

GUIDELINES FOR THE MANAGEMENT OF CRITICAL CARE

**Ministry of Health & Family Welfare
Govt. of India**

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(COPD)

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I. WHEN TO SUSPECT/ RECOGNIZE?

a) **Introduction:**

Chronic obstructive pulmonary disease (COPD) refers to a group of disorders characterized by chronic airflow obstruction/limitation. The airway obstruction is persistent and largely irreversible. It includes two distinct pathophysiological processes - chronic bronchitis and emphysema. Acute exacerbations of these disorders occur during the natural history of progression of this disease. Exacerbations are frequent, more so during winter, resulting in progressive loss of the functional capacity of the lungs leading to progressive dyspnea.

b) **Case definition:**

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

There are many definitions for what represents an acute exacerbation of COPD. One of the most widely used definitions evaluates the severity of exacerbation based on three symptoms:

- i. worsening dyspnea
- ii. increase in sputum purulence
- iii. an increase in sputum volume

Type I exacerbation (severe) have all three symptoms and Type 2 exacerbations (moderate) exhibit two of three symptoms. Type 3 exacerbation (mild) include one of the symptoms and at least one of the following: upper respiratory tract infection within the past 5 days, fever without apparent cause, increased wheezing, increased cough, or a 20% increase in respiratory rate or heart rate over baseline.

II INCIDENCE OF THE CONDITION IN OUR COUNTRY

COPD is currently the fourth leading cause of death worldwide behind cardiovascular disease, cancer and cerebrovascular diseases. The Global Burden of Disease Study estimated that in 1990, the worldwide prevalence of COPD was 9.34 per 1000 men and 7.33 per 1000 women. Depending on the severity of the disease, the 5-year mortality rate for patients with COPD varies from 40% to 70%. The three major causes of death have been identified as COPD itself, lung cancer and cardiovascular disease.

The prevalence rates of COPD in males varied from 2.12% to 9.4% in studies conducted in north India and from 1.4% to 4.08% in south India. The respective ranges for females were 1.33% to 4.9% in north India and 2.55% to 2.7% in south India. A majority of cases with chronic COPD (57.4%) were found to suffer from a mild form and only 16% had severe COPD.

A large-scale study in Hyderabad city and its surrounding municipalities, covering a population of more than 54 lakh and 28 hospitals/health posts, was done in 2001 to collect cause-specific morbidity data. The rates of hospital admissions of cases with COPD showed an age differential. While the rate was 47.84/100,000 persons at the community level, it was 57.28 for those 18 to 64 years of age and 546.17 for those above 65 years of age. Treatment cost of a patient with COPD per year (in Rs) according to Guidelines is Rs 2126 for moderate to severe disease and Rs 10,538 for acute exacerbation.

III DIFFERENTIAL DIAGNOSIS

Acute exacerbation of COPD should be differentiated from the following disorders

- Congestive cardiac failure
- Bronchial asthma
- Bronchiectasis
- Interstitial lung disease
- Chronic thromboembolic pulmonary disease
- Obesity induced dyspnea
- Chronic destructive lung disease due to old tuberculosis
- Occupational lung disease

IV PREVENTION AND COUNSELING

Avoidance of smoking is the single most important factor in prevention of exacerbation of COPD. Yearly influenza vaccine and 5 yearly Pneumococcal vaccine has also been found to be helpful. Education regarding starting early antibiotics with evidence of exacerbation. Avoidance of pollution is advisable. Early consultation with physician should be strongly encouraged and patient should be educated about the warning signs of acute exacerbation.

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**

a) **Clinical Diagnosis:**

Patient usually presents with a history of chronic cough and exertional breathlessness with recent increase in cough, breathlessness, increased volume and purulence of sputum. There are usually associated constitutional symptoms like fever, malaise and lack of appetite. Patient may be orthopneic and have swelling of feet,

On examination there is increase in respiratory rate, tachycardia, flapping tremor and drowsiness (if retention of carbon dioxide) . Some patients who have predominant chronic bronchitis show features of chronic cor pulmonale (Blue Bloaters) like pedal edema, raised jugular venous pressure, puffy face, central cyanosis, loud pulmonary heart sound and parasternal heave due to right ventricular hypertrophy. On the other patient with predominant emphysema (Pink Puffers) are usually thin built, plethoric due to associated secondary polycythemia, disproportionately dyspneic, features of hyper-inflated lungs like obliteration of liver and cardiac dullness, silent chest.

b) **Investigations:**

- Chest Xray ó To rule out Pneumothorax. Look for consolidation, pleural effusion, cardiomegaly and features of lung hyperinflation. Look for features of past tuberculosis
- Pulse Oximetry
- Sputum for gram stain, Culture and sensitivity, Acid Fast Bacilli stain.
- Hemogram, blood urea, serum creatinine, serum electrolytes
- Electrocardiogram

c) **Treatment:**

- Oxygen therapy: Controlled humidified oxygen therapy with a Venturi mask (fixed performance device) or low oxygen flow (1-2 litres) with nasal cannula or simple face mask (variable performance device) to keep Spo₂ 90-92%. Higher oxygen saturation and high concentration of inspired oxygen should be avoided.
- Bronchodilators:
 - Nebulised beta 2 adrenergic receptor agonists (salbutamol) in patients who are very dyspneic ó 2.5-5 mg nebulised every 4-6 hours and as necessary. Watch for tachycardia or arrhythmias

- Inhaled beta 2 adrenergic receptor agonists in patients who are able to take metered dose inhalers (180 mcg) every 2-4 hours
- Nebulised anticholinergic agent (ipratropium bromide) 0.5 mg every 4-6 hrs
- Inhaled Ipratropium bromide 18-36 mcg every 2-4 hours
- Corticosteroids: Five to 10 days of oral or intravenous corticosteroids is advocated in most cases. Prednisolone 40-60 mg orally or methylprednisolone 60-120 mg intravenously may be used. Appropriate stress ulcer prophylaxis with Ranitidine or Proton Pump inhibitors should be started. Inhaled corticosteroids may be added later when patient has stabilized.
- Antibiotics: The most common organisms identified in acute exacerbation are Streptococcus pneumonia, moraxellacatarrhalis and hemophilus influenza. In patients with more severe and recurrent disease gram negative organisms like Klebsiella pneumonia and Pseudomonas aeruginosa should also be considered. Initial antibiotic choice is empirical. Usually a macrolide antibiotic like azithromycin or clarithromycin or a quinolone like levofloxacin or moxifloxacin is given. Broader spectrum antibiotics are used for severe disease.
- Methylxanthines like aminophylline. Though commonly used in India but given the frequent and severe side effect profile, narrow therapeutic window and lack of evidence demonstrating improved outcomes routine use of these agents is not recommended
- There is no role of mucolytic or chest physiotherapy commonly used practices in acute exacerbation of COPD.

d) Referral criteria:

Following category of patient should be referred to higher centre.

- Patient who will benefit from non invasive ventilation and if this facility is not available in the primary centre
- Patients in need for intubation and mechanical ventilation
- Patient with hemodynamic instability
- Patient not responding to maximal medical treatment
- Patient with acute exacerbation complicated by associated pneumonia, pneumothorax.
- Patient in whom diagnosis is uncertain and needs further investigation.

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

- a) **Clinical Diagnosis:** As in situation 1
- b) **Investigations:**

- Arterial Blood gas analysis ó look for hypercarbia and respiratory acidosis
- Echocardiogram- Low ejection fraction

- D DIMER, Pro BNP ó bio markers for venous thromboembolism and congestive cardiac failure respectively
- CT scan of Chest ó look for other pulmonary disease, pulmonary thrombus
- Venous Doppler of legs- to rule out deep venous thrombosis

c) **Treatment:**

- Noninvasive ventilation should be applied simultaneously to a patient in acute respiratory failure in addition to the rest of the treatment based on the clinical criteria, provided there is no contraindication

Non-invasive Positive Pressure Ventilation (NIPPV) is indicated in patients with appropriate diagnosis with potential reversibility and if patient has any two of the following clinical criteria are fulfilled.

- Moderate to severe respiratory distress
- Tachypnea, (RR more than 25 / min)
- Accessory muscle use or abdominal paradox
- Blood gas derangement pH < 7.35, PaCO₂ > 45 mm Hg
- PaO₂ / FiO₂ < 300 or SPO₂ < 92% with FiO₂ 0.5

CONTRAINDICATIONS

There are no absolute contraindications for the use of NIPPV. Some contraindications have, however, been suggested

- Non-availability of trained medical personnel
- Inability to protect the airways -Comatose patients, patients with CVA or bulbar involvement, confused and agitated patients. Upper airway obstruction
- Hemodynamic instability- uncontrolled arrhythmia, patient on very high doses of inotropes, recent myocardial infarction.
- Inability to fix the interface -Facial abnormalities, facial burns, facial trauma, facial anomaly.
- Severe GI Symptoms ó vomiting, obstructed bowel. Recent GI Surgery., Upper G.I. Bleed
- Life threatening hypoxemia
- Copious secretions
- Conditions where NIPPV has not been found to be effective

Protocol for application of NIPPV For successful noninvasive ventilation.

- a) Patient interface ó Nasal or oronasal mask
- b) Mode of ventilation:
 - 1) Bi-level positive airway pressure--Spontaneous or spontaneous timed mode in portable pressure ventilators or NIV option on conventional ventilators
 - 2) Pressure support /Pressure control /Volume control ó conventional ventilators
- c) Ventilator settings

Explain therapy and its benefit to the patient in detail. Also discuss the possibility of intubation.

- a) Choose the correct size interface. Oronasal mask in acute respiratory failure is preferred.
- b) Set the NIPPV portable pressure ventilator in spontaneous or spontaneous /timed mode. ,
- c) Start with very low settings. Start with low inspiratory positive airway pressure (IPAP) of 6 ó 8 cm H₂O with 2 to 4 cm H₂O of EPAP (Expiratory positive airway pressure). The difference between IPAP and EPAP should be at least 4 cm H₂O.
- d) Administer oxygen at 2 liters per minute.
- e) Hold the mask with the hand over his face. Do not fix it.
- f) Increase EPAP by 1-2 cm increments till all his inspiratory efforts are able to triggers the ventilator.
- g) If the patient is making inspiratory effort and the ventilator does not respond to that inspiratory effort, it indicates that the patient has not generated enough respiratory effort to counter auto PEEP and trigger the ventilator (in COPD patients). Increase EPAP further till this happens. Most of the patients require EPAP of about 4 to 6 cm H₂O. Patient who are obese or have obstructive sleep apnea require higher EPAP.
- h) When all the patient's efforts are triggering the ventilator, leave EPAP at that level.
- i) Now start increasing IPAP in increments of 1-2 cm up to a maximum pressure, which the patient can tolerate without discomfort and there is no major mouth or air leak.
- j) In some NIPPV machine, inspiratory time (Ti) can be adjusted. Setting the Ti at one second is a reasonable approach.

- k) Now secure interface with head straps. Avoid excessive tightness. If the patient has a nasogastric tube put a seal connector in the dome of the mask to minimize air leakage.
- l) After titrating the pressure, increase oxygen to bring oxygen saturation to around 90%.
- m) As the settings may be different in wakefulness and sleep, readjust them accordingly.

When NIPPV is being initiated for acute respiratory failure, close monitoring and the capability to initiate endotracheal intubation and other resuscitation measures should be available in the same setup. Start NIPPV preferably in the ICU or in the emergency room in acute respiratory failure.

Application of NIPPV using a Critical Care Ventilator

- a) The first step is to select a ventilator, which is capable of fulfilling the needs of the patient.
- b) Explain the therapy to the patient
- c) Choose the appropriate mode. Usually pressure support or pressure control modes are preferred. Standard critical care ventilators using flow by system (non invasive mode option) allow the patient to breathe without expending effort to open valves. In selected patients like those suffering from neuromuscular diseases, volume assist or volume control mode may be used.
- d) Choose an appropriate interface
- e) Silent ventilator alarms
- f) Keep FiO₂ 0.5

Using pressure support/control approach

- Start with low settings like inspiratory pressure support at 5-6 cm H₂O and PEEP at 2 cm H₂O.
- Initiate NIPPV while holding the mask in place and confirm optimum fit. If it is big or small or loose, change it.
- Hold the mask .do not fix the headgear
- Now increase PEEP till all his inspiratory efforts are able to triggers the ventilator

- If the patient is making inspiratory effort and the ventilator does not respond to that inspiratory effort, it indicates that the patient has not generated enough respiratory effort to counter auto PEEP and trigger the ventilator (in COPD patients). Increase PEEP further till this happens.
- Once the patient's all inspiratory efforts are triggering the ventilator then start increasing pressure support further, keeping certain patient's comfort in mind. (Reduce respiratory rate, reduced use of accessory muscle etc. Ensure that there are no major leaks.
- When there is significant mouth leak, there may be asynchrony. In that case, pressure control will be the preferred mode of NIPPV and one can set up the inspiratory time to avoid asynchrony.
- After adequate ventilation has been achieved, increase fraction of oxygen concentration to maintain Oxygen saturation more than 90%.
- Secure interface with headgear. It should be tight, but not over-tight. Small leaks are acceptable
- A peak inspiratory pressure more than 25 cm is rarely required in COPD, but higher pressures can be used when using NIPPV for other indications. PEEP is usually titrated between 5-10 cm H₂O to improve triggering and oxygenation.

Patient must be monitored very closely clinically. Look for sensorium, dyspnoea, respiratory rate, respiratory distress, use of accessory muscles, abdominal paradox, Mask comfort and vital signs pulse, blood pressure, ECG monitoring and arterial oxygen saturation, All this must be documented every 15 minutes for the first hour in the clinical notes. Patient will show improvement in parameters if NIPPV is effective. Arterial blood gas sample should be sent after 30mts to 1 hr after the application of NIPPV. In ventilator setting look for air leaks and patient's ventilator interaction.

Monitoring of noninvasive ventilation for acute respiratory failure

Subjective

- Mask comfort

- Tolerance of ventilator settings
- Respiratory distress
- Physical findings
- Respiratory rate

Other vital signs

- Accessory muscle use
- Abdominal paradox
- Ventilator parameters
- Air leaking
- Adequacy of pressure support
- Adequacy of PEEP
- Tidal volume (5-7 mL/kg)
- Patient-ventilator synchrony

Gas exchange

- Continuous oximetry (until stable)
- ABGs, baseline and 1-2 hrs, then as indicated

Initially give NIPPV continuously or as long as possible. Once patient is tolerating periods off NIPPV, start discontinuing during day time and give during nighttime. In two to three days patient can be weaned off from the NIPPV.

- Intubate and initiate mechanical ventilation in following group of patients
 - Those who have failed NIV trial.
 - Those who have contraindications of NIV
 - Excessive secretions
 - Hemodynamic instability
 - Extreme obesity
- Initial Ventilator settings in COPD patient should take into account patients need for prolonged expiration. Appropriate initial ventilator settings would be volume assist control, Tidal volume 8 ml/kg predicted body weight, rate 10-12/min, PEEP of 0-5 cm f H₂O , FiO₂ titrate for SpO₂ 90-92 % . High peak flow 70-90 L/min to keep I:E ratio 1:4 or more .
- Attempt should not be made to attain normal blood gas but to aim for patient's baseline values.
- Monitor for development of auto PEEP by end expiratory manouever or analyzing ventilator graphics.
- Judicious use of sedation and analgesia should be tried

- Neuromuscular blockers should be avoided
- Deep venous thrombosis prophylaxis, Stress ulcer prophylaxis and nutritional needs should be addressed.

VI FURTHER READING / REFERENCES

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ACUTE SEVERE ASTHMA

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II. WHEN TO SUSPECT/ RECOGNIZE?

c) Introduction:

It is a chronic inflammatory disease of the airways characterized by airway hyper reactivity and inflammation, bronchoconstriction and mucus hyper-secretion. Asthma is associated with considerable patient morbidity, a diminution in productivity and increase in health care utilization.

d) Case definition:

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

Acute severe asthma or status asthmaticus is defined as a prolonged episode of severe asthma that is unresponsive to initial standard medical therapy and may lead to respiratory failure.

The episode may be rapid in onset (in a matter of hours) or more typically progress during several hours to days. The former is referred to as asphyxic asthma and occurs in a minority of cases.

III. INCIDENCE OF THE CONDITION IN OUR COUNTRY

The estimated prevalence of asthma in India is 2468 per 100,000 population. Prevalence of acute asthma in age group 15-59 was found to be 40 per 1000,000 populations in India. Prognosis of asthma in general is good but 10-20% of patents continue to have severe attacks throughout their lives. Approximately 10% of patients hospitalized with asthma are admitted to the intensive care unit and 2% are intubated. Mortality rate ranges from 0.5-3% in hospitalized patients.

IV. DIFFERENTIAL DIAGNOSIS

The following should be should be considered in patients with severe breathlessness

- Upper airway obstruction
- Epiglottitis
- Vocal Cord Dysfunction
- Foreign Body aspiration
- Congestive heart failure

V. PREVENTION AND COUNSELING

Morbidity and mortality from asthma disproportionately affects the economically disadvantaged, due to prehospital factors such as access to health care, inadequate preventive therapy or delay in seeking medical treatment

Rapid onset asthma is often triggered by exposure to allergens, irritants, exercise, psychosocial stress, and inhaled illicit drugs. It may also develop after exposure to aspirin, non steroidal anti-inflammatory drugs, or beta blockers in susceptible individuals. Asthma attacks may be triggered by viral or atypical pulmonary infections.

Proper counseling regarding prevention of allergen or precipitating factors should be done. Compliance with anti asthmatic drugs should be ensured and education in its proper use should be done. Early consultation with physician during acute attack is advocated.

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

a) Clinical Diagnosis:

b)

History and Physical Examination

Clinically patients present with dyspnea, cough, chest tightness and wheezing . Severity of asthma may be assessed by the following

- Unable to speak full sentences

- Increased Respiratory rate
- Use of accessory muscle
- Increased Pulse rate
- Pulsus paradoxus (Inspiratory decrease in systolic blood pressure)
- Decrease in sensorium, fatigue
- Auscultation: Wheezes and crackles; silent chest signifies very severe airflow obstruction

b) Investigations:

- Peak expiratory flow rate (PEFR) is an objective measure of airflow obstruction: <30% of baseline/predicted would indicate likelihood of respiratory failure. Initially check every half hour to assess response to therapy
- SPO2: Hypoxia is usually correctable with supplemental oxygen. Refractory hypoxia should trigger search for pneumothorax, atelectasis, pneumonia or occult sepsis.
- Chest x-ray; To rule out pneumothorax, look for degree of hyperinflation, or any lung infiltrate suggestive of atelectasis or collapse consolidation.

c) Treatment:

Initial medical management

- Oxygen supplementation is continued to keep Spo2 more than 90%.
- Nebulized salbutamol 2.5 mg (0.5 ml of 5% solution in 2.5 ml saline) or levosalbutamol, repeat every 20 mins for 3 doses then less frequently dictated by patient's clinical response.
- More frequent and even continuous nebulization of salbutamol at a dose of 10 to 15 mg can be used within limits of toxic effects such as tachycardia and tremors.
- Ipratropium 0.5 mg nebulization every 20 mts should be included in initial treatment concomitantly with salbutamol for better bronchodilatation
- If nebulizer is not available use 4 puffs of salbutamol MDI through a spacer device. Treatment concomitantly with salbutamol for better bronchodilatation

- Corticosteroids should be initiated at the earliest to prevent respiratory failure.. The usual doses are: Inj Hydrocortisone 100 mg every q 6 hourly or methylprednisolone 60-125 mg q 6-8 hourly. Oral prednisolone 60 mg is equally effective.
- Aminophylline may be used as a second-line agent although its role is much debated. A loading dose of 5-6 mg/kg is followed by a continuous infusion of 0.6 mg/kg/hr. Avoid loading dose in case patient has been on oral theophyllines earlier.
- Antibiotics are not required routinely in bronchial asthma exacerbation and should be given only if there is evidence of infection. Quinolones or macrolide may be used only if there is evidence of infection, though most of these are viral in origin.

d) Referral criteria:

The following patients should be referred to higher centre as they have a probability of developing respiratory failure and respiratory arrest.

- Breathless at rest inspite of bronchodilators
- Pulsus paradoxus > 25 mm Hg
- Peak expiratory flow < 60% predicted
- Oxygen saturation < 90%
- Patient getting drowsy or confused
- Bradycardia (<60/min)
- Severe work of breathing and fatigue.

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

d) Clinical Diagnosis: as per situation 1

e) Investigation:

- Arterial blood gases: In asthma normal or elevated PaCO₂ signifies respiratory failure due to respiratory muscle fatigue. pH < 7.28 would raise the need for ventilatory support
- Doppler Echocardiogram to rule out cardiac cause of breathlessness

f) **Treatment:**

- Non-Invasive Ventilation: inspite of medical treatment if respiratory status worsens NIV may be tried as a temporizing measure. IPAP reduces work of breathing and EPAP overcomes auto PEEP. Extended trials of NIV may be warranted if the sensorium and patient comfort are improving. NIPPV is more useful in patients with COPD; there is limited data on its use in acute severe asthma.
- Monitor respiratory rate, SPO₂, heart rate and blood pressure continuously. Reassess every 30 mins until patient is stable and comfortable. Nursing attendance should be continuous.
- Intubate if indicated
 - Impending respiratory arrest
 - Hypotension
 - Altered sensorium: progressive drowsiness, agitation or severe restlessness
 - In a conscious patient no improvement or deterioration after 3-4 hours of optimal medical therapy and NIV support
 - PCO₂ > 55 mmHg and Ph < 7.28. However more than the absolute values the general appearance and degree of distress and fatigue of the patient are important.
- **Orotracheal intubation:** As far a possible a tube size of 8 or more is employed and therefore oro-tracheal route is preferred
- **Sedation and paralysis:** At the time of intubation short acting sedative or anaesthetic such as ketamine, propofol or midazolam and short acting neuromuscular blocking agent (succinylcholine or rocuronium) are used. For maintenance of sedation to assist MV midazolam/ propofol infusion can be used. Neuromuscular blocking agents should be avoided as infusion to prevent critical illness neuropathy.
- **Initial ventilator settings**

Setting	Recommendation
Respiratory rate	10-15 breaths/min
Tidal volume	8-10 ml/kg
Minute ventilation	8-10 l/min
PEEP	0 cm H ₂ O
Inspiratory flow	×100 l/min
I:E ratio	×1:3
FiO ₂	1.00

The goals of ventilation are to

- Maintain oxygenation ($SpO_2 > 90\%$)
- Reduce work of breathing
- Minimise auto-PEEP
- Accept hypercarbia, do not increase respiratory rate and tidal volume to reduce $PaCO_2$ if it increases auto-PEEP

- **Monitor:** Hypotension is usual after mechanical ventilation due to dehydration, use of sedative and intrinsic PEEP. It should be managed by giving fluid challenge

- Pplat (plateau pressure) reflects PEEPi or dynamic hyperinflation and should be kept < 30 cmH₂O. Peak airway pressure reflects only proximal airway pressure and is generally high.

- Magnesium sulfate 2gms infusion over 20 mins can also be tried in refractory cases although its role is unproven.

- **Liberation from mechanical ventilation:**
 - Once the airway resistance decreases as reflected by decrease in Pplat and hypercarbia, spontaneous breathing is then allowed by discontinuing paralysis and deep sedation.
 - PEEP may be titrated cautiously to counteract auto PEEP for easier triggering
 - The patient is given spontaneous breathing trials with a T-piece or low CPAP (equal to or less than 8 cm H₂O). After 30 -120 mins, if the trial is successful the ventilator is withdrawn.
 - In the event of failure of the trial, the patient is placed on assist-control or Pressure support modes. While on spontaneous breathing a PEEP of 5-8 cmH₂O may be applied to reduce inspiratory threshold load imposed by PEEP.
 - Further attempts at liberation are carried out after 24 hours to allow for return of diaphragmatic function.

- **Supportive Therapy.** Adequate DVT prophylaxis and stress ulcer prophylaxis is mandatory in these patients. Adequate nutrition support with less carbohydrate proportion to decrease CO₂ production in COPD patient is desirable.

VII. FURTHER READING / REFERENCES

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ACUTE RESPIRATORY FAILURE

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I. WHEN TO SUSPECT/ RECOGNIZE?

e) Introduction:

Respiratory Failure includes any condition that affects breathing and ultimately results in failure of the lungs to function properly. The main tasks of the lungs and chest are to get oxygen into the bloodstream from air that is inhaled (breathed in) and, at the same time, to eliminate carbon dioxide (CO₂) from the bloodstream through air that is exhaled (breathed out). In respiratory failure, either the level of oxygen in the blood becomes dangerously low, and/or the level of CO₂ becomes dangerously high.

f) Case definition:

Respiratory failure is defined as a failure of gas exchange manifested either as hypoxemia (PO₂ <60mm Hg on room air) i.e. inadequate blood oxygenation or hypercapnia (PaCO₂>45 mm Hg) i.e. excess of circulating carbon dioxide or frequently a combination of both types of gas exchange abnormalities.

Practically/ clinically diagnosed as respiratory fatigue.

VIII. INCIDENCE OF THE CONDITION

The problem in US

1. 360,000 cases per year
2. 137 cases per 100,000 population
3. With 36% failing to survive the hospitalization

The problem in India: not known but respiratory failure is a common occurrence either as a complication of other diseases or as a terminal event

IX. DIFFERENTIAL DIAGNOSIS/ TYPES:

Type 1

Type 1 respiratory failure is defined as hypoxemia without hypercapnia, and indeed the P_aCO_2 may be normal or low. The basic defect in type 1 respiratory failure is failure of oxygenation characterized by:

P_aO_2	low (< 60 mmHg (8.0 kPa) on room air
P_aCO_2	normal or low

This type of respiratory failure is caused by conditions that affect oxygenation such as:

- Parenchymal disease (V/Q mismatch)
- Diseases of vasculature and shunts: right-to-left shunt, pulmonary embolism
- Interstitial lung diseases: ARDS, pneumonia, emphysema.

Type 2

The basic defect in type 2 respiratory failure is characterized by:

P_aO_2	decreased
P_aCO_2	increased

Type 2 respiratory failure occurs as a result of alveolar hypoventilation and results in inability to effectively eliminate carbon dioxide.

The commonest cause of type II respiratory failure is COPD.

Other causes are:

1. Impaired central nervous system drive to breathe

Drug over dose
Brain stem injury
Sleep disordered breathing
Hypothyroidism

2. Impaired strength with failure of neuromuscular function in the respiratory system

Myasthenia Gravis
Guillain Barre Syndrome
Amyotrophic Lateral Sclerosis
Phrenic nerve injury
Respiratory muscle weakness secondary to myopathy, electrolyte imbalance, fatigue

3. Increased loads on the respiratory system

Resistive-bronchospasm (Asthma, Emphysema, Chronic Obstructive Pulmonary Disease)
Decreased lung compliance-Alveolar edema, Atelectasis, Auto peep
Decreased chest wall compliance- Pneumothorax, Pleural effusion, Abdominal distension
Increased minute ventilation requirement- pulmonary embolism by increase in dead space ventilation, sepsis and in any patient with type I respiratory failure with fatigue.

Type 3 and 4 occur in setting of perioperative period due to atelectasis and muscle hypoperfusion respectively.

X. PREVENTION AND COUNSELING

Treatment of underlying disease.

XI. 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**

e) **Clinical Diagnosis:**

Dyspnoea at rest, tachypnoea, tachycardia, hypertension, nasal flaring, pursed lip breathing, using accessory muscle of respiration. Evidence of central / peripheral cyanosis, asterexis or severe drowsiness in case COPD is feature of severe hypercapnia

f) **Investigations:**

Pulse oxymetric assessment of SpO₂ to assess blood oxygen content / hypoxia.

Chest x-ray: Details regarding evidence of consolidation, pulmonary edema, COPD and various other pathology

Complete blood count, electrolytes

Electrocardiogram

g) **Treatment:**

Oxygen therapy:

In the hypoxic self-ventilating patient, delivery of oxygen to the alveoli is achieved by increasing the environmental oxygen fraction (FiO₂), which involves application of supplemental oxygen.

Oxygen therapy will suffice if muscle strength or vital capacity is reasonable and upper airway is not compromised.

Pulse oxymetry is used to quickly titrate to the preferred levels of oxygen administration

Various oxygen delivery devices:

1. **Variable performance:**

Nasal cannula delivers oxygen at low gas flow 1-6lpm with FiO₂ from 21-44 %. Best device for patient with high PCO₂ as no rebreathing.

Face mask delivers oxygen at low gas flow 6-10lpm with FiO₂ upto 50%.
Nonrebreathing face mask with reservoir bag delivers oxygen at flow rates 9-15 lpm with FiO₂ from 85-90%.

Delivery of oxygen is dependent on the patient inspiratory flow rates.

2. Fixed performance:

Venture type mask ensures fixed FiO₂ above fixed flow.

- Nebulised bronchodilators to relieve bronchospasm
- Appropriate early antibiotics in case of pneumonia or in case of infective exacerbation of COPD or antimalarials or antivirals as per case requirement.
- IV steroids for acute exacerbation of COPD or bronchial asthma.
- IV diuretics for acute pulmonary edema.

h) Referral criteria:

Need for invasive mechanical ventilation in cases of worsening hypoxemia or respiratory muscle fatigue in spontaneous breathing patient or on NIV.

(Non-invasive ventilation in secondary care hospitals to be offered only if backed up by invasive mechanical ventilation)

Need for non-invasive ventilation for worsening hypercapnic respiratory failure in COPD patients.

Unable to wean the patient off the ventilator in 48-72 hrs in small set up.

Need for specialized treatment.

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

g) Clinical Diagnosis: As per situation 1

b) Investigations:

Arteial blood gas analysis

Echocardiogram

Lung Function test (Spirometry)

Ventilation Perfusion Scan

CT scan of Chest

Other investigations to look for underlying cause of respiratory failure

g) Treatment:

Non invasive positive pressure ventilation or CPAP:

Using a comfortable reasonably tight nasal or full face mask with ventilators used in cases of hypercapnic/ type II respiratory failure like COPD, sleep apnoea, bronchial asthma and hypoxemic respiratory failure as in acute cardiogenic pulmonary edema.

Mechanical ventilation with endotracheal intubation:

Indications:

1. Type I /hypoxemic respiratory failure where the patient is unable to meet the oxygen requirements of the body or is able to do so only at a very high cost that results in haemodynamic and metabolic compromise.
2. Type II/ hypercapnic respiratory failure where the ventilatory pump has failed.

Goals of mechanical ventilation

- Correct hypoxemia- PO_2 ~60 mmHg/ SpO_2 90%
- Correct hypercapnic- PCO_2 ~ 40mmHg
- Reduce work of breathing
- Reversal of respiratory muscle fatigue.

Complication of mechanical ventilation:

1. Related to intubation:

- Loss of protective airway reflexes leading to aspiration
- Autonomic stimulation causing either tachycardia and hypertension or bradycardia
- Hypotension in fluid depleted patients post induction with sedations.

2. Complication secondary to endotracheal tube: blocked, kinked and misplaced tube, unrecognised esophageal intubation
3. Pneumothorax
4. Ventilator associated pneumonias
5. Ventilator associated lung injury like volutrauma, atelectotrauma and barotrauma.

Supportive care:

1. Suctioning: Maintains airway patency
Increases oxygenation and decreases work of breathing
Stimulates cough and prevents atelectasis.
2. Nebulisation: Inline jet nebulizer / MDI
Delivery of bronchodilator drugs in aerosolised form.
3. Humidification: Prevents drying of secretions and maintains mucociliary function.
4. Physiotherapy: Prevents atelectasis, facilitates postural drainage, and prevents complication of mechanical ventilation.
5. Care of ETT: Proper fixing of the tube, measuring cuff pressure and maintaining it less than 25 mm of Hg.
6. Nutritional support: early enteral feeding, provide adequate calories, protein, electrolytes, vitamins and fluids, care of feeding tube.
7. Stress ulcer prevention: Early enteral feeding, H2 blockers or proton pump inhibitors for prophylaxis, minimise use of steroids and NSAIDS
8. DVT prevention: DVT prevention either by low molecular weight heparin or conventional heparin or by graduated compression stockings or sequential compression device in patient where heparin is contraindicated.
9. Head end elevation of 35-45°.
10. Bowel bladder care
11. Care of eyes
12. Daily sedation interruption
13. Prevention of pressure sore: positioning, prevent soiling, use of air mattress, meticulous cleaning and good wound care.
14. Adequate Analgesia for pain
15. Infection control.

Weaning:

Weaning is a gradual process, which involves withdrawal of mechanical ventilation and removal of artificial airway. It represents the period of transition from total ventilatory support to spontaneous breathing.

Indications for weaning and extubation:

1. Resolution of disease and its acute phase
2. Patient is able to breathe spontaneously
3. Patient able to oxygenate
4. Patient able to protect the airway

Criteria for weaning

1. Resolution of disease and its acute phase
2. Patient has adequate cough
3. Adequate oxygenation:
 - PaO₂ >60 mm Hg on
 - a) FiO₂ < 0.5-0.6
 - b) PEEP < 5-10 cm of H₂O
4. Stable haemodynamics without recent increase pressor requirement.
5. Adequate mentation or no recent deterioration in neurological status.

The best way to determine suitability for discontinuation of mechanical ventilation is to perform spontaneous breathing trial, which can be performed in following ways,

1. Check respiratory rate and tidal volume on no pressor- support and calculate Rapid Shallow Breathing Index and extubate.
(RSBI=respiratory rate/tidal volume in L)
If RSBI <105 breaths/min/L then patient is suitable for extubation
2. A T-piece trial involves patient to breathing through T piece for a set period of time (30 min to max 180 min) The chances of successful extubation are high if patient passes the T-piece trial.

3. An alternative variant is the use of CPAP(continuous positive airway pressure) via an endotracheal tube, which overcomes the imposed work of breathing through ETT and prevents airway collapse.

During spontaneous breathing trial (SBT) presence of any of the following amounts to failure of SBT:

- a. Change in mental status-somnolence, coma, agitation
- b. Onset or worsening of discomfort
- c. Severe diaphoresis
- d. Signs of increased work of breathing- Use of accessory muscles, thoraco-abdominal paradox.
- e. Increase in heart rate >20 bpm or blood pressure > 20 mm of Hg, or any evidence of haemodynamic instability or new onset arrhythmias.

If a patient fails an SBT, then it is important to look for a reason like occult heart failure, neuromuscular pathology, etc.

Suitability for extubation:

1. All of the above
2. The patient with adequate cough and gag reflexes.

Extubation failure:

The use of post extubation non invasive ventilators has decreased the use need for re-intubation.

Tracheostomy:

Tracheostomies to be considered if mechanical ventilation is expected for more than 7-10 days.

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ACUTE RESPIRATORY DISTRESS SYNDROME

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WHEN TO SUSPECT/ RECOGNIZE?

Introduction:

The acute respiratory distress syndrome (ARDS) is a sudden, life-threatening lung failure caused by an inflammatory injury to the lung that is characterized clinically by acute hypoxemic respiratory failure accompanied by pulmonary infiltrates.

Clinical disorders associated with the development of ARDS are divided into those associated with direct injury to the lung and those that cause indirect lung injury (summarized in Table 1). Severe sepsis from any cause is a common underlying disease. Falciparum malaria, leptospirosis, H1N1 influenza pneumonia, hantavirus infection, scrub typhus and severe pneumonias due to Legionella and the pneumococcus are common causes of ARDS and multiorgan failure in India.

Table 1. Clinical Disorders Associated with the Development of ARDS

DIRECT LUNG INJURY	INDIRECT LUNG INJURY
Common causes	Common causes
Pneumonia	Sepsis
Aspiration of gastric contents	Severe trauma with shock and
Less common causes	Multiple transfusions
Pulmonary contusion	Less common causes
Fat emboli	Cardiopulmonary bypass
Near-drowning	Drug overdose
Inhalational injury	Acute pancreatitis
Reperfusion pulmonary edema after lung transplantation or pulmonary embolectomy	Transfusion of blood products

Case definition:

The American-European Consensus Conference Committee definition is commonly used. It defines a spectrum of severity ranging from a milder form of lung injury, Acute Lung Injury (ALI), to a more severe Acute Respiratory Distress Syndrome (ARDS)

Table 2. 1994 American-European Consensus Conference Committee Definitions

Condition	Timing	Oxygenation	Chest Radiograph	Pulmonary Artery Occlusion Pressure
Acute Lung Injury (ALI)	Acute Onset	PaO ₂ /FiO ₂ <300 torr	Bilateral Infiltrates on Frontal chest radiograph	< 18 mmHg. when measured or no clinical evidence of left atrial hypertension
Acute Respiratory Distress Syndrome (ARDS)	Acute Onset	PaO ₂ /FiO ₂ <200 torr	Bilateral Infiltrates on Frontal chest radiograph	< 18 mmHg. when measured or no clinical evidence of left atrial hypertension

INCIDENCE OF THE CONDITION IN OUR COUNTRY

An early estimate by the National Institutes of Health (NIH) suggested that the annual incidence in the United States was 75 per 100,000 population. Most studies report a mortality of 40 %-60% from ARDS with most deaths being attributed to sepsis and multi-organ failure rather than a primary respiratory cause. Recent studies have shown a decreasing mortality from this disease to as low as 36% and 34%. This may be probably related to improved and more effective strategies for ventilation and treatment of sepsis and better supportive care of the critically ill patients.

There are no reliable data from India.

DIFFERENTIAL DIAGNOSIS/ TYPES:

- Cardiogenic pulmonary edema
- Fluid overload
- Bronchopneumonia
- Aspiration pneumonia
- Viral pneumonia
- Alveolar hemorrhage
- Pulmonary contusion
- Miliary tuberculosis

Extensive pulmonary metastases
Vasculitis

PREVENTION AND COUNSELING

Management of the underlying condition
Early management and control of sepsis
Prognosis is guarded with mortality of about 50%

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**

Clinical Diagnosis:

Features of the underlying condition
Breathlessness, tachypnea, respiratory distress, cyanosis, sweating, mental obtundation
Pulse oximetry show SpO₂ below 90%, or is maintained above 90% only with high flow oxygen

Investigations:

Blood count, cultures, Ultrasonography and other investigations to diagnose the underlying
Chest X-ray : Bilateral parenchymal infiltrates
Arterial blood gases: low PaO₂, low PaO₂ / FiO₂ ratio
Echocardiography: normal left ventricular function, may show signs of pulmonary hypertension and right ventricular dysfunction in severe cases

Treatment:

Treatment of the underlying illness
ALI / ARDS is not a disease of the lung alone; it is often a part of multiorgan dysfunction in systemic inflammation and sepsis. Thus ventilatory and pulmonary management are part of the overall management of the patient. Identifying and treating the inciting clinical disorder is of utmost importance while supportive therapy with mechanical ventilation gives time for the lungs to heal.
Oxygen therapy
Intubation and mechanical ventilation

- Use tidal volume of 6 ml/kg ideal body weight (approximately 350-400 ml for average height Indian male, and 300ml for average height Indian female), respiratory rate 15-30/min
 - Give 5-10 PEEP
- Increase PEEP and FiO₂ to maintain the following goals:
- Plateau Pressure P_{plat} < 30 cm H₂O
 - pH of 7.25-7.35
- PaO₂ 55mmHg ó 70mmHg, or SpO₂ 88%-95%
- Avoid ventilator induced lung injury: do not exceed tidal volume and plateau pressure limit
- Supportive care as outlined in Chapter on Respiratory Failure and Mechanical Ventilation
- Avoid fluid overload, use basic hemodynamic monitoring (see chapter on Hemodynamic Monitoring)

Mechanical Ventilation settings for Protective Lung Ventilation

Variable	Protocol
Ventilator mode	Volume assist-control
Tidal volume	< 6 mL/kg ideal body weight
Plateau pressure	P _{plat} < 30 cm H ₂ O
Ventilation set rate/min	6–35/min, adjusted to achieve arterial
pH goal	pH of 7.25-7.35 pH of 7.25-7.35 considered acceptable.
Inspiratory flow, I:E	Adjust flow to achieve I:E of 1:1–1:3
Oxygenation goal	PaO ₂ 55-80mmHg 88% < SpO ₂ < 95%
FiO ₂ /PEEP (mm Hg) combinations	0.3/5, 0.4/5, 0.4/8, 0.5/8, 0.5/10, 0.6/10, 0.7/10, 0.7/12, 0.7/14, 0.8/14, 0.9/14, 0.9/16, 0.9/18, 1.0/18, 1.0/22, 1.0/24
Weaning	Attempts to wean by pressure support required when FiO ₂ /PEEP are .40/8

Referral Criteria

- Undiagnosed underlying condition
- Severe underlying illness and multiple organ dysfunction (e.g., severe sepsis, renal failure, etc)
- Associated polytrauma with head injury
- High FiO₂ and PEEP requirement (FiO₂ > 0.5 and PEEP > 10)
- Requirement of deep sedation and neuromuscular blockade to allow smooth mechanical ventilation
- High plateau pressures > 30 cmH₂O despite tidal volume of 6 ml/kg
- Development of complications such as pneumothorax, ventilator-associated pneumonia
- Inability to wean patient

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

Clinical Diagnosis: As per situation 1

b) Investigations: as per situation 1 plus

Investigations to find the source of sepsis / underlying cause of ARDS
CT scan of the Chest: alveolar filling, consolidation, and atelectasis occurring predominantly in dependent lung zone. lung injury in ARDS is non-homogeneous, and basal, dependent lung regions are more severely affected by edema and consolidation.

Treatment:

- As in Situation 1 plus
- Continue protective lung ventilation strategy, high FiO₂ and PEEP
- Permissive hypercapnia
- Deep sedation and neuromuscular blockade
- Recruitment manoeuvres
- Prone ventilation
- Nitric oxide
- High frequency oscillation
- Extracorporeal membrane oxygenation
- Steroids may be considered but not recommended for routine use
- Continue supportive Care
- Prevent ventilator induced lung injury and ventilator associated pneumonia
- Start weaning the patient as soon as possible

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ACUTE LIVER FAILURE

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Introduction

Acute Liver Failure (ALF) is defined as acute hepatitis (elevation in AST/ALT) accompanied by elevation in INR >1.5 and any degree of mental alteration (encephalopathy) within 12 weeks of onset of symptoms, in the absence of chronic liver disease. Its presentation is rapid, dramatic and frequently leads to death over the course of a few days in the absence of emergency liver transplantation.

Incidence

The exact incidence of ALF in the Indian subcontinent is not known. However, viral hepatitis leading to acute liver failure is the commonest cause in our country. In western countries, the commonest cause of ALF is paracetamol poisoning and it is a relatively uncommon disease (e.g., it affects about 2500 patients in the United States each year). Since there is a high load of hepatotropic viruses in India, the incidence of ALF may probably be higher.

Prognosis

ALF carries a high mortality rate with 15-20% survival without orthotopic liver transplantation (OLT). In developed countries, liver transplantation has revolutionized the prognosis of this disease and survival rates are in the range of 59 to 79%, with liver transplantation. Moreover, it accounts for about 5-11 % of liver transplants among adults.

Hepatitis A, paracetamol overdose and ischemic insults typically present as hyper acute liver failure, and have a relatively good spontaneous survival rate of 36%, whereas idiosyncratic drug reactions and indeterminate causes present later, with only a 14% survival rate without OLT. The other etiologies with very poor prognosis include acute hepatitis B (and other non-hepatitis A viral infections), autoimmune hepatitis, Wilson's disease and Budd-Chiari syndrome. Patients presenting in grade III/IV encephalopathy also have a very poor prognosis.

Differential diagnosis

Differential diagnosis includes severe malaria, leptospirosis, rickettsial diseases, enteric fever, and Hanta virus infection.

Clinical features

The initial clinical features of ALF may be non-specific, and may include anorexia, fatigue, abdominal pain, jaundice and fever before progressing to hepatic encephalopathy.

Hepatic encephalopathy is graded from I to IV based on clinical features and neurological signs.

Grades of Hepatic encephalopathy

I	Changes in behaviour with minimal change in level of consciousness
II	Gross disorientation, drowsiness, possibly asterixis, inappropriate behaviour
III	Marked confusion, incoherent speech, sleeping most of the time but arousable to verbal stimuli
IV	Comatose, unresponsive to pain, decorticate or decerebrate posturing

This grading is clinically robust and increasing grades of hepatic encephalopathy have a strong negative correlation with outcome. The evolution to grade III/IV HE is a grave prognostic sign as this group is at risk of intracranial hypertension, and subsequent brain herniation.

Clinical signs suggestive of increasing intracranial pressure include worsening of hepatic encephalopathy, systemic hypertension and bradycardia (Cushing reflex), altered pupillary reflexes and decerebrate rigidity. All of these clinical signs occur late in the clinical course.

Causes

Etiological category	Specific causes
Viral	HAV, HBV±HDV, HRV, HSV Human herpes virus 6, CMV, EBV, VZV, Parvovirus B19, Yellow fever
Drug/toxin induced (dose dependent)	Paracetamol, <i>Amanita phalloides</i> , tetracyclines, <i>Bacillus cereus</i> , carbon tetrachloride
Drug/toxin induced (idiosyncratic)	Halothane, anti-tubercular therapy, co-amoxiclav, macrolides, ofloxacin, phenytoin, valproate, statins, NSAIDs, disulfiram, metformin, dapsone, amiodarone, labetalol, methyl dopa, HAART, etoposide, ecstasy/amphetamines, cocaine, herbal remedies, etc
Vascular	Ischemic hepatitis, Budd Chiari syndrome, right heart failure, veno-occlusive disease
Metabolic	Wilson's disease, acute fatty liver of pregnancy, HELLP

Miscellaneous	Autoimmune hepatitis, malignant infiltration, sepsis, heat stroke
Others	Cryptogenic

Criteria for hospital admission

All patients with clinical or laboratory evidence of moderate to severe acute hepatitis should have immediate measurement of prothrombin time and careful evaluation for subtle alterations in mentation. If the prothrombin time is prolonged by >4-6 seconds or more (INR>1.5) and there is any evidence of altered sensorium, the diagnosis of ALF is established and hospital admission is mandatory.

Criteria for ICU admission

Patient with any one of the following:

Altered sensorium: Patients in grade I and perhaps, grade II encephalopathy, could be managed in a ward. However, rapidly worsening encephalopathy or grade III/IV encephalopathy warrants ICU admission.

Respiratory distress, i.e., respiratory rate >30/m.

Any evidence of gastrointestinal bleeding

Any hemodynamic instability

Optimal diagnostic criteria, investigations, treatment and referral

A. Non metro/ Secondary hospital

Investigations

- 2) Prothrombin time(PT)/INR
- 3) Chemistries: serum sodium, potassium, chloride, bicarbonate, calcium, magnesium, phosphate, glucose
- 4) Liver function test: AST, ALT, alkaline phosphatase, GGT, total bilirubin, albumin
- 5) Renal function test : serum creatinine, blood urea nitrogen
- 6) Arterial blood gas (with arterial lactate, if possible)
- 7) Complete blood count
- 8) Blood type and screen
- 9) Viral hepatitis serologies: anti-HAV IgM, HBsAg, anti-HEV.
- 10) Ultrasound abdomen to look at the echotexture of the liver and rule out chronic liver disease/ Budd-Chiari syndrome.
- 11) Blood culture
- 12) Blood smear for malaria, serology for Dengue and Widal test in selected cases (based on clinical suspicion)

Laboratory monitoring

Frequency to repeat tests	Tests
Twice daily	Blood glucose (bedside glucoStix adequate)
Daily	PT, serum sodium and potassium Arterial blood gas
Alternate day	Blood count, serum creatinine
Twice weekly	Magnesium, phosphate

Treatment

- 1) Nutrition: A carbohydrate rich diet with protein restriction (60 g/day) is recommended. If enteral feeds are not tolerated, dextrose infusion should be started. A record of intake and output should be maintained and a positive balance of no more than 500 ml is acceptable.
- 2) Bowel decontamination with lactulose and antibiotic for gut sterilization (ampicillin / metronidazole / rifaximin)
- 3) Intravenous ranitidine or proton pump inhibitors.
- 4) Rehydration is required in many patients as they may be dehydrated at admission due to vomiting and anorexia. Subsequently, maintain euvoemia.
- 5) Careful and repeated neurological examination for grade of encephalopathy and evidence of cerebral edema is mandatory.
- 6) Avoid sedation in grades 1 and 2 encephalopathy.
- 7) All patients in grade 3 or 4 hepatic encephalopathy should be intubated electively for airway protection. In addition, respiratory support and mechanical ventilation should be provided for those with inadequate respiratory effort.
- 8) Treatment for clinical evidence of cerebral edema includes:
 1. Elevation of head end of the bed to 15-30°
 2. Head in neutral position
 3. Limiting all nonessential physical examination
 4. Maintaining normotension (mean arterial pressure atleast 70-80 mm Hg)
 5. Hydrotherapy for fever control; judicious use of paracetamol to control fever
 6. Prevent hypo and hyperglycemia
 7. Parenteral mannitol (for raised ICP) in 0.5-1 gm/kg boluses
 8. Look for and correct hypercapnia and hypoxemia
- 9) Give one dose of vitamin K. Fresh-frozen plasma transfusion is required for bleeding manifestations, as and when required. Platelet transfusion is required for platelet counts <10,000/mm³ or invasive procedures.
- 10) N acetyl cysteine should be given in patients with acetaminophen induced ALF.
- 11) The role of antibiotics is not definitive. However, in grades 3 and 4 encephalopathy, prophylactic antibiotics may be advisable. Third generation cephalosporin, e.g., Ceftriaxone, is adequate.

Referral

The following are reasons for referral to a higher centre:

- 1) Liver transplantation: Planning for transfer to a transplant center should begin in patients with grade I or II encephalopathy because they may worsen rapidly. Early transfer is important as the risks involved with patient transport may increase or even preclude transfer once stage III or IV encephalopathy develops.
- 2) Renal replacement therapy: Renal replacement therapy forms an integral part of care given to all patients with renal failure. Continuous modes of dialysis such as continuous veno-venous hemofiltration are better as hemodynamic stability is maintained and fluctuations in intracranial pressure are avoided.
- 3) Transfusion requirement: Patients with significant gastrointestinal bleed should be referred to an institution where blood products can be arranged adequately.

B. Metro/ Super specialty situation

Investigations

All those listed in the previous section. In addition, the following may be added:

- 1) Toxicology screen including acetaminophen level
- 2) Serum Ceruloplasmin
- 3) Serum ammonia (if possible)
- 4) Autoimmune markers: Antinuclear antibody, anti smooth muscle antibody, anti liver-kidney microsomal antibodies, Immunoglobulin G level
- 5) HIV status (liver transplant)
- 6) Liver biopsy (via the transjugular route) may be done, if expertise with this technique is available.

Laboratory monitoring

Frequency to repeat tests	Tests
Four times a day	Blood glucose (bedside glucostix adequate)
Twice daily	Serum sodium and potassium, Arterial blood gas
Daily	PT/INR, blood count
Alternate day	Serum creatinine, magnesium
Twice weekly	Serum phosphate, Liver function tests

Treatment

Treatment enumerated in the previous section should be instituted. The following are recommended, in addition.

- 1) Enteral nutrition is preferred and should be started through a nasogastric tube. Total parenteral nutrition may be considered, in case enteral nutrition is not tolerated or there are contraindications. However, the risk of fungal infections increases with parenteral nutrition.
- 2) Invasive hemodynamic monitoring in the form of intra-arterial blood pressure and central venous pressure monitoring.
- 3) Maintenance of adequate cerebral perfusion pressure
 - Keeping mean arterial pressure >80mm Hg.
 - PaCO₂ in the range of 30-35 mm Hg.
- 4) In ventilated patients, sedation should be instituted to avoid coughing and bucking on endotracheal tube. Bolus of lignocaine and sedation should be given prior to suctioning.
- 5) Pts with renal failure should be started on continuous renal replacement therapy to minimize fluctuations in intracranial pressure during dialysis.
- 6) Urgent hepatic transplantation is indicated in acute liver failure where prognostic indicators suggest a high likelihood of death.
- 7) Artificial and bio-artificial liver devices may be used as bridge to liver transplant

Complications

Infection

If antibiotics are not given prophylactically, surveillance for infection (including chest radiography and periodic cultures of sputum, urine and blood for bacterial and fungal organisms) should be undertaken. In case the patient develops ascites, spontaneous bacterial peritonitis should be ruled out. A low threshold for starting appropriate anti-bacterial or anti-fungal therapy should be maintained.

Bleeding

Replacement therapy for thrombocytopenia and/or prolonged prothrombin time is recommended only in the setting of hemorrhage or prior to invasive procedures. Prophylactic platelet transfusions are needed only for platelet count <10,000/mm³.

Criteria for referral for liver transplant

Several prognostic indicators suggest a high likelihood of mortality and in these patients, liver transplantation is the only option. Currently available prognostic scoring systems do not adequately predict outcome; nevertheless, the King's college hospital criteria (KCH criteria) have been most commonly used and most frequently tested of the several criteria proposed.

Kings College Hospital Criteria

Etiology of ALF	Criteria predicting death
Acetaminophen overdose	Arterial pH <7.30 OR All of the following: PT > 100 seconds (INR > 6.5) Creatinine level > 3.4 mg/dL Grade III/IV encephalopathy
Non-acetaminophen overdose	PT > 100 seconds (INR > 6.5) OR Any three of the following: Non A non B hepatitis/drug/halothane Jaundice to encephalopathy interval > 7 days Age < 10 years or > 40 years PT >50 seconds (INR >3.5) and bilirubin level >17.4 mg/dL

Prevention & Counseling: Hepatitis A & E, which spread mainly by faeco-oral contamination, can be controlled by clean and safe water supply & other hygienic measures. . Universal precautions, viral screening of blood for Hepatitis B & C should be made mandatory. Recycling of syringes should be discouraged and declared unlawful.

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RESOURCES REQUIRED FOR ONE PATIENT / PROCEDURE (PATIENT WEIGHT 60 KGS)

(Units to be specified for human resources, investigations, drugs and consumables and equipment. Quantity to also be specified)

Situation	HUMAN RESOURCES	INVESTIGATIONS	DRUGS & CONSUMABLES	EQUIPMENT
1)Non-metro	<p>1. Gastroenterologist or a general physician on daily basis</p> <p>2. One nurse per shift</p> <p>3. Intensivist for those who develop grade III ó IV encephalopathy</p>	<p>1) Once : GE serology</p> <p>2) Daily: PT, serum sodium, potassium, ABG</p> <p>3) Twice daily: blood glucose</p> <p>4) Alternate day: blood count, serum creatinine</p> <p>5) Twice weekly: LFT, Magnesium, phosphate, Chest x- ray</p> <p>COST: 1st day: Rs. 2500-3000</p> <p>Subsequent days: Rs. 1000-1500/day</p>	<p>Drugs: 3 generation cephalosporin, proton pump inhibitor, lactulose, mannitol.</p> <p>Fentanyl ,midazolam, atracurium</p> <p>Consumables :</p> <p>18 G velflon (2), Foleyø catheter, uroflow meter.</p> <p>Ventilator tubings, HME(2), Endotracheal tube,</p> <p>catheter mount, suction catheters</p> <p>COST: 1st day: Rs. 3000-5000</p> <p>Subsequent days: Rs. 1000-2000/day</p>	<p>Monitor with ECG, NIBP, SpO₂</p> <p>Ventilator</p> <p>Blood Gas Analyzer</p>
2)Metro	<p>As in situation 1</p> <p>Plus</p> <p>4. Surgeon with expertise in liver</p>	<p>1) Four times a day Blood glucose (bedside glucostix adequate)</p> <p>2) Daily: PT/INR, blood count, serum sodium, potassium,</p> <p>3) Twice daily : Serum sodium and potassium,</p>	<p>All of the above plus</p> <p>7 fr triple lumen Central venous catheter, mersilk, tegaderm, single lumen CVC, 20g velflon.</p> <p>Pressure Transducers(2)</p> <p>Endotracheal tube</p>	<p>As in situation 1</p> <p>Plus</p> <p>Dialysis machines , Liver Transplant OT, Endoscopy suit</p>

	<p>transplant</p> <p>5. Anaesthetist with expertise in liver transplant</p> <p>6. Radiologist</p> <p>7. Nephrologist</p>	<p>Arterial blood gas</p> <p>4) Alternate day: Serum creatinine, magnesium</p> <p>5) Twice weekly :Serum phosphate, Liver function tests</p> <p>6) Once :special investigations as listed in above document</p> <p>COST: 1st day: Rs. 3000-5000</p> <p>Subsequent days: Rs.1000-3000/day</p>	<p>Angiography sheet</p> <p>Surgical gown.</p> <p>COST: 1st day*: Rs. 8000-10000</p> <p>Subsequent days*: Rs. 2000-4000 per day</p> <p>*Excluding dialysis</p> <p>Cost of each session of CRRT= Rs. 15, 000</p>	<p>and Fully equipped advance ICU with ventilator</p>
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Note: Cost calculated above does not include oxygen/ventilation costs/hospital and physician charges

BRAIN DEATH TEST AND ICU MANAGEMENT

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WHEN TO SUSPECT/ RECOGNIZE?

Introduction:

It is important to recognize and diagnose brain death especially in patients who are potential organ donors. Early diagnosis, documentation and initiation of the organ donation process and appropriate management of brain-dead organ donors forms an important part of intensive care unit management.

Definition

Brain death is defined as the irreversible loss of all function of the brain, including the brainstem. The three essential findings to confirm brain death are coma (known irreversible cause), absence of brainstem reflexes, and apnea.

An evaluation for brain death should be considered in patients who have suffered a massive, irreversible brain injury of identifiable irreversible cause as established by history, clinical exam, lab testing or neuroimaging (CT scan or MRI). Once brain death criteria are met a person clinically determined to be brain dead is legally dead in the context of organ donation under the Transplantation of Human Organ Act 1994. Always consider Medico legal, philosophical and religious perspective.

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

The diagnosis of brain death is primarily clinical. No other tests are required if the full clinical examination, including each of two assessments of brain stem reflexes and a single apnea test, are conclusively performed. In the absence of either complete clinical findings consistent with brain death, or confirmatory tests demonstrating brain death, brain death cannot be diagnosed.

Differential Diagnosis

Neurologic states that can mimic brain death

- Locked-in syndrome (Present in case of GBS); Patient cannot move the limbs, grimace or swallow, but blinking and vertical eye movements remains intact.
- Vegetative state; No awareness of self and environment using a series of stimuli after CPR may take 1 month to become fully apparent and is permanent if no change after 3 months is observed.

Investigation

Brain death Examination

Exam prerequisites

1. Irreversible loss of clinical brain function.

(Definitive cause leading acute brain catastrophe compatible with diagnosis of brain death evidenced on clinical or neuroimaging)

2. Achieve Systolic Blood Pressure >100mmHg and core body temperature $^{\circ}$ C (>90 $^{\circ}$ F).

3. Exclusion of confounding factor in prognostication.

- Drugs (sedatives or neuromuscular blocking agents).
- Intoxication.
- Hypothermia (induced hypothermia therapy).
- Shock.

Brain death test

- Sufficient time period has been passed to exclude possibility of possible recovery of meaningful neurological function, several hours to days as per clinical factors.
- The relevant family member or appropriate party has been notified of the intention to initiate the determination of brain death.
- Neurological exam then proceeds with aim of determining three principle findings in brain death: coma, absence of brainstem reflexes and apnea (coma and apnea must coexist).
- Two physician as per local institutional protocol do the brain death test
- The second physician should not be involved in the patient's care.
- Neither physician should be involved with organ transplantation.
- Intensivist, neurologist or any physician competent doing brain death test appointed by the institute as per local law can do the brain death test, both physician do the test individually.

Determination of unresponsiveness (Coma)

- Absence of supraspinal motor response to pain in all extremities and no eye opening to pain (standardized painful stimuli - supraorbital pressure, TMJ pressure, sternal rub and nail bed pressure) Glasgow coma scale 3/15.

Examination of brain stem reflex

Pupillary reflex

- Dilated pupils at mid position (4-6 mm).
- Absence of bilateral pupillary responses to light.

Ocular movement

- Absent oculoccephalic reflex (doll's eye)
- Absent cold caloric responses (vestibulo-ocular reflex)

Absent Facial sensory and motor response

Absent Pharyngeal reflex and Tracheal reflex

- Absence of gag reflex.
- Absence of coughing in response to tracheal suctioning.

Apnea test

Prerequisites

- SBP > 100 mmHg.
- Core body temperature > 36.5°C (> 97°F).
- Euvolemia with appropriate fluid balance in the previous 6 hours.
- Normal PaO₂.
- Normal PaCO₂.

Procedure

- Connect SpO₂ probe and preoxygenation at 100% Fio₂ for 10 minutes, draw baseline ABG, Pao₂ > 200 mmHg and Paco₂ ~ 40 mmHg (may require to reduce ventilator rate to get eucapnia) is needed.
- Disconnect the ventilator.
- Delivering oxygen by tracheal catheter at carina with flow of 6 liters per minute or T-piece system using 12 l/min O₂ flow or use CPAP of 10 cmH₂O (less hypoxia with CPAP method).
- Observe the chest and the abdominal wall movement for respiration for 8 to 10 minutes and monitor the patient for changes in vital functions.
- Rate of rise of PaCO₂ is 3 mmHg per minute so 8 to 10 minutes are sufficient for apnea test to get rise of 20 mmHg of PaCO₂.
- Draw post test ABG and then reconnect the ventilator.
- Positive apnea test - Absence of respiratory drive at a Paco₂ of 60 mm Hg or 20 mm Hg above normal base-line values, apnea is confirmed.
- If respiratory movement occurs or any sign of hemodynamic instability, abandon the test, draw sample for ABG and then reconnect the ventilator.

Ancillary test

Routine use is not recommended.

Observation period between two examination

Depends on the age of the patient;

- 7 days to 2 month old minimum 48 hr interval.
- 2 month to 1 year old minimum 24 hr interval.
- >1 year to <18 years old minimum 12 hr interval.
- >18 years old, interval is optional, minimum 6 hr.

Number of Confirmatory tests

- Neonate < 7 days Brain death testing is not valid.
- 7 days to 2 months old, 2 confirmatory tests.
- >2 months to 1 year old, 1 confirmatory test.
- >1 year to <18 years old, optional.
- >18 years old, optional.

Brain death declaration

- If clinical criteria are met.
- No need of confirmatory test.

Documentation of brain death

- Etiology and irreversibility of condition.
- Absence of brainstem reflexes.
- Absence of motor response to pain.
- Absence of respiration with $Paco_2 \times 60$ mm Hg.
- Timing of first and repeat neurologic examination.
- Justification for confirmatory test and result of confirmatory test.
- Brain death time - time of rise of $Pao_2 >60$ mmHg after second set of test.
- Two physician signatures should be obtained.

Primary or secondary health care centre

É Brain death test are clinical.

É Brain death can be declared at these centers if all three criteria are fulfilled.

Communication with family and further decision making

After the clinical criteria of brain death have been met, the physician should inform the next of kin, who can be approached about organ donation. The physician is required to abide by state law with respect to organ donation.

Treatment

- Basic intensive care, cardiovascular, respiratory, hemodynamic and metabolic support

Routine ICU care and monitoring

- Nursing care.
- Skin care.

- Turning and positioning.
- Care of lines.
- Ryle's tube to prevent risk of aspiration.
- Pulse oximetry.
- Arterial and central venous pressure monitoring.
- Pulmonary artery catheter placement If necessary.
- Foleys catheter for urine out put monitoring.
- Core temperature monitoring.
- Antibiotic therapy.
- Anticipation of complications.
- Prevention and treatment of complications.
- Frequent assessment and titration of therapies.
- Nutrition.
- Maintenance of vital organ function;
 - Resuscitation.
 - Oxygen delivery to the tissues.
 - Hydration and perfusion.
- Routine laboratory testing ABG, CBC, SE, BUN, Cr and LFT.
- Testing for HIV, HBV & HCV on all donors after first apnea test.
- Additional tests may be necessary as per local protocol.
- Support of the family.

Counseling

- The family should be counseled that the patient cannot recover
- Family should be counseled for organ donation
- If the patient cannot become an organ donor, withholding or withdrawing of life support may be discussed with the family.

Referral Criteria

- If the patient is a potential organ donor, he should be transferred to a tertiary level centre that is certified by the competent authority and is capable of supporting the brain dead organ donor
- If in some cases further diagnostic studies are required to confirm brain death
 - Difficulty to determine coma.
 - Incomplete brain stem reflex testing.
 - Incomplete apnea testing.
 - Toxic drug levels.
 - Facial trauma.
 - Preexisting pupillary abnormality.
 - Sleep apnea or severe pulmonary disease resulting in chronic retention of CO₂.
 - Children younger than 1 year old (<1 year age not recommended).
 - As required by institutional policy.

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

a) Clinical Diagnosis: As per situation 1

b) Investigations: as per situation 1 plus

- EEG
- Bispectral index (BIS)
- SSEP
- Neuroimaging
 - Cerebral angiography (CTA, MRA) when ICP exceeds MAP angiography demonstrates absence of blood flow beyond carotid bifurcation.
 - Cerebral scintigraphy (technetium tc-99m brain scan)
 - Noninvasive study also known as a cerebral blood flow study.
 - Absent uptake of isotope in brain parenchyma is supportive of a diagnosis of brain death- Hollow skull phenomenon.
 - Single photon emission computed tomography(SPECT) at 48 hrs is 100 % diagnostic.
 - In case of barbiturate coma neuroimaging can be used without the necessary wait (5 half life provided normal renal and hepatic function) for the medication to leave the system.
 - Transcranial Doppler Ultrasonography

However, the clinical criteria of brain stem death are considered adequate under the Transplantation of Human Organ Act and special investigation are not mandatory to declare brain stem death in India.

Treatment as in Situation 1 above plus

ICU management of Brain dead organ donor

ICU management of the potential organ donor plays a key role in maintaining and increasing current number of donor organs aim is to improve organ survival.

- Early identification of potential donors;
 - Critically ill patient in an intensive care unit - severity of acute brain injury is such that there is a high probability of brain death occurring.
- Early notification of Organ Procurement Organization(OPO), State Authorization Committee, Zonal Transplant Coordinating Centre (ZTCC) or Local Authorization Committee(LAC) as per institutional protocol.
- Designated requestor ó OPO or LAC coordinator, as per institutional protocol.
- Requesting consent to organ donation from the family are ethical and professional responsibilities of the intensive care specialist.
- Preparation of the family.
- Consider family's psychological, religious and cultural needs.
- Enquiring about the stated wishes of the patient.
- Ensuring the wishes, dignity and privacy of the donor are respected.

- Provide sufficient information and time.
- Support family to make an informed decision concerning organ donation without undue pressure.
- Clarification of ongoing physiologic support despite brain death.
- The family should have adequate emotional and social support after giving consent to organ donation and during the follow up period.
- Details of all discussions with the families should be documented.

Supportive treatment should start early as soon as brain death has been recognized irrespective of the consent. Switch the focus of the management for elevated intracranial pressure and brain protection, to preservation of organ function and optimization of tissue oxygen delivery.

Hemodynamic support

Hypertension

- Hypertension and bradycardia preceding brain death characterize the Cushing's response.
- Ischemia of the vagal nucleus in the medulla oblongata results in uncontrolled sympathetic stimulation- catecholamine storm results in systemic hypertension, tachycardia and possibly tissue ischemia including;
 - Pituitary ischemia.
 - Myocardial injury - right and/or left ventricular dysfunction.
- Duration and severity of this storm varies but within hours results in depletion of catecholamine with subsequent generalized vasodilatation and hemodynamic collapse.
- Initial period of severe HTN is short acting β -blocker esmolol.

Hypotension

Most common problem seen in brainstem dead organ donors.

- Chronic maintenance phase of brain stem dead donors is frequently characterized by hypotension.
- Invasive monitoring of arterial and central venous pressure should be instituted.
- Proper fluid management is the cornerstone of therapy;
 - Fluid resuscitation may require several liters of fluid.
 - Combination of crystalloids and colloids is used.
 - Relying on urine output alone to determine adequacy of fluid resuscitation is misleading because of polyuria due to diabetes insipidus.
- Vasopressors;
 - If possible use of vasopressors should be minimized because of their splanchnic vasoconstrictive effects.
 - The first choice is usually Dopamine, preferably at a dose below 10mcg/kg/min.
 - Dobutamine should be used for impaired myocardial contractility; and
 - Norepinephrine or Epinephrine for severe systemic vasodilatation.
- In donors who remain unstable despite routine management, pulmonary artery catheterization may help in determining the problem.
- Rule of 100's for management of brain death organ donor;
 - SBP 100 mmHg
 - U/O 100 ml/hr
 - PaO₂ 100 mmHg

- Hb 100 g/L

Arrhythmias

- Brady arrhythmias and tachyarrhythmia are common after brain death.
- Brady arrhythmias occurring as part of the Cushing reflex, during coning, do not require treatment.
- Correct acidosis, electrolyte abnormalities and try to optimize Inotropes.
- Atropine is ineffective for Brady arrhythmias after brain death has occurred.

Respiratory support

Ventilatory support

- *Increase ET cuff pressure immediately after BD declaration.*
- *HOB up 30°.*
- *Turning q2h.*
- *Pulmonary toilet.*
- *Paco₂ should be maintained in the normal range.*
- *Routine use of PEEP at 5 cm H₂O in brainstem dead organ donors is recommended to prevent microatelectasis.*
- *Plateau pressures should <35cmH₂O to reduce the risk barotrauma.*
- *FiO₂ <0.6 to reduce the risk of oxygen toxicity.*
- *PaO₂ of >100 and a saturation >95%.*
- *Monitor ABG's q2h or as required.*
- *Chest X-Ray.*
- *Bronchoscopy in some cases.*
- *CT chest in some cases*

Renal support

- Maintain urine output 1-3 ml/kg/hr.
- Avoid nephrotoxic drug.
- Maintain Euvolemia.
- Oliguria;
 - Despite adequate filling pressures and blood pressure, loop diuretics or osmotic diuretics should be used to initiate diuresis.
- Polyuria, a frequent finding in brainstem dead organ donors;
 - Diabetes insipidus.
 - Osmotic diuresis due to mannitol or hyperglycemia.
 - Physiologic diuresis due to massive fluid resuscitation.
 - Hypothermia.
 - Hypokalemia.

Neuro-Endocrine changes

As neurologic death occurs, alteration in the hypothalamic-pituitary-adrenal axis (HPA axis) is inevitable.

Diabetes insipidus

- DI results in problems with hemodynamic stability and fluid and electrolyte balance;
 - Urine volumes exceed 300ml/hr (or 7ml/kg/hr).
 - Hypernatremia (serum sodium greater than 150mEq/l).
 - Serum osmolality (>310mOsm/L).
 - Low urinary sodium concentration.
- Desmopressin (dDAVP) preferred;
 - (DDAVP) 1 mcg IV, may repeat x 1 after 1 hour.
 - 1-4 mcg every 8 to 12hrly SC.
 - Nasal spray.
- Vasopressin - splanchnic and renal vasoconstrictive effects.
 - 1-4 units/hr.
- Hypernatremia (>155mEq/L)
 - Free water, i.e. D5% or half strength 0.45% Saline.

Hyperglycemia

- Insulin 0.05-0.1U/kg/hour titrated to maintain glucose at 80-120.
- Hourly glucose checks so as to avoid hypoglycemia.

Thyroid hormone replacement

- Thyroid hormone administration typically with T3 (triiodothyronine) which is the active form of thyroid hormone.
- T3 is converted from T4 and T3 is 4 X more active than T4
- Use T3 preferably if not available use T4 (T3 dose 0.05-0.15 mcg/kg/hour) titrate to keep SBP >100
- Monitor Potassium levels closely.

Steroid

- Protocols may use hydrocortisone 1.5 mg/kg IV Q 6 hours (max dose of 100 mg) or single dose of methylprednisolone 15 mg/kg in adults and 1 mg/kg in children (max dose of 2 gm).
- The use of hormonal replacement therapy, Thyroxin, triiodothyronine (T3), corticosteroid and insulin, has been advocated to improve cardiovascular stability. At present, such therapies are regarded as experimental. Studies regarding ACTH and cortisol levels inconclusive. Unclear whether steroids make any significant improvement in organ preservation.

Hypothermia

- Core temperature should be monitored using rectal thermometers.
- Maintain above 35°C.
- É If core temperature <35°C

- É Warm inspired gas.
- É Warmed IV fluids.
- É Warming lights.
- É Warming blankets.
- É Hot packs in the axilla.

Infection

- Systemic infection is a relative contraindication to organ donation.
- All unnecessary indwelling devices should be removed.
- All lines and catheters must be inserted aseptically.
- Care of dressings and wounds is vital.
- Tracheal suction should be done with sterile precautions.
- Appropriate samples from suspected sources of infection should be sent for culture and sensitivity.
- Prophylactic antibiotics are indicated only immediately prior to organ retrieval.

Coagulopathy

- If clinically significant mucocutaneous bleeding, treatment with appropriate blood components is required.
- Keep hematocrit > 30%.

Ischemic reperfusion injury

- Keep FiO₂ <0.6.
- Avoid hyperthermia (>37°C).
- Avoid hyperglycemia (>180 mg/dl).
- Steroid and N-acetylcysteine may have short term and long organ survival.

Absolute Contraindications to organ donation

- Malignancy (except primary brain tumors, low grade skin malignancies and carcinoma in situ of the cervix).
- Uncontrolled sepsis.
- Active viral infections-hepatitis A and B, CMV, HSV, AIDS.

Age and Organ Harvesting

- Corneas 0 - 100 years (poor eyesight is not a contraindication).
- Heart Valves 0 - 60 years (Heart Attack not a contraindication).
- Trachea 15 - 60 years.
- Skin 16 - 85 years.
- Kidneys 0 - 75 years (Pediatric donors consider weight and size).
- Liver 0 - 70 years (size matching is usually recommended).

Organ Preservation Time

- É Heart ó 4 to 6 hours.
- É Lungs ó 4 to 6 hours.

É Small Intestines ó 4 to 6 hours.

É Liver - 12 hours.

É Pancreas ó 12 to 18 hours.

É Kidneys-72 hours.

Documentation

- Cause of irreversible brain injury.
- Absence of other potentially reversible causes of coma.
- Clinical and other findings that confirmed brain death.
- Time of brain death.
- Information to the patient's family on brain death and organ donation.
- Consent for organ or tissue donation.
- **Signatures required**
 - Medical officer treating the patient.
 - Neurologist/Neuro Surgeon (Where Neurologist/Neurosurgeon are not available, then anaesthetist/intensivist).
 - Authorized Specialist (from panel of experts approved by the Appropriate Authority).
 - Medical Administrator In charge of the hospital.

Conclusion

A severe shortage of organs the world over has led to increased pressure on the intensive care staff for early identification of the brain dead donor and optimum management of this condition. The diagnosis of brain death as per the Transplantation Human Organ Act 1994 is based on simple clinical bedside tests, no need of routine confirmatory test. This Act has made it possible in India to use this pool of patients for organ retrieval and transplantation. The process of organ donation and transplantation requires co-ordination between multidisciplinary teams operating almost simultaneously and sometimes in different locations like getting surgeons from different specialties together for both donor and recipient surgery.

Further reading

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EVALUATION OF NEW FEVER IN THE CRITICALLY ILL PATIENT

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1. When to suspect? Recognize?

a. **INTRODCTION:** New onset of fever in Intensive care unit is a very common finding, and triggers a response of various investigations and addition of new antibiotics which may not be needed many times. This leads to increasing cost and adds to increased utilizations of resources. All new fevers in ICU should be evaluated in a prudent and cost effective manner.

b. **CASE DEFINITION.**

- i. In non-immunosuppressed patient two consecutive temperature (core) of more than 101° F warrants further investigation.
- ii. In neutropenic patient a single temperature of 101° F should be considered important
- iii. New onset of fever below this range, in a hemodynamically stable patient requires a bedside assessment to look for a source of infection and non infectious fever and sending investigation appropriately.
- iv. Recording fever
 1. All patients in ICU should have hourly recording of temperature and recorded in nursing chart.
 2. Uniformity of scale (Centigrade or Fahrenheit should be maintained)
 3. The site of temperature recording should be recorded (Oral, axillary, rectal or tympanic)
 4. Larger ICUs should have access to core temperature (rectal, tympanic or bladder) measurement device
 5. The instrument should be properly calibrated and sterilized. Thermometers should not be shared between patients to reduce cross infection

2. Incidence of the condition in our country

30% patients become febrile during hospitalizations. Up to 90% critically ill patients with severe sepsis experience fever during ICU stay. ICU patients will generally present a newly elevated temperature at some point during their stay. Fever in ICU could be infectious, non-infectious or mixed origin and confirmation of source is difficult. A prudent, cost-effective assessment is necessary.

3. Differential diagnosis: Non-infectious causes of fever

- a. CNS: SAH, ICH, Infarction

- b. Cardiac: MI, Pericarditis
- c. Pulmonary: Atelectasis, PE, fibro-proliferative phase of ARDS
- d. Hepatobiliary & GIT: Acalculus cholecystitis, acute pancreatitis, active Crohn's disease, toxic megacolon, alcoholic hepatitis
- e. Rheumatologic syndromes: Vasculitis, SLE, RA, Good pasture's syndrome
- f. Endocrine: Hyperthyroidism, adrenal insufficiency, pheochromocytoma
- g. Other miscellaneous non-infectious causes:
 - i. Drug fever
 - ii. Transfusion reactions
 - iii. Neoplasms
 - iv. Malignant hyperthermia
 - v. Neuroleptic malignant syndrome
 - vi. Serotonin syndrome
 - vii. Opioid withdrawal syndrome
 - viii. Alcohol withdrawal syndrome
 - ix. Devitalized tissue secondary to trauma
 - x. Hematoma
- h. Infectious causes of fever
 - i. CNS: Meningitis, Encephalitis, Brain abscess, Epidural abscess
 - ii. Head & Neck: Acute suppurative parotitis, Acute sinusitis, ASOM, Para and retropharyngeal abscesses.
 - iii. CVS: Endocarditis, Catheter related infection
 - iv. Pulmonary & Mediastinal: Pneumonia, Empyema, Mediastinitis
 - v. Hepatobiliary & GIT: Appendicitis, Diverticulitis, Peritonitis, Intraabdominal abscess, Perirectal abscess, Infected pancreatitis, Acute cholecystitis, Cholangitis, Hepatic abscesses, Acute viral hepatitis
 - vi. Genitourinary: Bacterial or fungal cystitis, Pyelonephritis, Perinephric abscess, Tubo-ovarian mass, Endometritis, Prostatitis
 - vii. Breast: Mastitis, abscess
 - viii. Cutaneous: Cellulitis, Suppurative wound infection, Necrotizing fasciitis, Bacterial myositis, Herpes zoster
 - ix. Osseous: Osteomyelitis

4. **Prevention & Counseling**

Staff working in the ICU should be familiar with drug fever and non-infectious causes of fever. Strict asepsis, hand hygiene measures & universal precautions can bring down the infection related fevers. Regular surveillance can help in identifying non-compliant staff, which can be appropriately counseled.

5. **Optimal Diagnostic Criteria, Investigations, treatment & referral criteria**

*Situation1: At secondary Hospital/ Non-Metro situations: Optimal standards of treatment in situations where technology & resources are limited.

a. **Clinical Diagnosis:**

- i Patients are not febrile: eutermic or hypothermic → with life-threatening infection:
 1. Elderly
 2. Open abdominal wound
 3. Large burns
 4. Patients on ECMO, CRRT
 5. CHF
 6. End-stage liver disease, CRF
 7. Patients on anti-inflammatory or antipyretic drugs.
 - ii Symptoms and signs in the absence of fever, which mandate a comprehensive search for infection and aggressive, immediate empirical therapy: Unexplained hypotension, tachycardia, tachypnea, confusion, rigors, skin lesions, respiratory manifestations, oliguria, lactic acidosis, leukocytosis, leukopenia, immature neutrophils (i.e., bands) of 10%, or thrombocytopenia
- a. **Key elements in evaluation:** History & physical examination. Look at wounds, surgical incision sites, vascular access and pressure ulcers. Obtain/review Chest Xray, look for new infiltrates or effusions. Appropriate lab studies: Cultures, WBC, PBS. Remove CVC > 96 hrs Send tip for semi quantitative culture. Send stool sample in patients on ABx for > 3 days. C difficile toxin. Diagnostic thoracentesis, paracentesis, LP, Ultrasound/CT

4. INITIAL ASSESSMENT

- a. Focused history and bedside review of nursing chart and patients notes should be done. A detailed medication history, line manipulation, blood transfusion, appearance of new rash, diarrhea, or any new procedure performed should be enquired
- b. Focused physical examination should be performed looking for any source of sepsis or non-infectious cause of fever.
- c. Common infectious causes of new fever in ICU
 - Hospital acquired or Ventilator associated pneumonia- Intubated for more than 48 hours. New fever, purulent secretion, bronchial breathing
 - Central line sepsis-Line in place for more than 48 hours Erythema, purulent discharge at central line site.
 - Urinary catheter related infection ó Catheter more than 48 hours in place, suprapubic tenderness cloudy urine
 - Surgical site infection ó purulent discharge from wound site
 - Sinusitis- Nasogastric or nasotracheal tube, purulent nasal discharge

Parotitis- poor oral hygiene, unilateral tender parotid swelling

A calculus cholecystitis- abdominal tenderness, intolerance of feed

d. Common non infectious causes of fever in ICU

Rash- drugs (antibiotics,antiepileptics, NSAIDSetc.)

Unilateral painful swelling of limb- Deep Venous thrombosis

Thrombophlebitis

5. INVESTIGATION

Investigation to be performed (in all facilities)

- a. Total and differential white count
- b. Peripheral smear for toxic granules
- c. CRP
- d. Blood culture ó All ICUS should have a protocol for sending blood culture.
Recommendation for blood cultures:
 - **CULTURE NUMBER-** Obtain 3 to 4 blood cultures within the first 24 hrs of the onset of fever → first cultures before the initiation of antimicrobial therapy →drawn consecutively or simultaneously, →endovascular infection → separate venipunctures by timed intervals can be drawn to demonstrate continuous bacteremia.
 - Additional blood cultures to be drawn only: →clinical suspicion of continuing or recurrent bacteremia or fungemia or→? for test of cure, → 48ó96 hrs after initiation of appropriate therapy for bacteremia/fungemia.
 - Additional cultures should always bepaired.
 - For patients- **without an indwellingvascular catheter**→ at least 2 blood cultures using strict aseptic technique from peripheral sites → by separate venipunctures after appropriate disinfection of the skin.
 - For cutaneous disinfection, 2% chlorhexidine gluconate in 70% isopropyl alcohol is the preferred skin antiseptic; tincture of iodine is equally effective. Both require -30 secs of drying time before the culture procedure. Povidone iodine is an acceptable alternative; →it must be allowed to dry for 2 mins.

- e. Wound swab for gram stain, culture and sensitivity
- f. Endotracheal suction for gram stain C & S (semiquantitative)
- g. Urine for gram stain C&S (semi-quantitative)
- h. Central line tip for C&S
- i. Chest x-ray
- j. Abdominal USG
- k. X-ray sinus
- l. Transthoracic echocardiogram

Investigation to be performed in tertiary care center.

- a. Procalcitonin
- b. Chest CT
- c. Bronchoscopy with lavage
- d. CT sinus
- e. CT abdomen for any collection
- f. Four sets of blood culture
- g. Blood for fungal culture
- h. Stool for c. difficile toxin
- e. MIC or e-test of antibiotics
- f. Venous Doppler of legs
- g. Transesophageal Echocardiogram

- 6. MANAGEMENT.** It will depend on the underlying cause. Non specific treatment with antipyretic should be instituted in patients with central nervous system disorder, extremes of age, poor cardiac reserve.

Referral Criteria: If higher diagnostic tests and imaging techniques are not available and the patient is not improving, transfer to well equipped centres should be undertaken.

Suggested Reading

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HEMODYNAMIC MONITORING IN THE ICU

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WHEN TO SUSPECT/ RECOGNIZE?

h) Introduction:

Hemodynamic monitoring is an integral part of ICU care. Need for invasive monitoring should be assessed carefully. Attention to technical details correct interpretation of data, and its application in selecting therapy should be individualized within the clinical context.

a) Case definition:

For both situations of care

Basic hemodynamic monitoring: In any Secondary Hospital / non-Metro setup

- Clinical examination- Central and peripheral pulses, Manual blood pressure- look at the trend, compare with patients normal values, capillary refill, core temperature, peripheral temperature at extremities
- Noninvasive- Noninvasive blood pressure, Pulse oximetryplethysmographic signals
- Intraarterial pressure
- Central venous pressure
- Hourly urine output
- Screening Echocardiography
- Base deficit (ABG)
- Central venous oxygen saturation

Advanced hemodynamic monitoring in selected cases: In Superspeciality facility in a Metro location

- These should be initiated in patients on high vasopressors, high ventilator support, compromised cardiac and renal function, and where empirical fluid challenge may be harmful. These modalities include
 - Cardiac output- minimally invasive
 - Pulse contour analysis (e.g. Flotrac, PICCO, LiDCO)
 - Esophageal Doppler
- Pulmonary artery catheter
 - Pulmonary artery occlusion pressure
 - Continuous cardiac output
 - Continuous mixed venous oxygen saturation (SvO₂)
 - Derived and calculated variables
 - Pulse pressure/ Stroke volume variation
 - Continuous Scvo₂ monitoring
 - Lactate levels

Standard Operating Procedure

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

ARTERIAL CANNULATION

The ability of invasive blood pressure monitoring to identify beat to beat variability and long term trends is unsurpassed by any other currently available technology. In addition, presence of arterial catheter enables frequent sampling of arterial blood without arterial punctures in critically ill patients.

INDICATIONS:

- a) Hemodynamic monitoring
 - beat to beat monitoring of blood pressure
 - acutely hypertensive or hypotensive patients (shock)
 - use of vasoactive drugs
 - cardiac and cardiovascular surgery
 - induced hypotension
 - pulse contour cardiac output monitoring
- b) Frequent arterial blood gas sampling: critically ill patients including ventilated patient
- c) Arterial administration of drugs, thrombolytics
- d) Intra aortic balloon pump use

e) Noninvasive blood pressure monitoring not possible ó e.g., too obese, burned extremity

ABSOLUTE AND RELATIVE CONTRAINDICATIONS:

Severe injury to the limb

Lack of collateral circulation

Coagulopathy

Arteriovenous fistula in the same limb

- Pre-existing vascular insufficiency (Raynaud's phenomenon)

History of surgery disrupting lymphatic drainage to that limb e.g., mastectomy with lymph node dissection

Equipment:

Appropriate intravascular catheter

Fluid filled noncompliant tubing with stopcocks

Transducer

A constant flush device

Electronic monitoring equipment

Site selection:

The common sites of arterial line insertion are the radial, femoral, and dorsalis pedis arteries. Other sites: axillary dorsalis pedis brachial, ulnar, posterior tibial and superficial temporal arteries

Arterial Cannulation:

The arterial line can be inserted using a simple catheter-over-needle arrangement (with or without a guidewire) or a set based on the Seldinger technique.

Doppler or ultrasound can be helpful for difficult line insertion.

Set up of the pressure transducing system

- *The pressure transducing* assembly consists of a coupling system, pressure transducer, amplifier and signal conditioner, analog to digital converter, microprocessor which convert the signal received from the vein or artery into a waveform on the a bedside monitor
- *The flushing system* ó is set up using a 500 ml saline bottle encased in a bag

pressurized to 300 mm Hg. At this pressure the catheter will be flushed with 3 ml saline per hour and help keep the catheter patent. Heparinised saline is no longer routinely used

- The reference point is usually at the level of the heart where the transducer is zeroed.

RESOURCES REQUIRED FOR ONE PATIENT/PROCEDURE (PATIENT WEIGHT 60 KGS)

SITUATION	HUMAN RESOURCES FOR 4- 6 WEEKS	INVESTIGATION OF 4-6 WEEKS	DRUGS AND CONSUMABLES FOR 4-6 WEEKS	EQUIPMENT
1. At secondary hospital/non-metro situation	<p>One Each:</p> <p>1. Intensivist / Anaesthetist</p> <p>2. ICU Technician</p> <p>One in each shift:</p> <p>1. ICU/Ward Doctor</p> <p>2. Nurse</p> <p>3. Attendant</p>	<p>Once a week or more for 4-6 week long therapy</p> <p>a. Ultrasound</p> <p>1. Doppler of the cannulated artery</p> <p>2 For arterial canulation</p> <p>b. Arterial tip culture (femoral arterial line)</p> <p>c. Blood culture</p>	<p>1. Drugs for 4-6 week- Rs. 2000</p> <p>2 Lab investigation- Rs. 2000</p> <p>3. Consumables- Rs.7000</p>	<p>1. Ultra sonography machine</p> <p>2. Invasive arterial pressure monitor</p>

2. At super specialty facility in metro location	As in situation 1	As in situation 1	<p>a. For simple situation</p> <p>1. drugs for 4-6 weeks-Rs.2000</p> <p>2. Lab investigation-Rs. 5000</p> <p>b. For difficult situation</p> <p>1. use of long catheter for arterial canulation- Rs.6,000</p> <p>2. USG guided arterial canulation and using special arterial catheters with wire-guide - Rs.8,000</p>	<p>As in situation 1 with</p> <p>1. Long arterial catheter</p> <p>2. Arterial catheter with guide wire</p>
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RESOURCES REQUIRED FOR ONE PATIENT/PROCEDURE (PATIENT WEIGHT 60 KGS)

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- 6) March 1973 - Volume 38 - Issue 3> Complications of Percutaneous Radial-artery Cannulation: 1973 American Society of Anesthesiologists, Inc.
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Central venous catheter insertion and Central Venous Pressure Monitoring

Definition: Insertion of a catheter in a central vein, usually the superior vena cava, but also in the inferior vena cava or right atrium.

Indications: In recent years, central venous cannulation is practiced increasingly in anaesthesia and intensive care for a variety of indications

Measurement of Central Venous Pressure (CVP)

- Major surgery
- Anticipated major blood loss
- Anticipated major fluid shifts
- Significant cardiac disease
- Significant pulmonary disease
- Pulmonary hypertension

Intravenous access

- Rapid administration of fluids and blood
- Administration of Vasoactive agents and concentrated potassium infusions
- Measurement of central venous oxygen saturation during resuscitation from shock
- Measurement of cardiac output using some semi-invasive techniques
- Total parenteral alimentation
- Administration of Chemotherapeutic and other irritant drugs
- Frequent blood sampling
- Insertion of a pulmonary artery catheter
- Inability to cannulate peripheral veins

Therapeutic procedures

- Insertion of transvenous pacemaker
- Insertion of catheters for haemodialysis and plasmapheresis
- Aspiration of air emboli

Sites of central venous cannulation: The subclavian and internal jugular veins are the most commonly cannulated veins. Other veins that may be used are the arm veins (basilic, cephalic), external jugular and femoral veins.

Equipment Required

In all situations:

- Location of the vein by anatomical landmarks

Appropriate intravascular catheter

- catheter over guidewire using the Seldinger technique
- catheter through needle or cannula
- long cannula over needle

Fluid filled noncompliant tubing with stopcocks

Transducer

A constant flush device

Electronic monitoring equipment

Chest X-ray at the end of the procedure to confirm position of the CVC and rule out pneumothorax

In a superspeciality hospital in a Metro: in addition to the above

Location of the internal jugular vein by ultrasound

- Portable ultrasound machine with a high frequency probe
- Ultrasound probe with or without a needle guide
- Sterile jelly
- Sterile sleeve for ultrasound probe
- Antibiotic coated catheter may be used in case there is high risk of catheter related blood stream infection
 - Immunosuppressed patient
 - High baseline CRBSI rate in the unit
 - Anticipated prolonged duration of cannulation

Clinical Utilization of CVP Measurement

CVP is influenced not only by the volume status, but also by myocardial contractility, afterload, intrathoracic and intra-abdominal pressures.

A single measurement of the CVP helps somewhat in defining circulatory status but leaves considerable overlap in possible interpretations. Hence single values of CVP should not be relied upon. Instead, response to fluid challenge and the trend of values should be used in clinical decision making,

It is best not to remove PEEP for measurements.

- DO NOT subtract half or any other proportion of PEEP value to the CVP measurement to get an approximate of true CVP

In a non mechanically ventilated patient CVP of 8 -10 mm Hg is judged to be adequate.

Fluid Challenge

A controlled fluid challenge and response of CVP is the best method of interpreting volume status. The fluid challenge is performed in 4 steps:

- Select the type of fluid: usually normal saline or a colloid
- Infuse rapidly. Rate of infusion: 500ml of crystalloid or 200 ml of colloid over 20-30 minutes
- Target the Desired therapeutic response: the parameters are set empirically by the physician. These could be mean arterial pressure (MAP >70mmHg), HR <100/min, hourly urine output > 0.5ml.kg/hr.

- Set the Danger / safety limits. Again set empirically by the physician. E.g. CVP 16mmHg, or 4-5mmHg more than the baseline value
- Assess the response to the initial bolus of fluid
- Repeat bolus infusion of fluid if
 - Therapeutic target not reached AND
 - Danger CVP value is not reached
- Discontinue fluid infusion if
 - Therapeutic target is achieved OR
 - Danger value of CVP is reached
- Reassess at frequent intervals

Another way to perform a fluid challenge is to see the change in CVP in response to a fluid bolus. As a rule of thumb if the increase in CVP measured before and 5 minutes after a fluid bolus is 0-3 mmHg, more fluid should be given. If it is 3-5 mmHg he is probably adequately filled. If the CVP increases >5mmHg after the fluid bolus, fluid loading should be stopped.

RESOURCES REQUIRED FOR ONE PATIENT/PROCEDURE (PATIENT WEIGHT 60 KGS)

SITUATION	HUMAN RESOURCES FOR 4- 6 WEEKS	INVESTIGATION OF 4-6 WEEKS	DRUGS AND CONSUMABLES FOR 4-6 WEEKS	EQUIPMENT
1. At secondary hospital/non-metro situation	One Each: 1. Intensivist / Anaesthetist 2 ICU Technician One in each shift: 1. ICU/Ward Doctor 2. Nurse 3. Attendant	Once a week or more for 4-6 week long therapy a. Ultrasound 1. Doppler of the vein 2. For CVC: a. Blood count b. CVC tip culture c. Blood culture	1. Drugs for 4-6 week- Rs. 2000 2. Lab investigation- Rs. 2000 3. Consumables- Rs.8000	1.Ultra sonography machine 2.Muliparameter monitor with invasive pressure monitoring
2. At super specialty facility in metro location	As in situation 1	As in situation 1	a. For simple situation 1. drugs for 4-6 weeks-Rs.2000 2.Lab investigation-Rs. 7000 b. For difficult situation 1.antibiotic coated catheter 2000-4000 2. USG guided canulation	As in situation 1 with

Echocardiography

While resuscitation efforts are underway , a quick assessment with bedside echocardiogram can guide clinician in rationalizing use of volume resuscitation, inotropes and vasopressors . This can be repeated to assess response to therapy.

Using bedside Echocardiogram one can assess

- The Left ventricular (LV) function,
- Right Ventricular (RV) function,
- Presence of pericardial effusion and tamponade,
- Pre load assessment, fluid responsiveness
- Valve lesions.

Equipment requirement

Portable Echocardiography / Ultrasound machine with Probe : Rs. 15,00,000.00

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

Pulmonary artery catheter insertion and monitoring

Introduction: Swan & Ganz introduced the balloon tipped pulmonary artery catheter into clinical practice in early seventies. This brought the catheter out of the domain of radiologists and at the bedside of the patients in intensive care. Notwithstanding the controversies regarding the utility of pulmonary artery catheter in improving outcome, the clinician in the operating room and ICU needs to conversant with the use of pulmonary artery catheter.

Indications for insertion of PAC: Pulmonary artery catheterization can be used for diagnostic purpose, to monitor therapy, and to evaluate the effects of drugs. The indications for PAC insertion are:

Management of complicated myocardial infarction

- É Hypovolemia vs cardiogenic shock
- É Ventricular septal rupture (VSR) vs acute mitral regurgitation
- É Severe left ventricular failure
- É Right ventricular infarction
- É Unstable angina

- É Refractory ventricular tachycardia
- Assesment of respiratory distress**
- É Cardiogenic vs non-cardiogenic pulmonary edema
- Primary vs secondary pulmonary hypertension**
- Assessment of type of shock**
- Assessment of therapy**
- É Afterload reduction
- É Vasopressors
- É Beta blockers
- É Intra-aortic balloon counterpulsation
- Assessment of fluid requirement in critically ill patients**
- É Hemorrhage
- É Sepsis
- É Acute renal failure
- É Burns
- Management of postoperative open heart surgical patients**
- É Assessment of valvular heart disease
- É Assessment of cardiac tamponade/constriction
- Contraindications / Cautions:**
- É Coagulopathy
- É Inexperienced clinician
- É Pulmonary hypertension

Pulmonary artery catheter insertion can only be performed at well equipped tertiary care centres.

Use of the Pulmonary Artery Catheter

The 4 most important measurements obtained from the PAC are

- Pulmonary artery occlusion pressure (PAOP)
- Pulmonary artery diastolic pressure (PADP)
- Thermodilution cardiac output
- Mixed venous oxygen saturation
- The fluid challenge (as described with CVP) remains the best method of assessing the PAOP during mechanical ventilation with PEEP.

Mixed venous oxygen saturation (SvO₂) / Central venous oxygen saturation (ScvO₂)

. An SvO₂ below 65% implies low oxygen delivery, while a value below 60% indicates that there is a serious risk of tissue hypoxia if corrective measures are not taken.

A low SvO₂ (< 40 %) implies critical oxygen supply / demand imbalance. In some disease states, cells in some tissues are unable to assimilate and/or process the needed oxygen.

If SvO₂ is high(>80%) then the demand has declined, the O₂ supply has increased, or the cells are unable to utilize oxygen.

Thus a falling or low SvO₂ is an important indicator that the oxygen delivery is compromised and is deficient relative to the needs of the tissues.

An alternative is to measure central venous oxygen saturation (ScvO₂). Central venous catheterisation is a simpler and safer procedure, and is commonly used.

In this case a catheter is positioned in the Superior vena cava or upper Right atrium.

The goals of early resuscitation, within six hours of septic shock is to keep SVO₂ > 65% or Scvo₂ > 70%

SvO₂ and ScvO₂ can be measured continuously with oximetric catheters, or blood can be drawn intermittently and the analysed using a co-oximeter on the blood gas machine

Cardiac Output monitoring

Cardiac output is the amount of blood being pumped to the body by the heart every minute. In some patients, cardiac output monitoring may be useful to make a diagnosis and to refine therapy.

Cardiac output monitoring should be performed only in well equipped tertiary care centres.

Indications

Management of complicated myocardial infarction

- É Hypovolemia vs cardiogenic shock
- É Severe left ventricular failure

Assessment of type of shock

Septic shock

Assessment of therapy

- É Afterload reduction
- É Vasopressors
- É Beta blockers
- É Intra-aortic balloon counterpulsation

Assessment of fluid requirement in critically ill patients

- É Hemorrhage
- É Sepsis
- É Acute renal failure
- É Burns

Management of postoperative open heart surgical patients

Methods of monitoring cardiac output

Thermodilution (intermittent or continuous) using the pulmonary artery catheter has been the classical method of cardiac output monitoring. However insertion of a pulmonary artery catheter is demanding and complicated. Other less invasive methods include

PiCCO: using bolus transpulmonary thermodilution cardiac output and pulse contour derived continuous cardiac output measurement are obtained. A central venous catheter, special thermistor tipped femoral artery catheter and monitor are required. The main advantages over the pulmonary artery catheter is PiCCO is far less invasive, easy to place requiring routine skills of placing a central line and arterial line. The additional advantages are the values of extravascular lung water, global end-diastolic volume and the stroke volume variation (a dynamic measure of preload).

Lithium Dilution Cardiac Output (LidCO): uses lithium dilution technique, instead of transpulmonary thermodilution (used by PiCCO). The principle of pulse contour analysis for continuous cardiac output measurement is similar.

- Advantages: Existing arterial line and venous lines can be used, even central venous access is not mandatory. Therefore cardiac output monitoring can be established fast.
- Disadvantages: requires lithium injection

Flotrac: Arterial Pressure based Cardiac output (APCO) system calculates the stroke volume from pulse pressure, which is the standard deviation of blood pressure. A special transducer is connected to an existing arterial line and the cardiac output monitor.

- Advantages: does not require a central venous catheter or any bolus injection to estimate cardiac output, easy and rapid set up

Preload Responsiveness

Preload responsiveness is the increase in cardiac output in response to fluid loading.

Dynamic parameters predict the response to fluid loading without having to give a fluid challenge. Hence they may avoid the potential hazards of a fluid challenge.

Stroke volume variation, Systolic pressure variation and Pulse pressure variation with respiratory cycle and are referred to as dynamic indicators of preload responsiveness.

Values >13% is indicative of fluid responsiveness

These parameters are available on minimally invasive cardiac output monitors such as Flotrac, PiCCO, LIDCO.

Visible variation in the diameter of the inferior vena cava on echocardiography can also be used to predict fluid responsiveness.

SPV, PPV and SVV cannot be used in patients with spontaneous breathing activity and / or with arrhythmias. They are not reliable in patients ventilated with low tidal volume and in patients with increased intraabdominal pressure

In these cases Passive leg raising is an alternative choice.

Passive leg raising maneuver is an endogenous fluid challenge. A continuous monitor of stroke volume or SVV / PPV is required. Increase in stroke volume > 10%, increase of Aortic blood flow >10% in response or decrease in SVV / PPV after PLR predict a good response to fluid loading

A comparison of the costs of Disposables required for the Pulmonary artery catheter (PAC), Flotrac and PICCO is given in Table 2:

Table 2: Costs of Disposables for cardiac output monitoring

	PAC (Cost in Rs)	PiCCO (Cost in Rs)	Flotrac (Cost in Rs)
Essential disposables	9500 (CCO-SvO ₂ catheter)	9000	9500
Transducers	2	1	0
Total cost	1500	750	0
CVC	0	1000	0
Art. Line	70	0	70
Saline, syringes	400	200	200
Total Initial Set up Cost (Does not include capital cost of hemodynamic monitors)	11,470	12750	9770 Add Presep continuous ScvO ₂ catheter 8000 Total: 17700
Daily monitoring cost (based on an average of 3 days monitoring, does not include professional fees)	4500-5000	4500-5500	3500-4000 6000-7000 including Presep

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ACUTE PULMONARY EMBOLISM (PE)

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I. WHEN TO SUSPECT/ RECOGNIZE?

i) Introduction:

Venous thromboembolic conditions leading to acute respiratory failure is common in critically ill medical and surgical patients. This may be the presenting diagnosis on ICU admission or may develop secondarily in patient admitted to ICU for other conditions. PE presentation is variable presenting suddenly as a cardio respiratory arrest or may be asymptomatic .Mortality can be reduced by prompt diagnosis and therapy . Despite significant advances in the prevention and treatment of VTE, pulmonary embolism remains the most common preventable cause of hospital death, being responsible for approximately 150,000 to 200,000 deaths per year in the United States

j) Case definition:

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

PE refers to obstruction to main pulmonary artery or one of its branches by material (e.g., thrombus, tumor, air, or fat) that originated elsewhere in the body. This topic review focuses on PE due to thrombus. PE can be classified as acute or chronic. Patients with acute PE typically develop symptoms and signs immediately after obstruction of pulmonary vessels. In contrast, patients with chronic PE tend to develop slowly progressive dyspnea over a period of years due to pulmonary hypertension

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

The incidence of DVT in India as reported is one percent of the adult population after the age of forty and is 15% to 20% in hospitalized patients. The risk of DVT is 50% in patients undergoing orthopedic surgery, particularly involving the hip and knee, and it is 40% in patients undergoing abdominal or thoracic surgery. 1/100 who developed DVT can develop PE which can be fatal. As per India-specific ENDORSE data presented at Geneva, 1 of 2 hospitalized patients in India is at high risk of developing VTE at any point in time.

An autopsy data from PGI Chandigarh, where 1,000 consecutive autopsies were performed between 1997 and 2002. 14.4% showed evidence of pulmonary thromboembolism (PTE). 1.45 % of all hospital deaths were due to PTE

The mean age was 37 years with a male preponderance in the ratio of 1.82:1

Clinical suspicion was present in 29.17 % of cases

The most common underlying cases were

- Sepsis (40.28%)
- Respiratory illness (10.42%)
- Malignancies (9.72%)
- Renal disease (8.3%)
- Hepatobiliary disease (7.64%)
- Cardiovascular disorder (6.94%)
- Gastrointestinal tract disorder (3.47%)
- Vasculitis (2.78%)

III. DIFFERENTIAL DIAGNOSIS /TYPES

Acute PE can be further classified as massive or sub massive:

- Massive PE causes hypotension, defined as a systolic blood pressure <90 mmHg or a drop in systolic blood pressure of $\times 40$ mmHg from baseline for a period >15 minutes. It should be suspected anytime there is hypotension accompanied by an elevated central venous pressure (or neck vein distension), which is not otherwise explained by acute myocardial infarction, tension pneumothorax, pericardial tamponade, or a new arrhythmia.

All acute PE not meeting the definition of massive PE are considered submassive PE.

A saddle PE is a PE that lodges at the bifurcation of the main pulmonary artery into the right and left pulmonary arteries. Most saddle PE are submassive.

Acute PE should be differentiated from other causes of acute breathlessness

- Pneumonia
- Pneumothorax
- Acute Left Ventricular failure
- Acute exacerbation of COPD
- Acute bronchial asthma

IV. PREVENTION AND COUNSELING

Most of the acute PEs originate from deep venous thrombosis (DVT) of legs. Assessing patients at risk for DVT and preventing its occurrence decreases the incidence of acute PE

Assess the risk factors for PE and deep venous thrombosis (DVT) from past medical history as mentioned below:

Prior venous thromboembolism.

- Immobility for more than 48 hours, congestive heart failure, septic shock, surgery with general anesthesia, on mechanical ventilation.

Abdominal or lower extremity surgery or trauma.

Hypercoagulable states.

Malignancy.

Spinal cord injury.

Heparin-induced thrombocytopenia.

Pregnancy or use of oral contraceptives.

Indwelling central venous catheters

Obesity

Congestive heart failure

Initiate adequate DVT prophylaxis

Unfractionated heparin(UFH) 5,000 I.U. twice or thrice daily subcutaneously.

- Fractionated Low molecular weight heparin ó enoxaparin 40 mg sub cut once daily or equivalent Fondaparinaux
In patients with high risk of bleeding mechanical methods like intermittent pneumatic compression or graduated stockings may be tried.

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**

i) Clinical Diagnosis:

- PE should be suspected in all patients who present with new or worsening dyspnea, chest pain, or sustained hypotension without any other obvious cause
- **ASSESS CLINICAL PROBABILITY OF PE:** Clinical probability of PE is based on either clinical judgment or clinical decision rules (Wells and Revised Geneva Score) mentioned below.

Therevised Geneva score:

- ☞ Age older than 65 years (1 point)
 - ☞ Previous deep venous thrombosis or pulmonary embolism (3 points)
 - ☞ Surgery or fracture within 1 month (2 points)
 - ☞ Active malignant condition (2 points)
 - ☞ Unilateral lower limb pain (3 points)
 - ☞ Hemoptysis(2 points)
 - ☞ Heart rate
 - ☞ 75 to 94 beats/min (3 points) or
 - ☞ 95 beats/min or more (5 points)
 - ☞ Pain on lower-limb deep venous palpation and unilateral edema (4 Points)
-

The probability is assessed as follows:

- ☞ Heart rate Low-probability (0 to 3 points)
 - ☞ Intermediate-probability (4 to 10 points)
 - ☞ High-probability (> or =11 points)
-

j) **Investigations:**

ECG, XRAY CHEST (PA view) and ABG should be ordered in all these patients. Although these tests are nonspecific they do increase the index of suspicion.

k) **Treatment:**

Provide oxygen to maintain saturation at more than 90%

If the patient is hypotensive, administer 500 to 1000 ml isotonic crystalloid. Any more volume resuscitation should be given with caution as it may increase RV wall tension and cause ischemia and worsening of shock.

While diagnostic confirmation is awaited, anticoagulant treatment with subcutaneous low molecular weight heparin or intravenous unfractionated (UFH) heparin should be initiated as soon as possible in patients with a high clinical probability of PE if there are no contraindications.

UFH is preferred in hemodynamically unstable patients in whom thrombolytic therapy is being planned. UFH is also preferred in critically ill patients in the ICU with PE requiring numerous procedures. It is also preferred in patients with renal failure. Patients are considered to be hemodynamically unstable if they are in shock or have a systolic blood pressure of less than 90 mm Hg or a drop in systolic pressure of more than 40 mm Hg for more than 15 minutes in the absence of new onset arrhythmia, hypovolemia, or sepsis

Most patients with acute PE are candidates for initial anticoagulant treatment with subcutaneous low-molecular-weight heparin or fondaparinux or intravenous UFH. LMWH and Fondaparinux are preferred over UFH.

The usual doses of Anticoagulation for PE are:

1) UFH: Bolus of 80 units IV/kg or 5000 IU followed by infusion at 18 units IU /kg/hr. Keeping APTT between 1.5 and 2.5 to normal.

2) Weight based normogram of heparin infusion

3) Fondaparinux:

- Weight < 50kg - 5mg s/c once a day.

- Weight 50-100kg - 7.5mg s/c once a day

- Weight >100 kg 10mg s/c once a day.

4) Enoxaparin: 1 mg /kg s/c twice a day.

a) **Referral criteria:**

- All patients with massive PE should be referred to a higher centre

The risk of adverse outcome is also more in the following situations and these patients should be referred :

- Shock (SBP < 90mmof Hg) and/or BP drop \geq 40mm of Hg for >15min and sustained hypotension.
 - Immobilization due to neurological disease.
 - Age 75 years or more.
 - Cardiac, renal or respiratory disease or cancer
-

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

h) **Clinical Diagnosis:** As per situation 1.

i) **Investigations:**

- If the patient has a high probability of PE clinically or on the basis of a high probability score, and is safely transferable to CT room and is in a position to cooperate with breath holding, he should undergo multidetector CT (MDCT) for CT Pulmonary Angiography irrespective of his hemodynamic status.
- If the patient is hemodynamically unstable and has a high probability of PE clinically or on the basis of a high probability score and who is critically ill and can not be shifted, he should be subjected to Trans-esophageal Echo (TEE,), lower extremity ultrasonography and his blood sample sent for a D- Dimer level. A negative Echo and Venous Doppler, however, do not rule out clinically significant PE. Efforts should be made to stabilize this patient hemodynamically and once the patient stabilizes, he should be sent for MDCT CT Pulmonary Angiography, if doubt still remains about the diagnosis.
- If the patient is hemodynamically stable and has a low or medium probability score then order a high sensitivity D- Dimer level (ELISA). If it is positive (level more than 500ng/ml) further testing with CT chest is indicated.

- If it is negative the risk of PTE is very low (0.14%) and no further testing is required.
- A V/Q scan may be done in patients with a high probability of PE and where there is a contraindication for CT like renal failure or if CT scanning is not available.
- In pregnant women with clinical findings suggestive of PE, an MDCTchest should be done. The concern about radiation is overcome by the hazard of missing a potentially fatal diagnosis or exposing the mother and fetus to unnecessary anticoagulant treatment. Multidetector CT delivers a higher dose of radiation to the mother but a lower dose to the fetus than V/Q scanning. Venous ultrasonography can be done in these patients before MDCT.

j) Treatment:

CONSIDER THROMBOLYSIS:

- If the patient is hemodynamically unstable:
 - Admit in ICU
 - Start anticoagulation, preferably IV unfractionated heparin or LMWH. Keep APTT time 1.5-2.5 to normal.
 - Administer thrombolytic therapy if there are no contraindications (Table1).
 - Other supportive measure to stabilize the patient.
- Hemodynamically stable patients with right myocardial dysfunction and injury suggested by TEE and markers (raised Troponin and BNP) can also be given thrombolytic therapy if there are no contraindications (Table 2).

CONSIDER SURGICAL TREATMENT

Table 1

Thrombolytic therapy regimens for acute pulmonary embolism	
Drug	Protocol
Streptokinase	250,000 U IV (loading does during 30 mins; then 100,000 U/h for 24 hours)

Urokinase ^a	250,000 U IV (loading dose during 10 mins; then 2,000 U/lb/h for 12 to 24 hours)
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IV, intravenous; tPA, tissue-type plasminogen activator. 100 mg IV during 2h

Hemodynamically stable patient with PE without myocardial dysfunction or injury:

- Admit in ward.
- Anti-coagulate with LMWH or Fondaparinux or UFH.
- Closely watch for vitals and respiratory distress. Consider early mobilization.

Table2

Contraindication for thrombolytic therapy:

Absolute contraindications

- Prior intracranial hemorrhage (ICH)
 - Known structural cerebral vascular lesion
 - Known malignant intracranial neoplasm
 - Ischemic stroke within 3 months
 - Suspected aortic dissection
 - Active bleeding or bleeding diathesis (excluding menses) significant closed-head trauma or facial trauma within 3 months
-

Relative contraindications

- History of chronic, severe, poorly controlled hypertension
 - Severe uncontrolled hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)
 - Traumatic or prolonged (>10 min) CPR or major surgery less than 3 weeks
 - Recent (within 2-4 wk) internal bleeding
 - Non compressible vascular punctures
 - For streptokinase/anistreplase - Prior exposure (more than 5 d ago) or prior allergic reaction to these agents
 - Pregnancy
 - Active peptic ulcer
 - Current use of anticoagulant (e.g., warfarin sodium) that has produced an elevated international normalized ratio (INR) >1.7 or prothrombin time (PT) >15 seconds
-

INITIATE VITAMIN K ANTAGONIST (WARFARIN) THERAPY:

- Vitamin K antagonist should be initiated as soon as possible preferably on the first treatment day and Heparin should be continued. Heparin should be discontinued when INR reaches a level of 2.0 or higher for at least 24 hours. Duration of treatment is from 3 to 6 months.
- LMWH is preferred over Warfarin in Cancer and in pregnant women for longterm treatment.

: Inferior vena caval filters are indicated in the following conditions:

- Recurrent thromboembolism despite anticoagulant therapy
- Contraindication to anticoagulation therapy
- Bleeding while on anticoagulants.

Patient should be put on long term anticoagulant treatment in the following conditions:

- Idiopathic pulmonary embolism
- Recurrent PE
- Cancer

VI. FURTHER READING / REFERENCES

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SEVERE SEPSIS AND SEPTIC SHOCK

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I. WHEN TO SUSPECT/ RECOGNIZE?

k) Introduction:

Sepsis(from Greek *sepein* = to rot, putrefy)is a significant problem worldwide in the intensive care unit both in terms of the burden on the healthcare and the morbidity and the mortality it causes. Despite the advances in the treatment and the understanding of the pathophysiology of sepsis, the mortality has remained unforgivably high. The site of infection is difficult to estimate and even among those patients where the site is strongly suspected, cultures might be negative or of questionable significance. Though a positive blood culture would be diagnostic, the rate of positivity is only 30 to 50 % percent. It is easy to confuse the diagnosis of sepsis with conditions that simulate it such as pancreatitis or anaphylactic reactions or drug fever. Early identification and prompt treatment is the key to reduce mortality

a) Case definition:

Till 2001 there was no clear definition of sepsis. As a result there was no uniformity in the treatment guidelines. International sepsis forum defined sepsis in the following way

Systemic inflammatory response syndrome (SIRS)	Two or more of the following variables (1) fever > 38°C (100.40°F) or hypothermia <36°C (96.80°F) (2) tachypnea (>20 breaths/min) or PaCO ₂ < 32 mmHg (3) tachycardia (heart rate >90 beats/min) (4) Leukocytosis or leucopenia.i.eWBC > 12,000 cells/mm ³ , < 4,000 cells/mm ³ or > 10% immature band forms
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Sepsis	Systemic inflammatory response syndrome that occurs due to a known or suspected pathogen (bacteria, virus, fungal or parasite)
Severe sepsis	<p>Sepsis plus evidence of organ dysfunction or tissue hypoperfusion as follows</p> <ol style="list-style-type: none"> (1) Altered mental status. (2) ALI PaO₂/FIO₂ <250 (3) Thrombocytopenia < 100,000/ (4) Bilirubin >2mg/dl (5) INR >1.5 or aPTT > 60 seconds. (6) Urinary output of 0.5 ml/kg for at least 2hr or Scr >2mg/dl despite fluid resuscitation. (7) Tissue hypoperfusion as suspected by mottled skin, Capillary refilling time × 2 seconds or lactate >4 mmol/l (8) Hypotension Systolic blood pressure <90 mmHg or mean arterial pressure <70 mmHg.
Sepsis induced hypotension	SBP <90mmHg or MAP <70mmHG or SBP decrease >40mmHg
Septic shock	Sepsis induced hypotension despite adequate fluid resuscitation.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

The incidence of sepsis and the number of sepsis-related deaths are increasing, although the overall mortality rate among patients with sepsis is declining. The mortality rates associated with severe sepsis and septic shock are 25% to 30% and 40% to 70% respectively. Though we do not have exact statistics from India, one Indian study showed incidence of SIRS without organ dysfunction as 51.60%, SIRS with organ dysfunction as 17.10% patients, of which 76.50% were due to sepsis and 23.50% were not due to sepsis. ICU mortality of all admissions was 13.90% and that of severe

sepsis was 54.10%. Hospital mortality and 28-day mortality of severe sepsis were 59.30% and 57.60%, respectively.

III. DIFFERENTIAL DIAGNOSIS

Severe Sepsis and Septic shock should be differentiated from other common cause of fever and shock in ICU or hospital like -

- 1) Acute pancreatitis.
- 2) Drug fever.
- 3) Anaphylaxis and anaphylactoid reactions.
- 4) Adrenal crisis.
- 5) Cardiogenic shock, hemorrhagic shock or neurogenic shock.
- 6) Pulmonary embolism or pulmonary infarct.
- 7) Myxedema coma.
- 8) Thyrotoxicosis.
- 9) Poisoning or insect bite.
- 10) Burn, major surgery
- 11) SLE crisis.
- 12) Macrophage activation syndrome.

Although making the distinction of the above conditions from true sepsis becomes difficult, using different biomarkers and imaging studies might be helpful in making the diagnosis. Close monitoring and optimising the patient physiological variables will give us time to identify the exact insult.

IV. PREVENTION AND COUNSELING

Sepsis is a medical emergency. Awareness and recognition are the key of survival. The following action plan should be used to reduce global mortality from severe sepsis.

Build awareness of sepsis.

Follow standards guidelines of care.
Improve early and accurate diagnosis.
Increase the use of appropriate treatments and interventions.
Educate staff about sepsis diagnosis, treatment and management.
Data collection for the purposes of audit and feedback

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

Clinical Diagnosis:

The presentation of sepsis varies. The most important step towards improving survival is to identify the signs of sepsis very early.

General variables:

Altered mental status.
Fever.
Hypothermia.
Tachycardia.
Tachpnea.
Hyperglycaemia (plasma glucose >120 mg/dL or 7.7mmol/L) in the absence of diabetes.
Positive fluid balance.

Inflammatory variables:

Leukocytosis.
Leukopenia.
Normal WBC count with >10 % band forms.

Organ dysfunction variables:

- Respiratory óDecreased oxygen saturation
- Renal ó Acute oliguria urine output <0.5ml/kg/hr for atleast 2 hrs or rise in Creatinine > 0.5 mg/ dL.
- Haematological- Thrombocytopenia (platelet count <100,000/ µL) or coagulation abnormalities: International Normalised Ratio INR >1.5 or activated partial thromboplastin time aPTT > 60 sec.
Liver - Hyperbilirubinemia (plasma total bilirubin>4.0 mg/ dL or 70 mmol/ L).

Tissue perfusion variables:

Decreased capillary refill or mottling

Haemodynamic variables:

Arterial hypotension, Systolic Blood Pressure SBP <90 mm Hg, Mean Arterial Blood Pressure MAP <70 mm Hg, or SBP decrease >40 mm Hg.

l) Investigations:

Investigations should be directed at diagnosis, assessing the focus of sepsis, and the severity of the sepsis.

- 1) Hb
- 2) TLC
- 3) DLC
- 4) Blood Glucose.
- 5) Renal function tests (SE,BUN,Cr)
- 6) Liver function test (Bi,AST,ALT,ALKP,GGT,PT,INR,PTT)
- 7) Cultures with gram stain
- 8) Urine R/M
- 9) X-Ray
- 10) ECG

m) Treatment:

Standard Operating procedure

a. In Patient

Sepsis should be treated in the ICU, if recognized out side the ICU. Immediately start fluid resuscitation, collect blood culture and give broad spectrum antibiotics within 1 hr, culture collection should not delay antibiotic administration, and simultaneously organize ICUtransfer.

b. Out Patient

Resuscitation with fluid in the emergency department collect blood culture and give broad spectrum antibiotics within 3hrs , *culture collection should not delay antibiotic administration*, and shift the patient in the ICU.

c. Day Care

Do not admit septic patient in Day care setting.

n) **Referral criteria:**

Generally, patients can be considered for transfer for diagnosis, source control or further monitoring when they are hemodynamically stable with or without vasoactive drugs and when oxygenation and ventilation is maintained.

- a) Need Invasive monitoring devices such as arterial lines, centralline, flow trac.
- b) Mechanical ventilation, dialysis or CRRT required.
- c) Modern surgical facilities.
- d) Ultrasound and CT scan or MRI

Always communicate with receiving hospital physician, document the reason for transport and arrange appropriate staff, medication and instrument for transportation.

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

k) **Clinical Diagnosis:** As per situation 1

l) **Investigations:**

ABG

SCVO₂.

Serum lactate

Procalcitonin (PCT)

These biomarkers may be useful to distinguish between infectious and non-infectious causes of SIRS. PCT can be used to assess the severity of infection and prognostication. It also acts as a tool to guide Antimicrobial Therapy.

Ultrasonography (source identification)

CT scan if it is safe to do (source identification)

- USG or CT guided sample from the source ó minimally invasive approach is advisable to prevent change in physiology and keep in mind the risk of transportation to imaging department.

m) **Treatment:**

Follow the Surviving Sepsis Campaign (SSC) International guidelines for management of severe sepsis. Rapid diagnosis, expeditious treatment multidisciplinary approaches are critical and necessary in the treatment of sepsis. The management of patients with sepsis starts on arrival at the emergency room prior to ICU admission. Special focus on fluid and hemodynamic resuscitation and early antibiotics.

(1) Within the first 6 hours (Early goal-directed therapy)

Fluid therapy

1. Start resuscitation with fluid boluses if hypotension or serum lactate $>4\text{mmol/L}$ to maintain
 - Central venous pressure (CVP) more than or equal to 8-12 mm Hg and 12-15mmHg in mechanically ventilated patient or intra abdominal hypertension.
 - Mean arterial pressure (MAP) more than >65 mm Hg
 - Urine output more than 0.5 ml/kg/hr
 - Mixed venous oxygen saturation $\text{Svo}_2 >65\%$ and central venous oxygen saturation (ScvO_2).
 - Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement.
 - If mixed venous oxygen saturation $\text{Svo}_2 <65\%$ transfuse packed red blood cells to achieve a hematocrit of $>30\%$ and/or dobutamine infusion (up to a maximum of $20 \mu\text{g/kg/min}$).

Diagnosis

- 1) Cultures with gram stain- Obtain appropriate cultures before starting antibiotics *provided this does not significantly delay antimicrobial administration.*
 - Two or more blood cultures.
 - One or more BCs should be percutaneous.
 - One BC from each vascular access device in place for >48 hours.
 - Other site cultures as clinically indicated Eg. Tracheal culture, sputum culture, ascetic fluid culture, Urine cultures. (should be sent in lab within one hour)

Antibiotic therapy

1. Begin intravenous antibiotics early within the first hour of recognizing Severe sepsis or septic shock.
 - Broad-spectrum agents
 - Active against likely bacterial/fungal pathogens
 - Good penetration into the source

2. Reassess antimicrobial regimen daily
3. Combination therapy in Pseudomonas infections and in neutropenic patient.
4. De-escalation after culture sensitivity report.

Early and appropriate antibiotic therapy and control of the source of infection are the major therapies shown to improve survival in sepsis.

Source identification and control

1. Source of infection should be established as rapidly as possible and start measures to control the source within the first 6 hours of presentation as soon as the initial resuscitation is done e.g. abscess drainage, tissue debridement and removal of central line. In pancreatitis avoid early surgical intervention.
2. Source control measures must be directed at achieving maximal efficacy with minimal physiological upset.

Vasopressor

1. Use norepinephrine or dopamine through central line to keep MAP \times 65mmHg administered as the initial vasopressors of choice.
2. Epinephrine, phenylephrine, or vasopressin should not be used as the initial vasopressor in septic shock
3. Vasopressin 0.01 to 0.04 units/min may be subsequently added.
4. Epinephrine as the first alternative agent in septic shock when norepinephrine is not effective.
5. Do not use low-dose dopamine for renal protection.
6. In patients requiring vasopressors arterial catheter should be put as soon as practical.

Inotropic support

1. In case of myocardial dysfunction as evidenced by increased cardiac filling pressures and decreased cardiac output dobutamine can be used.
2. Dobutamine infusion (up to a maximum of 20 μ g/kg/min) if mixed venous oxygen saturation Svo₂ <65%.
3. Do not target predetermined supranormal levels of cardiac index.

(2) After initial resuscitation (24 hours goal)

Steroid

1. Consider use of low dose intravenous Hydrocortisone (300mg/day)

- a. Septic shock poorly responsive to fluid and vasopressors
 - b. Endocrine or corticosteroid history warrants it
2. Do not use steroids to treat sepsis in the absence of shock and wean it once vasopressors are no longer required
 3. Hydrocortisone is preferred to dexamethasone
 4. There is no role of ACTH stimulation test while determining whether the patient should receive hydrocortisone to treat septic shock.

Blood product administration

1. Packed red blood cells should be given to patients with hemoglobin less than 7.0 g/dL (<7.0 g/L). Achieve target hemoglobin of 7.0 -9.0 g/dL in adults. In certain special circumstances, a higher hemoglobin level may be required. (e.g.: myocardial ischemia, severe hypoxemia, acute hemorrhage, cyanotic heart disease, or lactic acidosis)
2. Erythropoietin must not be used to treat sepsis-related anemia
3. In case of active bleeding, fresh frozen plasma may be used. But its use for correcting laboratory clotting abnormalities is contraindicated unless an invasive procedure is planned.
4. Platelets should be transfused in case of -
 - Counts < 5000/ μ L regardless of bleeding.
 - Counts between 5000 to 30,000/ μ L and there is significant bleeding risk.
 - Higher platelet counts \times 50,000/ μ L in case of surgery or invasive procedures.

Mechanical ventilation of sepsis-induced acute lung injury (ALI)/ARDS

1. Target a tidal volume of 6mL/kg (predicted) body weight and plateau pressure \leq 30cmH₂O in patients with ALI/ARDS.
2. Positive end expiratory pressure (PEEP) should be set according ARDS NET protocol to avoid extensive lung collapse at end expiration and prevent over distention of normal lung.
3. Allow permissive hypercapnia if needed, to minimize plateau pressures and tidal volumes
4. Weaning protocol and a spontaneous breathing trial (SBT) regularly to evaluate the potential for discontinuing mechanical ventilation. (1A)
 - Daily SBT (spontaneous breathing trial)
 - Before the SBT, patients should:
 - be arousable
 - be hemodynamically stable without vasopressors
 - have no new potentially serious conditions
 - have low ventilatory and end-expiratory pressure requirement
 - require FiO₂ levels that can be safely delivered with a face mask or nasal cannula
5. Do not use a pulmonary artery catheter for the routine monitoring.
6. Consider early prone position or rescue therapy for refractory hypoxia.

7. Use a conservative fluid strategy for patients with established ALI/ARDS after initial resuscitation.

Lung protective ventilation strategy using low tidal volume ventilation reduces ventilator-induced lung injury like volutrauma, barotrauma, atelectrauma and biotrauma. This is the only ventilator manipulation that has been shown definitively to reduce injury and absolute mortality reduction of 9%.

Sedation, analgesia, and neuromuscular blockade in sepsis

1. Use sedation protocols with a sedation goal for critically ill mechanically ventilated patients.
2. Avoid neuromuscular blockers where possible. Monitor depth of block with train-of-four when using continuous infusions.

Glucose control

1. Aim to keep blood glucose 150 - 180mg/dL using a validated protocol for insulin dose adjustment.

Renal replacement

1. Consider early renal replacement therapy
2. Intermittent hemodialysis and continuous veno-venous hemofiltration (CVVH) are considered equivalent.
3. CVVH offers easier management in hemodynamically unstable patients.

Bicarbonate therapy

1. Do not use bicarbonate therapy to improve hemodynamics or reducing vasopressor requirements with lactic acidemia and $\text{pH} < 7.15$.

Deep vein thrombosis (DVT) prophylaxis

1. Use either low-dose unfractionated heparin (UFH) or low-molecular weight heparin (LMWH), unless contraindicated.
2. Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated.
3. Combination of pharmacologic and mechanical therapy high risk for DVT.

Stress ulcer prophylaxis

1. Provide stress ulcer prophylaxis using H2 blocker or proton pump inhibitor.

Consideration for limitation of support

1. Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations.

VI. FURTHER READING / REFERENCES

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SEVERE COMMUNITY ACQUIRED PNEUMONIA

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1. When to suspect/Recognize?

a. Introduction

Community acquired pneumonia affects 2 to 3 million patients per year and carries high mortality of around 30% in severe cases. As life expectancy is increasing and many patients with chronic diseases like cardiac failure, COPD are living longer, more patients in community like oncology and transplant with immunosuppressive therapy, incidence of community acquired pneumonia is increasing and distinction from hospital acquired pneumonia is getting blurred as these patients visit hospital frequently.

b. Case Definition

Patient usually presents with a constellation of respiratory symptoms like cough, purulent sputum and sometimes pleuritic pain associated with constitutional symptoms like fever, lack of appetite and myalgia. Chest x-ray revealing new infiltrate usually clinches the diagnosis.

c. Incidence of the condition

Community-acquired pneumonia is a major cause of morbidity and mortality, worldwide. Lower respiratory tract infections, including CAP, were ranked third in a list of the 30 leading causes of death worldwide. About 4 million CAP cases occur annually in the US; with about 20% requiring hospitalization. High mortality trends observed in patients hospitalized for CAP (5-20%) and in CAP patients admitted in ICU (up to 50%). Overall mortality rate of CAP is about 7.3%.

Typical CAP- Sudden onset fever, chills, pleuritic pain, productive cough. Raised TLC, ESR, CRP. Chest x-ray shows diffuse patchy opacities. 60-80% produced by bacteria like -Strep pneumoniae, Staphylococcus, Klebsiella, Haemophilus

Atypical CAP- The organisms: virus, mycoplasma, legionella, chlamydia psittaci, Coxiella burnetii. Presentation: Preceding airway symptoms, myalgias, fever without chills, headache, unproductive cough. TLC, ESR, CRP are either normal or show a mild rise. Chest x-ray shows- diffuse, patchy or ground glass shadows

Assessment of Severity

This is a crucial step as it will help in identifying patient who are prone to get complication and should be admitted in intensive care unit.

CURB 65 is a useful mnemonic for this

- Confusion
- Urea > 20 mg/dl
- Respiratory Rate >30/min
- Blood Pressure Systolic <90 mmHg
- Age > 65 years

INVESTIGATIONS

a. Investigations to be sent in all facilities

1. Complete Blood Count
2. CRP
3. Urea ,Creatinine
4. Liver Function Test
5. Blood Culture ó Two sets
6. Prothrombin Time
7. Na, K
8. Sputum for microscopy, gram stain, AFB stain, fungal stain, cytology
9. Sputum for culture and sensitivity
10. Chest X-ray
11. ECG

b. Investigation to be done at a higher centre

1. Procalcitonin
2. Chest CT scan
3. Chest ultrasound
4. Bronchoscopy with lavage
5. Echocardiogram
6. Urine for legionella and pneumococcal antigen
7. Serology for H1N1, HIV, ANCA , Legionella
8. Nasal Swab for MRSA, Viral Panel
9. NT PRoBNP
10. Venous Doppler legs
11. D Dimer

Treatment: Initial Choice of Antibiotic

A detailed history should be taken to identify patients who are at high risk of drug resistant infection.

- Previous hospitalization in 9 months
- Previous antibiotic in 3 months
- Comorbidity ó steroid use, liver failure, renal failure, COPD

Cover common organisms responsible for pneumonia: both typical and atypical

- Strep pneumoniae
- Legionella
- Staph aureus (MSSA)
- Gram negative bacilli (non ESBL)
- Hemophilus

Antibiotic choices in these patients

A beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) + azithromycin

OR

A beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) + a respiratory

Fluoroquinolone (levofloxacin or equivalent)

OR

For penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam

Additional organisms to be considered in patients at risk of drug resistant Infection

If ESBL or pseudomonas is a concern- An antipseudomonal, antipseudomonal beta-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) + either ciprofloxacin or levofloxacin (750 mg)

OR

The above beta-lactam PLUS an aminoglycoside and azithromycin

OR

The above beta-lactam PLUS an aminoglycoside and an antipseudomonal fluoroquinolone

(for penicillin-allergic patients, substitute aztreonam for above beta-lactam)

If MRSA is a concern- Add vancomycin or linezolid. Availability of other cephalosporin with betalactamase inhibitors combination (Cefoperazone + sulbactam, Cefepime Tazobactam, ceftriaxone-sulbactam) and Class 1 carbapenem- Ertapenem can be used to cover ESBLs as per the hospital antibiotic policy and local antibiogram.

Duration of Antibiotic therapy: Duration of antibiotic should be individualized based on clinical response, type of organism, biomarker response, development of complications and comorbidities. Minimum five days of antibiotic is recommended. Prolonged antibiotics up to two

weeks should be considered in selected cases like slow responders, pseudomonas and staph infection, lung abscess, empyema, metastatic infection.

Identification of Non-Responders

With appropriate antibiotic therapy some improvement in patients clinical course should be seen within 48 to 72 hours. This should be assessed clinically as radiographic resolution takes longer time. For non-responders following conditions should be considered.

1. Organism not covered by empiric choice of antibiotic
2. Atypical organisms ó Tuberculosis, strongyloidosis, melioidosis, H1N1 influenza etc
- 3 Complicated pneumonia- Lung abscess, empyema. Obstruction, Resistant organism
4. Nosocomial problem- Secondary infection.

Differential diagnosis: Heart failure, cryptogenic organizing pneumonia (COP), Malignancy, Pulmonary embolism, Pulmonary eosinophilia pneumonia, Hypersensitivity pneumonitis, vasculitis ó Wegeners granulomatosis

Referral Criteria

- Non-responders should be managed at a higher facility for appropriate workup.
- CAP patients with shock, multi-organ dysfunction

Suggested Reading

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I. WHEN TO SUSPECT/ RECOGNIZE?

1) **Introduction:**

Status epilepticus (SE) is a state of continuous seizure without return of consciousness. Any seizure type can progress to status epilepticus. Status epilepticus is a serious medical and neurological emergency which requires efficient management as delay is associated with worse outcome. The prognosis depends predominantly on the cause and duration of the SE and is good in rapidly reversible causes. Overall mortality is 15.8%. (1) Additional 10 to 23% of patients who survived from status epilepticus are left with disability.

Case definition: For both situations of care (*mentioned below**)

Clinically definition of SE based on manifestations of continuous seizure activity and incomplete recovery of consciousness between seizures for a particular duration. The criterion for duration is still ambiguous and evolving issue. For all practical purposes, a patient should be considered in status epilepticus if seizure activity lasting more than 5 minutes as very few single seizures will last this long.

Refractory Status Epilepticus (RSE): Appropriate definition is still not available. RSE is commonly defined as seizure activity that continues after failure of first and second line antiepileptic drug therapy (AED) therapy.

II. INCIDENCE OF THE CONDITION IN OUR COUNTRY

Chin et al in a recent systemic review reported incidence rates of SE between 3.86 to 38 per 100,000 per year in children and 6 to 27 per 100,000 per year in adults in Europe. (2) Incidence has bimodal distribution with peaks in children less than a year (135 to 156 per 100,000 per year) and elderly (14.6 to 86 per 100,000 per year). The annual incidence of Non convulsive status epilepticus (NCSE) is 2.6 and 7.8 per

100000. NCSE was documented in 8 % of all comatose patients without signs of seizure activity. Frequency of refractory status epilepticus in patients with SE ranged from 31 to 44 %.

There is hardly any incidence data available in India. In a recent study NCSE was documented as a cause of altered mental status in 10.5% of comatose patients without signs of seizure activity. The incidence of RSE in SE patients in Indian series ranges between 12 and 19 % . (3)

III. DIFFERENTIAL DIAGNOSIS

Disorders that may mimic seizures are benign conditions like myoclonus, fasciculations, tremors, tics, panic attack, psychogenic seizures and potentially dangerous conditions like basilar artery transient ischemic attack, metabolic encephalopathy and syncope. When doubt regarding diagnosis is present one should always request neurological consultation and electroencephalogram (EEG). Video- EEG monitoring may be useful for detection of ongoing subclinical seizures and should be considered in critically ill patient with unexplained altered mental status.(4)

IV. 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

a) Clinical Diagnosis:

SE is best divided into three categories:

Convulsive status epilepticus (CSE)

Non convulsive status epilepticus (NCSE)

Partial status epilepticus (PSE)

CSE is the most common form of SE characterized by rhythmic jerking of the body, limbs, tongue biting and loss of consciousness. With increasing seizure duration the movements may become reduced although generalized electrical activity continues in the brain.

NCSE may be difficult to diagnose and may be more common in the elderly population. Although there is no accepted classification of NCSE, two major types are partial complex ówhich is subdivided on the basis that whether the patient has underlying epilepsy or is in coma and petit mal.

In partial complex SE stereotypical movements such as lip smacking, chewing or picking at onesø clothes may occur and alteration of consciousness lasts more than 30 minutes as result of abnormal cortical electrical activity.

Physical examination should look for signs of occult head trauma, substance abuse, fever, meningismus and diabetes. Always check for Medical Alert bracelets or wallet information and try to contact relatives to determine prior medical and seizure history.

b) Basic Investigations

Complete blood count , electrolytes ,Blood urea nitrogen(BUN),serum creatinine,glucose,liver function test

c) Treatment

Initial general management:

- Assess basic life support
- Start supplemental oxygen, monitor oxygen saturation
- Initiate seizure precautions (e.g., padding bed rails)
- Monitor vital signs and ECG
- Adequate venous access and liberal hydration should be started with normal saline to prevent dehydration and rhabdomyolysis.
- Blood pressure should be monitored closely, especially if seizures persist for more than 30 minute
- Consider thiamine 100 mg IV and dextrose 25-50 g IV if blood

glucose is less than 60 mg/dl

- Treat fever with acetaminophen and icepacks

Initial Antiepileptic drug treatment

- In the setting of acute brain injury, treatment usually should be initiated after a single self limited seizure. Initial AEDs (viz. Lorazepam and phenytoin) should be given as soon as possible.
- Management of SE should begin within 5 minutes of seizure activity or after two seizures without full recovery in between.
- Give IV Lorazepam 0.1 mg/kg IV at 2mg/min If Lorazepam is not immediately available, diazepam 10-20 mg or midazolam 2-5 mg can be substituted
- Midazolam given intramuscularly is the promising treatment in prehospital settings
- Start phenytoin 20 mg/kg IV load at ≤ 50 mg/min

Referral criteria:

Patients of SE can be considered for transfer to superspeciality center if seizures are not controlled with benzodiazepine and first line antiepileptic drugs or patient has recurrent seizures after initial stabilization.

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

a) Clinical diagnosis (as per situation 1)

b) Investigation

- Blood and urine toxicology screen and when indicated pregnancy test and arterial blood gases, serum ammonia level
- Anticonvulsant medication levels
- CT or MRI scan and lumbar puncture may be necessary to establish underlying diagnosis once seizures are controlled.
- NCSE can only be diagnosed by EEG.
- Investigate to find the underlying cause of seizure

Common Aetiologies of seizures in critical care unit:

Neurological :

Cerebrovascular disease: infarct, haemorrhage, vascular malformation

Vasculitis

Infection: meningitis, encephalitis, brain abscess

Head trauma

Anoxia

Brain tumours

Neurosurgical procedure

Hypertensive encephalopathy/eclampsia/posterior reversible encephalopathy syndrome

Complication of Critical illness:

Acute systemic insult, sepsis, hypotension

Electrolytes imbalances: hyponatremia, hypocalcaemia, hypomagnesaemia, hypophosphatemia (especially in alcoholics), hypoglycaemia

Toxins

Illicit drug use, especially cocaine

Organ failure: renal, hepatic

Medications /substance withdrawal: Benzodiazepine, barbiturates, alcohol

If none of the above causes are identified consider **following less common aetiologies:** Anti NMDA receptor limbic encephalitis(LE), Anti glutamate receptor LE, Paraneoplastic LE, Hashimoto's encephalopathy.(5)

c) Treatment

Additional general management

- Consider intubation to maintain airway patency
- Monitor for arrhythmias, hypotension and respiratory failure

Antiepileptic drug treatment

- Start phenytoin 20 mg/kg IV load at ≤ 50 mg/min or Fosphenytoin at 20 mg phenytoin equivalents (PE)/kg at ≤ 150 mg PE/min
- **Seizure activity not resolving with two anticonvulsants:**
- Give **Phenobarbital** 10-20 mg/kg IV at <70 mg/min.
- Call for continuous EEG monitoring
- Consider neurological consultation
- Consider administration of following **alternative agents:**
- **Midazolam** drip: 0.2 mg/kg slow IV push, followed by 0.1-2 mg/kg/hr to stop electrographic and clinical seizures or
- **Propofol**: 2 mg/kg load and 2-10 mg/kg/hr to stop clinical and electrographic seizures or maintain burst suppression on EEG
- **Valproate** 15 mg/kg IV load may be useful as an adjunctive agent.
- **Pentobarbital** 3-5 mg/kg IV to induce burst suppression; in most adults pentobarbital bolus 400 mg over 15 min. every 15-30 min. until burst suppression appears is well tolerated, followed by infusion at 0.3-9.0 mg/kg/hr to maintain burst suppression.(7),(8)
- For all infusions, decrease infusion rate periodically to check EEG burst suppression pattern; if electro cerebral silence occurs, decrease the dose till bursts are seen again.(4)

V FURTHER READING / REFERENCES

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INITIAL MANAGEMENT OF SEVERE TRAUMA

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1. **When to suspect/Recognize?**

- a. **Introduction:** There is an increasing incidence of accidents and crimes in India with increasing urbanization and attendant emergency admission of trauma victims. A comprehensive trauma care is lacking in majority of places. As this malady affects predominantly young patients it is a heavy burden to the exchequer. Improving organized trauma care with easy accessibility is an urgent need in our country.
- b. **Case definition:** The American Trauma Society defines trauma as an injury caused by a physical force. More often, trauma is the consequence of motor vehicle crashes, falls, drowning, gunshots, fires and burns, stabbings, or blunt assaults.

Lot of emphasis has been placed on aggressive initial management of trauma. The concept of prehospital care is highlighted by the **Golden Hour**, which may be defined as the period during which all efforts are made to save a life before irreversible pathological changes can occur thereby reducing or preventing death in the second and third phase. This period may range from the time of injury to definitive treatment in a hospital. The first **platinum 10 minutes** becomes important to make this golden hour effective and should be distributed as follows to make it fruitful.

Time lines: Assessment of the victim & primary survey- 1-minute, Resuscitation & stabilization 6 5 min, Immobilization & transport to nearby hospitals 4 minutes.

2. **Incidence of the condition in our country**

India contributes to 10% of world trauma with vehicular accident every 3 min & death every 10 min. Road traffic injuries are a major cause of mortality responsible for 22.8% of death related to injuries. The lower and middle-income group countries, including India contribute about 90% of the global burden of injury mortality. Uncontrolled bleeding is a leading cause of death in trauma. In fact, death in trauma follows a trimodal distribution of death. First peak occurs immediately after an accident. Second peak occurs 1-4 hours later and the third peak occurs 1-5 weeks later.

The initial management is usually done by paramedics, and an adequately trained team with skills in maintenance of airway, control of external bleeding and shock, immobilization of the patient and transportation. This has to be tied to early arrival of trauma ambulance and a system of triaging and notifying the receiving hospital with a central coordination.

3. Differential diagnosis:

In Polytrauma, the assessment of the extent of injuries is very important. A head to toe examination facilitates identifications of brain & cervical spine trauma, thoracic or abdominal or major skeletal trauma. If shock persists after resuscitation, patient must be evaluated for any other covert internal injuries. All patients with head injury should be assumed to have a cervical spine injury as well unless proved otherwise clinically or radiologically.

4. Prevention & Counseling:

Road safety & pedestrian safety are two important issues. Most of the trauma victims are either pedestrians or bicyclists. Strict implementation of traffic rules and measures like wearing helmets, lane driving and implementing speed limits are important issues that need to be uniformly applied across India. A robust prehospital ambulance system manned by qualified emergency medical technicians will help in improving survival significantly.

Trauma victims are generally young and bread winners for their families. Any such death or disability is associated with significant financial and psychological trauma to the victim and his family. Adequate counseling and support is required for the trauma patients and their families.

5. 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**

Facilities required

1. Medical Personnel with basic training in airway management and resuscitation
2. Basic Airway management equipment
3. Cervical collar
4. Spine Board
5. Scoop stretcher
6. Basic Volume resuscitation items like i.v fluids and i.v cannulas
7. Continuous oxygen supply and suction
8. Chest tube drainage system
9. Fracture stabilization material

10. Surgical sutures and hemostatic forceps.
11. X-ray & ultrasound facilities
12. Abdominal paracentesis equipment
13. Access to Blood Bank
14. Routine hematology, biochemistry, coagulation testing facility
15. Transport to higher center.

Clinical diagnosis: This remains the mainstay of diagnosis.

Investigations: Facilities like CT scan/MRI etc. are not available. Simple x-ray & Ultrasound should be available. Basic investigations like hematology, biochemistry, coagulation parameters should be available.

Treatment: Quick identification and assessment of the extent of external injuries should be made. Basic care like intravenous access, fluid or blood resuscitation should be done. Splinting & bandaging of injured extremity or scalp should be done. Airway, breathing & circulation should get priority. Internal injuries and head injuries cannot be managed and should be referred to higher centres. These centers should have a clear policy on transfer of trauma patients and all patients who cannot be managed there should be shifted after initial treatment and resuscitation.

At Super Specialty Facility in Metro location where higher-end technology is available

Facilities required

1. Trauma Team with an on call rota and quick response time. The team should consist of a trauma surgeon or a general surgeon, intensive care or emergency medicine physician, Neurosurgical team, cardiothoracic team, orthopedician& anaesthesiologist.
2. The trauma team should be adequately supported by trained nurses and paramedical staff
3. Focussed abdominal ultrasound in trauma (FAST)
4. Portable X-ray facility
5. CT scan& MRI
6. Transport ventilator
7. Spine board
8. Scoop stretcher
9. Cervical immobilization devices
10. Difficult airway management equipment
11. Thoracotomy equipment
12. Portable echocardiogram
13. On site blood bank
14. Intravenous fluid warmed
15. Rapid i.v. infusion system

16. Central lines
17. Round the clock OT facility
18. Pericardiocentesis equipment
19. Trauma protocol to guide management

The principles followed in clinical diagnosis, investigations & treatment are same as above. However a more organized approach is used, which is described below.

1. **TRIAGE**: Triage is a process of determining the priority of patients' treatment based on the severity of their condition and the resources available to provide that treatment. . In multiple casualty incidents, the number of patients and the severity of their injuries do not exceed the ability of the trauma care facility. The patients with life-threatening injuries are treated first. In mass casualty incidents, the number of patients and the severity of their injuries exceed the capacity of the trauma care facility. Here, the patients with the greatest chance of survival are treated first.
2. **Primary Survey and Resuscitation**: Primary survey involves rapid early assessment of the patient. The life threatening conditions are identified and treatment priorities are established based on their injuries, vital signs and injury mechanisms. During the primary survey, the following aspects are assessed and rapid corrective measures taken.
 - a) Airway maintenance with C-Spine Control
 - b) Breathing and Ventilation
 - c) Circulation and /hemorrhage Control
 - d) Disability/ Neurological Status
 - e) Exposure/ Environmental Control

Airway with C-spine control

The patency of the airway should be assessed with special attention to foreign body or maxillo-facial fractures that may result in airway obstruction. Chin-lift or Jaw-thrust maneuver may be used to achieve airway patency simultaneously protecting the cervical spine. A definitive airway is warranted in a patient with an altered level of consciousness or a Glasgow Coma Score of 8 or less. It is critical to protect the spine. Spinal injury should be assumed in any patient of trauma unless specifically excluded.

Breathing and Ventilation

The patient's chest should be exposed to adequately assess chest wall excursion. Auscultation to detect adequate air entry, percussion to exclude air or blood in chest and visual inspection and palpation to detect injuries to chest wall should be carried out. Specific life threatening problems

such as tension pneumothorax, massive hemorrhage, flail chest and cardiac tamponade should be identified immediately and addressed during the primary survey

Circulation with Hemorrhage Control

Hemorrhage is the primary cause of shock in trauma patients. Rapid and accurate assessment of the patient's hemodynamic status and identification of the site of hemorrhage is therefore essential. It is critical to establish adequate intravenous access in a trauma patient. While the primary survey is going on, two intravenous lines should be established with short broad gauge cannula, preferably in the upper extremities, and resuscitation started with crystalloids.

Disability / Neurological Status

A rapid neurological evaluation is carried out at the end of primary survey after the resuscitation and before rapid sequence intubation. This assesses the patient's level of consciousness, pupillary size and reaction and focal neurological deficit. The level of consciousness may be described in terms of Glasgow Coma Scale (GCS).

Exposure / Environmental Control

The patient should be completely undressed to facilitate thorough examination and assessment. At the same time care should be taken to prevent hypothermia to the patient.

Adjuncts to Primary Survey and Resuscitation

- a) **ECG Monitoring:** The appearance of dysrhythmias may indicate blunt cardiac injury. Pulseless electrical activity, the presence of cardiac rhythm without peripheral pulse may indicate cardiac tamponade, tension pneumothorax or profound hypovolemia.
- b) **Urinary Catheter:** Urine Output is a sensitive indicator of the volume status of the patient and reflects renal perfusion. All trauma victims should be catheterized to enable monitoring of the urine output and plan intravenous fluid therapy. Transurethral catheterization is contraindicated in patients urethral transaction is suspected.
- c) **Gastric Catheter:** A gastric tube is indicated to reduce stomach distension and decrease the risk of aspiration. It should be passed via the orogastric route in patients with head injury and suspected base skull fracture.
- d) **X-rays and Diagnostic Studies:** The chest and pelvis x-ray help in the assessment of a trauma patient. Any trauma patient entering the red area of the emergency should undergo blood sampling. The blood should be sent for cross-match and arranging for packed cells, and important diagnostic parameters such as hemoglobin, renal parameters, ABG should be checked. Pulse oximetry is a valuable adjunct for monitoring oxygenation in injured patients.

- e) **FAST:** Focused Assessment by Sonography in Trauma is a rapid non- invasive tool used to assess free fluid in the abdomen, blunt abdominal injury and cardiac tamponade.
- f) **CT scan & MRI:** For brain, spinal cord trauma and in injury to internal organs._

Secondary Survey

Once the primary survey is accomplished, life- threatening conditions are managed and resuscitative efforts are underway, secondary survey is carried out. This is head to toe evaluation of trauma patient, which includes a complete history and physical examination and reassessment of all the vital signs. Each region of the body is completely examined. The care continues with regular re-evaluation of the patient for any deterioration and new findings, so that appropriate measures can be taken.

Reevaluation

After the completion of the secondary survey, the patient should be reevaluated beginning with the ABCs and thorough physical examination and examined for any missed injury such as fractures. Constant monitoring of the severely injured patient is required and may necessitate rapid transfer to the surgical intensive care unit, operating room or to another centre having better specialized facilities. The transfer to another centre should not be delayed for the want of investigations.

RESOURCES REQUIRED

SITUATION	HUMAN RESOURCES FOR 4-6 WEEKS	INVESTIGATION OF 4-6 WEEKS	DRUGS AND CONSUMABLES FOR 4-6 WEEKS	EQUIPMENT
<p>1. At secondary hospital/non-metro situation</p>	<p>One Each:</p> <ol style="list-style-type: none"> 1. Casualty Medical Officer (CMO) 2. X-ray Technician <p>One in each shift:</p> <ol style="list-style-type: none"> 1. CMO 2. Nurse 3. Attendant 	<ol style="list-style-type: none"> a. X-ray b. Ultrasound c. Hematology d. Biochemistry e. Blood grouping & cross matching 	<ol style="list-style-type: none"> a. Intravenous fluids- Crustalloids- Normal saline 50 , Ringer lactate 50 b. Intravenous fluid- Colloids- Hemaccel, HES 5 bottles each c. IV canula: 24,22,20,18,16 ,14 gauge (10 each) d. IV drip sep- 25 e. Compression bags for fast fluid delivery (5) f. Bandages (1-2 drums) g. Dressing material (1-2 drums) h. POP (100) i. Blood set (10) j. Leucoplast (5 rolls) k. Dynaplast (5 rolls) l. ICD tubes (10) different 	<ol style="list-style-type: none"> a. X-ray machine (portable) b. Ultrasound machine c. Orthopedic splints d. Spine board (1) e. Scoop stretcher (1) f. Ambu bag (2) g. Bain circuit (2) h. Oxygen cylinders (10) i. Blood storage refrigerator 1 j. Dressing set (1) k. Suturing set (1) l. Cervical collar m. Ambulance for transport

			<p>sizes</p> <p>m. Underwater seal (5)</p> <p>n. Nasopharyngeal & oropharyngeal airway (all sizes)</p>	
<p>2. At super specialty facility in metro location</p>	<p>As in situation 1</p> <p>a. Emergency Consultant-1</p> <p>b. CMO-2</p> <p>c. Technician-1</p> <p>d. Nurses- 3 per shift in addition to Incharge</p> <p>d. Ward boys 2</p> <p>e. Housekeeping 2</p> <p>f. Multiprofesional Trauma team as per the composition listed in the text.</p>	<p>As in situation 1 +</p> <p>a. CT scan</p> <p>b. MRI</p> <p>c. ECHO</p> <p>d. Coagulation parameters</p> <p>e. Blood and other fluid cultures (Microbiology)</p>	<p>In addition to all items listed above:</p> <p>1. Arterial canulae (10)</p> <p>2. Central venous lines (10)</p> <p>3. Cardiac monitors</p> <p>4. Defibrillator</p> <p>5.</p>	<p>As in situation 1 with</p> <p>1. Well equipped OT with C-arm</p> <p>2. Airway & breathing equipment</p> <p>3. Transport ventilator</p> <p>4. ACLS ambulance with ventilator, monnitor, defibrillator</p>

Referral Criteria

- Patients should have basic control of airway, breathing and circulation, and surgery to stop bleeding if possible before contemplating transfer
- Need for specialized surgery: thoracic, cardiac surgery
- Need for advanced intensive care after initial stabilization

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TRAUMATIC BRAIN INJURY

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I. a) When to suspect / recognize?

Traumatic Brain Injury is usually associated with road traffic accidents or criminal assault. It could also happen due to a fall or due to industrial mishaps. Nevertheless the disorder is usually obvious and history is generally clinching. In situations where the history is not forthcoming any injury or mishap associated with the change in the level of consciousness of the individual should be deemed to be associated with brain injury unless proved otherwise.

b) Case definition: The term TBI is self explanatory. However the course in hospital for a patient with TBI is characterized by 2 major injuries ó Primary and Secondary Primary injury is the injury sustained by the patient and is related to the mechanism of injury. Secondary injuries are those sustained during the transport and treatment of patients with TBI. This is the more common cause of altered consciousness amongst TBI patients. Some of the causes of secondary injury are

1. Seizures
2. Hypotension
3. Hypertension
4. High and Low blood sugars
5. Elevated body temperature.
6. Electrolyte imbalance.
7. Hypoxia

II. Incidence of the condition in our country

Incidence of road traffic accidents in India is amongst the highest in the world, and is rising. As per the report of the National Crime Records Bureau 2001, 2,710,019 accidental deaths, 108,506 suicidal deaths and 44,394 violence-related deaths were reported in India. A significant proportion of the deaths due to accidents and violence are due to head injuries. A study from NIMHANS revealed that minor, moderate and severe brain injuries (due to RTIs) were recorded in 60%ó65%, 16%ó20% and 15%ó20% of cases as per the Glasgow Coma Scale (GCS) grading. Mortality was higher among those with severe brain injuries. Polytrauma was documented in 1%ó21% of cases. Facial, chest, abdominal and limb injuries were documented in 48%, 3%, 1% and 10% of cases, respectively.

III. Differential Diagnosis:

The differential diagnosis of traumatic brain injury is generally straight forward. However when the history is not forthcoming, differential diagnosis should include

- Ischemic stroke
- Sub arachnoid hemorrhage
- CNS infections
- Toxic encephalopathies

IV. Optimal Diagnostic criteria, investigations, treatment and referral criteria:

Situation 1: In non metro situation with limited resources:

Investigations:

- CT Scan of the brain with or without contrast
- Serum electrolytes
- Blood sugar
- Chest X-ray

Treatment

- **Maintenance of oxygenation and blood pressure:** Hypoxia and hypotension are common causes of secondary brain injury. Mortality amongst patients whose saturations are < 60% is close to 50%. Duration of hypoxia is also a determinant of adverse outcomes.
 - **Intubation when GCS < 8 is recommended.** Mechanical ventilation is instituted to maintain PaO₂ and control PaCO₂
- Similarly, both pre and intra hospital hypotension are predictors of adverse outcomes. It is recommended that systolic blood pressure should not be less than 90 mm Hg. If hypotension does occur initially, all precautions need to be taken to avoid recurrent episodes. In resource limited settings management of TBI on the basis of Cerebral Perfusion Pressure may not be feasible and is recommended as an optional strategy.
- **Hyperosmolar therapy:** 20% Mannitol and Hypertonic Saline. Their use is indicated when raised intracranial pressure is suspected. Mannitol can either be used as a single short term agent or as a continuous therapy. However, repeated use of Mannitol over several days is not known to be effective.
- **Surgery,** indicated for evacuation of extradural or subdural hematoma, intracranial hemorrhage, depressed skull fracture, other surgery in case of associated polytrauma

- **Anaesthesia, analgesia and sedation:** Providing adequate analgesia and sedation is crucial for a patient with TBI with or without raised ICP. Morphine and midazolam can be used.
- **Infection Prophylaxis:** Prevention of other systemic infections is also important in TBI. Early extubation is recommended if the patient has an intact gag and cough reflex.
- **Thromboprophylaxis:** Patients with TBI are at a high risk of deep venous thrombosis. This risk increases with the increase in the severity of brain injury. Prophylaxis is either mechanical or pharmacological or both. The use of mechanical intermittent pneumatic compression (IPC) devices is strongly recommended for all patients with TBI except when there are coexistent lower extremity injuries.
 - A combination of IPC with low molecular weight heparin is superior to using either modality alone. However, initiating LMWH or Heparin within 24 hrs of surgery is not recommended. No specific agent is superior to the others. However, the use of pharmacoprophylaxis might be associated with a higher chance of intra cranial bleeding.
- **Anti Seizure Prophylaxis:** Post traumatic seizures can be early onset (<7 days) or late onset (>7 days). Both need to be prevented. Risk factors for PTS include
 - GCS<10
 - Cortical contusion
 - Depressed fracture
 - Sub dural hematoma
 - Epidural hematoma
 - ICH
 - Penetrating head wound
 - Seizure within 24 hrs of injury.

Phenytoin can be used for preventing early onset PTS. No role can be made out for prophylactic drugs to prevent late PTS. Valproate is as effective as Phenytoin in preventing PTS but is associated with higher mortality.

- **Hyperventilation:** Prophylactic hyperventilation is not recommended. It is a temporary measure. Whenever Hyperventilation is frequently required monitoring of SjVO₂ or brain tissue oxygen tension is recommended. Therefore such patients need to be referred to a centre with facilities to do so.
- **Steroids:** No role in the management of TBI

Transfer / Referral Criteria

- Non-availability of CT scan or neurosurgical expertise
- Persistent unconsciousness with GCS < 8, seizures
- Persistent high intracranial tension, clinically and on CT scan, despite medical and initial surgical management

- Polytrauma, especially associated chest trauma
- Ongoing requirement of mechanical ventilation, hemodynamic instability
- Requirement for intracranial pressure monitoring

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

a) Clinical Diagnosis: As per situation 1

b) Investigations: as per situation 1 plus

- MRI
- Intracranial pressure and cerebral perfusion pressure monitoring
- Serum osmolality
- EEG monitoring

c) Treatment: as in situation 1 plus:

- Hyperosmolar therapy: hypertonic saline. A close monitoring of the serum osmolality is warranted. A central venous access is preferable for administration of hypertonic saline
- **Intra cranial pressure (ICP) Monitoring:**

Indications:

- Patients with TBI who have a GCS < 8 and for those who have an abnormal CT scan. The abnormalities include hematomas, contusion, oedema, herniation and compressed basal cisterns.
- Age of the patient is > 40 years, patient has systolic pressure <90mm Hg or there is abnormal motor posturing.

The need for ICP monitoring is an indication for transferring the patient to a facility with the expertise in the technique. It is not recommended for use in non metro areas and resource limited settings.

ICP Monitoring methods:

The ventricular catheter connected to an external strain gauge is the best available tool for ICP monitoring. It is the least expensive and currently most accurate. It also gives a therapeutic option of CSF drainage. Fibreoptic transduced monitors are also accurate but more expensive.

- **ICP Thresholds:** Measures to regulate ICP should be initiated if the pressure exceeds 20 mm Hg. Treatment should be tailored on the basis of clinical and CT findings with ICP as a guide.
- **CPP Thresholds:** CPP should be maintained between 50-70 mmHg. Attempts to achieve CPP>70 are associated with a higher incidence of ARDS. CPP<50mm Hg should be avoided.
- **Brain oxygen monitoring:** Wherever facilities for jugular saturation monitoring are available, SjVO2 should be maintained >50%. If brain tissue oxygen tension is monitored

then Pbt_iO₂ should be maintained > 15mm Hg. Jugular venous oxymetry is recommended when hyperventilation is used with a therapeutic intent.

- Anaesthesia, analgesia, sedation, neuromuscular blockade
 - Propofol is recommended in moderate doses as a sedative for its beneficial effects on ICP and cerebral perfusion pressure. High dose propofol infusion can trigger Propofol Infusion Syndrome and is therefore not recommended.
 - Opioid analgesics and benzodiazepines are recommended. Morphine and Midazolam can be combined with opioid analgesics for sedation.
 - Barbiturate infusions are recommended for control of raised ICP.
 - If ICP remains high neuromuscular blocking agents may be considered.
 - Continuous EEG monitoring may be used wherever available to titrate the dose of sedatives.
- **Prophylactic Hypothermia:** The use of prophylactic hypothermia in patients with raised ICP is based on the fact that hypothermia decreases the metabolic activity of the injured brain. This reduces the cerebral metabolic rate for oxygen and minimizes the extent of brain injury. The target temperature is 32-33⁰C to be maintained for atleast 48 hrs. However, monitoring patients on hypothermia regimen needs core temperature monitoring and may not be available in resource limited settings. If patients are considered fit for transport, it is advisable to transfer them to a centre with the facilities and experience in using hypothermia.

d) References

1. Guidelines for the management of severe traumatic brain injury 3rd edition. Brain trauma foundation
2. Heegard W, Biros M. Traumatic brain injury Emerg Med Clin N Am 25 (2007) 655-678