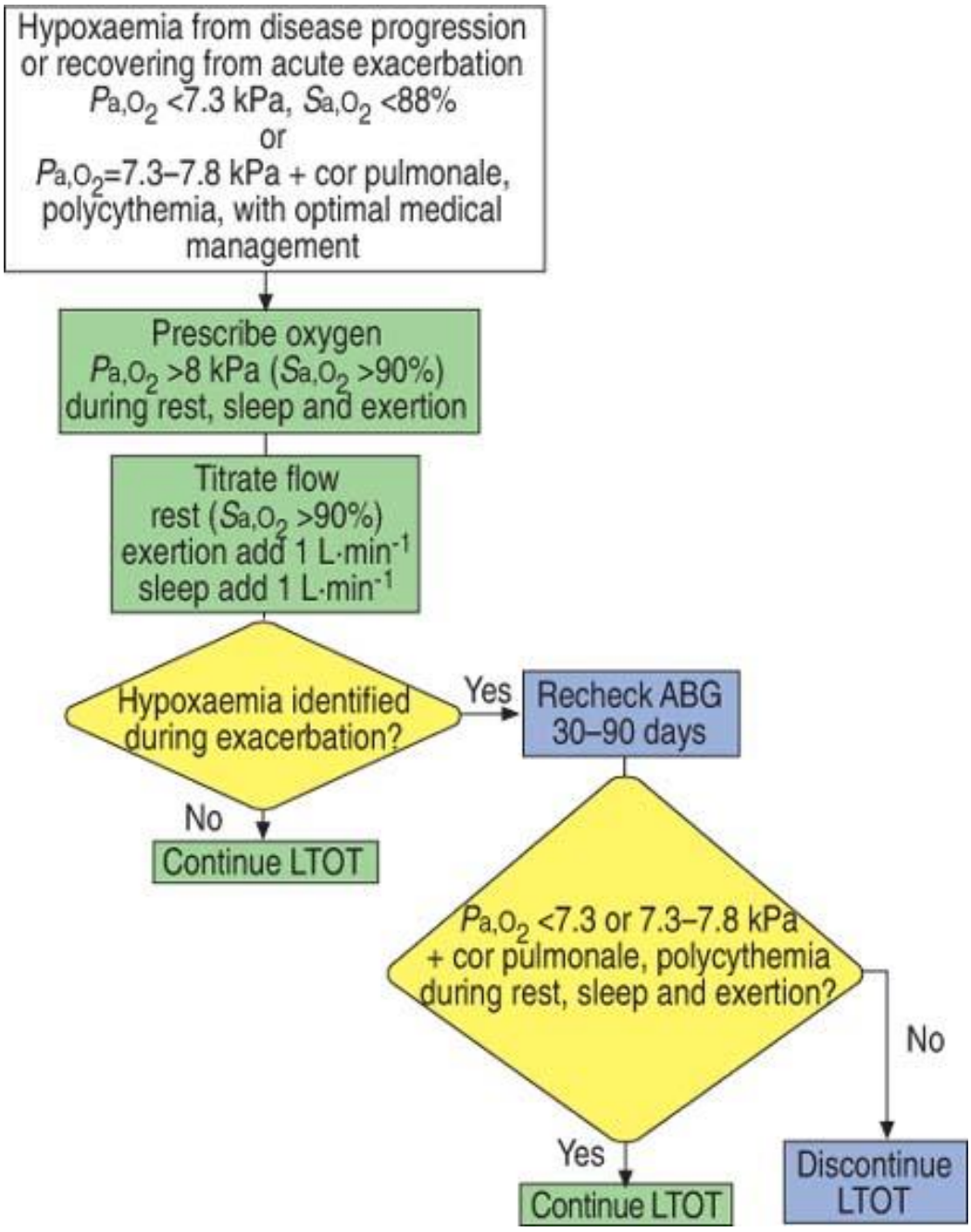
The algorithms for correction of hypoxia and long term oxygen therapy are given below.

Algorithm to correct hypoxaemia in an acutely ill COPD patient



For conversion of kPa into mmHg: 1 mmHg=0.133 kPa

Algorithm for long term oxygen therapy



b. **Out Patient**

- Same as in Situation 1 b)

c) Referral criteria:

Patients with very severe COPD who are not controlled even on maximal medical therapy and LTOT and who fulfill the selection criteria for lung transplantation should be referred to a specialist centre where expertise of lung transplantation is available.

VI. Who does what? and timeliness

***a. Doctor*:** Diagnosis and management including counseling

***b. Nurse* :** Implementation of orders and monitoring of patients

***c. Technician*:** Carrying out investigations

VII. FURTHER READING / REFERENCES

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	8. Physician 9. Nurse 10. Laboratory technician 11. Pulmonary function test technician 12. Radiographer 13. Physician trained in ECHO/ cardiologist	4. Chest radiograph 5. Hemogram 6. Pulmonary function tests 7. ABG 8. Eletrocardiogram 9. 2D-ECHO	7. Inhaled bronchodilators (salbutamol, ipratropium, tiotropium) 8. ICS (fluticasone/budesonide)+ LABA (formoterol/salmeterol) 9. Parenteral and oral bronchodilators (theophylline, terbutaline) 10. Parenteral and oral steroids (hydrocortisone, prednisolone) 11. Parenteral and oral antibiotics (Amoxycillin and clavulanate combination, cefadroxil, cefotaxime, Piperacillin and tazobactum combination)	7. Oxygen cylinder/concentrator 8. Nebulizers (both electric and electronic) 9. Spirometer along with 6-MW facility 10. X-ray machine 11. ABG analyzer 12. EKG machine 13. Echocardiography machine
2	Above plus 2. ICU staff with pulmonary training 3. Physiotherapist 4. Sleep laboratory technician 5. Thoracic surgeon 6. Psychiatrist 7. Cardiologist 8. Radiologist 9. Anesthetist	Above plus 1. CT Scan 2.Polysomnography 3.DEXA scan	Above plus 2. Higher generation antibiotics	Above plus 1. CT machine 2. ICU set up 3. Noninvasive and invasive ventilators 4. Polysomnography machine 5. DEXA machine 6. Operation theatre with trained staff

INTERSTITIAL LUNG DISEASE

I. WHEN TO SUSPECT/ RECOGNIZE?

a. Introduction:

Interstitial lung disease (ILD) is a heterogeneous group of disorders with a common clinico-radiological presentation, hence grouped together. These diseases are characterized by predominant involvement of lung 'interstitium' i.e. the space between alveolar basement membrane and pulmonary vascular endothelial membrane. As the disease progresses it encroaches alveolar spaces, terminal bronchioles and perivascular spaces, thereby ILDs are referred to as diffuse parenchymal lung disease (DPLD). ILDs due to systemic diseases such as connective tissue diseases, sarcoidosis, hypersensitivity pneumonitis, drugs, pneumoconioses and other miscellaneous conditions are termed as secondary ILDs. The primary pulmonary involvement is generally the Idiopathic pulmonary fibrosis (IPF/fibrosing alveolitis) or usual interstitial pneumonitis.

b. Case definition:

For both situations of care:
ILD is suspected in patients with onset of respiratory symptoms of relatively acute/ sub-acute duration of weeks to months. The predominant symptoms consist of breathlessness and dry cough. Weakness and weight loss are usually present. Chest pain/ heaviness and haemoptysis can occur in a few conditions. Elicitation of occupational history is mandatory. The chest X-ray film shows distinctly reticular, reticulo-nodular or nodular opacities which are patchy /basilar or diffuse in distribution. Chest X-ray can occasionally be normal. High resolution CT scan of the chest is usually characteristic. Investigations for the underlying disease are important to rule out a secondary cause especially in those with atypical HRCT findings. Pathological diagnosis with bronchoscopic/ thoracoscopic and other surgical modalities is required for confirmation in only a few cases.

II. INCIDENCE OF THE CONDITION IN INDIA

The exact incidence and prevalence of the disease is not known. The common causes of ILD in India include IPF, connective tissue related ILD (systemic sclerosis and rheumatoid arthritis) and sarcoidosis. In general, at most secondary-

level hospitals, 1-3 cases per month and at super-specialty hospitals, 1-3 cases per week of idiopathic ILD are likely.

III. DIFFERENTIAL DIAGNOSIS

Many disorders can present with symptoms similar to that of ILD and interstitial opacities on chest radiograph. The following are the common disorders that should be ruled out before making a diagnosis of ILD:

a) Tuberculosis
b) Atypical pneumonias (Mycoplasma and legionella)
c) Fungal pneumonias (Aspergillosis, crytococcosis)
d) Chronic bronchitis

Exclusion of a secondary causes such as a connective tissue disease, hypersensitivity pneumonia, pneumoconiosis, drug-toxicity is important before making the diagnosis of primary idiopathic ILD (such as IPF).

IV. PREVENTION AND COUNSELLING

Occupational and environment related interstitial lung disease may benefit from avoidance or decrease in intensity and duration of exposure. High index of suspicion and early recognition of interstitial lung disease can be helpful as it can prevent further deterioration of lung function by avoidance of exposure. Smoking cessation is another important caution which must be exercised.

The following are the few diseases in which avoidance of exposure can be advocated if ILD is detected early.

1) Silicosis (occupations-miners, sandblasting, workers in abrasive industries, such as stone, clay, glass, cement manufacturing and granite quarrying)
2) Asbestosis(asbestos manufacturing, construction trade, mining, milling and pipefitters)
3) Coal worker's pneumoconiosis
4) Chronic hypersensitivity pneumonitis (pigeon breeders, farm dust and grain husk containing thermophilic actinomyces)

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

While ILD can be suspected at any secondary-level hospital, the confirmation, exclusion of secondary causes and initiation of management lies essentially in the

domain of the specialty hospitals. Follow-up management afterwards can, however, continue at the secondary –level, referring hospital.

Diagnosis:

The diagnosis of ILD is based on the combination of clinical, radiographic, and histopathology criteria.

a. Clinical: i. Progressive breathlessness and/ or dry cough,

ii. Physical findings: basal end-inspiratory crackles- superficial, dry and velcro-like. Finger clubbing may be present in IPF.

b. Radiographic findings: A good quality postero-anterior chest radiograph should be initial investigation of choice followed by HRCT chest for confirmation of presence of ILD.
   i. Chest radiograph- presence of reticular, nodular or reticulonodular shadows, shrunken lung fields and obscuration of cardiac and diaphragmatic margins.
   ii. HRCT Chest- presence of reticular shadows (inter and intralobular septal thickening), patchy ground-glass opacities/consolidation (predominantly subpleural and peripheral) and honeycombing (indicates end-stage ILD)

c. Pulmonary function tests:
   i. Spirometry: A restrictive abnormality is classical of ILD with reduced total lung capacity (TLC), functional residual capacity, and residual volume. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) are reduced. FEV_1/FVC ratio is normal or increased. However, mixed (restrictive-obstructive)/obstructive pattern can be seen in patients with lymphangioleiomyomatosis, sarcoidosis, hypersensitivity pneumonitis due to involvement of small airways.
   ii. Diffusing capacity for carbon monoxide (DLCO): reduced in all patients with ILD except in alveolar hemorrhage syndromes in which it is increased.
   iii. Significant oxygen desaturation on exercise (>3-4%).
   iv. ECG and 2D ECHO for pulmonary hypertension/cor pulmonale.

d. Histopathology: The histopathology is required only in the presence of an early disease when the differential diagnosis is important from a treatable condition. The pattern varies according to the disease. Idiopathic pulmonary fibrosis is

characterized UIP pattern. Sarcoidosis, Wegener's granulomatosis and Churg-Strauss syndrome are characterized by granulomatous inflammation.

e. 6-minute walk test (6MWT): For baseline and follow-up

Treatment:

The management of the patients with ILD is difficult and unsatisfactory. Anti-inflammatory therapy with steroids, azathioprine or cyclophosphamide forms the main backbone of drug therapy. Interstitial lung diseases which respond well to immunosuppresive therapy include proliferative phase of NSIP, desquamative IP, cryptogenic organizing pneumonia, alveolar hemorrhage syndromes and sarcoidosis. Antioxidant and anti-fibrotic drugs such as N-acetyl cysteine and pirfenidone have some role for the treatment of idiopathic pulmonary fibrosis. None of the drugs are likely to provide benefit in advanced disease when only symptomatic treatment, home oxygen therapy, treatment of pulmonary hypertension, pulmonary rehabilitation and treatment of co-morbid diseases should be offered to improve quality of life and avoid unnecessary side-effects of the drugs.

REFERRAL CRITERIA: All patients in whom an interstitial lung disease is suspected or patients in whom alternative diagnosis like infection cannot be ruled out should be referred to a specialty hospital to confirm a diagnosis, identify the cause and initiate appropriate therapy.

VI. WHO DOES WHAT?

a. Doctor

Evaluate the patients, order investigations, make a diagnosis, advise proper treatment and perform follow-up

b. Nurse

Carry out the Investigations suggested by the doctors and help in follow-up of patients

c. Technical staff

Perform relevant investigations as per the advice of the treating physician

RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	14. Physician 15. Nurse 16. Laboratory technician 17. Pulmonary function test technician 18. Radiographer 19. Physician with training in echocardiography / cardiologist	10. Chest radiograph 11. Pulmonary function tests 12. ABG analysis 13. 2D-ECHO	12. Parenteral and oral steroids (hydrocortisone, prednisolone) 13. N-acetyl cysteine 14. Inhaled bronchodilators 15. Sildenafil, bosentan	14. Oxygen cylinder 15. Oxygen concentrators 16. Spirometer 17. Hand-held Spirometer 18. X-ray machine 19. ABG analyzer 20. ECHO machine
2	Above plus 10. ICU staff with pulmonary training 11. Radiologist 12. Pathologist 13. Physiotherapist	Above plus 1. CT Scan 2. Bronchoscopic biopsy (Transbronchial lung biopsy)	Above plus 3. Immunosuppressant drugs (azathioprine, cyclophosphamide, pirfenidone)	Above plus 1. ICU 2. Noninvasive and invasive ventilators 3. CT scan machine 4. Bronchoscope along with required facility

LUNG ABSCESS

VIII. WHEN TO SUSPECT/ RECOGNIZE?

e) Introduction:

Lung abscess is a common form of suppurative lung disease that is characterized by a localized necrosis of pulmonary parenchyma and circumscribed collection of pus in the lung that is usually greater than 2 cm in diameter. Many local causes and systemic diseases can result in lung abscess formation. *Primary* lung abscess is more common and develops as a result of necrosis of lung parenchyma due to an existing disease process that is occurring there, such as, untreated aspiration pneumonia especially due to staphylococcal klebsiella and anaerobic organisms,, or lung cancer. A lung abscess can also develop *secondary* to preexisting conditions, such as, bronchial obstruction, spread from an extrapulmonary focus of infection, bronchiectasis, or immunocompromised state. Acute and chronic is based on duration; acute <6 weeks and chronic > 6 weeks

f) Case definition:

(For both situations of care)

Primary lung abscess

i. A patient with an ongoing episode of pneumonia of 2 to 3 weeks duration, or, a history of pneumonia in the recent past presents with respiratory symptoms and signs consistent with a lung abscess, (such as, cough, sputum, that may be putrid and foul smelling, haemoptysis, pleuritic chest pain, shoulder pain, or heaviness in the chest) and systemic manifestations like fever, night sweats, anorexia, weight loss, and digital clubbing.
ii. Chest radiograph evidence of a cavity or cavities with a fluid level

IX. INCIDENCE OF THE CONDITION IN OUR COUNTRY

Globally, the incidence of lung abscess has declined by nearly 10-fold during the preceding few decades in comparison with the pre-antibiotic era. No definitive studies have been carried out till date to define the incidence of lung abscess from India and reliable epidemiological data are not available.

X. DIFFERENTIAL DIAGNOSIS

1. Non-infectious diseases
    - Embolism with infarction
    - Vasculitis
    - Pulmonary neoplasm
    - Pulmonary sequestration
    - Bullae or cysts with air fluid level
2. Infections
    - Infected bulla
    - Infected pulmonary infarct
    - Infected cyst
    - Bronchiectasis
    - Empyema with air fluid level

XI. PREVENTION AND COUNSELING

1. Measures for preventing aspiration of secretions in unconscious patients
2. Smoking cessation, good orodental hygiene
3. Early recognition of lung infections and institution of appropriate antibiotics in adequate dosage for appropriate duration.

XII. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

***Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited**

k) **Clinical Diagnosis**

Symptoms

1. The clinical manifestations of lung abscess may become evident coincident with the initial presentation of pneumonia or other underlying condition, or may develop later in the course of the illness.

2. Conditions predisposing the patient for aspiration and development of lung abscess, such as altered sensorium, depressed cough and gag reflex, diseases of the oral cavity, gastrointestinal disease, and neurological disease are usually present.

3. Patients with primary lung abscess often have an ongoing episode of pneumonia of 2-3 weeks duration, or, a history of pneumonia in the recent past. Presenting symptoms include fever, cough, sputum, that may be putrid and foul smelling. Pleuritic chest pain, shoulder pain, heaviness in the chest is also usually evident. Patients may also complain of chills, night sweats, anorexia, haemoptysis, weight loss, and digital clubbing. In patients with a secondary lung abscess, the clinical manifestations can develop over 48 to 72 hours.

4. Patients with hepatopulmonary amoebiasis may manifest abdominal symptoms, such as, right hypochondrium pain, bowel symptoms, among others.

5. In patients with perforation of the liver abscess into the lung, cough and expectoration of odourless anchovy sauce sputum may be evident.

Signs

1. Patients with an acute lung abscess appear sick and toxic. New and focal respiratory signsmay be evident on physical examination of the chest. Presence of physical signs depends on the proximity lung abscess from the chest wall.
2. Signs due to complications, such as, pleural effusion, empyema, sepsis syndrome may also be present.

l) **<u>Investigations</u>**

1. **Chest radiograph:** A chest radiograph is essential to establish the diagnosis of lung abscess. Lung abscess appears as an irregularly shaped cavity with an air-fluid level. The lesion may be solitary (primary lung infection), or sometimes, multiple (metastatic infection). Rapid pulmonary

cavitation within a dense segmental consolidation; and a rapidly enlarging nodular lesion, with or without cavitation suggest anaerobic infection.

2. **Ultrasonography of the chest:** Peripherally located lung abscesses, especially those in contact with pleura are detectable on ultrasonography of the chest.

m) Treatment:

Standard Operating procedure

a. In Patient

1. **General therapeutic measures**

1.1. Adequate drainage of the lung abscess is facilitated by encouraging the patient to cough and by chest physiotherapy and postural drainage.

2. Antibiotic treatment: clindamycin administered intravenously in a dosage of 600 mg, eight hourly, followed by 150 to 300 mg orally four times daily is considered to be the preferred treatment of choice for lung abscess. Other antibiotic options include intravenous penicillin plus metronidazole and amoxycillin-clavulanate plus metronidazole.

2.1. Antibiotic treatment is administered till the pulmonary infiltrates have resolved or until the residual lesion becomes small and stable; the duration of antibiotic treatment is usually for 6 to 8 weeks.

2. **Supplemental oxygen therapy**

In patients with hypoxaemia, spontaneous ventilation using a face mask with a high flow gas delivery system can be used to deliver a FIO_2 of up to 0.5 to 0.6.

b. Out Patient

Not applicable

n) **Referral criteria:**

1. Patients not responding to antibiotic treatment.

2. Occurrence of complications of lung abscess, such as, metastatic brain abscess, sepsis, empyema, broncho-pleural fistula, pleura-cutaneous fistula,

massive life-threatening haemoptysis, spontaneous rupture of the abscess into uninvolved lung segments, and failure to resolve.

***Situation 2: At Tertiary hospital where higher-end technology is available**

j) Clinical Diagnosis

As in situation V.1 a) above

k) Investigations

As in situation V.1b) above PLUS

1. Computed tomography: computed tomography (CT) of the chest helps in delineating the size and location of abscesses. It also facilitates identifying associated empyema, and detecting other conditions such as pulmonary infarction, infected bulla, and raising the suspicion of a cavitating lung malignancy. In lung abscesses that fail to communicate with a bronchus, the characteristic air-fluid level within a cavity will not be seen and instead, a focal, ground-glass infiltrate with indistinct borders may be evident.

2. Establishing microbiological diagnosis:

1. Ascertaining the microbiology of anaerobic infection of the lower airways requires a specimen devoid of contamination by the flora of the upper airways or quantitative cultures that can distinguish pathogenic bacteria from the normal flora.
2. Specimens obtained from blind, deep suctioning via an endotracheal tube; radiologically guided, percutaenous transthoracic aspirates, specimens obtained at thoracotomy, quantitative cultures of specimens obtained at fiberoptic bronchoscopy (FOB), either by bronchoalveolar lavage (BAL) or with the protected double-lumen catheter with a protected sampling brush are subjected to microbiological examination.
3.If the abscess is associated with an empyema, then culture of the empyema fluid may help in isolating the aetiological organisms.

l) Treatment:

Standard Operating procedure

a. In Patient

As in situation V.1c) a.1 above PLUS

1. Drainage procedures

Drainage procedures are usually reserved for patients with lung abscess who fail to respond to antibiotic therapy

1.1. Percutaneous catheter drainage (for peripherally located lung abscess)

1.2. Video-assisted thoracoscopic surgery (VATS)

2. **Surgery**

2.1. Surgery is indicated if airway obstruction (e.g., due to a tumour or a foreign body) limits drainage. The surgical procedures performed include lobectomy, wedge resection or pneumonectomy.

2.2. When associated empyema is present, adequate drainage with tube thoracostomy is required; in patients with multiloculated empyemas, open pleural drainage is indicated.

b. Out Patient

Not applicable.

XIII. WHO DOES WHAT? and TIMELINES

a. ***Doctor:*** Diagnosis and Management including counseling

b. ***Nurse:*** Implementation of orders, monitoring of patients and counseling

c. Technician: Investigations

XIV. FURTHER READING / REFERENCES

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1. Physician 2.Nurse 3.Radiographer	1.Chest X-ray 2.Ultrasonography of chest 3. sputum smear and culture 4. Blood culture and sensitivity	1. Oral and i.v. antibiotics 2. Streptokinase	1. X-ray machine 2. USG machine 3. Intercostal tubes 4. Negative suction machines
2	Above plus 1. Intensivist 2.Interventional Radiologist 3.Thoracic Surgeon 4.Nurse and Technician for assisting with bronchsocopy 5.Nurse and Technician for assisting with interventional radiology procedures 6.Nursing staff trained in assisting thoracic surgery 7.Respiratory therapist	Above plus 1.CT chest 2.Interventional radiology procedures 3.Bronchoscopy 4.Conventional and molecular microbiological diagnostic methods 5.Fiberoptic bronchoscopy	Above plus 1.Catheters and tubes for drainage procedures 2.Disposables for use during interventional procedures/ VATS/ surgical intervention	Above plus 1. CT machine 2.Facilities for conducting interventional radiology procedures 3.Bronchoscope and facilities for performing interventional pulmonology procedures 4.Microbiology laboratory service with facilities for conventional and molecular diagnostic testing 5.Video-assisted thoracoscope 6.Thoracic surgery operating theatre; recovery room and ICU

LUNG CANCER

I. WHEN TO SUSPECT/ RECOGNIZE?

g) Introduction:

Lung cancer is the commonest form of malignancy world over and is the most common cause of death. The disease is fatal if not treated early. Although, tremendous advances have taken place, the 5-year survival rate is still around 15%. Tobacco smoking is the most common cause of lung cancer and detection at the early stage is the key to successful treatment and prolonged survival.

h) Case definition:

(For both situations of care)

It is a malignant condition of the lung and the tumor usually arises from the bronchi although this can originate from the alveoli (bronchoalveolar cell carcinoma). Bronchogenic carcinoma is of 4 major sub types: squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma. The first three are known as non small cell lung cancer.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

Lung cancer is the commonest form of malignancy in our country. It has surpassed the oropharyngeal carcinoma which used to be the commonest form. ICMR cancer registry, hospital based as well as community based, reveal it to be the commonest form of cancer in males and is amongst the top ten cancers in females. There is an increase in the incidence of lung cancer in recent years. The cancer atlas program also shows that the north eastern region of the country has the highest prevalence/incidence. It is estimated that every year nearly 58,000 new cases of lung cancer are diagnosed in the country.

III. DIFFERENTIAL DIAGNOSIS

- Tuberculosis
- Pneumonia
- Lung abscess
- Lung cysts
- Pleural effusion of any cause

IV. PREVENTION AND COUNSELING

Tobacco smoking cessation is the most important preventive measure. People working in high risk occupations with exposure to asbestos, arsenic, pollution, mercury, lead, and other heavy metals and chemicals need to have regular chest X-ray done.

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

***Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited**

o) **Clinical Diagnosis**

Symptoms

Cough, expectoration, chest pain, haemoptysis, breathlessness, weight loss, anorexia, weakness, hoarseness of voice, dysphagia, superior vena cava (SVC) obstruction etc.

Signs

Clubbing, findings of collapse, mass lesion, haemorrhagic pleural effusion, hard lymph nodes and SVC obstruction are some of the common clinical findings.

p) **Investigations**

1. **Chest radiograph:** A chest radiograph is the cornerstone to establish the diagnosis of lung cancer which may reveal findings like mass, collapse, pleural effusion, or mediastinal lymph nodes. There may be consolidation particularly non-resolving. Bronchoalveolar cell carcinoma will have an alveolar pattern on chest radiograph.

q) Treatment:

Usually no treatment is possible at this level. The diagnosis need to be established first by other means as discussed below. However, the patients should be treated symptomatically with cough suppressants, pain relieving agents etc. Once the diagnosis and follow-up plan is made by a tertiary care

hospital, the patient can be looked after for palliative therapy like pain management, thoracocentesis, cough suppressants and oxygen therapy etc.

r) **Referral criteria:**

1. Diagnosis not clear.
2. It is important that the doctor at this level should be able to suspect a diagnosis of lung cancer from the chest X-ray. It is common for these patients to be misdiagnosed as having tuberculosis and continue receiving anti-TB treatment and important time is lost before a diagnosis is achieved. Even if this is missed, a patient of tuberculosis should respond to ATT within a period of 2 to 3 weeks, failing which the patient should be referred.

***Situation 2: At Tertiary hospital where higher-end technology is available**

m) Clinical Diagnosis

As above.

n) Investigations

1. Above plus
    2. CT scan of chest (abdomen and brain is done for staging)
    3. Sputum cytology
    4. Fine needle aspiration cytology and biopsy
    5. Bronchoscopy
    6. Very rarely thoracotomy
    7. Mediastinoscopy (rarely done now)
    8. Bone scan (only in symptomatic patients)
    9. PET Scan (if available)

o) Treatment:

a. Out Patient

It is important to get a histological diagnosis and staging of the disease. The performance status (ECOG and Karnofsky scale) is to be ascertained. The overall financial conditions of the patient are to be accessed.

There are four treatment options:

1) Early stage (Stage I to III A) - surgery

2) Stage III B and Stage IV -- chemotherapy
3) Radiotherapy is usually a localized form of therapy and can be given in localized disease as a specific therapy. Both chemotherapy and radiotherapy can be given as an adjuvant therapy to surgery or as neo adjuvant setting to downstage the disease so that the patient is operable.
4) Recently targeted therapy (molecular therapy) is available in certain types of lung cancers.
5) Palliative or supportive therapy like pleurodesis in massive and repeated effusions, care of nutrition, pain alleviation, management of chemotherapy related toxicities like nausea and vomiting, diarrhea or constipation, hair loss etc. One also needs to look after the terminal care of the patient.

Suggested chemotherapy regimens:
A cisplatin based 2-drug combination therapy is recommended.

a) cisplatin plus gemcitabine
b) cisplatin plus docetaxel
c) carboplatin plus paclitaxel
d) cisplatin and paclitaxel
e) cisplastin and irinotecan is a good and cheap combination therapy and can be used in our country.

Pemetrexed is a new anti-folate anti-metabolite useful in adenocarcinoma of the lung. It is to be given in combination with cisplatin. The above combinations is for non small cell lung cancer. For small cell lung cancer one can use cisplatin and irinotecan or etoposide.

Molecular therapy: epidermal growth factor receptor (EGFR) inhibitors like gefitinib and erlotinib are useful drugs for treating adenocarcinoma of the lung particularly in non-smoking and Southeast Asian female patients. Cetuximab is a monoclonal antibody also useful in these patients. Vascular endothelial growth factor receptor (VEGFR) inhibitors like bevacizumab are a new drug useful for non squamous cell type of non small cell lung cancer.

One should keep in mind that chemotherapeutic drugs are toxic and costly also. All the aspects should be explained to the patient as well as to the family before such a decision is taken.

VI. WHO DOES WHAT? and TIMELINES

a. ***Doctor:*** Usually the chest physician makes the diagnosis and the management should include a team of thoracic surgeon, medical oncologist and radiotherapist. However, a chest physician or an internist can handle such a case in delivering chemotherapy with proper training.

b. ***Nurse :*** Implementation of orders, monitoring of patients and counseling, management of side-effects.

c. Technician: Investigations

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1. Physician 2. Nurse 3. Radiographer	1. Chest radiograph 2. Hemogram and blood chemistry	1. Cough suppressant 2. Analgesics	1. X-ray machine 2. Hematology and biochemistry laboratory
2	All above plus 1. ICU staff (Physician, nurses) 2. Radiologist 3. Pulmonologist 4. Pathologist 5. Oncologist 6. Thoracic surgeon 7. Anesthetist 8. Nuclear medicine specialist 9. Radiotherapist 10. Nurse and technician for assisting with bronchsocopy 11. Nurse and technician for assisting with interventional radiology procedures 12. Nursing staff trained in assisting thoracic surgery 13. Respiratory therapist	Above plus 1. Sputum cytology 2. FNAC cytology and biopsy 3. Bronchoscopy 4. Arterial blood gases 5. CT scan 6. Bone scan 7. PET scan (if available) 8. SPECT-CT to detect bone metastases	1. Chemotherpay protocol (cisplatin, gemcitabine, docetaxel, paclitaxel, carboplatin) 2. Surgery protocol 3. Molecular therapy (gefitinib, erlotinib) 4. Radiotherapy	Above plus 1. Pathology laboratory (with facilities for special stains) 2. CT scan machine 3. ABG machine 4. Fiberoptic bronchoscope 5. Infusion pumps 6. PET scan machine (if available) 7. Bone scan machine 8. Operation theatre 9. Radiotherapy machine 10. SPECT-CT

SLEEP DISORDERED BREATHING

I. WHEN TO SUSPECT/ RECOGNIZE?

a) Introduction:

- Sleep disordered breathing (SDB) constitutes a spectrum of disorders of various severity with intermittent snoring as the mildest form at one end and obesity hypoventilation syndrome (OHS) , the most severe form at the other end of the spectrum. Heavy snoring and upper airway resistance syndrome (UARS); mild, moderate and severe sleep apnea lie in between these two extremes. Because of the uncertainty about what constitutes sleep apnea, the term SDB is used to describe events that do not satisfy criteria as apneas and hypopneas according to the conventional criteria, but which carry some of the same consequences, like, snore-arousals or respiratory effort-related arousal (RERA) or flow limitations.
- Apnea: cessation of airflow ≥10 seconds with or without respiratory effort
- Hypopnea: recognizable, transient reduction, but not a complete cessation of breathing ≥10 seconds. A≥50% decrease in the amplitude of a validated measure of breathing must be evident or a <50% amplitude reduction that is associated with either an oxygen desaturation of ≥3% or an arousal on electroencephalography (EEG)
- Respiratory effort - related arousal (RERA): is an event characterized by increasing respiratory effort for ≥ 10 seconds leading to an arousal from sleep, but which does not full fill the criteria for hypopnea or apnea.
- Apnea - Hypopnea Index (AHI): defined as the number of obstructive apneas and hypopneas per hour
- Respiratory Distress Index (RDI): is defined as the number of obstructive apneas, hypopneas, RERAs and flow limitations per hour averaged over the course of at least 2 hours of sleep as determined by nocturnal polysomnography (PSG).
- The term apnea-hypopnea index (AHI) is most commonly used conventional criteria to diagnose and quantitate the severity of sleep apnea, however recently as per the guidelines of American Academy of Sleep Medicine (AASM) the term respiratory disturbance index (RDI) is increasingly used to

diagnose and describe SDB which includes besides apneas, hypopneas other events such as RERAs, and flow limitations

b) <u>Case definition:</u>

Diagnostic Criteria for OSAS (1)

A Excessive Daytime Sleepiness (EDS) not better explained by other causes

B. Two or more of the following not better explained by other causes

- Choking or gasping during sleep
- Recurrent awakenings from sleep
- Un-refreshing sleep
- Daytime fatigue
- Impaired concentration

C. PSG showing AHI > 5 in adults and >1 in children

OSAS must fulfill A or B, plus criterion C

- The newly revised International Classification of Sleep Disorders defines OSAS as when a patient has an RDI of five or more than five per hour of sleep with the appropriate clinical presentation such as excessive daytime sleepiness, un-refreshing sleep, fatigue, insomnia, mood disorders or other neuro-cognitive disturbances. The severity of SDB is assessed by the number of abnormal breathing events per hour of sleep, degree of sleepiness and the degree of oxygen desaturation during sleep.

Mild	AHI or RDI	> 5-15/hour
Moderate	AHI or RDI	> 15-30/hour
Severe	AHI or RDI	> 30/hour

Severity Grading of OSAS (criteria for children) (2)

	AHI or RDI /hour	
	Adults	Children
Mild:	> 5-15	2-4
Moderate:	>15-30	5-9
Severe:	> 30	> 10

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

The prevalence of SDB varies from region to region. It has been found to be present in 4% of men and 2% of women. In India various studies have shown the prevalence of SDB of 2.6% to 4.9% in adult males and 1% to 3.6% in adult females. About 4.8% children and 10.3% of elderly population in India have SDB. No gender difference in the prevalence of SDB has been observed in children and elderly subjects.

The factors associated with the pathogenesis of SDB include anatomically small airway, obesity, and loss of upper airway motor tone during sleep and dysfunction of central respiratory control. The various risk factors are body habitus (especially percentage of predicted neck circumference), obesity, genetics, craniofacial morphology, chronic rhino-sinusitis with nasal obstruction, smoking and alcohol consumption.

III. DIFFERENTIAL DIAGNOSIS

- Narcolepsy
- insomnia
- Sleep hygiene disorder
- Depression
- Drug effect
- OHS
- Habitual snorers
- Restless leg syndrome

IV. CLINICAL FEATURES

The night-time symptoms of SDB include:

- Loud, disruptive snoring
- Nocturnal pauses in breathing
- Gasping or choking for air during sleep
- Restless sleep
- Nocturia

The daytime symptoms of SDB include:

- Feeling of excessive daytime sleepiness
- Grogginess and morning headache
- Memory or leaning problems
- Not being able to concentrate at work
- Depression and irritability
- Sexual dysfunction
- Dry throat upon awaking
- Frequent nocturnal enuresis

The symptoms seen in women include:

- Report typical symptoms less frequently
- Under-report snoring and underestimate symptom severity as compared to men
- Non-specific somatic complaints such as insomnia, fatigue, myalgias, and morning headache
- Amenorrhea and dysmenorrhea
- Depression, anxiety and social isolation
- Women tend to be more obese than men for the same degree of severity

PRESENTATION IN CHILDREN

Nocturnal symptoms in children include

- Snoring
- Restless sleep
- Mouth breathing
- Struggle to breathe/ gasp for air
- Bed wetting

Daytime symptoms in children include

- Feels depressed, sad or irritable
- Sleepy during the day
    - Feels fatigued or tired during daytime
    - Excess activity, short attention span
    - Learning difficulties
    - Falling school performance
    - Difficulty to concentrate and memory lapses
    - Enlarged tonsils and adenoids

Consequences of SDB are as follows:

Physiological

- Cardiovascular – Metabolic syndrome, hypertension, cerebrovascular accidents, coronary artery disease
- Alterations in inflammatory biomarkers

Behavioral

- Tiredness in the morning
- EDS in permissive situation
- Increased risk of motor vehicle accidents
- Losses of concentration and productivity
- Epworth Sleepiness Score & psychomotor vigilance test are abnormal
- Behavioral effects can be variable amongst patients
- Behavioral measurement alone are insufficient

Social effects

- Principally related to snoring
- Disrupts social harmony by disturbance of bed-partner and others in a home
- Falling asleep at social gatherings
- Subjective measures are commonly used
- Bed-partner scoring

V. PREVENTION AND COUNSELING

Risk factor reduction:

- Weight reduction
- Avoid alcohol and cigarette smoking
- Treatment of nasal congestion

- Surgical treatment of tonsillar and adenoid hypertrophy
- Good sleep hygiene
- Awareness about sleep disorders
- Diagnosis and timely treatment of hypothyroidism

VI. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

*Situation 1: At Secondary Hospital/ Non-Metro situation: Optimal Standards of Treatment in Situations where technology and resources are limited

s) **Clinical Diagnosis**:

The diagnosis of SDB depends on properly taken history from the patient and the bed-partner regarding the typical daytime and night-time symptoms. Co-morbid conditions like hypertension, diabetes and other metabolic and hormonal problems. Good physical examination taking into account body mass index (BMI), neck length, percentage of predicted neck circumference (PPNC), cranio-facial anomalies like micrognathia and retrognathia, and evaluation of the upper airway using clinical examination scores, eg. Friedman score, X-ray cephalometry, CT scan, MRI, and videoendoscopy. For the localization of the site of the obstruction multi-channel pressure measurement has also been used with some success.
The gold standard test for the diagnosis and severity assessment of SDB is clinical polysomnography (PSG); however, there are many practical considerations and clinical caveats in PSG interpretation in sleep related sleep disorders.

History should include any history of sleep problem, sleep diary, medication history, medical problems, work history-shift work, alcohol or drug use, periodic limb movement disorders, dream history and teeth grinding.
Physical examination should include measurement of body mass index (BMI; kg/m^2), neck circumference and waist/hip ratio, examination of nose, oral

cavity, oropharynx, bony structure of head and neck. Sleep endoscopy is rarely needed to confirm airway collapse.

t) **<u>Investigations</u>**:

- Thyroid function tests
- Blood sugar (fasting and post-prandial)
- Serum insulin (fasting and post-prandial)
- HbA_1c
- Lipid profile
- ECG and echocardiography
- Pulmonary function testing (if overlap with chronic obstructive airway disease is suspected)
- Arterial blood gases [if overlap with chronic obstructive airway disease or obesity-hypoventilation syndrome (OHS) is suspected]
- Polysomnography
    - Full-night diagnostic study
    - Split-night with CPAP titration
    - Home study
    - Multiple Sleep Latency Testing (MSLT) if narcolepsy is suspected

Requirement for standard diagnostic nocturnal polysomnography (PSG) includes recording and analysis of the following parameters: EEG, (EOG), (EMG), oro-nasal airflow, chest wall effort, body position, snore microphone, ECG, and oxyhemoglobin saturation. The duration of a diagnostic NPSG is at least 6 h with the exception of the diagnostic portion of a split-night study, which is at least 2 h in duration.

The various levels (types) of PSG are as follows

Type 1- gold standard, in-lab, attended PSG

Type 2- Comprehensive portable monitoring, unattended

Type 3- cardio-pulmonary sleep study or modified portable sleep apnea testing

Type 2 and Type 3 are acceptable in attended setting for patients without co-morbidity when scored by a trained physician

Type 3 underestimates the severity of SDB

Type 4- continuous single or dual bio-parameter recording -underestimates severity

Indications of polysomnography are as follows:

- For the diagnosis of SRBD and CPAP titration
- Symptomatic patients with negative portable studies.
- Full night PSG is required for CPAP titration of documented case of SDB; RDI > 15/hour or RDI > 5 with EDS
- Evaluation of narcolepsy, and parasomnias
- Before and after the application of dental appliances to assess the therapeutic benefits
- Before and after upper airway surgery for snoring and SDB
- After significant (10%) weight gain or weight loss
- Patients with specific medical condition
    - Coronary artery disease
    - Congestive heart failure
    - History of stroke
    - Treatment of transient ischemic attack (TIA)
    - Significant tachy- or brady- arrhythmias

Indications for split-night study include:

- AHI $\geq$ 40/hour of at least 2 hours of sleep.
- AHI between 20 and 40 in the presence of repetitive lengthy obstructions and major de-saturations.
- CPAP titration must be carried out for more than 3 hours.
- PSG documentation of abrogation of all events with CPAP.

u) Treatment:

Treatment decision is based on evaluation of the patient's history, anatomy, disease severity, symptoms and presence of co-morbidities. The severity of disease depends on

- Severity of symptoms
- Apnea hypopnea index (AHI)
- Degree of oxygen desaturation
    - Minimum O_2 desaturation
    - Sleep time spent below 90% oxygen saturation

- Effect on sleep architecture
    - Presence or absence of REM and Delta sleep
- Respiratory distress index (RDI)
    - Includes arousals with apneas and hypopneas

All modes of treatments should be discussed and these include behavioral treatments, use of oral appliances, positive airway pressure (PAP) therapy and surgical therapy while providing real information about success with each mode of treatment.

The behavioral modifications

- Can reduce or eliminate OSA without the need for medication, device use or surgery.
    - Sleep hygiene counseling
    - Sleep position therapy
    - Lifestyle modification and weight reduction
    - Avoidance of sedatives and alcohol
    - Smoking cessation
    - Avoidance of large meals before bedtime

Continuous positive airway pressure (CPAP) is the gold standard for treatment of OSAS. It acts as a pneumatic splint to keep airway patent. The benefits of CPAP include the following.

- Minimally invasive and reversible
- Reduction and/or reversal of OSA-related signs and symptoms

  Like snoring, excessive daytime sleepiness, un-refreshing or fragmented sleep, cognitive impairment
- Decrease risk of accidents
- Increased productivity
- Decrease long-term complications of OSA like hypertension, heart disease, stroke, and death

Common adverse events of CPAP are as follows:

<u>Minor (30-50% of Patients)</u>

- Inconvenience

- Skin ulceration due to mask
- Poor mask fit
- Claustrophobia
- Various nasal problems (15-45%)

Major

- Massive epistaxis
- Pneumocephalus – following recent surgery or trauma causing CSF leak.

Guidelines for titration

- Patient should be evaluated for awake respiratory failure, congestive cardiac failure, and marked nocturnal hypoxemia.
- CPAP titration should ideally be done in the hospital under supervision of a trained technician.
- Patient should receive adequate PAP education, hands on demonstration, careful mask fitting and acclimatization
- CPAP should be increased till all the obstructive events: apneas, hypopneas, RERAs, snoring and desaturation dissapear.
- Recommended minimum pressure is 4 cm and maximum of 15 cm (<12 yrs) and 20 cm H_2O (> 12 yrs)
- CPAP pressure of 1 cm H_2O should be increased with an interval no shorter than 5 min.
- CPAP pressure should be increased by 1 cm H_2O
    - 1 apnea (<12 yrs) or 2 apneas (> 12 yrs)
    - 1 hypopnea (<12 yrs) 3 hypopneas (> 12 yrs)
    - 3 RERAs (<12 yrs) 5 RERAs (> 12 yrs)

- Use of BiPAP is recommended if CPAP titration pressure is > 15 cm H_2O
- Titration algorithm is same for split-night study

Titration in patients with cardio respiratory failure

- Requires close supervision by trained technician or physician while commencing CPAP.
- Many patients might require endotracheal intubation or urgent tracheostomy.
- The patient may become confused or delirious due to deranged blood gases.

- In trained hands, judicious use of CPAP or BiPAP can control breathing disturbances.
- Auto CPAP should not be used

CPAP adherence

- No clear field standard exist
    - Too few studies to define amount of adherence needed to treat common sequelae
- Average patient uses CPAP about 5 hours per night
- Most clinicians generally recommend CPAP use for more than 4-5 hours per night on ≥ 70% of all nights

Predictors of CPAP adherence

- Early use patterns predict long-term adherence
    - Patients appear to establish their patterns of use by the first month (as early as 4 days)
    - Adherence at 1 month appears to predict adherence at 3 months
    - Since adherence is established by 3 months, alternative forms of therapy should be considered for non-adherent patients

Factors affecting CPAP adherence

Patient related factors:

- Lesser severity of symptoms
- Little or no perceived benefit from therapy
- Failure to understand importance of or directions for CPAP use
- Use of prescription/non-prescription drugs or alcohol
- Lack of social support
- Other medical illnesses or fatigue
- Physical limitations (i.e. vision, hearing, hand coordination)

II. *Therapy related factors:*

- Complexity of therapy/device use
- Increased rate of adverse reactions that go unaddressed
- Lack of efficacy
- Expense of therapy
- Chronic nature of illness

- Compliance decreases over time

III. *Clinician related factors*

- Poor relationship with patient
- Lack of clinician follow-up
- Expression of doubt concerning therapeutic potential or creating falsely elevated expectations
- Poor communication skills
- Failure to identify concomitant use of alcohol and sedatives by the patient

<u>Measures to improve CPAP adherence:</u>

Technological interventions:

Auto-titrating CPAP

- Pressure delivery is auto-adjusted during changing airway conditions overnight

Bi-level positive pressure (BiPAP)

- Set inhalation pressure with a lower set exhalation pressure

Flexible pressure delivery (C-Flex, EPR)

- Slight reduction in pressure during early exhalation

Heated humidification

- Decreases nasal/oral dryness for comfort
- Improves nasal resistance

Pressure ramp feature

- CPAP starts at lower pressure (2-4 cmH_2O) and gradually ramps up to prescribed pressure over set time period (5-45 min)

Behavioral interventions:

- Patient education
- Systematic desensitization and sensory awareness (for claustrophobia)
    - Wearing device for progressively longer periods
- Cognitive behavioral therapy/Motivational Enhancement Therapy

Reducing side effects:

PROBLEM	**SOLUTIONS**
Skin breakdown/irritation	• Refit mask • Try nasal pillows
Eye irritation	• Refit mask • Saline eye drops

	• Eye mask
Mouth leaks	• Chin strap • Switch masks
Mask leaks/discomfort	• Refit or switch masks
Nasal congestion	• Heated humidification • Nasal saline sprays • Nasal steroids ± decongestants ± antihistamines • Correct any anatomic obstruction
Epistaxis	• Heated humidifiers and saline
Rhinorrhea	• Heated humidifier, nasal saline ± antihistamines
Aerophagia	• Reduce CPAP pressure • Consider APAP, BiPAP
Claustrophobia	• Switch to nasal pillows • Desensitization
Difficulty in exhalation	• Ramp feature • Consider switching to APAP, BiPAP, flexible PAP • Consider re-titration

Treatment with oro-dental appliances: useful for mild to moderate cases of OSAS who are not tolerant/ willing to use CPAP treatment

- Improve upper airway baseline dimensions
    - Pulling tongue forward – tongue retaining device
    - Moving mandible forward – nocturnal airway patient device (NAPA)

- Effectiveness of oral appliances
    - Significantly reduce or completely eliminate snoring
    - Significantly reduce AHI
    - Subjective improvement in daytime function but objective evidence of improvement in sleepiness lacking
    - Adverse events include excessive salivation, temporo-mandibular joint arthritis, and overall lower compliance (50%)

Patient selection for oro-dental appliances:

- Factors associated with better response
    - Younger age
    - Lower BMI
    - Lower AHI
    - Good protrusive range
    - Presence of adequate healthy denture

- However, some studies have demonstrated success even in patients with more severe OSA

Surgical treatment for OSAS

- Patient selection for surgery depends on
    - OSA severity
    - Individual patient anatomy
    - Patients option for surgery
    - Presence of co-morbidities

- Procedures used for localization of the site of obstruction
    - X-ray cephalometry, CT and MR imaging, video endoscopy under sedation and multi channel pressure measurements.

- Points of discussion while considering surgical option
    - Patient's expectations and preferences
    - Patient's expectation regarding cure of their snoring, apnea and symptoms of tiredness.
    - Presence of co-morbidities
    - Type of surgery
    - Pain and complication rates
    - Expected consequences
    - Morbidities
    - Cost
    - Need for evaluation following surgical procedure and possible need for subsequent surgeries

- Procedure on the upper airway, which may improve PAP use and compliance.
    - Adeno-tonsillectomy
    - Nasal surgery for hypertrophied turbinate, deviated nasal septum or nasal polyps.
- Surgery that improves OSA without surgically altering the upper airway
    - Tracheostomy
    - Bariatric surgery

- Surgery that directly alters the upper airway

Tracheostomy

- Done on a temporary basis in the pre/peri-operative period
- Not done routinely because of its associated hygiene and social burden
- Typically reserved for morbidly obese patients who can't tolerate PAP
- Morbidly obese patients with OHS who require upper airway bypass and nocturnal ventilation
- Patients who are unable to tolerate PAP with significant co-morbidity

Bariatric surgery

- Bariatric surgery has a potential to reduce body weight significantly as a significant number of OSA patients are obese.

Indications

- BMI > 40
- BMI > 35 with significant co-morbidities

- Has the advantage of treating other co-morbidities associated with obesity

Surgery that alters the upper airway

- Uvulopalatopharyngoplasty (UPPP)
- Tongue advancement
- Hyoid suspension
- Maxilo-mandibular advancement (MMA)

ALGORITHM FOR TREATMENT OF OSA & TREATMENT GOALS

Mild (AHI >5-15)

No symptoms

Behavioral modification

Symptoms

Behavioral modification

- Consider oral appliance
- Consider PAP
- Consider surgical intervention

Moderate (AHI >15-30)

No symptoms

Behavioral modification

- Consider PAP
- Consider oral appliance
- Consider surgical intervention

Symptoms

Behavioral modification

PAP

Surgical intervention for PAP failures

Consider oral appliance

Severe (AHI>30)

Symptoms or no symptoms

Behavioral modification (rarely sufficient alone)

PAP

Surgical intervention for PAP failures

- Consider tracheostomy if other treatments fail and significant symptoms or co-morbidities exist
- Co-morbidities should also be taken into account when discussing the strength of recommendations
- Patients with BMI >35 and co-morbidities or BMI>40 should be considered for bariatric surgery
- Interventions should typically be applied in the order listed. Proceed down the list until success is reached.

Follow up

Follow-up after medical and surgical intervention is critical to ensure that the patient has benefited from the chosen treatment and to provide an opportunity to implement further recommendations in case partial treatment response.

v) **Referral criteria:**

Patient should be referred when following are present:

- Severe OSAS/OHS having cardio-respiratory failure
- Co-morbidities
- Overlap syndrome (COPD or ILD with OSAS)
- Poor compliance to CPAP treatment
- Severe, intractable adverse events
- Refusal for CPAP therapy
- Consideration for oro-dental appliances and surgery
- Requiring advanced investigations like nasal endoscopy, CT or MRI etc
- Patients with complex sleep apnea

***Situation 2: At Super Specialty Facility in Metro location where higher-end technology is available**

p) Clinical Diagnosis:

Same as mentioned in Situation 1

q) Investigations:

Same as mentioned in Situation 1

Level I polysomnography

Patients requiring advanced investigations like nasal endoscopy, CT or MRI etc

r) Treatment:

Titration and treatment of patients with severe cardio-respiratory failure

Treatment and counseling of patients with poor CPAP adherence

Oro-dental appliances and surgical treatment

As mentioned above

VII. WHO DOES WHAT? and TIMELINES

- **a.** ***Doctor*** Diagnosis and Management including counseling
- **b.** ***Nurse*** Implementation of orders, monitoring of patients and counseling
- ***c. Technician*** Investigations

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1. Physician with sleep medicine training 2. Nurse 3. Radiographer 4. Laboratory technician 5. Biochemist 6. Sleep laboratory technician 7. Cardiologist/ Physician with echocardiography training	1. Pulmonary function test 2. Arterial blood gas 3. Thyroid function test 4. Blood sugar 5. Lipid profile 6. Electrocardiogram 7. Serum insulin 8. Echocardiography 9. Polysomnography	1. Tongue retaining devices 2. Nocturnal airway patient device 3. CPAP machine with humidifier	1. Polysomnography machine 2. Pulmonary function test machine 3. Pathology laboratory 4. Biochemistry laboratory 5. Echocardiography machine 6. ABG analyzer 7. Body composition analyser
2	Above plus 1. Radiologist 2. ENT Surgeon 3. Anesthetist 4. Bariatric surgeon	Above plus 9. X-ray cephalometry 10. Nasal/oral video endoscopy 11. CT scan 12. MRI scan	As above	Above plus 1. CT scan machine 2. MRI machine 3. Nasal/oral video endoscope 4. Operation theatre 5. DEXA scan

PLEURAL DISEASES

I. WHEN TO SUSPECT/ RECOGNIZE?

i) Introduction:

There are 4 types of pleural diseases: pleurisy, pleural effusion, pneumothorax and pleural mesothelioma. Pleural mesothelioma is a malignant condition of pleura related to asbestos exposure occurring rather infrequently in our country compared to other lung cancers and is beyond the purview of this review.

j) Case definition:

For both situations of care:

1. Pleurisy is defined as an acute inflammation of the pleura. The inflammation can be primary or secondary due to spread from an adjacent structure.
   1.1. Primarily, viral infections of the pleura result in pleurisy. Secondarily, the pleura may be involved due to pneumonia or pulmonary infarction. The present review is restricted to 'primary' pleurisy.

2. Pleural effusion is defined as an excessive accumulation of fluid in the lungs. There are mainly two types of pleural effusions: transudative and exudative pleural effusion.
   2.1. Fundamentally, transudative pleural effusions reflect a systemic pathology and exudative pleural effusions reflect a local pleural pathology. Generally, transudative effusions are usually bilateral, whereas exudative effusions are usually unilateral.
   2.2. The common causes of transudative pleural effusions are congestive heart failure and hypoalbuminemic states (cirrhosis, nephrotic syndrome).
   2.3. The common causes of exudative pleural effusions are tuberculosis, malignancy and traumatic hemothorax. Uncommon causes include pancreatitis, connective tissue diseases, non-traumatic hemothorax (embolism, malignancy) and chylothorax (tumors, filariasis)

3. Pneumothorax is defined as air in the pleural cavity resulting in collapse of the whole lung or some part of the lung. It may be traumatic or spontaneous.
   3.1. Traumatic pneumothorax can result in a life-threatening condition due to tension pneumothorax.

3.2. Spontaneous pneumothorax may occur without any associated underlying lung pathology (primary) or may be associated with underlying lung pathology (secondary).

3.2.1. The common secondary causes include tuberculosis and chronic obstructive airway disease. Smoking and marfanoid habitus are important risk factors. Secondary pneumothorax is a more critical condition as the underlying lung is already compromised.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

No systematic robust epidemiological studies are available from India

III. DIFFERENTIAL DIAGNOSIS

1. Pleurisy

- Cardiac: post-myocardial injury syndrome (Dressler syndrome)
- Renal: chronic renal failure

2. Pleural effusion

- Amebic liver abscess
- Lower lobe collapse
- Mass lesion

3. Pneumothorax

- Pulmonary embolism
- Acute coronary syndrome
- Large bulla

IV. PREVENTION AND COUNSELING

Optimal treatment of primary systemic illness. Abstinence from smoking, alcohol and other substance abuse.

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

<u>*Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited</u>

w) **Clinical Diagnosis**

Symptoms

1. Pleurisy: sharp pain in the lateral hemithorax characteristically increasing on inspiration and coughing.
2. Pleural effusion: may be asymptomatic or associated with dull aching pain on the affected site. Dyspnea, dry cough may also be present. Symptoms of underlying systemic pathology may be associated.
3. Pneumothorax: sudden onset excruciating pain associated with dyspnea especially in a smoker.

Signs

1. Pleurisy: acute history of fever, pleural rub.
2. Pleural effusion: findings of primary systemic disease, local examination reveals decreased tactile fremitus, stony dull note on percussion and absent breath sounds on auscultation.
3. Pneumothorax: marfanoid habitus, local examination reveals decreased tactile fremitus, tympanitic note on percussion and absent breath sounds on auscultation.

x) **Investigations**

1. Pleurisy: No specific investigation *per se*. Patients with pleurisy normally improve in 7-10 days.

2. Pleural effusion:
   2.1 Chest X-ray (PA and lateral views of chest radiographs): 50 ml fluid can be appreciated on lateral chest radiograph as a meniscus in the posterior costophrenic angle. Lateral decubitus film helps in differentiating a loculated effusion from a free fluid effusion.
   2.2 Ultrasound: USG helps in confirming a pleural effusion as compared to pleural thickening, which many times cannot be appreciated on a chest radiograph. It is also useful in diagnosing loculated effusions, subpulmonic and subdiaphragmtic pathology like an amebic liver abscess.
   2.3 Pleural fluid (PF) evaluation

2.3.1 Diagnostic thoracocentesis performed with/without US guidance is the investigation of choice to differentiate between a transudative and exudative pleural effusion. This differentiation is the sheet anchor of further management.

2.3.2 Colour

2.3.2.1 Pale yellow: transudative

2.3.2.2 Turbid : exudative

2.3.2.3 Frank pus : empyema

2.3.2.4 Blood-like : traumatic tap, hemothorax

2.3.2.5 Milky : chylothorax

2.3.3 Biochemistry {Protein and lactate dehydrogenase (LDH)}

Light's criteria have a high (> 98%) sensitivity and specificity to classify PF. There are 3 criteria as follows:

a. PF protein/serum protein> 0.5
b. PF LDH/ serum LDH> 0.6
c. PF LDH> 2/3 upper limit serum LDH

Exudative PF: any one of 3 criteria present

Transudative: even if one of the 3 criteria are absent

2.3.4 pH: normal PF pH is 7.64.

2.3.5 Cell cytology for polymorphonuclear or lymphocytic predominance

2.3.6 Malignant cytology (if available at secondary level)

2.3.7 Bacteriology: Gram stain and culture sensitivity in addition to pH are very important investigations to decide regarding the management in cases of parapneumonic effusion vis-à-vis empyema.

2.3.8 Adenosine deaminase (ADA) levels (if available at the secondary level) Higher ADA levels with lymphocytosis point to a diagnosis of tubercular pleural effusion

2.3.9 Hematocrit (Hct): PF hct > 50% blood Hct signifies hemothorax differentiating from a traumatic thoracocentesis

3. Pneumothorax

3.1. Chest radiograph: collapsed lung at the hilum with absence of lung markings in the periphery.

3.2. Important to evaluate the contralateral lung radiographically-normal or abnormal for management.

y) Treatment:

Standard Operating procedure

a. In Patient

1. Pleurisy: symptomatic treatment with non-steroidal inflammatory drugs. If symptoms persist, evaluate for pleural effusion.

2. Pleural effusion
   2.1. Therapeutic thoracocentesis - symptomatic relief of dyspnea
   (Caveat: not more than 1 litre of pleural fluid should be removed to prevent post thoracocentesis shock and re-expansion pulmonary edema in one sitting)
   2.2. In a transudate, the primary cause has to be managed.
   2.3. Exudative effusions
      2.3.1. Tuberculosis: as per Revised National Tuberculosis Control Program (RNTCP) guidelines
      2.3.2. It needs to be remembered that in cases of suspected empyema, establishing the diagnosis as early as possible after admission is the key. A delay in the institution of ICD even by a few more hours results in more fibrosis and loculations, which further complicate the long term management.
      2.3.3. At admission, the following criteria help in deciding the plan in these patients

PF bacteriology	PF pH	Chest tube drainage
Culture and/or Gram stain -	> 7.2	No
Culture and/or Gram stain +	< 7.2	Yes
Frank pus	< 7	Yes

3. Pneumothorax
   3.1. Primary spontaneous:
      3.1.1. Small pneumothorax requires observation.
      3.1.2. Large pneumothorax requires simple aspiration. If lung does not expand then tube thoracostomy.
   3.2. Secondary spontaneous
      3.2.1. Tube thoracostomy
   3.3. Traumatic

3.3.1. Depends on size- simple observation to thoracostomy

3.4. Tension

3.4.1. Medical emergency

3.4.2. Large bore needle in second intercostal space. If air gushes out, tube thoracostomy

b. Out Patient

Treatment of primary systemic illness

z) **Referral criteria:**

1. Diagnosis not clear
2. Response to therapy not optimal
3. Recurrent pneumothorax
4. Persistent air leak
5. Unexpanded lung after 3 days of tube thoracostomy

***Situation 2: At Tertiary hospital where higher-end technology is available**

s) Clinical Diagnosis

As in Situation V.1 a) above

t) Investigations

10. Pleurisy: As in situation V.1b) above

11. Pleural effusion: As in situation V.1b)2. above PLUS

11.1. CT scan to accurately define the anatomy of lung parenchyma (lung abscess) and pleura (empyema by the split pleura sign, loculated effusion, pleural masses)

11.2. Special investigations

11.2.1. PF triglyceride > 110 mg/dl for chylothorax

11.2.2. PF antinuclear factor for systemic lupus erythematosus (SLE) [specific but not very sensitive]

11.2.3. PF Rheumatoid factor and anti-citrullinated protein antibody (anti-CCP)

11.2.4. PF amylase for pancreatitis

11.3. Pleural biopsy

11.4. Medical thoracoscopy and video-assisted thoracoscopy (also has therapeutic potential)

12. Pneumothorax: as in situation V.1b)3. PLUS

12.1. Computed tomography to assess for blebs and associated pulmonary disease

u) <u>Treatment:</u>

<u>Standard Operating procedure</u>

a. In Patient

3. Pleurisy: As in situation V.1c)a.1 above

4. Pleural effusion: As in situation V.1c)a.2 above PLUS

4.1. Pleurodesis with doxycycline – recurrent malignant pleural effusion

4.2. Chest tube instilled fibrinolytic therapy (streptokinase) - parapneumonic effusions

4.3. VATS (thoracotomy, if VATS not available)- non-resolving empyema

4.4. Pneumothorax as in V.1c)a.3 above PLUS

4.4.1. VATS with pleurodesis/bleb resection

b. Out Patient

Treatment of primary systemic illness

VI. WHO DOES WHAT? and TIMELINES

a. ***Doctor:*** Diagnosis and Management including counseling

b. ***Nurse:*** Implementation of orders, monitoring of patients and counseling

c. Technician: Investigations

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	8. Physician 9. Surgeon 10. Nurse 11. Radiographer 12. Laboratory technician	10. Chest radiograph 11. Pleural fluid examination (total and differential cell count, malignant cytology, *Mtb* smear and culture, PCR, fungal smear and culture, protein, LDH, glucose, ADA) 12. USG chest and abdomen 13. Arterial blood gas analysis 14. Echocardiography 15. Blood biochemistry	3. Anti-tuberculosis therapy (DOTS) 4. Intercostal tube	4. X-ray machine 5. USG machine 6. Cytopathology and histopathology laboratories 7. Microbiology laboratory service 8. ABG analyzer 9. ECHO machine
2	Above plus 14. Radiologist 15. Pathologist 16. Thoracic surgeon 17. Anesthetist 18. Nursing staff trained in assisting thoracic surgery	Above plus 13. Malignant cytology 14. Pleural fluid triglyceride 15. Pleural fluid antinuclear antibody, anti-CCP antibody 16. Markers for connective tissue diseases 17. Pleural Biopsy 18. Video-assisted thoracoscopy 19. CT Scan	Above plus 11. Streptokinase 12. Doxycycline	Above plus 6. CT scan machine 7. Pleural biopsy needle 8. Immunology laboratory services 9. Video-assisted thoracoscope 10. Thoracic surgery operating theatre; recovery room and ICU

COMMUNITY ACQUIRED PNEUMONIA (Bacterial)

I. WHEN TO SUSPECT/ RECOGNIZE?

k) Introduction:

Pneumonia, an infection of the pulmonary parenchyma is a commonly encountered, potentially life-threatening condition in clinical practice. In light of the recent pandemics of multidrug-resistant bacterial infections world-over, pneumonia has been categorized as either community-acquired pneumonia (CAP) or health care-associated pneumonia (HCAP). The subcategories of HCAP include hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). In spite of the availability of potent new antimicrobials, CAP is associated with considerable morbidity and mortality, particularly in elderly patients and those with significant co-morbid illnesses.

l) Case definition:

For both situations of care:

1. Symptoms and signs consistent with an acute lower respiratory tract infection (productive cough, rusty sputum, pleuritic chest pain, etc.); presence of at least one systemic manifestations (either a symptom complex of sweating, fever, shivers, aches and pains and/or temperature of >38 ^{o}C or more).
2. New focal signs on physical examination of the chest.
3. New chest radiograph evidence of pneumonic consolidation which is at least segmental or present in more than one lobe and is not known to be previously present for which there is no other explanation.
4. Confirmation of aetiological diagnosis by blood culture/sputum culture and/or molecular diagnostic methods.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

Estimates form the developed world suggests that CAP occurs in 8 to 15 per 1000 persons per year; the highest rates are at the extremes of age. No systematic studies have been carried out till date to define the incidence of CAP in India and reliable epidemiological data are lacking.

III. DIFFERENTIAL DIAGNOSIS

1. Common
    - Pulmonary embolism/infarction
    - Pulmonary oedema
    - Bronchogenic carcinoma
    - Pulmonary tuberculosis
    - Bronchiectasis

2. Uncommon
    - Pulmonary eosinophilia/eosinophilic pneumonia
    - Cryptogenic organising pneumonia
    - Pulmonary alveolar haemorrhage
    - Foreign body
    - Congenital pulmonary abnormality (eg. lobar sequestration)
    - Radiation pneumonitis

IV. PREVENTION AND COUNSELING

1. Persons hospitalized with CAP who smoke should be counseled regarding smoking cessation.
2. Respiratory hygiene measures, including the use of hand hygiene and masks or tissues for patients with cough, should be used in outpatient settings and casualty as a means to reduce the spread of respiratory infections

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

*Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited

aa)**Clinical Diagnosis**

Symptoms

The onset of CAP is acute. Patients present with symptoms suggestive of acute lower respiratory tract infection, cough, rusty sputum, pleuritic chest pain, and constitutional symptoms, such as, fevers, sweating, chills, rigors, body aches and pains; temperature of >38 ^{o}C or more.

Signs

Patients with CAP look sick and toxic. New and focal signs of pneumonic consolidation (reduced movements and expansion, increased tactile vocal fremitus, dull note on percussion, tubular bronchial breathing, increased vocal resonance, aegophony and whispering petriloquy; pleural rub) are present on physical examination of the chest. Signs due to complications, such as, pleural effusion, empyema, sepsis syndrome may also be present.

bb) **Investigations**

1. **Chest radiograph:** A chest radiograph is the cornerstone to establishing the diagnosis of CAP or an alternative diagnosis, and to assess the extent of the disease and the presence of complications such as pleural effusion, lung abscess etc.
2. In all admitted patients:
    2. 1. Pulse oximetry: pulse oximtery is useful for assessment of gas-exchange status.
    2.2. Sputum Gram's stain, culture; smear examination for acid-fast bacilli; blood culture.
    2.3. Full haemogram.
    2.4. Serum biochemistry (blood urea, serum creatinine, liver function tests).
3. Arterial blood gas (ABG) analysis: ABG analysis is helpful in detecting acute respiratory failure that may complicate the course of CAP.
4. Assessment of severity: This is best assessed by CURB-65 scoring system [confusion, urea >7mmol/L, respiratory rate >30/min, blood pressure (systolic <90 mmHg or diastolic <60 mmHg), Age >65yrs] and guides admission to ICU and antibiotics administration. Pneumonia Severity Index (PSI) a prognostic model to identify those with low risk of death.

cc) Treatment:

Standard Operating procedure

a. In-Patient

1. **General therapeutic measures**

1. SpO_2 monitoring by pulse oximetry.
2. Adequate circulation and blood pressure is ensured using volume infusion and/or vasopressors.

3. Decision to admit

3.1. The decision to admit patients with one or more adverse factors (confusion, respiratory rate > 30/min; systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg; age more than 65 years) without severity factors (hypoxaemia, bilateral or multilobar involvement on chest radiograph) should be individualized.

3.2. Patients with one or more severity factors listed above need hospitalization

3.3. Admission into an ICU: for patients with septic shock requiring vasopressors or with acute respiratory failure requiring intubation and mechanical ventilation, direct admission into ICU will be required. Admission to an ICU is also recommended for patients with 3 of the following minor criteria for severe CAP: respiratory rate >30 breaths/min; PaO_2/FIO_2 ratio$\leq$ 250; multilobar infiltrates; confusion/ disorientation; uraemia (blood urea nitrogen level >20 mg/dL); leukopenia (total leukocyte count, < 4000 cells/mm^3), thrombocytopenia (platelet count <100,000/mm^3), hypothermia (core temperature <36^{o}C); and hypotension requiring aggressive fluid resuscitation.

4. Antibiotic treatment of the aetiological cause of CAP

4.1 In-patient antibiotic therapy

4.1.1 In-patients, non-ICU treatment

When admitted, these patients are treated with intravenous beta-lactam **plus** macrolide (Table 1).

Table 1

Choice of antibiotics for in-patient treatment of CAP

Choice of drug	Daily dosage	
	Intravenous beta-lactam	*Macrolide*
First choice	Cefotaxime 2 g q8h	Azithromycin 500 mg qd
Second choice	Ceftriaxone 1 g q12h	
Third choice	Co-amoxyclav 1.2 g q8h	

4.2 Duration of antibiotic therapy is 7 to 10 days based on clinical response

4.3 A switch to oral therapy can be made at 48-72 hours as most patients with CAP will have an adequate clinical response within 3 days, which includes improvement in cough and dyspnoea, absence of fever, decreasing white blood cell count and functioning gastrointestinal tract with adequate oral intake.
4.4 Patient may be discharged on the same day if medical and social factors are favorable.
4.5. Pleuritic pain should be relieved using drugs such as paracetamol.

2. **Supplemental oxygen therapy**

In patients with hypoxaemia, spontaneous ventilation using a face mask with a high flow gas delivery system can be used to deliver a FIO_2 of up to 0.5 to 0.6.

b. **Out Patient**

Out-patient antibiotic therapy

The choice of antibiotics for out-patient treatment of CAP is as follows. For previously healthy patients and those who have not used antimicrobials within the previous 3 months, treatment with oral macrolide (e.g., azihtromycin) is indicated. For patients with comorbidities such as chronic heart, lung, liver or renal disease, diabetes mellitus, alcoholism, malignancies, asplenia, immunosuppressing conditions or use of immunosuppressing drugs, or use of antimicrobials within the previous 3 months, and patients in regions with a high rate (>25%) of infection with high-level [minimum inhibitory concentration (MIC) $\geq$16 mg/mL] macrolide-resistant *Streptococcus pneumoniae,* oral treatment with co-amoxyclav in combination with macrolide is recommended.

dd) **<u>Referral criteria:</u>**

1. Patients presenting with two or more adverse factors (confusion, respiratory rate> 30/min; systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg; age more than 65 years) or one or more severity factor (hypoxaemia, bilateral or multilobar involvement on chest radiograph).

2. Diagnosis not clear.
3. Patients not responding to therapy

***Situation 2: At Tertiary hospital where higher-end technology is available**

v) Clinical Diagnosis

As in situation V.1 a) above

w) Investigations

As in situation V.1b) above PLUS

13. Two blood cultures (minimum 20 ml)
14. Sputum or other respiratory tract specimen for Gram stain, bacterial culture and sensitivity tests; molecular diagnostic methods (e.g., polymerase chain reaction for respiratory pathogens)
15. Pleural fluid, if present, for microscopy, culture and pneumococcal antigen detection.
16. Investigations for Legionella pneumonia:
    4.1 Urine for *Legionella* antigen
    4.2 Sputum or other respiratory tract specimens (for *Legionella* culture and direct immunofluorescence) (if available)
5. Investigations for atypical bacterial pathogens:
    5.1 If available, sputum or other respiratory sample for PCR or direct immunofluorescence (or other antigen detection test) for *Mycoplasma pneumoniae*, Chlamydia spp, *Pneumocystis jirovecii* (if at risk)
6. Imaging studies: ultrasonography of the chest is useful for detecting complications such as pleural effusion, empyema. In non-responders, computed tomography of the chest can help in detecting an underlying malignancy and complications, such as, lung abscess.
7. Bronchoscopic procedures: should selectively be used in individual patients for aetiological confirmation and ruling out an alternative diagnosis, such as, malignancy.

x) Treatment:

Standard Operating procedure

a. In Patient

As in situation V.1c)a.1 above PLUS

1. General therapeutic measures

1.1. Patients should be assessed for volume depletion and may require intravenous fluids.

1.2. Prophylaxis of venous thromboembolism with low molecular weight heparin should be considered for all patients who are not fully mobile.

1.3. Nutritional support should be given during prolonged illness.

1.4. Airway clearance techniques should be considered if the patient has sputum and difficulty in expectoration or in the event of a pre-existing lung condition.

2 Antibiotic therapy

As described under V.4 above PLUS

2.1 In-patients, ICU treatment

- A beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **plus** azithromycin are recommended.
- For penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended.
- If *Pseudomonas* is a consideration, an antipseudomonal beta-lactam (e.g., piperacillin tazobactam, cefepime, imipenem, or meropenem) **plus** either ciprofloxacin or levofloxacin (750 mg) are recommended.
  or
  The above beta-lactam plus an aminoglycoside and azithromycin
  or
  The above beta-lactam plus an aminoglycoside and an antipseudomonal fluoroquinolone are recommended.
- For penicillin-allergic patients, aztreonam may be substituted for above beta-lactam)
- **Prior to use of respiratory fluoroquinolones, active pulmonary tuberculosis should be excluded.**
- If community acquired methicillin-resistant *Staphylococcus aureus* is a consideration, vancomycin or linezolid can be added.

2. **Supplemental oxygen therapy**

All patients should receive appropriate oxygen therapy with monitoring of oxygen saturation and inspired oxygen concentration with the aim to maintain PaO_2 at 60 mm Hg or above and SpO_2 between 94%–98%.

2.1. High concentrations of oxygen can safely be given in patients who are not at risk of hypercapnic respiratory failure.

2.2. Oxygen therapy in patients at risk of hypercapnic respiratory failure complicated by ventilatory failure should be guided by repeated ABG measurements.

3. **Ventilatory support**

Patients with CAP who develop acute respiratory failure require mechanical ventilation for maintaining gas exchange with minimal complications.

4. Management of complications

4.1 Parapneumonic effusion/empyema

4.1.1. Early thoracocentesis is indicated for all patients with a parapneumonic effusion.

4.1.2. Patients found to have an empyema should have effective pleural fluid drainage and appropriate antibiotic therapy. Streptokinase may be instilled if loculation(s) present.

4.2 Lung abscess

This condition is described in detail in another chapter

b. Out Patient

Not applicable.

VI. WHO DOES WHAT? and TIMELINES

a. ***Doctor:*** diagnosis and management including counseling

b. ***Nurse:*** implementation of orders, monitoring of patients and counseling

c. Technician: investigations

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1.Physician 2.Nurse 3.Radiographer 4. Laboratory technician	1.Chest X-ray 2. USG chest 3. Pulse oximetry 4. ABG 5. Serum biochemistry 6. Hemogram 7. Sputum smear and culture 8. Sputum for AFB 9. Blood culture 10. HIV ELISA for high risk group	1.Oral and i.v. antibiotics 2. Streptokinase	1. X-ray machine 2. USG machine 3. Pulse oximeter 4. ABG machine 5. Oxygen cylinders 6. Nebulizers 7. Microbiology laboratory services 8. Hematology and biochemistry laboratory services
2	Above plus 1.Intensivist 2.Nurse and technician for assisting with bronchsocopy 3.Nursing staff trained in ICU care 4.Pathologist	Above plus 1.CT chest 2.Bronchoscopy	Above plus 1.Oxygen supply 2.Tubes and other disposables for thoracocentesis (when indicated)	Above plus 1.CT machine 2.Bronchoscope and facilities for bronchoscopy 3.Clinical pathology laboratory service 4.Microbiology service with conventional, serological and molecular diagnostic facilities for aetiological diagnosis confirmation 5.ICU 6.Noninvasive and invasive ventilators

PULMONARY HYPERTENSION

I. WHEN TO SUSPECT/ RECOGNIZE?

a) Introduction:

The diagnosis of pulmonary hypertension requires strong clinical suspicion in practice. It is usually found secondary to various systemic causes, the list of which is long but the usual causes include the rheumatic heart disease, and diseases of the respiratory system, including the obstructive airway diseases and the diffuse parenchymal pulmonary diseases. Dilation and hypertrophy of the right ventricle develops in response to diseases of the pulmonary vasculature and/or lung parenchyma, which is known as cor pulmonale. Pulmonary hypertension may also occur as primary idiopathic disease due to the mutation of certain genes, such as BMPR-2.

b) Case definition:

Secondary hospital: presence of a pulmonary artery systolic pressure more than 40 mmHg at rest, calculated by the tricuspid velocity jet by trans-thoracic echocardiography.

Super-speciality hospital: presence of a mean pulmonary artery pressure (PAP) of more than 25 mmHg at rest, pulmonary capillary wedge pressure < 15 mmHg, accompanied by increased pulmonary vascular resistance (PVR) (more than 160 dynes/s/cm^5), by right heart catheterisation.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

No systematic studies till date to define the incidence of pulmonary hypertension in our country

III. DIFFERENTIAL DIAGNOSIS

1. Pulmonary artery hypertension (PAH)

1.1 Idiopathic

1.2 Heritable

1.2.1 BMPR2 (chromosome 2, autosomal dominant)

1.2.2 ALK1, endoglin (with or without hereditary haemorrhagic telangiectasia)

1.3 a) Drugs: aminorex, fenfluramine, dexfenfluramine, cocaine, phenylpropanolamine, amphetamines, L- tryptophan, methamphetamines, chemotherapeutic agents, fluoxetine, pergolide, oral contraceptives, oestrogen

b) Toxins: toxic rapeseed oil

1.4 Associated with (APAH)

1.4.1 Connective tissue diseases
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart disease
1.4.5 Chronic haemolytic anaemia: sickle cell anaemia
1.4.6 Schistosomiasis

1* Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

2. Pulmonary hypertension due to left heart disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular heart disease

3. Pulmonary hypertension due to lung diseases and/or hypoxia

3.1 Chronic obstructive pulmonary disease (COPD)
3.2 Diffuse parenchymal lung disease (DPLD)
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep related breathing disorders (SRBDs)
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

4. Chronic thrombo-embolic pulmonary hypertension

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

5.1 Haematological disorders: myeloproliferative disorders, splenectomy.
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis,
lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher's disease, thyroid disorders
5.4 Others: tumoural obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

IV. PREVENTION AND COUNSELING

Early diagnosis by strong clinical suspicion in clinical settings, and appropriate treatment of the underlying cause.

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

***Situation 1: At Secondary Hospital/ Non-Metro situation: Optimal Standards of Treatment in Situations where technology and resources are limited**

ee) **Clinical Diagnosis**:

Patient presents with dyspnoea on exertion, fatigue, chest pain, palpitations, syncope, and lower extremity oedema. Examination reveals raised jugular pressure, left parasternal lift, right ventricular S_4 , accentuated P_2, early systolic click, midsystolic ejection murmur or early diastolic murmur at pulmonary area (Graham Steell)

ff) **Investigations**:

To confirm pulmonary hypertension, and determining the underlying cause.

- Electrocardiogram
- Chest radiograph
- Trans-thoracic 2-D Doppler echocardiography

- Pulmonary function test
- Arterial blood gas analysis

gg) <u>Treatment:</u>

General measures

- Avoid heavy physical exertion or isometric exercise
- Sodium restricted diet (less than 2.5 g per day)
- Annual immunization against influenza
- Avoid pregnancy (female patients)
- Anticoagulants : idiopathic/chronic thrombo-embolism
- Diuretics
- Long-term oxygen supplementation to maintain oxygen saturation > 90%

Specific treatment

- Treat the underlying cause of pulmonary hypertension
- Pulmonary hypertension-specific agents
    - Sildenafil*

*20 mg 24 hourly gradually increased upto 20 mg 8 hourly with careful blood pressure monitoring. The drug can be used in PAH secondary to connective tissue diseases, chronic pulmonary thromboembolism and idiopathic pulmonary artery hypertension.

hh) **<u>Referral criteria:</u>**

- Diagnosis not confirmed with echocardiography and patient requires right heart catheterisation
- Underlying cause not clear, before labelling as idiopathic pulmonary artery hypertension
- Worsening clinical condition of the patient
- Suspected thrombo-embolism

<u>*Situation 2: At Super Specialty Facility in Metro location where higher-end technology is available</u>

y) <u>Clinical Diagnosis</u>: Same as level 1

z) <u>Investigations:</u>

Same as level 1, in addition

- CT pulmonary angiography (CTPA)
- Ventilation-perfusion scan
- Multi-detector CT chest
- Overnight supervised polysomnography
- Connective tissue disease work up : ANA/RF/ANCA/ anticentromere antibodies
- HIV ELISA, CD4 count, plasma viral load (screening for pulmonary hypertension not indicated routinely in ART clinics)
- Functional tests : 6-minute-walk test, cardio-pulmonary exercise test
- Right heart catheterization with acute vasodilator testing

aa) <u>Treatment:</u>

Same as level 1, in addition

- Pulmonary hypertension-specific agents
  - Calcium channel blockers (only in patients with positive acute vasodilator test)
  - Sildenafil* 20 mg 24 hourly gradually increased upto 20 mg 8 hourly with blood pressure monitoring
  - Bosentan* 62.5 mg 12 hourly for 4 weeks, followed by
    125 mg 12 hourly (monitor liver functions monthly)

* These drug can be used in PAH secondary to connective tissue diseases, chronic pulmonary thrombo-embolism and idiopathic pulmonary artery hypertension.

Surgical intervention

- Pulmonary thrombo-endarterectomy for chronic thrombo-embolic pulmonary hypertension
- Atrial septostomy
- Lung and combined heart-lung transplantation (for refractory cases)

VI. WHO DOES WHAT? and TIMELINES

a. **Doctor**
   Screening, diagnosis, treatment and follow-up
b. **Nurse**
   Investigations and follow-up
c. **Technician**
   Investigations

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1.Physician 2.Nurse 3.Radiographer 4.Lab technician 5.Physician with training in echocardiography/ cardiologist	1.Electrocardiogram 2.Chest X-ray 3.Trans-thoracic 2-D echo 4. Arterial blood gas analysis 5. Pulmonary function test	Sildenafil	1.X-ray machine 2.ECG machine 3.ECHO machine 4.Spirometer along with 6-MWT facility 5.ABG analyzer
2	Above plus 1.Radiologist 2.Physician with sleep medicine training 3.Cardiologist 4.Cardiothoracic and vascular surgeon 5.Microbiologist 6.Nursing staff for OT, catheterization laboratory 7.Technician for sleep laboratory 8.Technician for clinical laboratory services 9.Nuclear Medicine expert	Above plus 1.Contrast-enhanced CT chest, High-resolution CT chest for underlying pulmonary parenchymal disease, CTPA (CT pulmonary angiography) 2.Ventilation-perfusion scan 3.Overnight polysomnography 4.Connective tissue disease work up : ANA/RF/ANCA/ anticentromere antibodies 5.HIV ELISA*, CD4 count, plasma viral load 6.Functional tests : 6-minute-walk test, cardio-pulmonary exercise test 7.Right heart catheterization with acute vasodilator testing	1.Sildenafil 2.Calcium channel blockers 3.Bosentan	Above plus 1.USG with Doppler machine 2.CT machine 3.Sleep laboratory 4.Rheumatology laboratory service with facilities for connective tissue disorders work-up 5.Cardiopulmonary exercise testing laboratory 6.Cardiac catheterization laboratory 7.ICTC centre for HIV testing, facilities for CD4 cell counts, plasma viral load estimation 8.CTVS operating theatre, recovery room and post-op facilities

SARCOIDOSIS

I. WHEN TO SUSPECT/ RECOGNIZE?

a) Introduction:

Sarcoidosis is a systemic disorder of unknown origin characterized by granulomatous inflammation in a variety of organs, most commonly the lungs. It affects people of all racial and ethnic groups. Sarcoidosis cases are increasingly being reported from India since the second half of the last century. The accurate diagnosis of sarcoidosis and the ability to differentiate it from tuberculosis are challenges to physicians especially in countries with high prevalence of tuberculosis.

b) Case definition (for both situations of care):

Patients with sarcoidosis may present to different specialties as sarcoidosis is a multiorgan disorder. The clinical feature may vary depending on the ethnicity, duration of illness, site and extent of organ involvement and activity of the granulomatous process. Lung manifestations are seen in almost all (> 90%) patients. Predominant pulmonary symptoms (30-50%) include dry cough [Indian patients experience frequent exacerbation (especially dry cough and wheezing) with seasonal change], dyspnea and chest pain.

Organs other than lungs, usually involved in sarcoidosis include skin (macules, papules, plaques, erythema nodosum and rarely lupus pernio), joints (arthralgias more common than arthritis), eye (anterior and posterior uveitis), liver and spleen (granulomatous hepatitis, hepatic cirrhosis and portal hypertension), peripheral lymph nodes, parotid, salivary glands (commonly parotid, rarely lacrimal and submandibular glands), nervous system [cranial nerve palsies (facial nerve involvement being commonest), headache, ataxia, cognitive dysfunction, weakness and seizures), heart (conduction blocks, tachy- and brady- arrhythmias cardiomyopathy with or without congestive cardiac failure, and sudden death), kidney (hypercalciuria more common than hypercalcemia, and renal failure) and. Sarcoidosis is an unusual cause of fever of unknown origin. Constitutional symptoms such as fever, night sweats, fatigue and weakness, anorexia and weight loss are found to be more common in Indian patients. Many asymptomatic patients (30-50%) are discovered when a chest radiograph is obtained for screening purposes. Tuberculin skin testing frequently reveals anergy.

II) Incidence of the condition in our country

The true burden of sarcoidosis in India is not clearly known as systematically documented reliable epidemiological data are not available. In general, at a secondary level hospital, 1-2 cases per month and at a specialty hospital, 1-3 cases per week are likely to be seen.

III) Differential Diagnosis from other granulomatous diseases (as below)

1. **Diseases due to Infective agents**
    - **a) Mycobacterial**
        - **i.**Tuberculosis
        - ii.Atypical mycobacterial infection
    - **b) Fungal**
        - **i.** Histoplasmosis
        - ii. Coccidiodomycosis
    - **c) Bacterial**
        - **i.** Brucellosis
        - ii. Chlamydia infection
        - iii. Tularemia
    - **d) Parasitic**
        - **i.** Leishmaniasis
        - ii.Toxoplasmosis
2. **Diseases due to exposure of organic or inorganic agents**
    - a) Chronic hypersensitivity pneumonitis (Farmer's lung)
    - b) Pneumoconiosis (especially silco-tuberculosis)
    - c) Talc
    - d) Granulomatous diseases related to metals
        - i**.** Titanium
        - ii. Aluminium
        - iii. Zirconium
        - iv. Chronic beryllium disease
    - e) Methotrexate pneumonitis
3. **Neoplasia**
    - a) Lymphoma
    - b) Tumour-related granuloma
4. **Autoimmune disorder**
    - a) Granulomatous vasculitis (Wegener's)

b) Primary biliary cirrhosis
c) Churg-Strauss syndrome

IV) Prevention and counseling

Sarcoidosis is considered as a benign disease with a tendency to wax and wane either spontaneously or in response to treatment. It has been reported that 60-70% of patients have spontaneous remission and 10-30% of patients have a chronic course. Permanent sequelae are observed in 10-20 % of patients.

V) OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

*Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited

a) Diagnosis

Secondary hospital

1. History (occupational and environmental exposure; symptoms)
2. Physical examination with emphasis on lung, skin, eye, liver, heart, nervous system and salivary glands
3. Peripheral blood counts (white blood cells, red blood cells, platelets)
4. Serum chemistry (calcium, liver enzymes, creatinine, blood urea nitrogen and angiotensin converting enzyme)
5. Urine analysis (routine and 24-hr urinary calcium)
6. Chest radiograph (postero-anterior view)
7. Abdominal ultrasound
8. Tuberculin skin test
9. Spirometry
10. Electrocardiogram (ECG)
11. Biopsy of superficial organs (e.g. skin, lymph nodes)

A provisional diagnosis of sarcoidosis can be made based on clinic-radiographic findings with a negative tuberculin skin test result. Sarcoidosis is a possibility when chest radiograph shows bilateral hilar adenopathy in an asymptomatic patient. In some cases, erythema nodosum and bilateral hilar adenopathy on chest radiographs with fever and arthritis (Lofgren syndrome) suggests sarcoidosis. The diagnosis can be established when clinic-radiographic findings are supported by histological evidence of non-caseating granulomatous inflammation in one or more of the involved organs; other causes of granulomas should be excluded. A diagnosis of sarcoidosis is reasonably certain without biopsy in patients who present with Löfgren's syndrome. In all other cases, a biopsy specimen should be

obtained from the involved organ that is most easily accessed, such as the skin, peripheral lymph nodes, lacrimal glands, or conjunctiva. If diagnosis requires pulmonary tissue, transbronchial biopsy by means of bronchoscopy has a diagnostic yield of at least 85% when multiple lung segments are sampled. If biopsy of a deep organ is required, the patient may require referral to a specialty hospital.

***Situation 2: At Tertiary hospital where higher-end technology is available**

In addition to the investigations suggested under secondary hospital, the following investigations should be available at the super-specialty hospital.

1. Contrast enhanced and high resolution chest tomography.
2. ^{18}F-fluorodeoxyglucose positron-emission tomography (^{18}FDG PET-CT) may be useful in assessing the extent of organ involvement and in pinpointing the candidate organ(s) for diagnostic biopsy.
3. Pulmonary function tests [spirometry, lung volumes, carbon monoxide diffusing capacity (DLCO), and 6-min walk test (6MWT)
4. Arterial blood gas analysis
5. Biopsy to obtain histological confirmation of non-caseating granulomas (with special stains and cultures to exclude tuberculosis, fungal diseases and malignancy)
6. Fibreoptic bronchoscopy including endobronchial and transbronchial lung biopsy and bronchoalveolar lavage to rule out infectious etiology
7. Ophthalmic evaluation with slit-lamp examination
8. Other tests depending on clinical presentation and suspicion of extrathoracic disease
9. Mediastinoscopy, video-assisted thoracoscopic surgery (VATS), open lung biopsy

c) Treatment

Secondary hospital

Asymptomatic patients with normal lung function and patients with minimal, well tolerated symptoms, mild functional abnormalities and with chest X-ray stage 1 should be observed without treatment because of the potential for spontaneous improvement. These patients require treatment only if symptom develops or lung function deteriorates. Patients with symptoms and with chest X-ray stages 2 to 4 can be treated with corticosteroids. Pulmonary sarcoidosis is treated with

prednisolone (30-40 mg/day, gradually tapered to 5-10 mg/day over 2-3 months; Indian patients don't require higher dosages). Treatment should be continued for a minimum duration of 12 months. Patients with cough alone can be treated with inhaled corticosteroids. Topical steroids have also been found to be useful in

some patients with skin sarcoidosis, nasal involvement, or uveitis. Hydroxychloroquine should be added in patients with cutaneous and joints manifestations. Sarcoidosis patients with multi-organ involvement, requiring further investigations and alternate forms of treatment can be referred to a tertiary care super specialty hospital.

Super-specialty hospital

In addition to the treatment recommended for patients at secondary hospital, patients with severe ocular disease, neurosarcoidosis, cardiac sarcoidosis and malignant hypercalcaemia require treatment with oral corticosteroids as the first-line treatment. Several patients (~25%) relapse after discontinuation of corticosteroid therapy and some with frequent relapses may require indefinite therapy.

Patients with sarcoidosis requiring long-term corticosteroids therapy and those with comorbidities e.g. diabetes, hypertension and who suffer from major side-effects of steroids can be offered steroid-sparing alternative treatments. Relapses of sarcoidosis may also require alternate steroid sparing drugs. Prednisolone requirement has been found to be considerably reduced in patients receiving methotrexate (5-15 mg weekly) for six months. Folic acid 1 mg/day may reduce toxicity of methotrexate. Other cytotoxic drugs for sarcoidosis are azathioprine (50-200 mg/day) and cyclophosphamide (50-150 mg/day). The antimalarial drugs chloroquine and hydroxychloroquine (200-400 mg/day for 6 months) have been found to be useful in lupus pernio, nasal sarcoidosis, disfiguring skin sarcoidosis and hypercalcaemia. As hydroxychloroquine is found to be less toxic, it can be used for prolonged periods without retinal damage. Hydroxychloroquine has also

been reported to be useful in chronic pulmonary sarcoidosis and also in neurosarcoidosis failed on corticosteroid treatment. Refractory sarcoidosis can be treated with infliximab intravenously 3-5 mg/kg (2wkly for 2 doses initially and later on 3-10mg/kg every 4-8 wkly

VI) WHO DOES WHAT? and TIMELINES

a. ***Doctor*** Diagnosis and Management including counseling

b. ***Nurse*** Implementation of orders, monitoring of patients and counseling

c. ***Technician*** Investigations

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RESOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1. Physician 2.Nurse 3.Laboratory technician 4.Pulmonary function test technician 5.Radiographer	1.Chest X-ray 2.Hemogram, serum chemistry 3.Serum ACE levels 4.Pulmonary function tests 5.Electrocardiogram 6. Tuberculin skin test 7. ABG analysis 8. 2D-Echo	Oral corticosteroids Tuberculin PPD, syringes	1.X-ray machine 2.Spirometer 3.EKG machine 4.Clinical laboratory services including serum ACE levels 5. ABG analyzer 6. ECHO machine
2	As above plus 1.Interventional radiologist, 2.Thoracic surgeon 3.Anaesthetist 4.Pathologist 5.Nuclear medicine expert 6.Opthalmologist 7. Nursing staff trained in assisting thoracic surgery	Above plus 1.Contrast-enhanced CT chest and High-resolution CT chest for underlying pulmonary parenchymal disease 2.Tissue biopsies 3.Ophthalmic evaluation 4.PET-CT scan (if available) 5.Mediastinoscopy, VATS	Above plus methotrexate, hydroxychloroquine, azathioprine, cyclophosphamide, infliximab	Above plus 1.CT machine 2.Bronchoscope 3.Pathology service for interpretation of histopathological specimens 4.Ophthalmic evaluation setup including slit lamp examination 5.Nucelar medicine facility for PET-CT (if available) 6.Mediastinoscope 7.Video-assisted thoracoscope

RESPIRATORY FAILURE

I. WHEN TO SUSPECT/ RECOGNIZE?

a) Introduction:

The respiratory system performs the vital function of gas exchange. Respiratory failure results when the respiratory system fails in one or both of its gas exchange functions of oxygenation and carbon dioxide elimination. Depending on the rapidity of development, respiratory failure can also be classified into (i) acute; (ii) acute on chronic; and (iii) chronic respiratory failure. Acute respiratory distress syndrome (ARDS) is a special type of acute respiratory failure and has been dealt with in a separate chapter and will not be discussed in this chapter.

b) Case definition:

For both situations of care *(mentioned below*)*

Based on the arterial blood gas (ABG) analysis, respiratory failure may be classified as (i) type I (hypoxaemic) respiratory failure; and (ii) type II (hypercapnic) respiratory failure. Type I respiratory failure is characterized by arterial oxygen tension (PaO_2) less than 60 mm Hg with a normal or low partial pressure of arterial carbon dioxide ($PaCO_2$). Type II respiratory failure is characterized by arterial hypoxaemia (PaO_2 less than 60 mm Hg) and a $PaCO_2$ greater than 50 mm Hg. Acute respiratory failure develops over minutes to hours; chronic respiratory failure develops over several days or longer.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

No systematic studies have been carried out till date to define the incidence of acute or chronic respiratory failure in India and reliable epidemiological data are lacking.

III. DIFFERENTIAL DIAGNOSIS

Even though, several conditions (e.g., bilateral diaphragmatic paralysis, obstructive sleep apnoea) may mimic respiratory failure clinically, ABG analysis is essential for establishing a diagnosis of respiratory failure.

IV. PREVENTION AND COUNSELING

1. Optimal treatment of underlying diseases that can result in respiratory failure.
2. Abstinence from smoking, alcohol and other substance abuse drugs.
3. Early diagnosis by a high index of clinical suspicion in relevant clinical settings and institution of appropriate treatment of the underlying cause.

V. OPTIMAL DIAGNOSTIC CRITERIA, INVESTIGATIONS, TREATMENT & REFERRAL CRITERIA

***Situation 1: At Secondary Hospital: Optimal Standards of Treatment in Situations where technology and resources are limited**

The following clinical scenarios raise the suspicion of respiratory failure. However, ABG analysis is eventually required to diagnose respiratory failure.

a) **Clinical Diagnosis**

Acute respiratory failure

Symptoms

Symptoms at presentation in patients with acute respiratory failure can be due to hypoxaemia, hypercapnia and the manifestations due to the aetiological cause.

1. Manifestations of hypoxaemia

1.1 Acute onset hypoxaemia results in dyspnoea, irritability, impaired intellectual function, altered sensorium, progressing convulsions, coma and death

1.2 Cardiac arrhythmias may develop especially if there is dyselectrolytaemia or if the patient is also receiving diuretics or digitalis

2. Manifestations of hypercapnia

2.1 Patient with rapidly developing hypercapnia often manifests irritability, confusion and somnolence.

2.2 The skin may be warm and flushed

2.3 Tachycardia may be present

2.4 The peripheral pulse may be bounding

2.5 Increased cerebral blood flow and intracranial tension may manifest as papilloedema

2.6 Asterixis, tremor, myoclonic jerks, and seizures may also develop

2.7 Coma may ensue

3. *Manifestations due to aetiological cause*

3.1 Patients presenting with pneumonia may present with a history of a febrile illness, cough and sputum production.

3.2 When acute respiratory failure develops in the setting of human immunodeficiency virus (HIV) infection, or organ transplantation, *Pneumocystis* pneumonia, bacterial and fungal pneumonias constitute important treatable causes of acute respiratory failure.

3.3. In persons with acquired immunodeficiency syndrome (AIDS), paradoxical worsening of opportunistic infections, termed immune reconstitution inflammatory syndrome (IRIS) has been described shortly after the initiation of highly active antiretroviral therapy (HAART).

3.4. A history of poisoning with substances such as organophosporus pesticides, sedatives, hypnotics, and other drugs with potential for causing respiratory depression may sometimes be evident.

3.5. In the setting of sepsis syndrome, trauma, pancreatitis, onset of acute respiratory failure may indicate development of ARDS (also known as non-cardiogenic pulmonary oedema)

Signs

1. Physical examination of the respiratory system may reveal localising clues in patients with conditions such as pneumonia, pulmonary oedema, asthma, or chronic obstructive pulmonary disease (COPD).

2. Central cyanosis, tachycardia and peripheral vasodilatation may be evident.

3. Presence of pulsus alternans, evidence of left atrial hypertension in the form of left parasternal heave, loud pulmonary component of the second heart sound, gallop rhythm, cardiac murmurs, clicks, rub, may point to cardiogenic pulmonary oedema as the cause of respiratory failure, while their absence may point to ARDS.

4. Areflexic flaccid quadriparesis in a febrile patient should arouse a suspicion of acute anterior poliomyelitis.

5. Ascending paralysis suggests a possibility of acute inflammatory demyelinating polyneuropathy (AIDP).

6. Trismus, muscle spasms suggest a possibility of tetanus.

7. Acute respiratory failure requiring mechanical ventilation due to myasthenic crisis may be the first manifestation of myasthenia gravis.

Chronic respiratory failure

Symptoms

Symptoms at presentation in patients with chronic respiratory failure can be due to hypoxaemia, hypercapnia and the manifestations due to the aetiological cause

1. Manifestations of chronic hypoxemia

1.1 When it develops gradually, hypoxaemia is surprisingly well tolerated and dyspnoea on exertion may be the only complaint.

1.2 Patients with chronic respiratory failure due to interstitial lung disease, pneumoconiosis, fibrosing alveolitis often complain of progressively worsening dyspnoea.

2. Manifestations of chronic hypercapnia

2.1 Headache on waking up in the morning may be a common complaint.

Signs

1. The skin may be warm and flushed
2. Tachycardia may be present
3. Peripheral pulse may be bounding.
4. Increased cerebral blood flow and intracranial tension may manifest as papilloedema.
5. Asterixis, tremor, myoclonic jerks, and seizures may also develop.
6. Central cyanosis and signs of cor-pulmonale may also be evident.
7. Kyphoscoliosis, thoracic cage abnormalities, findings suggestive of underlying causes such as hypothyroidism, motor neuron disease or muscular dystrophy may be present.

b) **Investigations**

1. Pulse oximetry: pulse oximetry helps in detecting arterial hypoxemia
2. Chest radiograph: chest radiograph can help in identifying cause of respiratory failure and ruling out other causes such as pneumothorax.
3. Echocardiography: useful in differentiating acute respiratory failure from cardiogenic pulmonary oedema.
4. ABG analysis: ABG analysis is necessary to confirm the diagnosis of respiratory failure

c) Treatment:

Standard Operating procedure

a. In Patient

General therapeutic measures

1. SpO_2 monitoring by pulse oximetry
2. Treatment of the aetiological cause of acute respiratory failure (e.g., antibiotics for bacterial pneumonia).
3. In acute exacerbation of COPD, nebulized beta-2 agonists, ipratropium and parenteral corticosteroid administration.

Supplemental oxygen therapy

Acute type I respiratory failure

1. Initially, spontaneous ventilation using a face mask with a high flow gas delivery system can be used to deliver a FiO_2 of up to 0.5 to 0.6.
2. Continuous positive airway pressure (CPAP) may be added to improve PaO_2 without increasing FIO_2.

Acute type II respiratory failure

1. In patients with type II respiratory failure, high flow oxygen therapy can be detrimental. *Controlled oxygen delivery* can be administered through nasal prongs at 1 to 1.5 L/min or by a Venturi mask with the flow set to deliver 24% to 28% oxygen (the Venturi mask has the advantage of delivering a predictable FiO_2, but the nasal prongs are better tolerated by the patient).

b. Out Patient

Acute respiratory failure is managed in an intensive care (ICU) unit setting.

d) Referral criteria:

1. Diagnosis not clear. Even though clinical manifestations of hypoxemia and hypercapnia may raise the suspicion of respiratory failure, ABG analysis is essential for diagnosing respiratory failure. Hence, patients with suspicion of respiratory failure should be referred to a tertiary hospital where higher-end technology is available.
2. Hemodynamic instability

***Situation 2: At Tertiary care hospital where higher-end technology is available**

a) **Clinical Diagnosis**

As in situation V.1 a) above

b) **Investigations**

1. As in situation V.1b) above PLUS
2. Computed tomography of chest
3. *Tests for pulmonary thromboembolism*
   3.1 Doppler studies for deep vein thrombosis
   3.2 CT pulmonary angiography
   3.3 D-dimer estimation
   3.4 V/Q scanning
4. Diagnostic testing to establish the aetiological cause of respiratory failure

c) **Treatment:**

As in situation V.1 c) above PLUS

1. Respiratory stimulants

In patients with type II respiratory failure, hypercapnia and acidosis, who are awaiting initiation of non-invasive ventilation (NIV), when NIV is not available or is poorly tolerated respiratory stimulants such as doxapram (initial dosage 5 mg/min, reducing according to the response to 1 to 3 mg/min; maximum dosage 600 mg) for short periods (24 to 36 hours) can be tried.

2. Ventilatory support

If the arterial hypoxemia does not get corrected with the measures described above, ventilatory support may be required.

2.1 Non-invasive ventilation

2.1.1 NIV modalities such as continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP) are used in the management of acute respiratory failure.

2.1.2 NIV has been particularly found to be useful in the management of acute respiratory failure due to acute exacerbations

of COPD, decompensated congestive heart failure with mild to moderate degree of pulmonary oedema, *Pneumocysits* pneumonia and if severe co-morbid illnesses are present, among others. However, NIV should be considered as a therapeutic option only at centers equipped with facilities for tracheal intubation and mechanical ventilation. Excessive secretions and unconscious patient are contraindications for NIV.

2.2 Mechanical ventilation

2.2.1 When other measures fail to maintain adequate respiratory effort, tracheal intubation and assisted mechanical ventilation will be required.

2.2.2. The mode of ventilation should be individualised to suit the needs of the patient. Following the initiation, the ventilator settings should be adjusted based on the patient's underlying

disease process, gas exchange, lung mechanics, and response to mechanical ventilation.

2.2.3. Aims of assisted ventilation in patients with respiratory failure due to COPD and asthma include decreasing the load of the respiratory muscles, ensuring adequate oxygenation, and minimizing the development of dynamic hyperinflation and its associated adverse consequences. Care must be exercised to avoid causing further hyperinflation, and the set level of external PEEP should always be less than the level of intrinsic PEEP.

2.2.4. In patients with acute severe asthma, development of dynamic hyperinflation can be minimised by delivering the lowest possible minute ventilation in the least possible time.

3. Weaning from mechanical ventilation

3.1 A patient who has stable underlying respiratory status, adequate oxygenation, intact respiratory drive, and stable cardiovascular status should be considered for weaning.

c. Out Patient

1. Acute respiratory failure is managed in an intensive care (ICU) unit setting

2. Chronic respiratory failure can be managed in the out-patient setting, ideally, at a tertiary health care level; however, many patients are managed at secondary level health care also.

2.1 Drug treatment

Drugs, such as, including medroxyprogesterone, acetazolamide, protriptyline, and almitrine bismesylate can be used for the management of chronic ventilatory failure.

2.2 Domiciliary oxygen therapy

Patients with COPD and chronic respiratory failure must be encouraged to ambulate. Controlled, low flow oxygen therapy (1 to 2 L/min) is administered for at least 15 hours a day. Compressed gas cylinders, liquid oxygen and oxygen concentrators have been used for domiciliary

oxygen therapy. Delivery devices that have been used include nasal prongs, cannulae and face masks. Since long-term oxygen therapy (LTOT) is expensive, oxygen conserving devices such as reservoir oxygen

delivery; electromechanical pulsing devices; and trans-tracheal catheter delivery can be used. For the outdoor activities, very light weight battery operated portable oxygen concentrators can be used, but, these are 4-5 times more expensive than the usual concentrators. Alternatively, light-weight oxygen cylinders which can be refilled by the oxygen concentrators can be used.

VI. WHO DOES WHAT? and TIMELINES

a. ***Doctor.*** Diagnosis and management including counseling

b. ***Nurse.*** Implementation of orders, monitoring of patients and counseling

c. Technician Investigations

d. Respiratory physiotherapist For administering supportive care to patients admitted in ICU

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SOURCES REQUIRED FOR ONE PATIENT

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1	1. Physician 2. Nurse 3. Radiographer 4. Technicians for performing pulmonary function testing 5. Physician with training in echocardiography	1. Pulse oximetry 2. Chest X-ray 3. ABG analysis 4. Echocardiography 5. Pulmonary function testing	1. Oxygen 2. Inhaled bronchodilators (salbutamol, ipratropium) 3. ICS (fluticasone/ budesonide)+ LABA (formoterol/salmeterol) 4. Parenteral and oral bronchodilators (theophylline, terbutaline) 5. Parenteral and oral steroids (hydrocortisone, prednisolone) 6. Parenteral and oral antibiotics	1. Oxygen cylinder 2. Oxygen concentrator 3. Ventilator for NIV 4. Mechanical ventilator 5. Nasal prongs 6. MC mask 7. X-ray machine 8. Pulse oximeter 9. Spirometer 10. ABG machine 11. Echocardiography machine
2	Above plus 1. ICU staff with pulmonary training 2. Respiratory physiotherapists 3. Radiologist 4. Nuclear medicine expert	Above plus 1. Computed tomography including CT pulmonary angiography 2. Doppler studies 3. D-dimer estimation 4. V/Q scanning	Above plus 1. Respiratory stimulants 2. Higher antibiotics	Above plus 1. CT machine 2. USG with Doppler machine 3. V/Q scanning machine 4. Clinical pathology laboratory service for D-dimer estimation 5. ICU set-up 6. Noninvasive and invasive ventilators