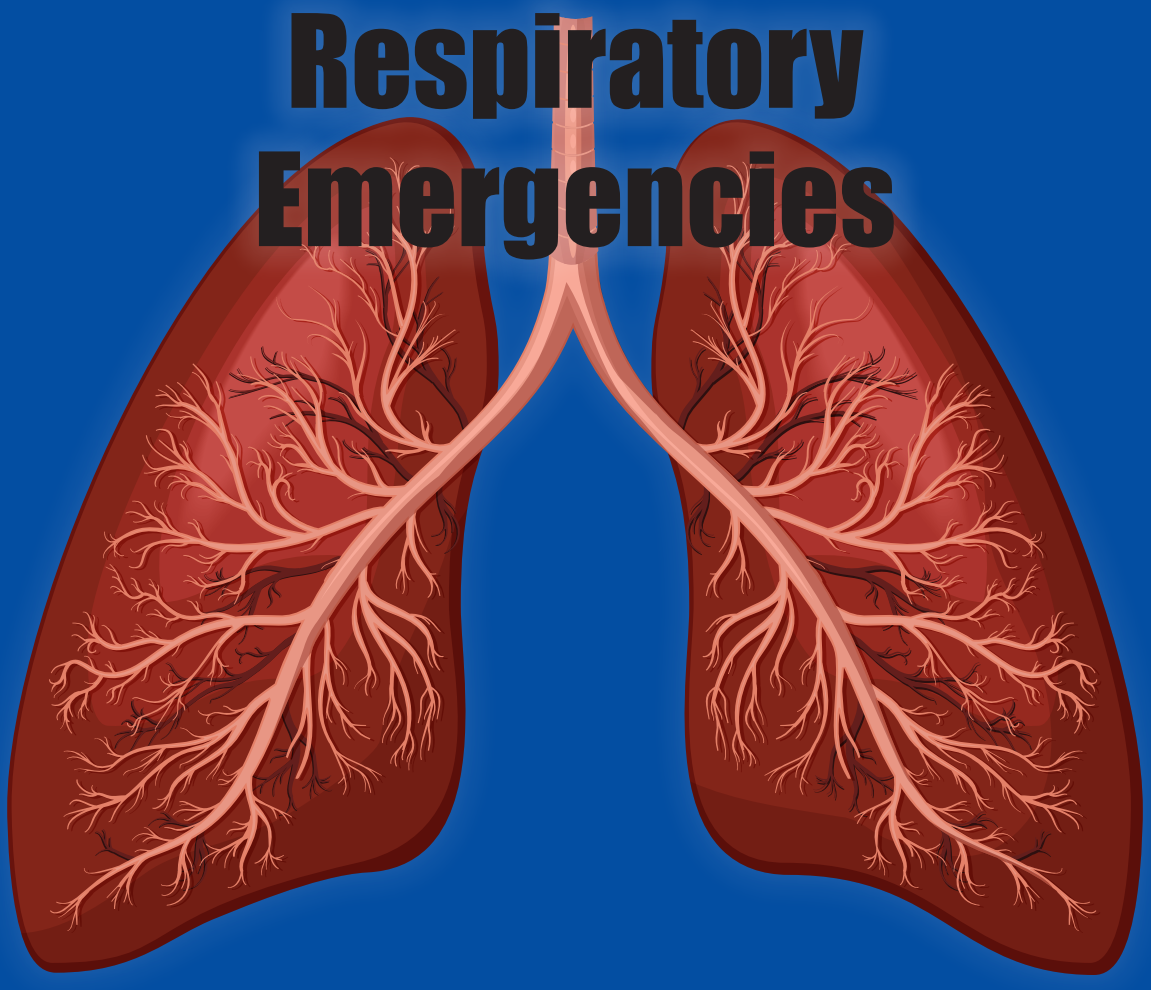
Under the auspices of
Indian College of Physicians
Academic wing of
Association of Physicians of India

MONOGRAPH

Respiratory Emergencies



Chief Editor
M. Sabir

Executive Editor
Vitull K Gupta

'Respiratory Emergencies":
Chief Editor - Dr. M. Sabir; Executive Editor - Dr. Vittul Gupta.

Printing of this Monograph has been made possible by the unconditional academic support from M/S Cipla Ltd.

First Edition 2020

ISBN:.....

Printed at.....

RESPIRATORY EMERGENCIES

MONOGRAPH

Editorial Board

Published Under the Auspices of Indian College of Physicians, Academic Wing of Association of Physicians of India by Malwa Branch, Bhatinda

Dedicated to.....

Our Parents

.....who brought up & inspired us

Our teachers

.....who taught us

Our patients

.....who facilitate our learning

and

Our family members & friends

.....who support us

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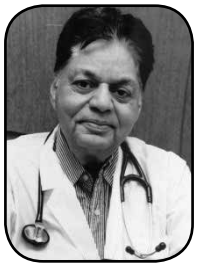
Foreword



Dr. K. K. Pareek

To,

Dr. Mohd Sabir

Chief Editor - "Monograph on Respiratory Emergencies"

Dear Dr. Sabir & Dr. Vitull,

It is a pleasure and a great honor to write the foreword for the "Monograph on Respiratory Emergencies".

Respiratory Respiratory diseases are a significant health burden to human morbidity and mortality. Recently all of us have witnessed a great surge in the acute and chronic respiratory disorders and all the more it is such a common disorder, that every doctor comes across respiratory emergencies in their day to day practice. It has become very much necessary to keep abreast with the latest updates in the diagnosis, management and guidelines of respiratory diseases.

Many times it becomes very difficult for a practicing physician to diagnose and manage respiratory emergencies. Definitely this monograph will cover the knowledge gap between the diseases and management of respiratory emergencies.

It will be a great opportunity at this Corona time, publishing this monograph will be of much utility to the clinicians as the maximum morbidity and mortality is because of pneumonia and respiratory failure in COVID-19 patients.

This monograph includes almost all emergencies of respiratory disorders and the chapters have been contributed by eminent and learned faculty of national reputation.

Dr. Sabir, Chief Editor of this "Monograph" is a distinguished and learned physician, ex professor and Past President of Indian Chest Society having vast clinical & research experience of pulmonary medicine, which has proved to be of great benefit in editing this monograph.

I congratulate Dr.Sabir, Dr. Vitull & other members of editorial team for their untiring and dedicated efforts in publishing this comprehensive monograph; under the auspices of Indian College of Physicians and hope that this monograph will be of great value to our physicians in managing respiratory emergencies in their day to day practice.

I wish great success for this monograph on 'Respiratory Emergencies'.

Jai Hind. Jai API

With kind regards,

Dr. KK Pareek,
MD, FICP, FACP,FRCP (Glasgow, Edinburgh)
Past Dean of ICP
Past President of API
Founder President of Rajasthan State RSSDI

List of contributors

(updated 13.07.2020, to be made alphabetical)

1.	**Dr. M. Sabir,** MD (Medicine) Senior Consultant Physician & Pulmonologist, Kothari Medical Research Institute, **Bikaner-334001** Retired Professor & Head, Respiratory Division., Department of Medicine, S.P. Medical College, Bikaner-334001 Former President & Founder Editor, Public Forum Indian Chest Society
2.	**Dr. Sushila Gahlot,** MD (Physiology) Retired Senior Professor, Department of Physiology, S.P. Medical College, **Bikaner-334001**
3.	**Dr.Vikas Chaudhary** PG Student, Department of Physiology, S.P. Medical College, **Bikaner-334001**
4.	**Dr. Harshit Kiran kumar Mehta** Senior Consultant, Emergency Medicine, Shalby Hospitals, **Ahemadabad-380015**
5.	**Dr. Kapil Chahar** Assistant Professor, Critical Care, Department of Medicine, S.M.S. Medical College, **Jaipur**
6.	**Dr. Mansoor Ahmed, DM** (Cardiology) MO & Cardiologist, SMS Hospital, **Jaipur**
7.	**Dr. A.S. Rathod** Senior Consultant ENT, Kothari Medical & Research Institute, **Bikaner-334001** Retired Professor ENT, S.P. Medical College,
8.	**Dr. Pushpendra Shekhawat** Consultant, Kothari Medical & Research Institute, **Bikaner-334001**
9.	**Dr. Rajesh Swarankar,** MD, DNB, DTCD, MNAMS, FCCP (USA) National Secretary, Indian Chest Society Director & Chief Consultant Pulmonologist, Department of Respiratory, Critical Care, Sleep Medicine and Interventional Pulmonology Getwell Hospital & Research Institute, Dhantoli, **NAGPUR - 440012**
10.	**Dr. Angira Dasgupta,** MD, DNB (Resp. Dis.), MRCP (UK), FCCP Sr. DMO, Dept. of Medicine & Pulmonary Medicine, B R Singh Hospital & Centre for Medical Education and Research, Eastern Railways, **Kolkata**
11.	**Dr. Bodhisattwa Saha,** PhD, DST-Inspire Faculty, Institute of Genomics and Integrative Biology**,** **New Delhi**
12.	**Dr. Govinda Narke**, MD Chest Research Foundation, Marigold Premises, Kalyaninagar, Pune
13.	**Dr. Sundeep Salvi,** MD Director, Chest Research Foundation, Marigold Premises, Kalyaninagar, **Pune**
14.	**Dr Lalita Fernandes,** Professor, Department of Pulmonary Medicine, Goa Medical College, **Panji**

15.	**Dr. Ashwini Pednekar** (details awaited)
16.	**Dr. A.M.Mesquita.** (details awaited)
17.	**Dr. Virendra Singh** Director, Asthma Bhawan, Former Professor & Head Pulmonary Division, Department of Medicine, Superintendent, SMS Hospital., SMS Medical College, **Jaipur** Former President Indian Chest Society
18.	**Dr. Bharat Bhushan Sharma** Professor, Department of Medicine, SMS Medical College, **Jaipur**
19.	**Dr. Dr. Surya Kant Tripathi** Professor & Head, Department of Respiratory Medicine King George's Medical University UP **,Lucknow -**226003 (UP)
20.	**Dr. Amitesh Gupta, MD** (Respiratory Medicine) Asst. Professor, Department of Respiratory Medicine Sri Lal Bahadur Shastri Govt. Medical College& Hospital, Mandi At Ner Chowk, **Himachal Pradesh, 175001**
21.	**Dr Parul Mrigpuri, MD** (Respiratory Medicine) Assistant Professor, Department Of Respiratory Medicine, Sri Lal Bahadur Shastri Govt. Medical College& Hospital, Mandi At Ner Chowk, **Himachal Pradesh, 175001**
22.	**Dr K.Sailaja** Prof. Pulm. Med. Hyderabad (details avaited)
23.	**Dr Vitull Gupta** Former Professor, Dept of Medicine, AIMSR. Bhatinda. Consultant, Kishori Ram Hospital & Diabetes Care Centre, Bhatinda (Punjab)
24.	**Dr. Meghna Gupta,** MBBS PG Resident, Dept of Psychiatry, MM Medical College and Hospital, **Kumarhatti, Solan.**
25.	**Dr.Varun Gupta, MD** (Thoracic Surgery) Resident Thoracic Surgery, Lungenklinik Hemer, Hemer, **Germany.**
26.	**Dr. Surendra Verma** Professor, Department of Medicine, S.P. Medical College, Bikaner (Rajasthan)
27.	**Dr Neeraj Gupta**. MD, FCCP (USA), FICS, FNCCP, FIASR Senior Professor, Department of Respiratory Medicine JLN Medical college, Ajmer (Rajasthan)
28.	**Dr Akhilesh Verma** Medical Officer, Dept of Respiratory Medicine, JLN Medical College, **Ajmer** (Rajasthan)
29.	**Dr Don Gregory Mascarenhas,** MD,DNB Assistant Professor, Dept of Respiratory Medicine Fr Muller Medical College, **Kankanady, Mangalore**
30.	**Dr. Kumar Utsav Samaria,** MD (Respiratory Medicine) Ex. Registrar, Department of Respiratory Diseases, B.J. Medical College, Ahmedabad Consultant Pulmonologist & Interventionist, Centre for Research & Treatment of Allergy, Asthma & Bronchitis, **Varanasi- 221005**

31.	**Dr. J.K. Samaria,** MD FNCCP, FIACM, FICP, D.Yoga, FCCP (USA), FICS Former Professor & Head, Department of Chest Diseases, Institute of Medical Sciences, B.H.U, Varanasi Director & Chief Consultant, Centre for Research & Treatment of Allergy, Asthma & Bronchitis, **Varanasi**
32.	**Dr Mridul Mahanta** DM Resident, Hero DMC Heart Institute, Dayanand Medical College & Hospital, **Ludhiana**
33.	**Dr. Gurpreet Singh Wander** Prof. & Head of Cardiology Unit Hero DMC Heart Institute Dayanand Medical College & Hospital, **Ludhiana** Former President Association of Physicians of India
34.	**Dr. Rohit Bhatia,** MD, DM, DNB Professor, Department of Neurology, Neurosciences Centre, **AIMS, New Delhi.**
35.	**Dr. Nishita Singh** Department of Neurology, Neurosciences Centre, **AIMS, New Delhi.**
36.	**Dr. S.P. Chauhan,** MS (Gen. Surg.), FAIS, FAIGES, FMAS Senior consultant Surgeon, Dean & Head, Department of Surgery, Kothari Medical & Research Institute, **Bikaner** Retired Professor & Head, Department of Surgery, S.P. Medical College, **Bikaner-334001**
37.	**Dr. Vamshi Krishna Gone** Junior Resident, Final Year DNB, General Surgery, Kothari Medical & Research Institute, Bikaner-334001 (Raj.)
38.	**Dr. N. K. Jain** Retired Senior Professor & Head & Medical Superintendent, Department of Pulmonary Medicine., SMS, Medical College, **Jaipur** Consultant & Director, Jain Chest Care Center, **Jaipur**
39.	**Dr Nitin Jain** Consultant. Jain Chest Care Center, **Jaipur**
40.	**Dr. Mohd.Yunus Khilji** Associate Professor, Department of Anesthesiology, SP Medical College, **Bikaner**
41.	**Dr. Sadik Mohammed** Associate Professor, Department of Anesthesiology & Critical Care, AIIMS, **Jodhpur**
42.	**Dr. Dhruva Chaudhry**, MD (Med.), DNB (Med.), DM (Pulm. & Critical Care Med.) Senior Professor and Head, Department of Pulmonary & Critical Care Medicine, PGIMS, **Rohtak**
43.	**Dr. Mansi Gupta,** MD (Pulm. Med.), DM (Pulm.& critical care Med.) Department of Pulmonary & Critical Care Medicine, PGIMS, **Rohtak**
44.	**Dr. Brijesh Prajapat,** MD (Pulm.Med.), DM (pulmonary and critical care) Department of Pulmonary & Critical Care Medicine, PGIMS, **Rohtak**

45.	**Dr. Sanjay Kumar Kochar** Senior Professor & Head: Respiratory Division & I/c Malaria Research Center, Nodal officer: Medical Education Unit & Multidisciplinary Research Unit Bikaner Coordinator: COVID-19 Department of Medicine, S.P. Medical College, Bikaner - 334003 (Raj),
46.	**Dr. Rishabh Kochar,** MD (Medicine) Senior Resident, Department of Medicine, Lady Harding Medical College and Associated Hospitals, New Delhi, 110001
47.	**Dr. V. K. Jain** Senior consultant &Professor & Head, Dept. of Tuberculosis & Chest Diseases, MGM College, **Jaipur** Retired Senior Professor & Head, Dept. of Tuberculosis & Chest Diseases, Former Additional Principal, S.P. Medical College, **Bikaner-334001**
48.	**Dr.Valliappan Muthu** Senior Research Associate, Department of Pulmonary Medicine, PGI,**Chandigarh,**
49.	**Dr. Ritesh Agarwal** Professors, Department of Pulmonary Medicine, PGI, **Chandigarh, India**
50.	**Dr. Digambar Behera** Professor & Head, Department of Pulmonary Medicine, (WHO Collaborating Centre for Research & Capacity Building in Chronic Respiratory Diseases) Post Graduate Institute of Medical Education and Research **Chandigarh.** Chairman, National Task Force, RNTCP

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Basic Applied Lung Physiology

Shushila Gahlot, Vikas Chaudhary

In clinical practice knowledge of anatomy and physiology of the respiratory tract is important not only in the field of pulmonology but also in critical care and anesthesiology. Such knowledge has influence on patient care related to anesthesia, airway management, and management of cases with respiratory disorders including emergencies, respiratory procedures and surgeries. It is also important for optimizing ventilator strategies in respiratory emergencies and designing airway devices.

Primary function of respiratory system is to obtain oxygen from environment for use by body cells & eliminate carbon dioxide that is produced (by cells) as a result of energy production and other chemical reactions necessary for normal functioning of human body.

Secondary functions include acid-base buffering, hormonal regulation and host defense.

To achieve these goals of respiration, three main functional components of the respiratory system are:

- *Mechanical structures*: Chest wall, respiratory muscles and pulmonary circulation.
- *Membrane gas exchanger*: interface between airspace and pulmonary circulation, and
- *Regulatory system:* network of chemical and mechanical sensors throughout the circulatory and respiratory systems.

All three components are tightly integrated, and dysfunction of one can lead to respiratory abnormalities or failure.

During act of respiration about 10,000 lit. of fresh air (rich in oxygen) is inhaled (taken in to the lungs) through nasal cavities (also through oral cavity), pharynx, larynx, trachea, branches of bronchi and through bronchioles, then ultimately to alveoli (site of gas exchange). After giving up oxygen and taking up carbon dioxide air is exhaled out of lungs through the same path.

Respiratory tract- structure

- The respiratory system, functionally, can be separated in two zones; conducting zones (nose to bronchioles) a path for the conduction of the inhaled gases to respiratory zone (alveolar duct to alveoli) where the gas exchange takes place. Anatomically, respiratory tract is divided into upper respiratory tract (organ outside thorax - nose, pharynx and larynx) and lower respiratory tract (organ within thorax - trachea, bronchi, bronchioles, alveolar duct and alveoli).

- Nose and nasal cavity are divided into two halves by the nasal septum. The lateral wall of the nose consists of three *turbinates or conchae* (superior, middle and inferior). The passage inferior to inferior turbinate is preferred passage for nasotrachealintubation.The pharynx is a tube-like passage that connects the posterior nasal and oral cavities to the larynx and oesophagus. It is divided into nasopharynx, oropharynx and laryngopharynx.

- There are three narrowest portions of pharynx; passage posterior to the soft palate (retro palatal space), passage posterior to the tongue (retroglossal space) and passage posterior to epiglottis (retroepiglotic space). There is significant reduction of these spaces with sedation and anesthesia, which would lead to upper airway obstruction.

- *Nose* plays important role in removing impurities from the air. Hair, mucus, blood capillaries, and cilia that line the nasal cavity filter, moisten, warm, and eliminate debris from the passing air and are thrown out during sneezing.

- *In Nasopharynx* two auditory (Eustachian) tubes connecting ears with throat that equalize air pressure in the middle ear also enter here. The pharyngeal tonsil (adenoid) prevents (to some extent) bacteria from entering lungs lies at the back of the nasopharynx.

- *Oropharyrnx* &*Laryngopharynx*receives air from the nasopharynx and food from the oral cavity& passes food to the esophagus and air to the larynx. Tonsils are located here.

- *Larynx*consists nine pieces of cartilage, joined by membranes and ligaments. Epiglottis, the first piece of cartilage of the larynx, which prevents entrance of food in the wind pipe during swallowing. A forward projection of the cartilage (thyroid cartilage) appears as the Adam's apple.

- *Vocal cord* (apparatus for producing voice) contain elastic ligaments that vibrate when skeletal muscles move them into passage of air. Various sounds, including speech, are produced in this manner.

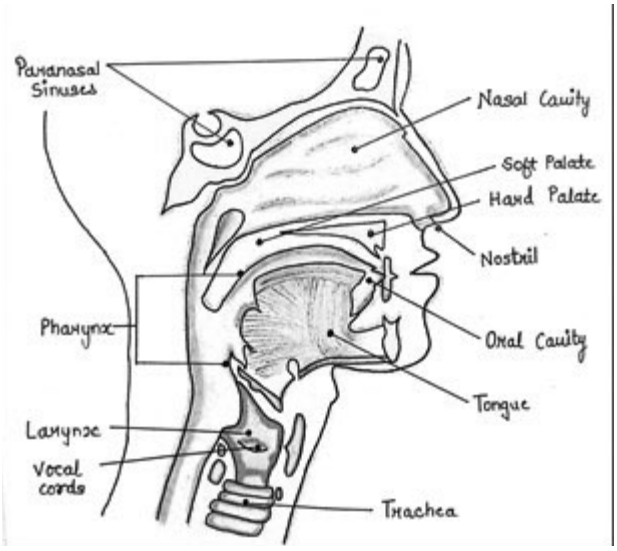

Figure 1 : Upper airways

- *Trachea* is a flexible tube, 10 to 12 cm (4 inches) long and 2.5 cm (1 inch) in diameter contains 16 to 20 C-shaped cartilaginous rings, helps in maintaining its lumen.
- *Bronchial tree* - its primary job is to spread the air received through trachea over a very wide area in the lungs *Primary bronchi* are two tubes that branch from the trachea to the left and right lungs. In lungs, each primary
- *Bronchus* divides repeatedly into branches (like an inverted tree) of smaller and smaller diameters, forming *secondary lobar bronchi & tertiary (segmental) bronchi.*
- *Bronchopulmonary segments* are the division of lung separated by connective tissue septums, so eachbronchopulmonary segment can surgically removed without affecting other segments. There are ten segments in right lung and eight in left lung.
- Segmental bronchi divide into many primary bronchioles (1 mm or less in diameter), which further divide into terminal bronchioles (0.5 mm in diameter).
- Each of terminal bronchioles which gives rise to several respiratory bronchioles, which go on to divide into two to 11 alveolar ducts (terminal part of the bronchial tree)
- The air flows through three interconnected regions--*upper airways,conducting airways*,and *alveolar airways*. Between the trachea and the alveolar sacs the airways divide 23 times.
- The first 16 generations of passages from the *conducting zone* of the airways (*bronchi,bronchioles* and *terminal bronchioles*).

- The remaining seven generations form the alveolar or respiratory zones where gas exchange occurs and are made up of *respiratory bronchioles, alveolar ducts* and *alveoli.*
- The multiple successive branching of the airways greatly increases the total cross sectional area of the airways from 2.5 cm square in the trachea to *12000 cm square in thealveoli.*
- The most important function of the respiratory passages is to keep them open and allow easy passage of air to and from alveoli.
- The *Trachea and bronchi have cartilage* in their walls with little smooth muscle which keep them open.

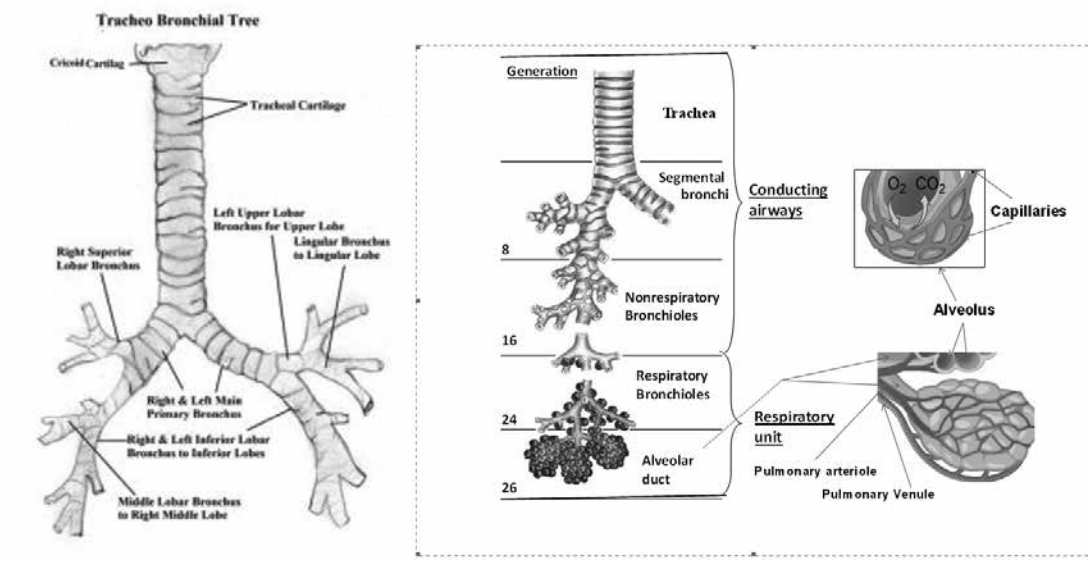

Figure 2 : Tracheo bronchial tree & respiratory apparatus.

- The *cilia* in their wall along with mucus layer allows for the trapping of foreign bodies.
- The walls of bronchioles and terminal bronchioles do not contain cartilage and they contain more smooth muscle of which the largest amount is present in the terminal bronchioles.
- *Bronchioles and terminal bronchioles* are kept open by same trans pulmonary pressure which expand alveoli. The diameter of smaller airways can change much more than that of the larger airways in obstructive lung disease, it is smaller Airways that offer most of resistance.

- It is estimated that totao number of alveoli is 300 milionhaving total surface area 70 m2 lined pneumocytes:
  - *Type I*areflat cellswith large cytoplasmic extensions and are the primary liningcells
  - *Type II*are granularpneumocytes which are thicker and contain numerous lamella
  - *lymphocytes, plasma cells, alveolar macrophages, mast cells* & many more.
  - *Inclusion bodies* - these cells secrete lung surfactant which maintains the stability of thealveoli.

  The deficiency of surfactant leads to Respiratory distress syndrome the lungs also contain specialized cells pulmonary alveolar macrophages which are actively phagocytic and when they ingest large amount of smoke or other irritants they may release lysosomal products into extra cellular space to cause inflammation.

Mechanics of respiration

The act of respiration includes two processes:

- External respiration – is the uptake of O2 and excretion ofCO2 in the lungs
- Internal respiration – Exchange of gases e.g. Oxygen & Carbon di Oxide between the cells and capillary blood

The quality of these respiration processes depends on:

- Pulmonary ventilation –inflow and outflow of air between the atmosphere and the lung alveoli.
- Diffusion of O2 and CO2 between the alveoli and the blood.
- Perfusion – of lungs with blood.
- Transport of O2 and CO2 in the blood.
- Regulation of respiration.

Non-respiratory functions of respiratory system:

- In voice production.
- Protective reflexes (apnoea, laryngospasm).
- Defensive reflexes (cough, sneeze).
- In thermoregulation.

Ventilation

Inspiration **-** occurs as alveolar pressure drops below atmospheric pressure due to expansion of thoracic cage along with pleura and lung tissue due to contraction of diaphragm and external intercostal muscles.

Expiration **-** occurs as alveolar pressure rises above atmospheric pressure due to shrinking of thoracic cage as diaphragm and ext intercostals muscles relax and elastic tissues of lung recoil back to the resting state.

Both inspiration and expiration can be modified.

The larger and quicker the expansion of thoracic cage the larger the gradient and the faster the air movement, down its pressure gradient.

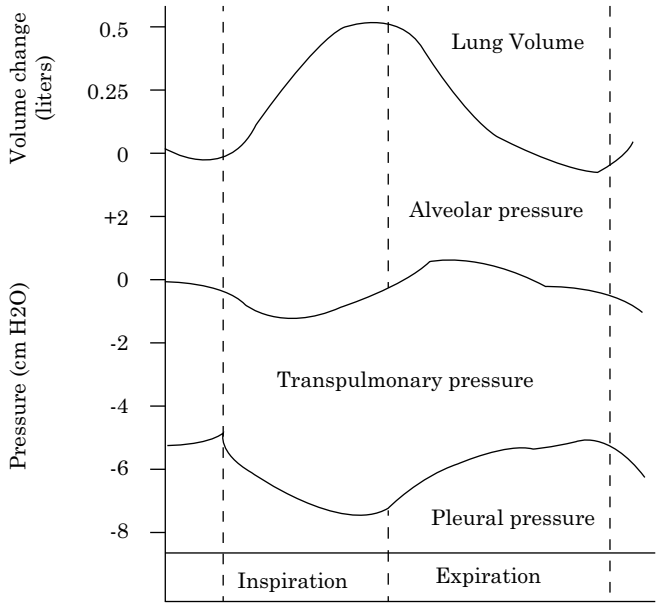

Figure 3 : Changes in lung volume, alveolar pressure, pleural pressure, and transpulmonary pressure during normal breathing

Table 1 : Lung volumes and capacities

Parameters	Measurements
Tidal volume (TV)	500ml
Inspiratory reserve volume (IRV)	3300 ml
Inspiratory capacity (IC)	3800ml
Expiratory reserve volume (ERV)	1000ml
Vital capacity (VC) = ERS + TV+IRV	4800ml
Residual volume (RV)	1200ml
Total lung capacity (TLC) = RV + VC	6litre
Respiratory minute volume	6 litres
Maximum breathing capacity	150/170 litres per min

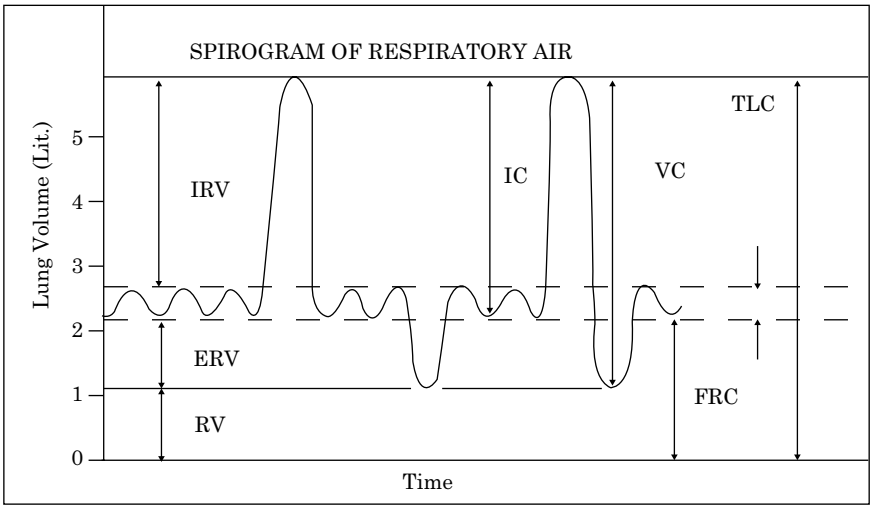

Figure 4: Lung volumes and capacities

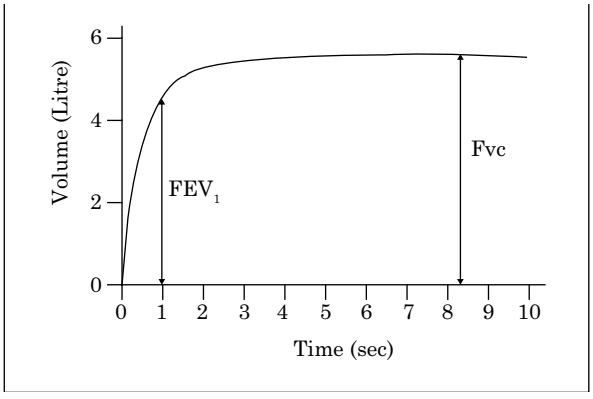

Figure 4: Ratio of Forced Vital Capacity (FVC) to Forced Expiratory Volume in one second (FEV_1)

- FEV or timed vitalcapacity
  - FEV1- < 83% of TVC
  - FEV2- 94% of TVC
  - FVC- 97% of TVC
  - Peak Expiratory flow rate (PEFR) - 400L/min
  - FEV1/FVC very important in differentiating obstructive and restrictive lung diseases.

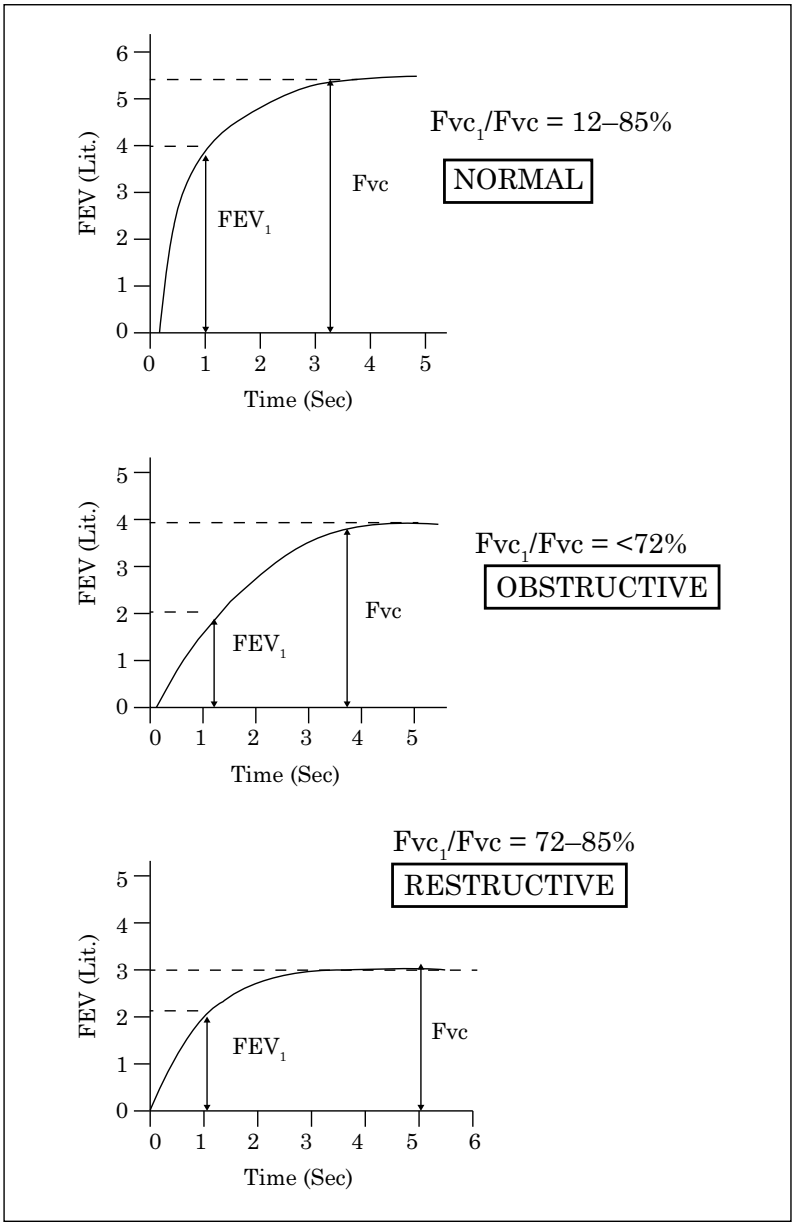

Figure 5 : Altered airflow in disease

Work of breathing

- It is performed by respiratory muscles in
- Stretching the elastic tissues of the chest wall and lung (65%)
- Moving inelastic tissues i.e. viscous resistance (7%)
- Moving air through air passages i.e. airway resistance (28%)

The energy cost of breathing in normal individuals represents less than 3% of total energy expenditure. Work of breathing greatly increased in diseases such as emphysema asthma and heart failure with dyspnea.

Ventilation t / perfusion in

In upright position the bases of lungs are better perfused and better ventilated than the apices but the relative change in blood flow from apex to base is greater than the relative change in ventilation so the V/F ratio is lower at the base and higher at the apex

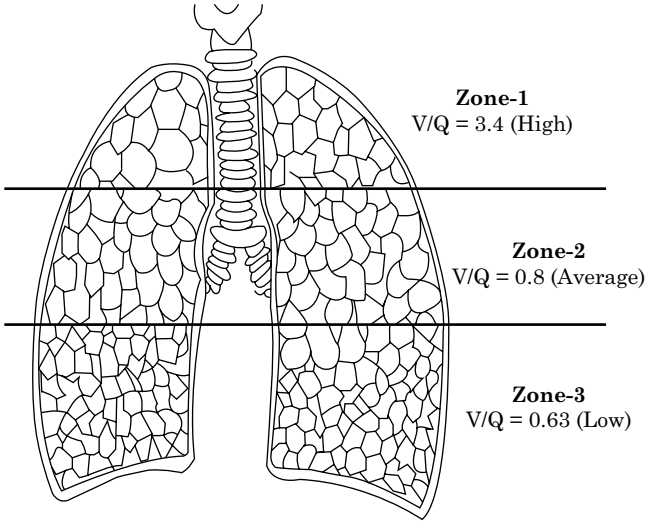

Figure 6 : Diagram showing differences in ventilation and perfusion in the normal lungs in the upright position.

Outlined areas are representative of changes in alveolar size (not actual size). Note the gradual change in alveolar size from top (apex) to bottom. Characteristic differences of alveoli at the apex of the lung are stated.

At apex: Intrapleural pressure is more negative & transmural pressure is greater. Alveli are large with lower intravascular pressure so there is less blood flow, leading to less ventilation & perfusion. (V/P)

Pulmonary circulation

The amount of blood ejected by heart into pulmonary circulation is same as the amount ejected into systemic circulation. The pulmonary circulation is a low pressure circulation in comparison to the systemic circulation due to low resistance offered by the pulmonary vessel the total resistance in pulmonary circulation is about one tenth of systemic circulation but they have high compliance to accommodate large amount of blood.

Pulmonary diffusion

It occurs through the Respiratory membrane or alveolar capillary membrane. This membrane allows Rapid exchange of respiratory gases through it because of huge capillary network it consists of several layers made up of epithelium of alveoli and endothelium of pulmonary capillaries, thickness of this membrane is about. 5 micrometre and total surface area available for diffusion is 70 square metre while total amount of blood in lungs at any moment is 150 ml so this small quantity of blood in lungs spreads and naturally facilitatediffusion.

Diffusion capacity

It is the volume of gas that diffuses through the respiratory membrane each minute for a pressure gradient of 1 mmHg.

Diffusion capacity of oxygen is 20 to 25 ml per minute per mm of Hg, during exercise it can increase up to 65 ml per minute.

Diffusion capacity for Carbon dioxide is about 20 times more than that for oxygen that is 400 to 500 ml per minute, during exercise it can increase up to 1200 mm to 1300 mm per minute.

Diffusion capacity is;

- directly proportional to the *membrane surface area, diffusion coefficient of gas* and *partial pressure difference of the gas* and
- Inversely proportional to *membrane thickness.*

Diffusion of oxygen from alveoli to blood - partial pressure of oxygen in alveoli is 104 mmHg and partial pressure of oxygen in blood is 40 mm Hg so pressure gradient of 64 mm Hg allows diffusion of oxygen when blood passes through pulmonary capillaries. RBCs are exposed to O2 only for 5 seconds so diffusion of oxygen must be quicker and effective.

Diffusion of carbon dioxide from blood to alveoli - diffusion of carbon dioxide occurs from blood to alveoli because pressure of carbon dioxide in blood is 46 mm of Hg as opposed to 40 mm of Hg in alveoli.

Transport of gases

Blood plasma can't transport enough oxygen and corbon di oxide to meet physiological needs so oxygen is carried in reversible combination with hemoglobin and carbon di oxide in plasma as bicarbonate ions and lesser amount of CO_2 is bound to Hb or dissolved in plasma. If pO_2 increases Hb binds O_2 and when pO_2 falls it releases O_2. At a given pO_2 the Hb will release more O_2; if pH falls or temperature increases, the situation seen at tissue level. Oxygen delivery in tissues and pickup at lungs is regulated by rising p CO_2 levels and coordination of lung perfusion and alveolar ventilation.

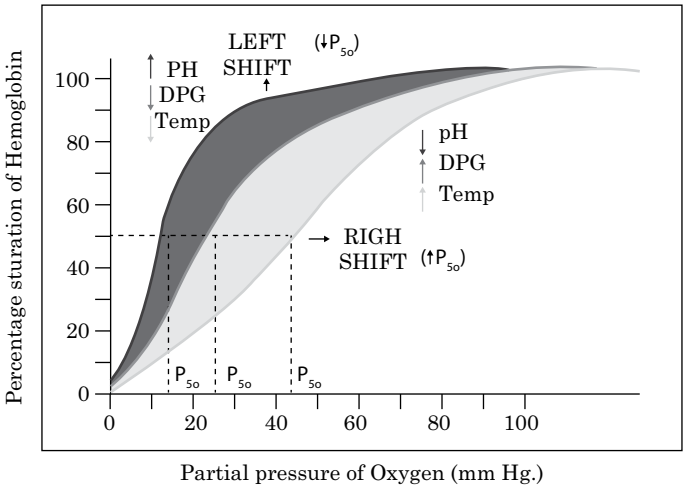

Figure 7 : Effects of temperature and pH on the oxygen–Hemoglobin dissociation curve

Control of respiration

It is exerted voluntary and Automatic Voluntary centres are in cerebral cortex as well as in reticular formation. The automatic pace of respiratory rhythm is set by centres in medulla oblongata. The rate and depth of respiratory rhythm is adjusted by two centres in pons.

Five sensory modifiers of Respiratory centres are- Central and peripheral chemoreceptors sensitive to pCO2, pO2 and pH of blood or CSF.

In general CO2 levels rather than O_2 levels are primary drivers of respiratory activity

- Baroreceptors in aortic or carotid sinuses
- Stretch receptors which respond to changes in lung volumes
- Irritant physical and/or chemical stimuli in respiratory tract

Other sensations like pain, change in body temperature and abnormal visceral sensations also affect respiratory activity..

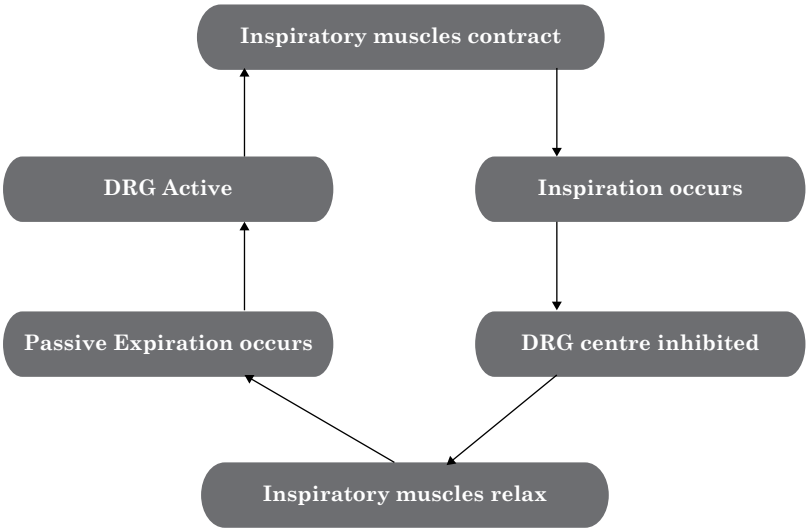

Figure 8 : Quiet Breathing

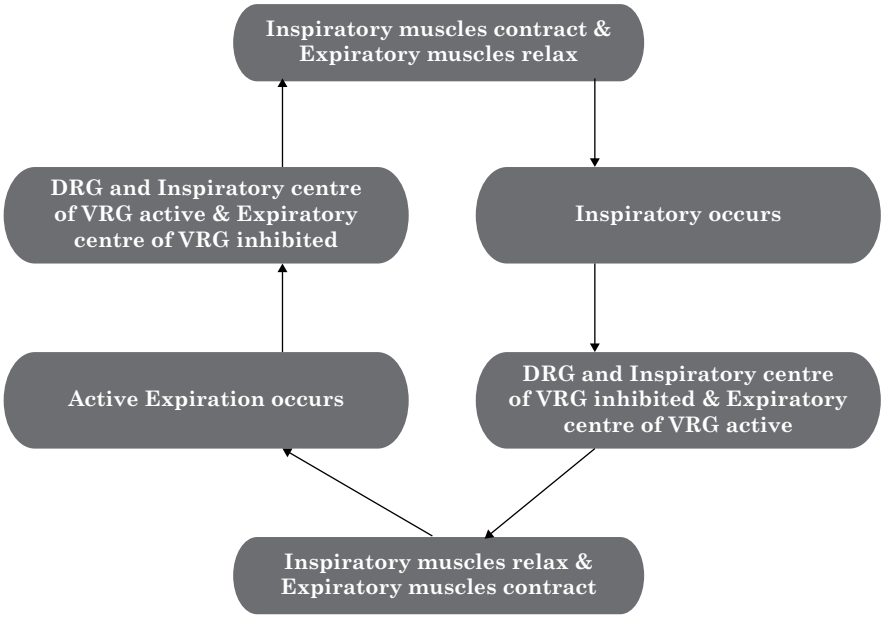

Figure 9 : Forced breathing

Abbreviations: DRG-dorsal respiratory group of neurons, VRG - Ventral respiratory group of neurons

Respiratory adjustment to stresses in health

Respiratory adjustment is the specific change in respiratory system undergone in response to different stresses which can be

1. Respiratory adjustment during exercise
   - Greater oxygen consumption and CO2 production
   - Increase pulmonaryventilation
   - Increase uptake of oxygen by blood in thelungs
   - Increased pulmonary bloodflow
   - Shift of hemoglobin oxygen dissociation curve to right
2. Respiratory adjustment at low atmospheric pressure at high altitude
   - Increased alveolarventilation.
   - Increased arterial partial pressure of Oxygen and decrease in arterial partial pressure of carbondioxide

- pulmonaryhypertension
- diffusion capacity of gasesincrease

3. Respiratory adjustment at high barometric pressure
   - respiratory resistance increases
   - dynamic lung volumes are reduced as the pressureincreases
   - decompression sickness can be avoided if the divers trained to ascend slowly with short stay at regular intervals.

4. Respiratory adjustment on exposure to cold and heat
   - on exposure to heat : Evaporation of water water in expired air through lungs and painting in some animals.
   - on exposure to cold : 38% of total heat produced by muscular activity is due to respiratory muscle activity

5. Respiratory at birth
   - pulmonary fluid is replaced by air
   - fall in arterial pressure of Oxygen and rise in pressure of carbondioxide
   - high intra plural pressure about 60 mmHg.

Disturbances of respiration

1 Abnormal respiratory patterns

- Apnoea : temporary cessation of breathing Types
  - Voluntary apnoea
  - Apnoea after Hyperventilation
  - Deglutition Apnoea
  - Breath holding attacks
  - Vagal apnoea
  - Adrenalin eapnoea
  - Sleep apnoea

- Hypoventilation : decrease in rate and force of respiration
- Hyperventilation : increase in rate and force of respiration
- Dyspnea : difficult or distressed breathing, commonly known as air hunger
- Dyspnea Point : level at which there is increased ventilation with severe breathing discomfort

Causes :

Physiological - severe muscular exercise Pathological

- Respiratory disorders - bronchial asthma, emphysema, pneumonia, pulmonary edema, Pneumothorax
- Cardiac failure - left ventricular failure decompensated mitral stenosis
- Metabolic disorders - diabetic acidosis uremia and increased hemoconcentration

- Periodic breathing - abnormal or uneven respiratory rhythm. It is of two types:
  - Chyne stokes breathing - Characterized by rhythmic hyper Apnea and Apnea at regular intervals. Occurs during deep sleep, in high altitude, newborn babies, during cardiac disorders, renaldiseases etc.
  - Biots's breathing - hyper Apnea and apnea occurs at regular intervals
    Causes - doesn't occur in physiological conditions, Pathological conditions related to nervous disorders like injury to brain

2 Disturbances related to respiratory gases

- Hypoxia : deficiency of oxygen supply at tissuelevel
  - Hypoxichypoxia
  - Anemichypoxia
  - Stagnanthypoxia
  - Histotoxichypoxia
- Hypercapnia : increase arterial partial pressure of carbon dioxide associated with respiratory acidosis. this occurs due to defective elimination of carbon dioxide or accidental inhalation of carbon dioxide.
- Hypocapnia : decrease partial pressure of carbon dioxide associated with respiratoryalkalosis
- Asphyxia : characterized by combination of hypoxia and hypercapnia. Clinical stages of asphyxia : 3 threestages
  - stage 1 - stage of hyperpnea (1minute)
  - stage 2 - stage of convulsions (1minute)
  - stage 3 - state of collapse (3minutes)
- Carbon monoxide poisoning

3 Pulmonary diseases

- **Obstructive lung diseases**
  - Asthma
  - Chronic Bronchitis and emphysema
  - Chronic obstructive pulmonary diseases
- **Restrictive lung diseases**
  - Lung parenchymal diseases
  - Pulmonary tuberculosis
  - Atelectasis
  - Pulmonary edema

Depending upon the disease process, anatomy & physiology of respiratory system undergoes vital alterations, which have implications not only on respiratory function but also have effect on others tissues of body. While managing respiratory emergencies these changes must get due consideration. It will help in correct evaluation and positive outcome of treatment.

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Respiratory Emergencies – Classification

Harshil Kiran kumar Mehta

Respiratory emergencies refer to a state of disturbance with respiratory functions to such an extent that endangers life. The term is not limited to an acute disturbance of ventilation but it's a much wider range of conditions can properly be regarded as respiratory emergencies. Respiratory emergencies are one of the leading causes of Emergency department visits in India. Around 12.5%[1] of patients presenting to Emergency are having respiratory problems whereas worldwide the rate is around 10.5%.[2] Common respiratory symptoms that bring patients to Emergency Department include dyspnea, cough, wheezing, chest pain, hemoptysis, confusion etc.

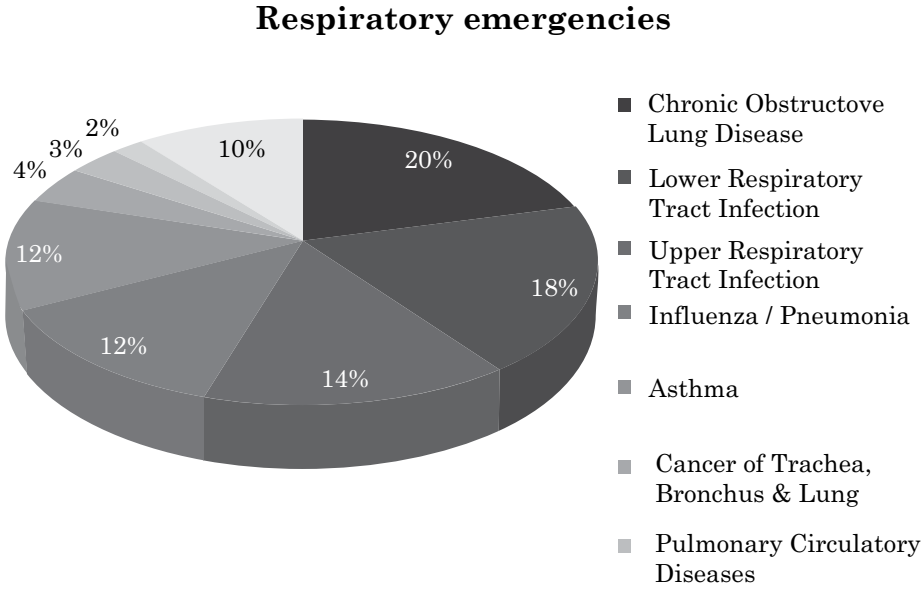

Figure 1 : Incidence of Respiratory emergencies[3]

In literature, there is no definite classification of respiratory emergencies is found. In this chapter, we will classify respiratory emergencies on the basis of Anatomical locations of abnormality. Respiratory system includes Upper airway, lower airway,

lung parenchyma, Chest wall and pleura, vasculature, and nervous system controlling respiratory activities. Some metabolic and endocrinal disturbances do contribute to respiratory distress.

Respiratory emergencies related to respiratory organs

Respiratory Tract

Respiratory tract starts from nose and ends at alveoli. It is divided in to Upper and lower airway divided by vocal cords. Nose, Nasal passage, Paranasal sinuses, Pharynx (Nasopharynx, Oropharynx, Hypopharynx), Epiglottis and portion of larynx above vocal cords are considered as upper airway. Lower airway starts from vocal cords till alveoli including, trachea, bronchi and bronchioles and lungs.

Upper Airway

Acute upper airway emergencies mainly occur due to mechanical obstruction leads to asphyxiation.[4] In adults, clinically significant obstruction may happen anywhere in upper airway. Obstruction is caused by wide variety of pathology i.e. Infection, Inflammation, Foreign Body inhalation, Neoplasia, trauma, scar formation, skeletal deformities having in common a local mechanical effect causing the symptoms. Upper airway obstruction tends to produce stridor.

Nasal Obstruction doesn't produce significant distress as compared to pediatric patients.[9] Inhalational injuries in nose must be looked for to decide further course of management especially in Burns.

Pharyngeal pathologies that created respiratory emergencies are mostly infective in origin. Tonsillitis, Peritonsilar abscess, Laryngitis, epiglottis, Diphtheria etc produce significant breathing difficulties in acute conditions. Neoplasia of pharyngeal structure is a dreadful condition to maintain patent airway.

Sleep apnea is mainly seen in obese males above 40 years of age. Pharyngeal tube doesn't have bony support unlike to Nasal airway, oral airway and trachea. Hence its collapsible and pharyngeal muscle strength is dependent on arousal state. Due to excessive Carbon dioxide retention in body such patients may present to emergency department.

Asphyxiation due to obstruction at laryngeal level is a nightmare to manage in emergency as placement of advanced airway is highly difficult and cricothytotomy may be the only option available at the time. Hence such condition must be anticipated in advance and Airway should be secured electively in such scenarios.

On inhalation, vast number of chemicals causes Upper Respiratory Tract injuries and diseases or secondary problems due to absorption in blood. Various gases e.g. Acetaldehyde, Acrolein, Ammonia, Cadmium Oxide, Carbon Monoxide etc can cause respiratory discomfort acutely.

Foreign bodies usually cause acute manifestations when lodged in Pharynx or larynx. They may pass up to bronchi almost unrecognized. Urgent investigation and removal foreign body is the need of time

Table 1 : Causes of respiratory emergencies related to respiratory system.

<table>
<tr><th colspan="4">LUNGS</th></tr>
<tr><th colspan="2">Upper Airway</th><th colspan="2">Lower Airway& paranchyma</th></tr>
<tr><td>Nose
• Nasal congestion
• Nasal Foreign body
• Inhalation Injuries
Pharynx
• Sleep Apnea
• Tonsillitis
• Peritonsillar abscess
• Retropharyngeal abscess
• Ludwig's Angina
• Inhalational Injuries</td><td>• Influenza
• Neoplasm
• Foreign body
Larynx
• Anaphylaxis
• Foreign Body
• Epiglottis
• Trauma
• Laryngomalacia
• Inhalational Injuries
• Neoplasm</td><td>Main stem bronchi
• Foreign Body
• Papilloma
• Hemangioma</td><td>Alveoli & interstitium
• Cystic fibrosis
• Pulmonary hemorrhage
• Pneumonia
• Pulmonary edema
• COPD
• Interstitial lung diseases
• Respiratory failure
• Aspiration Pnemonitis
• ARDS
• Drowning
• Toxicological injuries</td></tr>
<tr><th colspan="4">CHEST WALL & PLEURAL CAVITY</th></tr>
<tr><td colspan="2">Chest Wall
• Diaphragmatic Hernia
• Flail Chest
• Neoplasm</td><td colspan="2">Pleural cavity
• Spontaneous Pneumothorax
• Chylothorax
• Empyema
• Hemothorax
• Pleural effusion</td></tr>
</table>

Lower airway

Wide variety diseases presents with common pathology of Lower Respiratory tract obstruction. The pathophysiology of the conditions causing lower respiratory tract induced symptoms are Infection, Inflammation, Bronchoconstriction, obstruction, mucous plugging, hemorrhage, alveolar damage, parenchymal destruction or a combination of factors. Such conditions are generally chronic and get aggravated due to certain stimulating factors.

Obstruction at the level of bronchi is largely due to mechanical in nature contributed by either foreign body or any abnormal mass irrespective of their parent tissue (papilloma, hemangiomaetc)

Asthma is the most common etiology of lower airway obstruction. Apart from it, Bronchiolitis, cystic fibrosis and pulmonary hemorrhage due to abnormal connection between vasculature and bronchiolar connection secondary to inflammatory of neoplastic activities contribute to Lower Respiratory Tract Obstruction.

Alveoli are basic functional unit of lung that exchange gases with blood. Damage to alveoli or lung parenchyma disrupts gas exchange and cause respiratory failure. Understanding of the pathology will make physician efficient to treat such complicated conditions. ARDS is a consequence of various bacterial/viral infection/inflammation that require true critical care. Drowning as well as toxicological injuries are extra-ordinary circumstance that initiates chemical inflammation and disrupts alveolar lining. Pulmonary edema due to various pulmonary or extrapulmonary causes need to differentiated and treated accordingly.

Chest wall & pleural cavity

Physiologic process of chest wall contributing to respiration is complex. Any mechanism that obliterates pleural space and restricts lungs from expansion during respiration causes significant respiratory distress.

When integrity of nonmuscular part of chest wall (the thoracic spine, ribs, costovertebral joints, abdominal wall, and sternum) is severely compromised, respiratory failure may ensue.

The pathophysiology of such disorders is mostly connected to the imposition of excessive elastic load placed on respiratory muscles. With flail chest, such load is acute. Sometimes Diaphragmatic hernia, as well as any neoplasm that limit elasticity of chest wall result in acute respiratory distress.

Pleural effusion is the most common manifestation of pleural disease, and its etiologies range in spectrum from Tuberculosis, systemic diseases (e.g., lupus), disorders of individual organ systems (e.g., chronic pancreatitis, congestive heart failure [CHF]), trauma and surgery, and iatrogenic interventions (e.g., drug related).

Pneumothorax is defined as abnormal air in pleural cavity with subsequent collapse of adjacent lung.[4] It is classified according to its etiology as Spontaneous (Primary or secondary) and Traumatic. Other than air, if chyle or blood or pus is present in pleural cavity then it is described as Chylothorax, Hemothorax or empyema respectively.

Non-respiratory causes of respiratory emergencies

Cardiovascular

Cardiac and pulmonary systems are closely interconnected. Cardiac diseases can result in respiratory problems by variety of mechanisms. Not only cardiac, but peripheral vascular diseases also contribute to respiratory pathology.

Abnormal cardiac functioning resulting from Myocardial Infarction or Congestive cardiac failure or arrhythmia or myocarditis results in pulmonary congestion and shows Acute respiratory emergencies.

Pulmonary Embolism is a common cause of mortality and morbidity especially in patients hospitalized surgical or medical illness. The incidence of this condition is 1 in 1000 in USA.[5,6] Incidence in India is not determined however it is not expected to be different from western countries.[8]

Pulmonary vasculitis is usually a manifestation of a systemic disorder leading to inflammation of vessels of different sizes by a variety of immunological mechanisms.[7]

Table 1 : Non respiratory Causes of respiratory emergencies.

<table>
<tr><th colspan="4">Non respiratory causes of respiratory emergencies</th></tr>
<tr><th colspan="2">Cardiovascular</th><th colspan="2">Neurological</th></tr>
<tr><td>Cardiac
• CHF
• Arrhythmia
• Myocardial Infarction
• Myocarditis
• Pericardial effusion</td><td>Vascular
• Pulmonary Embolism
• Systemic Vasculitis</td><td>Brain with brainstem
• Central apnoea
• Infection
• Seizures
• Stroke
• Cerebral edema with Mass effect
Spinal cord
• Transverse Myelitis
• Infection
• GBS</td><td>Peripheral Nervous system with Muscles
• Myasthenia Gravis
• Muscular Dystrophy
• Botulism
• Diaphragmatic paralysis</td></tr>
<tr><th colspan="2">Gastrointestinal</th><th colspan="2">Metabolic</th></tr>
<tr><td colspan="2">• GERD -TracheoesophagealFistulla
• Abdominal distension</td><td colspan="2">• Metabolic acidosis
• Dehydration
• Sepsis
• Toxicology symptoms</td></tr>
<tr><th colspan="4">Others</th></tr>
<tr><td colspan="2">• Hyperventilation syndrome</td><td colspan="2">• Anxiety neurosis</td></tr>
</table>

Neurological

Respiratory distress may be a symptom of a primary neurologic disease. Spinal cord disease such as spinal muscle atrophy may present with progressive respiratory insufficiency or frequent lower respiratory tract infections due to inability to handle secretions. Peripheral neuropathies affecting the neuromuscular junction or muscles of respiration, such as myasthenia gravis, botulism, or muscular dystrophy, can also result in shortness of breath.

Gastrointestinal

In geriatric age group and moribund individuals Poor lower esophageal tone and frequency of being in supine position especially In geriatric age group and moribund individuals predisposes patients to Gastroesophageal reflux. This leads to reflex bronchospasm and mimics to bronchial asthma. Significant abdominal distension also leads to respiratory difficulty due to impaired diaphragmatic movement.

Metabolic

Infrequently, respiratory distress can be a symptom of some other systemic disorder. Metabolic acidosis, sepsis, dehydration etc would result in increased work of breathing as compensation for acidosis. Toxicological syndromes that result in metabolic acidosis will also cause respiratory distress. It is prudent to keep in mind, especially when patients are not responding to the therapeutic interventions.

Others

Some disease causing respiratory distress that don't have any structural or interconnected pathophysiological abnormality with respiratory system should not be missed out. Hyperventilation syndrome and anxiety neurosis are the examples.

Above mentioned diseases are affecting normal physiologies or respiration either at ventilation or perfusion or diffusion or all of them. All pathologies are connected at any of the three steps of respiration. It is necessary for physician to find out the anatomical and physiological aspects of diseases to treat them efficiently.

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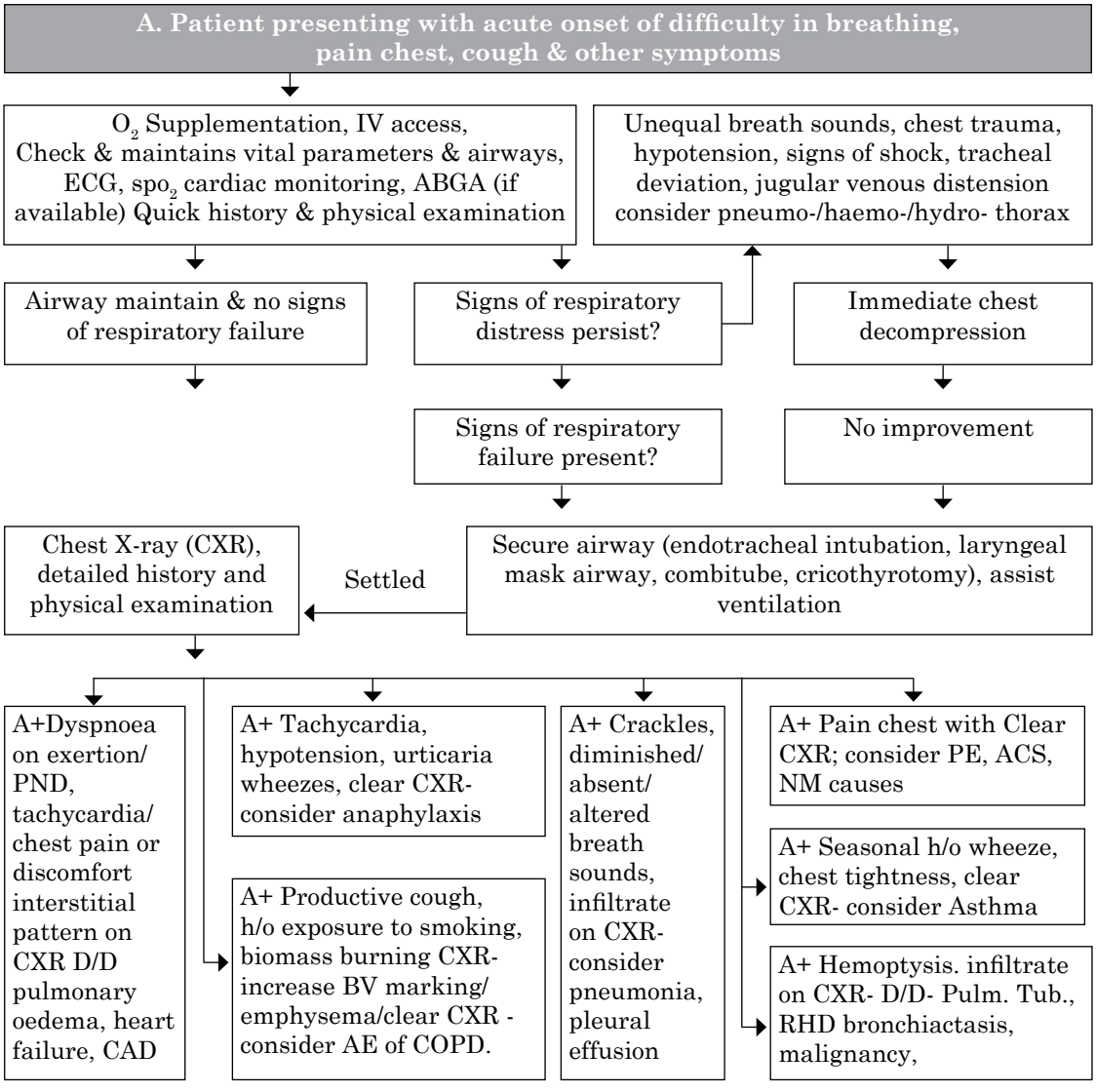
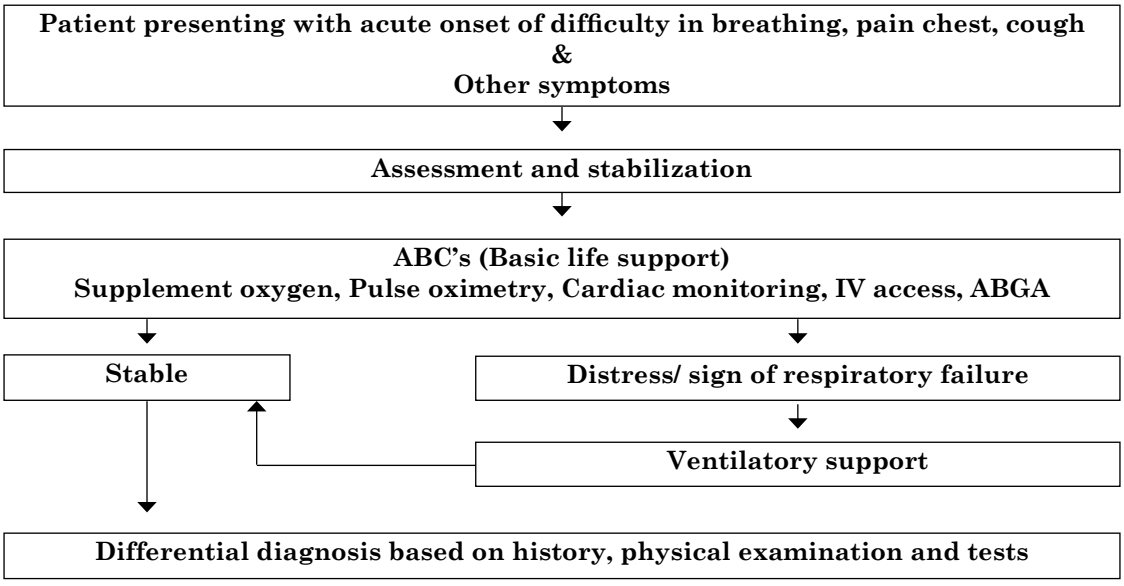
Patient with complaints of difficulty in or inability to breath

Figure 2 : Algorithm for managing respiratory emergencies



Abbreviations : O2 Oxygen; spo2-Oxygen saturation by Pulse oxymeter; IV-Intravenous; CXR-Chest X-Ray; PND-proxysmal nocturnal dyapneoa; PE-pulmonary embolism; ACS-acute coronary syndrome; NM-neuromuscular; CAD-coronary artery disease; RHD-rheumatic heart disease.

Figure 1 : Algorithm for diagnosis of Respiratory Emergencies.



Evaluation	Clinical Presentation
History	Onset of symptoms, Positional changes, Orthopnea, PND, Exertional dyspnea, Fever, Chest pain, Trauma, Associated symptoms, Allergy, Rashes, Weight loss, Past illness, Medications and events leading to present illness
General appearance	Cachcxiz, Weight loss, Sniffing position, Barrel chest, Pallor, Clubbing, Anemia
Vital signs	Tachypnea, Tachycardia, Hypotension
Chest	Wheeze, Rhonchi, Diminished sounds, Hemoptysis, Crepitations on palpation, Flail segment
Cardiac	JVP, Murmur, Muffled heart sounds, Gallop
Extremities	Edema, Calf tenderness, Cyanosis
Neuromuscular	Focal deficits, Diffuse weakness, Ascending weakness, Hyporeflexia
Ancilliary testing	CBC, Chemistry, BUN/creatinine, S.Electrolytes, B.glucose, Chest X-ray, ECG
Relevent Specific investigation	USG, CT/MRI, 2D-ECHO, Spirometry, Waveform capnography, PEFR measurement, Cytochemical examination of pleural fluid

Table - 2 : Approach to a patient with respiratory emergency- Differential diagnosis

S. No.	Resp. Emergency	History	Symptoms	Examination		Relevent Specific investigation
				General Physical	Systemic	
1.	Pulmonary embolism	Long time Immobility (travel, DVT, recent surgery, malignancy, hypercogulability)	Abrypt onset of dyspnea, pleuritic pain	Tachycardia, tachypnea, hypotension, low grade fever, JVD	Rales, Murmer, S3 or S4 gallop, S2 accentuation, calf tenderness	Pulmonary angiogram
2.	Pneumo -thorax	Trauma, chest pain, lung infection	Abrypt onset of dyspnea	Tachycardia, tachypnea, hypotension, low grade fever,	Decreased breath sounds, subcutaneous emphysema, chest wall wound	USG
2.	AE COPD	Smoking, mining worker, farmer, exposure to biomass fuel burning, productive cough (more in winter)	Shortness of breath, air hunger, diaphoresis, sputum production, wt. loss	Clubbing, tobacco stain, Barrel chest, tripoding position, stridor, in severe cases cachexia, oedema feet,	Wheeze, rhonchi, chest retractions, in severe cases accessory muscle use, cynosis, basal crepts	USG, Waveform capnography, on recovery spirometry
4.	Attack of asthma	Recurrent seasonal attacks, more in early morning medication noncompliance, family history,	Shortness of breath, cough, chest tightness,	signs of skin, nasal, conjuctival allergy, hives, rash, bruising in chronic steroid use	Wheeze, rhonchi, chest retractions, in severe cases accessory muscle use, cynosis	Peak expiratory flow rate (if possible), on recovery spirometry
5.	Pleural effusion	Fever, past medical history of : CHF, malignancy, tuberculosis etc	Dyspnea, chest pain, fever	May have cachrxia, weight loss, edema, clubbing	Unilateral decreased chest movements & breath sounds, dullness on percussion, decreased tactile fremitus, asymmetrical chest expansion, pleural friction rub	Thoracentesis for fluid examination (routine, LDH, Protein, cholesterol, glucose level)
5.	Anaphy- laxis	Exposure to allergen, bite or sting, excersise	Itching, oral swelling, rashes, nasal congestion, sneezing, hoarseness, dyspnea, dysphasia,	Tachycardia, hypotension, tachypnea, hives, rash, urticaria	Wheeze, rhonchi, stridor, angioedema	May help: serum tryptase, 24 hour urinary histamine or 5-hydroxyindole -acetic acid, IgE levels

S. No.	Resp. Emergency	History	Symptoms	Examination		Relevent Specific investigation
				General Physical	Systemic	
6.	Pneumonia (infection)	Fever, cough, chest pain	Cough, fever, shortness of breath, chest pain,hemoptysis	Tachycardia, tachypnea, low grade fever	Rales, decrease breath sounds over affected area, bronchophony & bronchial breathing +/-	USG specially to rule out syn-pneumonic effusion
7.	Traumatic chest injury	Trauma	Chest pain, dyspnea	Tachycardia, hypotension,	Stridor, subcutaneous emphysema, chest wall wound, flial segment, crepitance on palpation	CT chest, USG
7.	CHF	Gradual onset dyspnea initially on exertion, diabetes, recent MI or CHF	Dyspnea, hemoptysis, cough, orthopnea, PND	Tachypnea, tachycardia, may be hypotension, JVD	Wheezes, rales, Peripheral edema	2D-ECHO
8.	Cardiac tamponade/ Pericardial effusion	Trauma, past medical history of: malignancy, uremia, CTD, HIV or other chronic infection	Associated to chronic disease, chest pain, dyspnea	Hypotension, tachypnea, tachycardia, JVD, hepatomegaly, dysphoria	Muffled heart sound, pulses paradoxus, kussmaul sign, ewart sign,	2D-ECHO, specific investigations to rule out chronic disease as per clinical findings
8.	Stroke, ICH	Diabetes, hypertension, family history, sudden onset of weakness, visual defects, vertigo	Weakness, diplopia, dysarthria, ataxia, vertigo, aphasia	May have signs of raised ICT, high/low BP, tachy -cardia, confusion, low GCS	Abnormal respiratory pattern, hypopnea Focal deficits, cognitive defects	CT/ MRI brain, Fundus examination
8.	Neuro-muscular	Family history, CTD, difficulty in movements balancing, swallowing, speaking, breathing, visual defect	Tremmers, cramps, Twitching, movement issues, numbness, tingling	Muscle weakness- ascending or descending , muscle wasting, sensory loss, faciculations,	Symmetrical deficits, atrophy, spasticity, visual impairments, defect in pelvic girdle or shoulder muscles	EMG/ NCS study, muscle biopsy, fundus examination

Relevent General Investigations for all patients: Routine biochemical, Pulse oximetry, ECG, CXR , ABGA if available (especially when Pulmonary embolism CHF , Cardiac tapenade, Pericardial effusion etc are diagnosed or suspected).
Abbreviations: GCS-Glasgow Coma Scale

Approach to Management of Respiratory Emergencies – An Overview

Dr. Kapil Chahar

Respiratory emergencies are characterized by respiratory distress or difficulty in breathing or inability to breath. If pain is one universal symptom to bring patient to doctor, respiratory distress is other one to bring patient directly to emergency department. Patients presenting with respiratory distress in emergency department, generally complaints of shortness of breath, difficulty in breathing, air hunger, uneasiness and restlessness. Respiratory distress is a combination of multiple signs and symptoms rather than a specific disease process or syndrome. Signs of respiratory distress include tachypnea, dyspnea, wheezing, abdominal paradox, intercostals retractions, diaphoresis and altered mentation.

Initial care of patient (assessment and stabilization):

Figure 1 Outlines of approach to a patient with respiratory emergency.

Initial care (assessment and stabilization, see figure 2) of patient must be performed rapidly and life threatening or critical causes (see table 1) should be ruled out and managed initially. Critical diagnoses should be promptly considered for the best treatment options to stabilize the patient. After stabilization a thorough medical history, physical examination and ancilliary testing is done and a diagnosis is made. Uncommonly the cause of dyspnea cannot be identified by history, physical examination or ancilliary tests, and specialized testing, including cardiac stress testing echocardiography, CT scan of chest or combined cardiopulmonary testing is indicated. Despite the increasing availability of ancilliary tests, the assessment of patients still begins with an accurate history and a careful physical examination.

Table 1 Critical causes

Diagnostic Approach

Respiratory distress has many different potential causes which can be divided into acute and chronic causes of which many are pulmonary. Other etiologies include cardiac, neuromuscular (NM), metabolic, traumatic and hematological.

History

Onset and Duration of Symptoms

sudden onset of symptoms may be due to pulmonary embolism, spontaneous/ tension pneumothorax or due to chest trauma. Acute spells of dyspnea may be due asthma or copd exacerbations, pulmonary embolism (PE), allergen or foreign bodies. Progressive dyspnea that builds slowly over hours or days may represent a flare of asthma, COPD, pneumonia, congestive heart failure (CHF), malignancy or renal failure.

Positional

orthopnea and paroxysmal nocturnal dyspnea is common with left sided heart failure. Sniffing position is seen in epiglottitis. In COPD/ asthma with severe distress tripod position is seen.

Symptoms

Associated symptoms may indicate towards a diagnosis. Fever suggests a infectious cause. Anxiety may indicate panic attack. Chest pain may point towards myocardial infarction, pleural effusion, PE, pleurisy and spontaneous pneumothorax.

Table - 2 : Approach to a patient with respiratory emergency- Differential iagnosis

Physical examination

***Signs*:** Physical signs may point towards or consistent with specific illness. Tachypnea and tachycardia are found in many illnesses like pneumonia, pneumothorax, traumatic chest injury and asthma / COPD exacerbations. If hypotension is present then tension pneumothorax and cardiac tamponade must be ruled out. Hypopnea may point toward intracranial insult or drug/ toxin ingestion. Cachexia or weight loss may indicate malignancy, immune disorder or mycobacterium infection. Bruising when present over chest wall indicates rib fracture or pneumothorax and diffusely indicates thrombocytopenia, chronic steroid use or anticoagulation. Stridor is consistent with upper airway edema, foreign body, traumatic injury and anaphylaxis. Jugular venous distention indicates tension pneumothorax, fluid overload, pulmonary embolism and congestive heart failure. Abnormal respiratory pattern is indicative of intracranial insult. In pneumothorax and tracheobronchial rupture subcutaneous emphysema is found. Thoracoabdominal desynchrony is found in diaphragmatic injury and cervical

spinal cord trauma. Murmur, s_3 or s_4 galloop or s_2 accentuation is seen in pulmonary embolism. Focal neurological deficits suggests stroke, intracranial hemorrhage. Diffuse weakness is generally due to metabolic/ electrolyte abnormalities like hypocalcemia, hypomagnesemia, hypophosphatemia and anemia. Edema over extremities is seen in CHF.

Ancilliary studies

Findings observed after careful history and physical examination are used to determine which tests are needed.

Bedside pulse oximetry or selectively ABGA are useful in determining the degree of hypoxia and need for supplemental oxygen or assisted ventilation.

Electrocardiogram may be useful to diagnose or rule out dysrhythmia, acute coronary syndrome, and pulmonary embolism.

Serum electrolytes may suggests less common causes.

Severe anemia or thrombocytopenia can be identified with complete blood count.

Blood urea nitrogen/ serum creatinine are helpful in diagnosis of acute or chronic renal failure. ***Glucose estimation*** is helpful for diagnosis of hypoglycemia and diabetic ketoacidosis.

Chest radiograph is a very important investigation to diagnose many pulmonary pathologies like rib fracture, pneumothorax, pleural effusion, local consolidation, interstitial edema, infiltrates, bowel herniation, cavitatory lesion, bony deformity, cardiomyopathy, fluid overload, lytic lesions, malignancy, foreign body and mediastinal adenopathy.

Investigations like; NT-proBNP for heart failure, troponin for cardiac ischemia, D-dimer for abnormal clotting activity can be ordered when there is suspicion of such diseases.

Special testing like V/Q scan, pulmonary angiogram, MRI, CT scan, bronchoscopy and laryngoscopy may be done if diagnosis is not made with history physical examination and basic investigations.

Table - 2 : Approach to a patient with respiratory emergency- Differential diagnosis.

Outlines of Management and disposition

1. In a case of respiratory emergency firstly most critical cause must be considered and take appropriate action as necessary.
2. Unstable patients must be stabilized and these may require admission to an intensive care unit or assisted ventilation.
3. Those patients who have improved in emergency department may be shifted to high dependency units.
4. After stabilization when a specific cause is found then treat the underlying cause.
5. Those patients who are in danger of deterioration without proper treatment also require admission for observation and treatment.
6. If dyspnea persists despite therapy and no diagnosis is made then hospitalize the patient for ongoing evaluation and treatment.
7. If pneumonia or infectious cause is suspected then initiate appropriate empirical antibiotic or antifungal or antiviral agent according to clinical suspicion and send blood and sputum culture.
8. In a case of trauma do FAST (focused assessment with sonography in trauma),
9. If tension pneumothorax is there do immediate chest decompression by needle or tube thoracostomy.
10. Asthma/COPD exacerbations are treated with inhaled ß – agonist, steroids and treat concurrent infection.
11. When anaphylaxis is diagnosed then secure airway when needed (endotracheal intubation, cricothyrotomy), use of epinephrine (IV or SC), steroids, inhaled ß agonist and H_1/H_2 blocker.
12. In case of cardiac disease like acute coronary syndrome (ACS) and dysrhythmia consult a cardiologist as early as possible.

Figure -2. Algorithm for managing respiratory emergencies

Table 1 Critical causes

Organ system	Diagnosis	
Pulmonary	Airway obstruction	Pulmonary embolus
	Anaphylaxis	Ventilator failure
	Pneumothorax	
Cardiac	Pulmonary edema	Myocardial infarction
	Cardiac tamponade	Pericarditis
Traumatic	Tension pneumothorax	Flial chest
	Hemothorax, diaphragmatic rupture	
Metabolic	Diabetic ketoacidosis	Toxic ingestion
	Renal failure	
Hematological	Acute chest syndrome	
Neuromuscular	CVA,	Head injury

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Acute Breathlessness It is Respiratory or Cardiac?

Mansoor Ahmed

Breathlessness is the perception of an inability to breathe comfortably1. Breathlessness is a common chief complaint among patients who come to the emergency department. Acute severe breathlessness may be due to mild unimportant clinical condition to severe life-threatening illness. The adult patient come to emergency department with acute Breathlessness presents difficult challenges in diagnosis and management. The cause of breathlessness is composed of four general categories: cardiac, respiratory, and mixed cardiac or respiratory, and noncardiac or nonrespiratory3,. Most cases of breathlessness are due to cardiac or respiratory disease, which is readily identified with a careful history and physical examination. Chest radiographs, electrocardiograph, spirometry, peak flow meter and echocardiography, ABG are commonly performed diagnostic tests that can provide valuable information to determine the cause of breathlessness.[11,12,13,16,19.]

Table 1 : Causes of Acute or/and severe Breathlessness usually present in emergency department[1, 2, 3, 20]

Respiratory	Cardiac	Others (continue..)
• Angioedema • Anaphylaxis • Infection of the pharynx • Vocal cord dysfunction • Foreign body • Trauma- rib fractures/flailchest/ lung contusion/hemothorax • Pneumomediastinum • COPD exacerbation • Asthma attack • Pulmonary embolism • Pneumothorax • Pleural effusion • Pneumonia • Acute respiratory failure • Hemorrhage • Lung cancer • Exogenous allergic alveolitis • Diaphragmatic paralysis	• Ac. coronary syndrome/ myocardial infarction • Ac. decompensated CHF • Acute LVF • Pulmonary edema • High-output failure • Cardiomyopathy • Tachy-arrhythmia • Valvular heart disease • Pericardial tamponade **Others** • Organophosphate poisoning • Salicylate poisoning • Carbon monoxide poisoning • Ingestion of other toxic substances • Diabetic ketoacidosis	• Sepsis • Fever • Anemia • Encephalitis • Traumatic brain injury • Acute renal failure • Drugs (e.g., beta-blockers, ticagrelor) • Hyperventilation • Anxiety • Intra-abdominal process • Ascites • Pregnancy • Obesity • Stroke • Neuromuscular disease.

Diagnostic approach

The differences of the treatment strategies in respiratory and cardiac diseases and probability of worsening of the primary disease with wrong treatment modality necessitates early and correct diagnosis.

Proper diagnostic approach include detailed clinical history, including past history, drug history occupational and social history, onset, time course, severity,associated sign and symptoms, relation with position, pattern of breathlessness, general and systemic physical examination and Investigations including ECG, X-Ray chest, ABG, Echocardiography and lab investigation, and other specific tests.[4,5,10,11,12,16.]

Clinical history

Careful history-taking is the most useful first step in elucidating the cause of breathlessness. Several factors need to be addressed in the clinical history when constructing the initial differential diagnosis.[17]

Time course

- *Acute breathlessness of sudden onset* with rapid progression in a matter of minutes typically indicates acute and severe conditions that may be life-threatening, for examples acute pulmonary embolism, acute heart valve insufficiency, pneumothorax, anaphylaxis and foreign body aspiration.
- *Acute worsening of pre-existing symptoms* may occurs in acute pulmonary edema due to cardiac disease, acute asthmatic attack, acute exacerbation of COPD
- *Acute breathlessness of insidious onset* with progress within minutes to hours includes myocardial infarction, or pulmonary edema, cardiac tamponade.
- *Subacute dyspnoea* develops over hours to days. Common causes include acute asthma, exacerbation of COPD, or pulmonary edema or cardiac tamponade.
- *Recurrent acute breathlessness* may indicate paroxysmal tachycardias or intermittent complete heart block.

Associated symptoms

- *Acute breathlessness* often occurs with other symptoms, and their co-existence may help to localize the origin of dyspnoea to the involved organ system and help to narrow the differential diagnosis.

- *Fever* manifests with breathlessness and cough suggests infectious and inflammatory conditions, including pneumonia, viral syndromes (e.g., severe acute respiratory syndrome [SARS]), vasculitides and sepsis.[7,8,12,13]
- *Central chest pain* may suggest coronary artery disease, pulmonary embolism, pneumothorax, pneumomediastinum, or foreign body aspiration. Pleuritic chest pain may indicate pneumonia, pneumothorax, pulmonary embolism, or pleuritis.[5]
- *Palpitations* may be present in paroxysmal tachyarrhythmia, pulmonary embolism, valvular heart disease, or anxiety attacks.
- *Syncope* may accompany dyspnoea associated with tachyarrhythmias or pulmonary embolism._
- *Wheezing* may indicate asthma, COPD, pulmonary edema, bronchiolitis, or aspiration of a foreign body. Cough may be present in bronchitis, acute infectious pneumonia, acute eosinophilic pneumonia, interstitial lung disease, COPD, asthma, bronchiectasis, or chronic pneumonitis. Chronic sputum production may indicate COPD or bronchiectasis.
- *Change in the pitch of the voice* may occur with foreign body in respiratory tract.
- *Haemoptysis* may accompany dyspnoea in patients with, exacerbation of bronchiectasis,, acute infectious pneumonia, pulmonary embolism, cocaine toxicity, or diffuse alveolar haemorrhage.
- *Dysphagia or odynophagia* may be present in a dyspnoeic patient with foreign body aspiration, tetanus, and epiglottitis
- *Muscle weakness or myalgias* associated with dyspnoea may indicate muscular dystrophies, acute polio or post-polio syndrome, Guillain-Barre syndrome.[18]
- *Visual disturb*ances may occur with dyspnoea in myasthenia and tetanus, and headache may be present in carbon monoxide poisoning.

Positionality

- *Orthopnoea* is the presence of dyspnoea while supine, with an improvement in the upright position. It is characteristically linked with congestive heart failure but may also be present in asthma, COPD.
- *Platypnoea* is the worsening of dyspnoea on assuming an upright position, with alleviation while supine. It is typical of patent foramen ovale, abdominal muscle deficiency, or hepatopulmonary syndrome.

- *Trepopnoea* is an infrequent finding in which dyspnoea is present only in the lateral decubitus position. It is associated with congestive heart failure, sinus of Valsalva aneurysms, or after a pneumonectomy.

Pattern of dyspnoea

- Seasonal dyspnoea or shortness of breath related to cold, pets, exercise, or non-specific irritants may suggest asthma or reactive airway disease.[4, 5, 8]

Past medical history

- *Breathlessness* in a patient who recently was in labor, post operative, prolonged immobilization or history of DVT may indicate pulmonary embolism.
- *Past history of Bronchial asthma, COPD, CAD, Valvular heart disease, cardiomyopthy.*

Physical examination

Careful physical examination helps to differentiate cause of acute breathlessness.

- Vital signs: Hypotension, tachycardia, and tachypnoea may indicate acute myocardial infarction, pulmonary embolism, acute valvular insufficiency, cardiac tamponade, or an acute infectious process with sepsis.
- ***Hypertension*** in a dyspnoeic patient may point to hypertension-related diastolic heart failure with pulmonary edema.
- ***Pulsus paradoxus*** may be a sign of asthma, COPD, or cardiac tamponade.

General examination

- *Mental status* change may be present with dyspnoea in some conditions, including hypoxemic or hypercarbic respiratory failure related to congestive heart failure, pulmonary edema, asthma, and COPD, pneumonia, sepsis, or CNS infections.
- *Frequent sighing* may accompany hyperventilation and anxiety state.
- *Cyanosis* may indicate acute respiratory failure caused by exacerbated COPD, pulmonary embolism, acute airway obstruction, acute drug toxicity, congenital cyanotic valvular disease, mechanical valve malfunction, cardiac tamponade, pulmonary arteriovenous malformations, aspiration, or methaemoglobinaemia.

- *Facial edema* may be present in dyspnoeic patients with CHF or anaphylaxis.
- *Clubbing* may be present in lung cancer, interstitial lung disease, portopulmonary hypertension, or pulmonary arteriovenous fistulas.
- *Increased abdominal girth* may indicate congestive heart failure, hepatic cirrhosis with ascites and pleural effusions, or constrictive pericarditis.
- *Urticarial rash* may accompany dyspnoea in systemic anaphylaxis.

Cardiovascular exam

- *Neck vein* engorgement may present in dyspnoeic patients with congestive heart failure, COPD, pneumothorax, or cardiac tamponade. Elevated neck veins, extra heart sound (S3 gallop rhythm), and fluid retention indicate congestive heart failure. Chronic dyspnoea resulting from pericardial constriction and effusions may be accompanied by elevated neck veins, pulsus paradoxus, a pericardial knock, pericardial rub, and Kussmaul's sign.
- An irregular or fast *heart beat* may lead to a diagnosis of a tachyarrhythmia or atrial fibrillation. A loud S2 may be associated with pulmonary hypertension and cor-pulmonale. A systolic heart murmur may indicate acute valvular insufficiency, mechanical valve malfunction, or congenital or rheumatic valvular disease.[7,10]
- *Lower extremity edema* may indicate congestive heart failure with pulmonary edema, volume overload, pulmonary thromboembolism, myocardial infarction, arrhythmias, constrictive pericarditis, pulmonary hypertension, inferior vena cava thrombosis, hypothyroidism, or cardiac tumours.

Respiratory examination

- *Pursed lip* breathing may be present in a patient with COPD.
- *Stridor* in a dyspnoeic patient is usually caused by upper airway obstruction with a foreign body, infectious or inflammatory edema (e.g., diphtheria, tetanus, epiglottitis, angio-edema),
- A *barrel chest* (increased anteroposterior diameter) is seen in emphysema and cystic fibrosis.
- The *trachea may deviate* away from the lesion in tension pneumothorax or a large pleural effusion.

- *Unilateral dullness* to percussion may be due to pleural effusion, atelectasis, foreign body aspiration, pleural tumours, or pneumonia. Hyper-resonance may indicate pneumothorax or severe emphysema. Subcutaneous emphysema may indicate the presence of pneumomediastinum.
- *Unilateral decreased or absent breath sounds* may be due to pleural effusion, atelectasis, foreign body aspiration, or pneumothorax. Pulmonary hypertension is suggested by a loud P2 on auscultation. Distant breath sounds suggest a pleural effusion.
- *Wheezing* accompanies dyspnoea in asthma, COPD, anaphylaxis, vocal cord dysfunction, pulmonary congestion and edema, cystic fibrosis, or pulmonary embolism. In COPD, wheeze is associated with acute dyspnoea and a laryngeal descent of at least 4 cm.
- *Pulmonary rales* may indicate pulmonary congestion (fine, bibasal) or edema, acute or chronic pneumonia, or some interstitial lung diseases, including sarcoidosis, hypersensitivity pneumonitis, or idiopathic pneumonitides. Velcro crackles should alert the clinician to the possibility of interstitial lung disease.
- A *prolonged expiratory phase* may be observed in asthma, COPD, cystic fibrosis, bronchiectasis, or bronchiolitis.[7, 8, 13, 20]

Neurological exam

- Cranial nerve palsies may accompany dyspnoea in botulism. Ptosis may be present in myasthenia gravis, myotonic dystrophy, or botulism.

Investigations

After a detailed history and physical examination, if the diagnosis still remains unclear, five investigations would clarify the situation in almost all causes

a. ECG

ECG should be seen carefully in the light of the clinical presentation. A severely breathless patient may have a near normal ECG. This is common in BA, COPD, ARDS, pulmonary embolism and many causes of left ventricular failure such as hypertension, myocarditis, and dilated cardiomyopathy. ECG findings of common causes of acute breathlessness of cardiac and respiratory causes are mentioned here.

- *Myocardial infarction* with acute LVF - ST elevation (or new LBBB),ST depression, inverted T wave,Q wave.
- ECG in congestive *cardiomyopathy***.** Arrhythmias, especially atrial fibrillation and ventricular tachycardia, First degree block, Right or left atrial enlargement, Low amplitude QRS complexes, Left anterior hemiblock, Left bundle branch block, Right bundle branch block, Left ventricular hypertrophy, Nonspecific ST segment and T wave changes.
- *Mitral stenosis* - Atrial fibrillation, Left atrial hypertrophy, Right ventricular hypertrophy
- *Mitral regurgitation*- Atrial fibrillation, Left atrial hypertrophy, Left ventricular hypertrophy
- *Aortic stenosis* - Left ventricular hypertrophy, Incomplete left bundle branch block (i.e. loss of Q waves in leads V_5-V_6), Left bundle branch block
- *Aortic regurgitation* - Left ventricular hypertrophy, Prominent but narrow Q wave in lead V_6, Left anterior hemiblock, occasionally, left bundle branch block.
- Pulmonary embolism; Key ECG findings include:
  - Sinus tachycardia : the most common abnormality; seen in 44% of patients.
  - Complete or incomplete RBBB : associated with increased mortality; seen in 18% of patients.
  - Right ventricular strain pattern :T wave inversions in the right precordial leads (V1-4) ± the inferior leads (II, III, aVF). This pattern is seen in up to 34% of patients and is associated with high pulmonary artery pressures.
  - Right axis deviation : seen in 16% of patients. Extreme right axis deviation may occur, with axis between zero and -90 degrees, giving the appearance of left axis deviation ("pseudo left axis").
  - Dominant R wave in V1: a manifestation of acute right ventricular dilatation.
  - **Right atrial enlargement (P pulmonale) :**peaked P wave in lead II > 2.5 mm in height, Seen in 9% of patients.
  - **S_I Q_{III} T_{III} pattern**: deep S wave in lead I, Q wave in III, inverted T wave in III. This "classic" finding is neither sensitive nor specific for pulmonary embolism; found in only 20% of patients with PE.

– **Clockwise rotation :** shift of the R/S transition point towards V6 with a persistent S wave in V6 ("pulmonary disease pattern"), implying rotation of the heart due to right ventricular dilatation.

– **Atrial tachyarrhythmias (AF, flutter, atrial tachycardia**) :Seen in 8% of patients.

– **Non-specific ST segment and T wave changes**: including ST elevation and depression, Reported in up to 50% of patients with PE.

– COPD - P pulmonale : (Tall, peaked P-wave ≥ 2.5 mm height in inferior leads II, III and aVF), Increased R wave voltage in leads V1, V2, Right axis deviation usually between +90° and +180°, Low voltage QRS complex (<5 mm height) in limb leads, Poor R wave progression, Supraventricular dysrhythmias – Atrial Premature Complexes (APCs), Atrial Flutter, Atrial Fibrillation, Paroxysmal atrial tachycardia and Multifocal atrial tachycardia

b. Chest X-Ray

A good chest film will diagnose pleural effusion, pneumothorax, pneumonia, ARDS, and cardiogenic pulmonary edema. Just like with EGG, a severely breathless patient may have near normal X-ray chest as in BA, COPD, pulmonary embolism, foreign body aspiration, metabolic cause, psychogenic causes and pulmonary edema due to hypertension, acute MI and early myocarditis. Radiological changes take several hours to develop, therefore cases presenting early may not show radiological features and x-ray may have to be repeated if clinical suspicion is strong : X ray findings of common causes of acute breathlessness of cardiac and respiratory causes are mentioned here

- *Acute LVF* - cardiomegaly, cephalization of blood vessels, interstitial edema (eg, "Kerley B" lines, peribronchial cuffing), and vascular congestion. Pleural effusions may be present.
- *Pneumonia /ARDS* - Infiltration of lung field
- *COPD and asthma* – Large lung volumes and a flattened diaphragm on CXR suggest air trapping, which occurs with COPD or asthma.
- *Pneumothorax and pleural effusion*- are easily visible in CXR
- *Pulmonary embolism* - X Ray may be Normal or Atelectasis or parenchymal density, Pleural Effusion, Pleural based opacity, Elevated diaphragm, Prominent central pulmonary artery,Westermark's sign,Cardiomegaly, Pulmonary edema.[12,13,20]

c. Arterial Blood Gas analysis (ABG)

- It should be performed without giving oxygen at presentation and after giving oxygen to the patient for at least 30 minutes. Findings of ABG are dependent on the severity and duration of the disease-state.
- One should notice first whether breathlessness is associated with hypoxia or not.
- Dyspnea without hypoxia is psychogenic or metabolic. In setting of acute breathlessness hypoxia with hyper apnea occurs in COPD with acute exacerbation, BA, pulmonary edema and ARDS.

Table 1 : ABG finding of diseases causing acute breathlessness

S. No.	Disease	PH	pO2	pCO2	HCO3	SaO2
1.	Bronchial Asthma	N	Low	Low	N	Low
2.	LVF	N or low	Low	Low	N	Low
3.	ARDS	N	Low	Low	N	Low
4.	COPD	N or low	Low	Increase	Increase	Low
5.	Metabolic	Low	Increase	Low	Low	N
6.	Psychogenic	N or increase	Increase	low	N or increase	N

d. Bedside Pulmonary Function Test (PFT)

- This should include Peak expiratory flow rate (PEFR) and Forced expiratory volume in first second (FEV|) assessment.
- Both these parameters are necessary to determine the severity of BA and COPD and their response to drugs.[16]

e. Echocardiography

- This is not an essential investigation in a usual case of severe dyspnea. However it does help in cases that have coexistent respiratory and cardiac disease. It is essential when cardiac tamponade is suspected.

f. Other Investigations

- High-resolution CT scan;
- V/Q scan;
- Radioallergosorbent test (RAST) measurement or skin prick testing to common aero-allergens.
- Blood tests including Troponin T, Tropnin I, BNP, D-Dimer level may be important tool to determine cardiac or respiratory cause of dysponea.[10,14,15]

The recovery and survival of patient of acute breathlessness depends on ability of treating physician to identify the underlying cause and treat promptly. Cause of acute breathlessness whether Cardiac or pulmonary is determined in most cases by the systemic approach and basic tests including X-ray chest, ECG, bed side PFT, ABG, bed site Echocardiography. However preexisting cardiac or pulmonary diseases may require more extensive investigations.

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Acute Large Airway Obstruction Including Foreign Body Aspiration

A. S. Rathod, Pushpendra Shekhawat

And I wonder if Beethoven held his breath,
the first time his fingers touched the keys.
the same way a soldier holds his breath,
the first time his finger clicks the trigger.
We all have different reasons for forgetting to breathe.

Andrea Gibson

After evolution of life from sea, it was whole lot of different environment for life to sustain, and in the same pursuit, respiratory system was also differentiated from the sea to earth. Homo sapiens developed complex but sophisticated tracheo- bronchial tree. Men found eternal Bliss to Breath, Speak and Sing. This segment of publication is for a brief outline of Acute Obstruction of same sophisticated system i.e. Upper Airway Obstruction with some light on Foreign Body Aspiration.

Most ancient treatment to relieve airway Obstruction in human Is Tracheostomy, there are few surgical procedures which gives dramatic turn to the event, and Tracheostomy is one of them.

The tracheostomy is one of the oldest surgical procedure .Amazingly, a tracheostomy was portrayed on Egyptian tablets dated back to 3600 BC.Asclepiades of Persia is credited as the first person to perform a tracheotomy in 100BC Prasovala in 15th century. The first successful tracheotomy was performed by Prasovala in 15th century. in the 16 th century Guidi invented an original method of Tracheotomy.

Magnitude of Upper Airway Obstruction (UAO) demands necessary and prompt Action. This chapter will review the options available to us and their judicious use.

Our intention is to provide least invasive method providing maximum relief to patient and appropriate control to clinicians. This sounds easy but sometimes the most difficult part of entire situation, because of concurrent clinical situations and medical history. The most appropriate example is road traffic accident and dealing the case onsite, assessment of airway for obstruction difficult due to lack of attending paraclinics and

resources. Furthermore, it is possible that in an attempt of securing the airway, it may cause further injury.

Clinical presentation of airway obstruction

Sometimes the symptoms are so nonspecific and may mimic different respiratory conditions. Commonest symptoms are cough, dyspnoea and change in voice which may or may not be associated with pain and dysphasia.

The most important symptom is dyspnoea and if it is increasing may herald complete upper airway Obstruction.

Stridor

The cardinal sign of upper airway Obstruction is stridor, it's a noisy breathing due to narrowing of larynx or trachea. Stridor is always high pitched. Obstruction of pharyngeal Airway produces low pitched noise as in snorers and it is called Stertorous.

Type of Stridor - in relation of phase of respiration is clinically useful to ascertain the level of Obstruction

- *Inspiratory stridor*-indicates the level at Glottis.
- *Expiratory stridor* -associated with Obstruction at intrathoracic airway
- *Biphasic stridor* - indicates tracheal obstruction.

In human respiratory cycle, the extra thoracic Airway tends to collapse on inspiration and to increase in diameter on expiration, this is the exact reason of Stridor in inspiratory phase because effect of reduction in diameter more marked during inspiration.

Similarly, pedunculated lesion and soft tissue oedema in supraglottic airway sucked into the Glottis on inspiration and expelled out of the way during expiration. The same situation occurs in Stertorous breathing in pharyngeal obstruction.

Opposite is true for the intrathoracic airway, which is guided by intrapleural pressure changes. During inspiration, the negative intrapleural pressure exerts an outbound force on the intrathoracic airway and thus increases diameter. During expiration, opposite happens, and positive intrapleural pressure causes a relative collapse of intrathoracic airway, which is exacerbated by any narrowing.

Trachea is discerningly different characteristics because of its cartilage rings, so any narrowing of lumen remains same in both phases of respiration and so is stridor.

Hoarseness

Hoarseness in UAO developes because of abnormal vibrations of vocal cords.

Wide range of injuries may produce this response.

Vocal cord paralysis, oedema, mucosal tears, laryngeal trauma or reduced flow of air through vocal cords due to benign or malignant neoplasm are to name a few of them. As a rule severity of hoarseness is directly proportional to level of Obstruction in airway. Aphonia is almost always associated with very severe injury.

Suprasternal retraction

Airflow obstruction leads to more active efforts by the patient, more inspiratory efforts need accessory muscles to work.This leads to suprasternal retraction, intercostal recession and fairing of nostrils. Working of accessory muscles should never be missed to assess and diagnose the UAO.

Restlessness

Restlessness and suprasternal retraction requires immediate attention and urgent respiratory support.

Restlessness commonly attributed to anxiety but hypoxia due to UAO is also very common, beside that parenchymal lung damage and haemorrhagic shock may also cause hypoxia and in turn restlessness.

Restlessness due airway Obstruction followed by calmness inspite of without respiratory support should be looked and registered very judiciously.As the patient starts to tire from the extreme respiratory efforts,so they become less restless, which may be the imminent sign preceding complete respiratory failure.

Haemorrhage and drooling of saliva

Haemorrhage is due to trauma in mucosa of oropharynx, larynx or upper airway. Careful examination with proper illumination is needed to find the source of bleeding.A good headlight with halogen or LED illumination is always helpful in such situations. in patient of multiple trauma sometimes it's very taxing to find out the exact location of bleeding.

Drooling of usually due to pain, where patient avoid a painful stimulus of deglutition. Drooling is due Trauma or infection.both these may affect neuromuscular coordination in 2ndstage of deglutition.

Surgical emphysema and fractures

Surgical emphysema may happen in case of laryngotrachealinjury.This always implies the disruption of aerodigestive tract, with air leak into the surrounding soft tissue. sometime surgical emphysema is so severe that it may produce UAO.

Fractures of Trachea,Larynx, mandible and maxilla may produce UAO.A thorough examination is mandatory to look for the fractures.

Assessment of Upper Airway Obstruction

As the traditional teaching of emergency medicine goes, it's A,B,C. The initial assessment of airway in patients of airway Obstruction is of paramount importance.The assessment should be prompt and rapid but must not be hasty. Promptness should not compromise the thoroughness of the examination. Sometimes in the heat of the moment clinicians unknowingly overlooks the reversible cause of the airway Obstruction.

Breathing and circulation should be checked and resuscitation should be done if needed at all.

Following this a full assessment of patient should be done to find out if there is any other injury or medical conditions.

At this juncture of time if we found any doubt in securing airway .we should secure the airway by least invasive method without waiting.

A careful examination and assessment of signs and symptoms will,in most of the cases, provide enough evidences for further management of the situation. After securing a stable airwayif we are still unable to find out the reason and nature of disease,it becomes absolutely necessary to do an examination of airway and flexible fiberoptic examination is appropriate tool for this.

Flexible fiberoptic examination is far better option than indirect laryngoscopy for the several reasons,its better tolerated,can be done in drowsy or moribund patient, better ability to provide details of every nook and cranny and findings can be recorded for further examination, clinical or legal purpose, as need may arise.

If there is any suspicion of cervical trauma, it makes story somewhat different. Cervical spine skiagram becomes need of the hour and there is any trauma to cervical spine positioning of neck becomes crucial for conventional endotracheal intubation as well as tracheostomy. Flexible fiberoptic examination again a fairly good choice in such happenings.

Radiograph rarely provide any useful information except in one condition that is Foreign Body in laryngotracheal passage specially if it's a child of 1 to 5 years age. A complete collapse of one lung, shifting of tracheal shadow, compensatory emphysema with a clear history of choking and bout of coughing with respiratory distress without any pyrexia indicates foreign body in respiratory passage. It's not uncommon that ingestion was several months ago. An emergency bronchoscopy is the only answer in such children after stabilizing.

Soft tissue radiograph of neck, facial view, barium swallow and arteioriography may occasionally, be indicated.

Treatment

- When we treat upper airway Obstruction one idea should be kept in mind and that is "DO NOT VACILLATE".
- As discussed earlier, the intervention depends on the experience of the clinician and results of the examination. Intervention required to overcome the UAO can be a single definitive treatment or it could be a combination of treatment modalities. This is more true in case of progressive obstruction in spite of therapy.
- There are certain cardinal principal to follow in management
- Treatment of choice should beleast invasive, most effective and straightforward and should be of standardized technique, and it should adequately secure the passage
- Any method of management/treatment should overcome or bypass the obstruction. The lowest level of Obstruction should be overcome.
- Pre or coexisting medical or surgical conditions should be carefully addressed and plan of relieving the Obstruction should not deteriorate these, as mentioned earlier in case of cervical trauma.

The medical conditions should be carefully managed after securing the airway.

Medical Treatment and Noninvasive Procedures

- There is a famous statement and almost universal *truth "the time to do Tracheostomy is when you first think of it."* This should always kept in mind, but in present time state of the art critical care unit and ICUs demands more pragmatic approach.
- There are situations when minor trauma, infections or neoplasm may cause moderate to severe obstruction but stable, in these conditions a brief period of close observation with judicious use of specific treatment can be given.

- This can only be followed at that institute level where staff is fully trained to identify the deterioration in conditions and efficient enough to intubate or perform Tracheostomy.
- This should be clearly understood that period of observation in these situations are dangerous and patient should only be kept under observation if he is otherwise stable
- There should be a standard protocol in every establishment and should be clearly understood by the residents and consultant. On passing a certain criteria there should not be any delay from observation to intervention.
- During the period of observation some of the nonsurgical treatments are briefly described.

Heimlich Manoeuvre

Heimlich first published his views about the maneuver in a June 1974 informal article in *Emergency Medicine* entitled, «Pop Goes the Cafe Coronary». On June 19, 1974, the *seattle post intelligencer* reported that retired restaurant-owner Isaac Piha used the procedure to rescue a choking victim, Irene Bogachus, in Bellevue, After a tumultuous course of time and endless efforts by American heart association, American red cross and different safety councils Heimlich manoeuvre is still popular, tested and proven method to dislodge foreign body usually food bolus from larynx. It should start with sharp blow to the back of the patient. Hugging the patient from behind so as to apply pressure in the region of xiphisternum,uses the residual air in the lung to expel out the bolus from Glottis.If the procedure fails to relieve the bolus or Foreign Body than immediate cricothyrodotomy should be carried out.

Heimlich manoeuvre if successful derives dramatic results in saving life but it is not without complications, which includes pneumomediastinum, pneumoperitoneum, surgical emphysema and rupture of stomach. Keeping all these possibilities in mind patient should be kept under monitoring even after Heimlich manoeuvre is successful to remove bolus. In spite of such potentially fatal complications different meta-analysis depicted decrease in death rate from inhaled foreign bodies since the introduction of the Heimlich manoeuvre.

Oxygen and Heliox

Humidified oxygen by face mask or by nasal cannulae improves hypoxia. Some patients develops pulmonary oedema due to negative pulmonary pressure and upper airway Obstruction combined, humidified oxygen helps to breakdown the secretion and make them easier to expel out.

Heliox is mixture of 80% Helium and 20% oxygen, since 1930 it has been used for various respiratory disorders. Patient of UAO feels reduced resistance during breathing with Heliox. Helium has unique properties like low density and high viscosity and make it less prone to turbulent flow than air or pure oxygen. This is of proven benefit in the obstructed patient. Surprisingly it has been observed effect of Heliox is more pronounced in more severe degree of Obstruction.

Steroids

Steroids are very effective in reducing the oedema and they play overtly significant role in reducing the inflammatory, infective and traumatic oedema.

When using steroids it should be always used in correct dose. Underdosing of steroids is common mistake rather than overdosing.

There is no detrimental effect in presence of infection if steroids are used as short term therapy.

Antibiotics

Antibiotics should be immediately started if there is infection and evidence of mucosal injury.A broad-spectrum antibiotic or sometime specific antibiotic is needed egAc. Eoiglottitis need IV cephalosporin.

Alternative Airways

If non invasive procedures are not producing desired effect condition is deteriorating than it has to be decided what should be most suitable alternative Airway.As the earlier guidelines states it should be least invasive, adequately bypass the Obstruction for required amount of time. Experience of the staff should be enough to place the device effectively.

Oral Airway

Figur 1 : Oral airway

Oral Airway bypass nasal and oral obstruction, commonly present in Road traffic injuries.Nasal and oral injury is bypassed by oral Airway. This is semirigid device and easy to place.Patient must still have normal ventilatry drive and normal anatomical architecture beyond oral cavity and nasopharynx.This device is not very well tolerated by conscious patient and easy to get dislodged.This is good device in unconscious and comatose patient,it is simple, maintain the airway well and facilitate suction.A facemask and ambubagcan also be used with this device.

Nasopharyngeal Airway

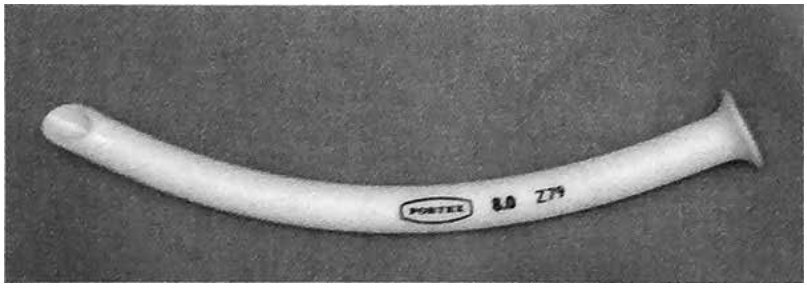

Figure 2 : Nasopharyngeal airway

As in oral Airway,a normal respiratory drive is needed in nasopharyngeal Airway. They are made of soft in consistency and can be used when problem lies in oropharynx for example Ludwig's angina

Tongue base is pushed back in this situation and trauma in oropharynx also produce the same situation.oral Airway doesn't go far enough down the airway and make a conduit to undamaged part of Airway. Nasopharyngeal Airway is again easy to insert and provide access to suction, but it's not uncommon when it Leeds to epistaxis and blocks both Airway

Endotracheal Intubation

Both of the above mentioned devices are useful only when respiratory drive is there. If nasopharyngeal and oral device are not serving the purpose due this reason. Endotracheal Intubation is the treatment of choice for assisted ventilation,or in case of progressive upper airway Obstruction.

To facilitate endotracheal Intubation there should be array of endotracheal tube available beside this a bougie,a laryngoscope preferably having fiberoptic LED illumination and good suction are necessary equipments.

Commonest method of intubation is transoral but there are some relative contraindications to transoral intubation. They are as follows:

- *Cervical spine fractures* - hyperextension of neck is part of transoral intubation, this may result in exacerbation of incomplete or unstable spinal injury.
- *Maxillofacial trauma*- haemorrhage, oedema, bony instability and ankylosis of TM joint leading to trismus may all combine and make it very difficult to view the larynx.
- *Laryngotracheal injury*- Endotracheal tube may further cause trauma to already injured larynx and upper tracheal segment.

As mentioned earlier they are all relative contraindications. It all depends on the experience and experty of clinician. At any indication of above problem if transoral intubation is found inappropriate, transnasal intubation can be attempted. Traditionally transnasal intubation is a blind procedure and it needs greater experience and skill. Transnasal intubation is having again potential problems of injury to nasal passage and further bleeding in already compromised Airway. Since advent of flexible fiberoptic system for illumination, transnasal flexible fiberoptic endoscopes are the best system available for transnasal intubation under vision.

A transnasal laryngobronchoscope is passed beyond the vocal cords in trachea, and an appropriate sized endotracheal tube is passed /threaded over the endoscope into the position. The use of endoscope turns a blind procedure into a much illuminated and safer procedure performed under vision.It looks good but again

This needs additional skill and resources. in patients of excessive secretion and bleeding, visibility of larynx is compromised and makes even fiberoptic intubation difficult.

Transtracheal Cannulation

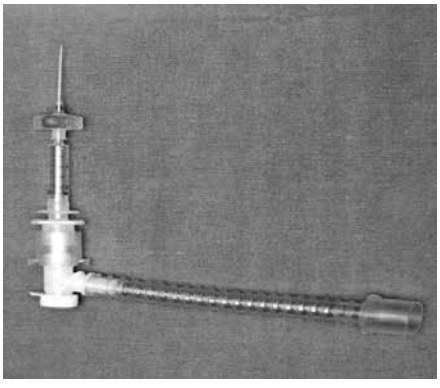

Figure 3 : Device for transtracheal cannulation

It is a very temporary procedure to secure the airway after after doing transtracheal cannulation, patient has to be shifted for either Tracheostomy or intubation by appropriate method. In extreme emergency situation cricothyrodotomy membrane is punctured with a large bore intra venous canulathis is connected to a syringe which inturn connected to 7 mm endotracheal tube adaptor. An adequate oxygenation can be achieved with this method but CO2 is not efficiently cleared that's why an emergency tracheostomy has to be performed .

Cricothyrodotomy

Sometimes a complete Airway obstruction and inability to ventilation heralds a panicky situation. Cricothyrodotomy can be performed in such happenings . It can be performed with minimum of equipment and associated with lease complications. A no.15 blade with BP knife handle is the only instrument needed and cricothyrodotomy membrane is punctured in midline and dilated with a simple artery forceps. Once the airway has been secured, a formal Tracheostomy should be performed.

Tracheostomy

Tracheostomy is gold standard to relieve upper airway Obstruction.Again it needs a great experience and skill to do a emergency Tracheostomy, because sometime patient is restless and not able to stay in supine position,they are only comfortable in sitting position to use accessory muscles better and allay the air hunger.Emergency Tracheostomy is performed under local anaesthesia and by vertical incision .

The terms *Tracheotomy* and *Tracheostomy* are often interchanged but are technically different. A*Tracheotomy* is generally described as a procedure that involves opening the Trachea. *Tracheostomy* is a procedure that exteriorizes the Trachea to the cervical skin, resulting In a more permanent Tracheostomy fistula, therefore term Tracheostomy should be reserved for these particular procedure. Indications of Tracheostomy in upper airway Obstruction are difficult to enumerate but some of clear indications are as follows

- Severe maxillofacial trauma in which injuries make the airway inaccessible for transoral intubation.
- Significant laryngeal trauma in which intubation may potentially cause more damage.
- Excessive haemorrhage or emesis obscuring landmarks required for successful intubation.
- Cervical spine injury with vocal cords that are difficult to visualise,and
- Following failed transoral intubation.

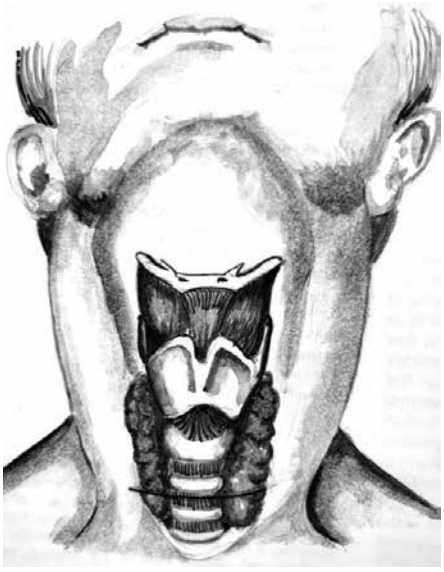

Figure 4 : Tracheostomy site and landmarks

Emergency Tracheostomy is done by vertical incision, after retracting the strap muscles, isthmus of thyroid is encountered which can be retracted up, down or divided as the situation demands. First tracheal cartilage is avoided to open the Trachea, usually 3rd or 4th tracheal cartilage level is chosen for making Tracheotomy opening.

Foreign bodies in upper airway

General Considerations

Foreign body aspirations in upper airway are important cause of morbidity and mortality in paediatric population in India. Different eating and playing habits make this situation different from UK and US in terms of incidence and type of foreign bodies.

The peak incidence of foreign bodies in upper airway is between the ages of 1and 3 years of age.

Different studies conclude that only 12% of inhaled foreign bodies impact in larynx and most passing through the vocal cords into the tracheobronchial tree. In children they tend to lie more centrally and 53% are within the Trachea and 47% are distal to Carina. Adult population are less affected by foreign bodies and in them it tends to lodge in right main Bronchus.

Pathogenesis

Children under 3 years have a peculiar habit and this is called *oral exploration* that makes them the most probable age-group. Increased mobility and ingestion of adult food add to the risk of inhalation.

Lack of dentition or immature dentition and immature neuromuscular coordination in 2nd stage of swallowing may also play a significant role.

Food is the most commonly inhaled or aspirated foreign body.

Long standing foreign bodies in upper airway can lead to multiple complications, and complications are directly proportional to the length of time foreign body has been present. Granulation tissue formation, erosive lesion, pneumonia and ultimately lung abscess may develop over the period of time. Early diagnosis and endoscopic intervention can prevent all these possibilities.

Prevention

Foreign body aspiration is an accident and as in every accident protocol prevention is the most important intervention. Parent's education and awareness play big role in prevention of upper airway foreign bodies. However, it is not always possible to keep a vigilant watch every time if the day on infants and toddlers.

Children older than 5 years of age are more prone to aspirate school supplies like eraser, lead pencil part or cap of pen. Careful explanation of potential complications to this age group should be part of bringing up the child.

On part of government authorities it is welcome idea if they come up with legislation on using the size of objects in toys(>3.17 cm in diameter and >5.71cm in length),but it is very difficult to regulate and follow.

Clinical findings

Choking episode and sudden onset of extensive bout of coughing with respiratory distress always present suspicion of foreign body aspiration. Sometimes history suggests that child was playing with some object or eating peanut, beetle nut or cashew and it started suddenly coughing. This can be followed by symptom-free period if object lodges in lower airway.

Partial obstruction of main stem bronchi produce characteristic wheeze over one side of the chest by auscultation and hyperinflation of lung by skiagram.But it is not necessarily present in all cases. The hyperinflation of the chest can be explained by 'ball-valve effect'. Negative intra-thoracic pressure on inspiration dilated the bronchial lumen around

the foreign body and let a small volume of air inside of lung. On expiration, positive intra-thoracic pressure compress the main bronchi and make it closely approximated to foreign body and thus no air can be escaped from distal portion to foreign body from affected lung.

Foreign body aspiration most of the time leads to dramatically devastating clinical symptoms and signs but still 20% of patient may not have initial presenting complaints and these patients' presents after several days with secondary respiratory complications. A high index of suspicion and early option of bronchoscopy should always be kept in mind.

Imaging studies

Simplest approach is to start with X-ray. A posteroanterior view of chest is mainstay added with posteroanterior and lateral view of neck. Radio-opaque foreign bodies are easy to find.

Foreign body in Bronchus produce different characteristic features in X-ray chest.

- Localised atelectasis or infiltrates
- Unilateral hyperinflation or obstructive emphysema due to earlier mentioned 'ball-valve' effect.
- Mediastinal shift are some of them.

However high clinical intuition and strong history always are indications for the rigid bronchoscopy even if X-ray findings are normal.

CT scan of thorax may or may not help in definitive diagnosis of foreign bodies.

If foreign body goes untreated common sequelae are pneumothorax or pneumonia. Smaller foreign bodies may produce granuloma formation, signifying aggressive search for foreign body in every new case of bronchial granuloma. Longstanding foreign body in tracheo-bronchial tree may lead to lung abscess or bronchiectasis and this may eventually lead to indication of lung resection.

Differential diagnosis

Clinical presentation of foreign body Bronchus so varied that lot conditions can be kept under differential diagnosis but history and suspicion of foreign body rule out most of possibilities.

Sometimes chronic cough and wheezing are the presenting complaints and this may result in common misdiagnosis of

- Bronchial asthma
- Croup
- Pneumonia

In children with these diagnoses who continue to visit paediatrician, pulmonologist and general physician and getting partial response with appropriate treatment, the presence of airway foreign body should be considered.

Complications

Complications can be classified as early and late.

Early complications are severe like Cyanosis, respiratory distress and even respiratory arrest. A ball valve effect can do hyperextension of affected lung, and complete occlusion may cause partial or total collapse of lung.

Late complications are pneumonia, empyema, bronchial fistula and pneumothorax.

Treatment

The treatment of choice for foreign body Bronchus is rigid bronchoscopy and removal under general anaesthesia. It is often matter of debate between flexible and rigid fiber optic bronchoscopy but every unsuccessful flexible bronchoscopy has to be converted in rigid

Bronchoscopy method

Figure 5 : A ventilating bronchoscope with attached telescope.

A flexible fiber optic bronchoscopy is helpful in diagnosis of suspected foreign body in tracheo-bronchial tree.

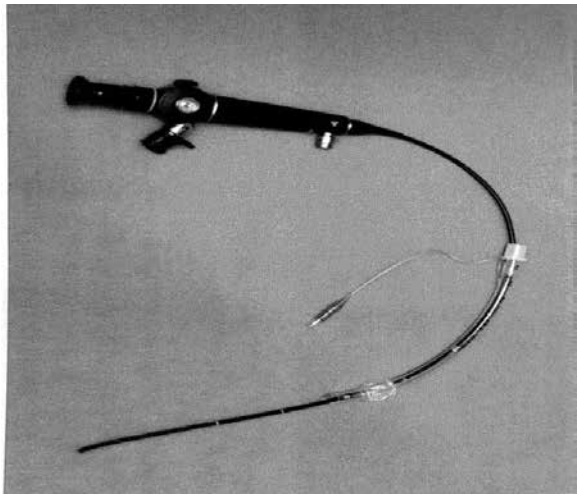

Figure 6 : A fibreoptic flexible laryngobronchoscope.

Foreign body aspiration is an emergency and Bronchoscopy should be done when it is presented in Emergency room or OPD. If child is not fasting, a rapid sequence technique is preferred for general anaesthesia to prevent aspiration.

A thorough discussion between surgeon and anaesthesiologist is necessary regarding the case. Both the clinician must perform this procedure in complete harmony because they both have to share common airway. Operating ENT surgeon should be gloved; all the attachments of bronchoscope, light source, video equipments and suction machine should be ready. Induction of anaesthesia should be done after everything is ready and at place.

During anaesthesia spontaneous respiration can be maintained with inhalational agents, topical lignocaine spray can be used to anesthetize vocal cords. Direct laryngoscopy performed and rigid bronchoscope passed through vocal cords into trachea under direct vision. Once the bronchoscope is passed in trachea anaesthesiologist may connect it to ventilation port. Once the foreign body is identified clinician should not rush to grab it and remove. A proper and careful suction around foreign body should be done. Telescope of optical forceps used to correctly see the lie, orientation and place of foreign body. Optical forceps used to retrieve the foreign body under vision. Only a small foreign body can be removed through lumen of bronchoscope. Whole unit i.e. bronchoscope, optical forcep and foreign body should be withdrawn.

Care should taken to avoid premature release of foreign body while withdrawing, subglottic area is narrower in children and foreign body Bronchus will be converted in laryngotracheal foreign body which preclude ventilation and could be catastrophic.

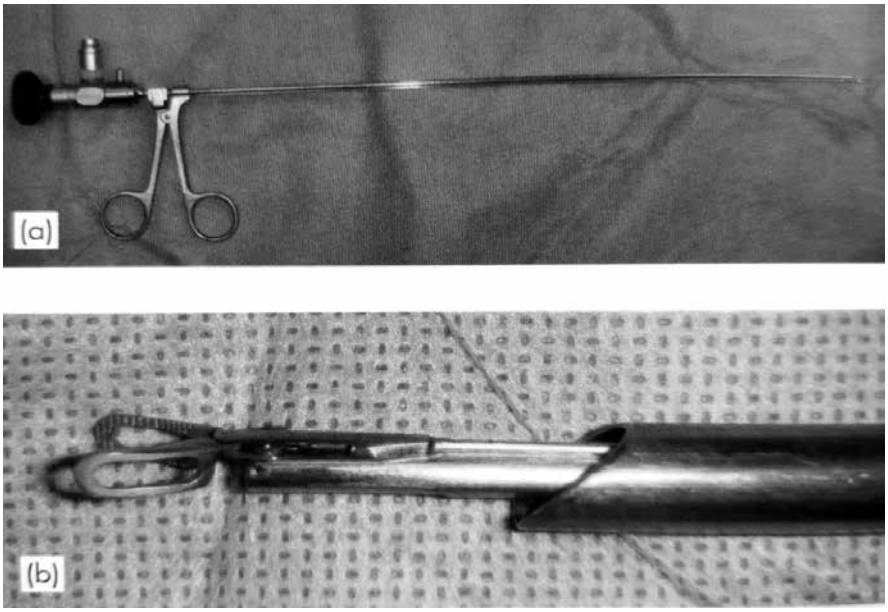

Figure 7 : (a). Optical forceps with attached telescope. (b). Open jaw of peanut optical forceps passed through ventilating Bronchoscope.

Surgeon should communicate with anaesthesiologist to confirm the depth of anaesthesia so that laryngoscopy can be avoided upon withdrawal of the bronchoscope. Bronchoscope should be passed again to rule out further foreign bodies in distal airway, it's not uncommon to have second foreign body distal to previous.

Beetle nut, cashew and groundnut may require multiple attempts to remove whole of foreign body.

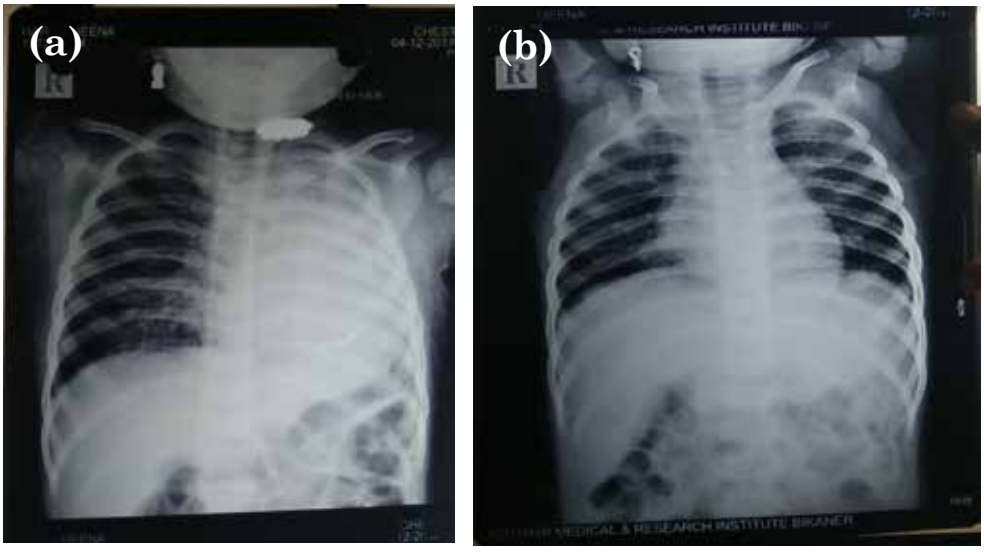

Figure 8 : (a). Collapse of left lung, mediastinal shift and obstructive emphysema due to 'Ball-valve' effect. (b). 12 hours after bronchoscopy and removal of foreign body, improved lung ventilation and mediastinal shift.

Care should be taken to avoid mucosal trauma otherwise mucosal bleeding will make it difficult to see residual foreign body.

A careful and thorough suction done, pent up secretion distal to obstruction usually copious and suctioning will help in ventilation of collapsed part of lung. Mucosal bleeding can be controlled by application of adrenaline soaked patties.

Patient can be shifted to general ward and kept under observation. A prophylactic antibiotic can be started. A short course of steroids started with bolus during anaesthesia may help to control postoperative oedema and inflammation due to instrumentation.

Depending on the presenting illness child may require postoperative skiagram chest and close follow up to rule possibilities of pneumonia and late complications.

Prognosis

Majority of children will make full and extremely satisfactory recovery without late complications or sequelae from foreign bodies of Bronchus and tracheo-bronchial tree. Delays in diagnosis of foreign body cause most severe morbidity. Children who have long standing foreign body and technically difficult extraction should be kept under observation in hospital setting until improvement in X-ray findings. They should no longer require airway support.

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Acute Exacerbation of Asthma

Rajesh Swarnakar

Acute asthma exacerbations are defined as episodes of worsening of asthma symptoms and lung function, characterized by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function.

They may be the presenting manifestation of asthma or may occur in patients with a known asthma diagnosis presenting as change from the patient's usual status occurring in response to a "trigger" such as an allergen or irritant exposure, viral upper respiratory infection, lack of adherence to controller medication, or an unknown stimulus.[1] Asthma exacerbations are a major cause of disease morbidity, increases in healthcare costs and in some patients, a greater progressive loss of lung function.[2]

Classification of asthma severity[3]

Considering clinical presentation and PEF or FEV1 levels Asthma exacerbations can be classified as mild, moderate or severe or life threatening (Table 1)

Table 1: Classification of severity of asthma

Degree of severity	Symptoms and signs	Initial PEF (or FEV1)	Clinical course
Mild	Mild Dyspnea only with activity (assess tachypnea in young children)	PEF ≥ 70 % of predicted or personal best	• Home treatment • Inhaled SABA • Possible short course of OSC
Moderate	Dyspnea interferes with or limits usual activity Talks in phrases	PEF 40 to 69 % of redirected or personal best	• Usually requires office or ED visit • Frequent Inhaled SABA • Short course of OSC • Some symptoms last for one to two days after treatment begins

Degree of severity	Symptoms and signs	Initial PEF (or FEV1)	Clinical course
Severe	Dyspnea at rest; interferes with conversation Talks in words	PEF < 40 % of predicted or personal best	• Usually requires ED visit & likely hospitalization. • Partial relief from frequent inhaled SABA & OSC. • Some symptoms last for more than three days after treatment begins • Adjunctive therapies are helpful
Subset: life threatening	Too dyspneic to speak; perspiration, drowsy, silent chest	PEF < 25 % of predicted or personal best	• Requires ED visit/hospitalization • Possible admission in ICU. • Minimal or no relief from frequent inhaled SABA • Intravenous corticosteroids • Adjunctive therapies are helpful

Abbreviation: SABA- short-acting beta2 agonist; OSC-oral systemic corticosteroids; ED - emergency department

Triggers for exacerbations of asthma

Asthma exacerbations are caused by an accentuation of existing inflammatory processes and a loss of disease control. Several triggers have been identified to be associated with asthma exacerbations

- **Viral infections :** Viral infections are the most common triggers for asthma exacerbations. The respiratory viruses implicated are human rhinovirus, particularly subtypes A and C, H1N1 virus, Coronaviruses, human metapneumoviruses, parainfluenza viruses, adenoviruses, and bocaviruses.[4]

- **Bacterial infections :** Impair mucociliary clearance leading to an increase in mucus production in the lung and may cause chronic lower airway inflammation. Evidence linking bacterial infections to acute asthma exacerbations has been limited.[5,6]

- **Allergen exposure :** Environmental allergens lead to mast cell activation by allergens.[7,8] This causes the release of histamine, prostaglandin D2, and cysteinyl leukotriene generation to cause airway smooth muscle constriction, increased microvascular permeability, mucus secretion, and enhanced inflammation. Allergic sensitization also is also associated with diminished innate immune responses and may be a susceptibility factor to viral-induced wheezing. This allergen associated inflammation also increases airway responsiveness.[9]

- **Pollutants** such as tobacco smoke, ozone, and particulate matter, along with occupational exposures, provoke asthma exacerbations[4]
- Other triggers also include moulds, fungi, animal dander, dust, dust mites and cold air.

Risk factors for exacerbations of asthma

Several risk factors have been identified in patients with exacerbations of asthma. These include

- **Medications:** High SABA use (use of more than 1 canister per month; inadequate ICS (not prescribed ICS, poor adherence, incorrect inhaler technique).
- **Comorbidities:** obesity, chronic rhinosinusitis, GERD, confirmed food allergy, pregnancy.
- **Exposures : Triggers,** Smoking, air pollution, exposure to allergens
- **Major psychological or emotional problems.**
- **Lung function:** Low FEV1 especially < 60% of predicted, high bronchodilator reversibility.
- **Blood eosinophilia.**[10]
- **Ever intubated** or in the intensive care for asthma.
- **Asthma exacerbation** - one or more than one in the last 12 months.

Presentation of a patient with acute exacerbation of asthma

An asthma exacerbation is an acute or subacute episode of progressive worsening of symptoms of asthma, including shortness of breath, wheezing, cough, and chest tightness. Exacerbations are marked by decrease from baseline in objective measures of pulmonary function, such as peak expiratory flow rate and FEV1.

Diagnosis

Laboratory tests are not required for most patients with acute exacerbations. The history of asthma and the patient symptoms can help in making the diagnosis of acute exacerbation of asthma. Some useful tests include complete blood count, and basic chemistries. Chest radiography is not routinely recommended because it does not alter the treatment of patients with an uncomplicated asthma exacerbation. Measurement of arterial blood gases is indicated if hypoventilation is suspected. Electrocardiography is indicated in patients with a history or suspicion of cardiac disease

Approach to management

It would be prudent to adopt an approach of early recognition and intervention, before attacks become severe and potentially life-threatening.

- Assess the severity of the attack and risk for asthma-related death
- Assess potential triggers
- Use an inhaled short-acting beta agonist (SABA) early and frequently
- Start systemic glucocorticoids if there is not an immediate and marked response to the inhaled SABA
- Use of high dose of inhaled corticosteroids in the emergency department after presentation within the first hour reduces the need of hospitalization in patients who are not receiving systemic corticosteroids.
- Make frequent objective assessments of the response to therapy until definite, sustained improvement is documented
- Advise patients who are not responding to initial home or office management to go to an acute care facility or see their asthma provider immediately, especially if they have a history of near-fatal asthmatic attacks
- Educate patients about the principles of self management for early recognition and treatment of a future attack and develop an "asthma action plan" for recurrent symptoms
- **For patients with one or more risk factors for exacerbations**
  - Prescribe daily ICS containing medication, provide a written asthma action plan, review more frequently than for low risk patients
  - Identify and address modifiable risk factors (smoking)
  - Consider non pharmacological methods such as smoking cessation, breathing exercises, avoidance of allergens

Table 2 : Investigating a patient with poor symptom control and exacerbation despite treatment (GINA 2019)[10]

Adherence	Observe inhaler technique Discuss adherence issues
Confirm diagnosis	Spirometry Consider challenge test
Comorbidities ; risk factors	Check for risk factors Assess/ manage comorbidities
Consider treatment step up	Consider step up to the next treatment level

Home treatment

Early treatment is critical for managing asthma exacerbations. It is important to teach patients how to monitor signs and symptoms, and take appropriate action. Physicians can give patients a written asthma action plan and if the patient complies and takes the appropriate medication early, mild exacerbations may be managed at home, but for most patients in our setup it is difficult to execute because of many factors e.g. illiteracy, ignorance, patients' priority, poor accessibility of expert consultation, financial constrai & many more.

Key components of an asthma action plan include standard written instructions; criteria based on symptoms or PEF (compared with personal best) to trigger action; two to three action points; and individualized, written instructions on the use of inhaled or oral corticosteroids.[11] Patients at risk of asthma-related death may need more intensive treatment in the hospital and must approach a hospital at the earliest

The patient can be trained to use the peak expiratroy flow (PEF) meter as a guide for treatment action. Inhaled short-acting $beta_2$ agonists are the cornerstones of treatment for patients with acute asthma

Table 3: Peak Expiratory Flow (PEF) reading based treatment approach

PEF reading	Action
PEF of 50 to 79 *% of their personal best*	Up to two treatments of two to six inhalations of a short-acting $beta_2$ agonist may be safely employed at home. Treatments should be 20 minutes apart followed by a reassessment of PEF and symptoms.[3]
Patients who do not achieve a PEF of at least 80 % of their personal best after two treatments	Should contact their physician for further instructions
Patients whose **PEF declines after treatment**	Should contact their physician and seek emergent care.[3]

Table 4 : Management of Asthma Exacerbations: Home Treatment Algorithm

Assessment of severity

- Patients at high risk of a fatal asthma attack require immediate medical attention after initial treatment.
- Symptoms and signs suggestive of a more serious exacerbation require initial treatment and immediate consultation with a physician:
  - Marked breathlessness,
  - Inability to speak more than short phrases,
  - Use of accessory muscles,
  - Drowsiness,
- Less severe signs and symptoms can be treated initially with assessment of response to therapy.
- If available, measure PEF; persons at 50 to 79 percent of predicted or personal best need quick-relief medication.
- Depending on the response to treatment, consultation with a physician also may be needed.
- Persons with PEF below 50 percent need immediate medical care.

↓

Initial treatment

Inhaled short-acting beta2 agonist: up to two treatments, 20 minutes apart, of two to six puffs by metered-dose inhaler with spacer or nebulizer treatments.

NOTE: Medication delivery is highly variable; children and persons who have exacerbations of lesser severity may need fewer puffs.

↓

Good response

No wheezing or dyspnea (assess tachypnea in young children) PEF ≥ 80 % of predicted or personal best

- Contact physician for follow-up instructions and further management
- May continue inhaled short-acting beta2 agonist every three to four hours for 24 to 48 hours.
- Consider short course of oral systemic corticosteroid

Incomplete response

Persistent wheezing and dyspnea (tachypnea) PEF of 50 to 79 % of predicted or personal best

- Add oral systemic corticosteroid
- Continue inhaled short-acting beta2 agonist
- Contact physician immediately for further instructions

Poor response

Marked wheezing and dyspnea PEF < 50 % of predicted or personal best

- Add oral systemic corticosteroid
- Repeat inhaled short-acting beta2 agonist immediately
- If distress is severe and nonresponsive to initial treatment: call physician and proceed to the emergency department.

Adapted from the National Heart Lung and Blood Institute. National Asthma Education and Prevention Program. 12

Figure 1. - Algorithm for management of asthma exacerbations in primary care.

Management of asthma exacerbations: Emergency department / hospital based treatment

In the ambulatory and emergency department settings, the goals of treatment are correction of severe hypoxemia, rapid reversal of airflow obstruction and reduction of the risk of relapse by intensifying therapy and carefully monitoring response. If the patient can tolerate a measurement of PEF or forced expiratory volume in one second (FEV_1), an initial value should be obtained and repeated to monitor treatment response.

Table 5 : Treatment options for Management of Asthma Exacerbations

Treatment options	Mechanism of action	Comments
Oxygen	Correction of severe hypoxemia[4]	• A saturation of at least 94 percent is recommended in patients presenting with a moderate to severe asthma exacerbation. • Oxygen should be administered as soon as possible[4]
Inhaled corticosteroids (ICS)	ICS can reduce the number of airway eosinophils[4]	• ICS improve disease control and reduce asthma exacerbations. • In new onset, untreated persistent asthma, low-dose ICS decreases asthma exacerbations by about 50%. • If asthmatic patients are already taking moderate doses of ICS, but are poorly controlled, high-dose of ICS further reduced severe asthma exacerbations & reduced the need for systemic corticosteroids, by 50% • Pre emptive use of higher doses of ICS at the onset of a respiratory tract infection and continued for 10 days, reduced the need for oral corticosteroids
Inhaled short-acting beta2 agonist (SABA) treatment for rapid reversal of airflow obstruction (albuterol or levalbuterol,)	SABA use leads to rapid reversal of airflow obstruction (bronchodilatation) and resolves acute symptoms of asthma	• Mainstay of office or emergency department treatment of moderate to severe asthma exacerbations. • SABA can initially be used every 15–20 minutes for the first hour during acute asthma. • Levalbuterol, the R-enantiomer of albuterol, and albuterol are equivalent

Treatment options	Mechanism of action	Comments
		• In very severe asthma exacerbations, continuous nebulization should be considered. It is based on evidence of reduced admissions & improved pulmonary function • SABAs provide symptomatic relief but have no effect on airway inflammation or sustained benefit.[4]
ICS+ LABA (Long acting beta-2-agonists) .	• ICS+LABA, attenuate allergen-induced airway eosinophilia and improve lung function better than ICS alone. • The combination treatment has a synergistic effect in suppressing the induction of rhinovirus-generated chemokines in bronchial epithelial cells.	• ICS+LABA have consistently been shown to prevent exacerbations in patients with more severe exacerbations • The benefit of ICS/LABA is seen in patients requiring higher doses of ICS4
Early use of systemic corticosteroids (500 mg hydrocortisone sodium succinate injection or 125 mg Methylprednisolone Sod. Succinate Inj.)	Systemic glucocorticoids accelerate the rate of improvement when persistent airflow obstruction exists despite bronchodilator treatment.	• Early use of systemic corticosteroids can reduce the risk of relapse4. • A short course of oral corticosteroids following ED treatment of acute asthma exacerbations reduces the rate of relapse. • Although the duration of therapy is not fully established, courses longer than 5 days did not provide additional benefit4
Anti-leukotrienes or Leukotriene receptor antagonists (Montelukast, zafirlukast)	Leukotriene receptor antagonists reduce airway inflammation	• Reduce asthma exacerbations • Montelukast reduces asthma exacerbations secondary to viral Infections • Adding montelukast to ICS is as effective as doubling the dose ofICS with no difference in exacerbation rates and asthma free day

Treatment options	Mechanism of action	Comments
The anticholinergic drugs (Ipratropium bromide, tiotropium bromide)		• Reduces the frequency of asthma exacerbations • Tiotropium decreases rates of exacerbations and improved asthma control in patients with moderate symptomatic asthma already receiving medium-to-high doses ICS or ICS/LABA • Adding ipratropium bromide to an inhaled SABA in severe exacerbations, decreases rates of hospitalizations and shortens ED stays in patients with severe or moderate to severe asthma exacerbations.
Targeted biologic therapy (Omalizumab)	• Omalizumab is a humanized monoclonal antibody directed against IgE and reduces the risk for asthma exacerbations in allergic asthmatic patients. • Omalizumab improved antiviral defenses by increasing release of IFN-α from peripheral blood mononuclear cells to RV stimulation • In addition to anti-inflammatory effects of omalizumab, a restoration of anti-viral activity may prevent exacerbations.	• Omalizumab is indicated for use in patients six years of age and older with allergies and uncontrolled, persistent asthma despite moderate-to-high dose ICS. • Omalizumab reduces asthma exacerbations when given with ICS and shortens the duration of exacerbations

Treatment options	Mechanism of action	Comments
Anti-Interleukin (IL)-5 monoclonal antibodies (mepolizumab & reslizumab)	• IL-5 contributes to airway eosinophilic inflammation. • Approximately 40–50% of difficult-to-control asthma patients have persistent airway eosinophilia despite treatment with high dose ICS • Asthma patients with blood eosinophil counts greater than 400 cells/μL experience more frequent severe exacerbations, and serves as a convenient biomarker for anti-IL-5 therapy.	• Approved as maintenance therapy for patients with uncontrolled, persistent eosinophilic asthma with an exacerbation phenotype despite high dose ICS. • Mepolizumab, given subcutaneously, reduces exacerbations by approximately 50% in patients with severe asthma who have blood eosinophil counts 150 cells/μL or greater • Reslizumab is indicated as - add on, maintenance therapy of severe asthma in patients 18 years or older with an eosinophil count of 400 cells/μL or higher. • In clinical trials, intravenous reslizumab reduced asthma exacerbations by approximately 50 percent. • Biologic therapy may also be beneficial in the acute treatment of asthma exacerbations to prevent subsequent events.

Points to note

1. Nebulized magnesium sulfate does not have a significant effect on respiratory function and hospital admission rates in adults
2. The addition of intravenous aminophylline to conventional therapy has no additional benefit in reducing hospital admissions. However, it significantly increases the risk of adverse effects such as vomiting, palpitations, and arrhythmias.
3. There is inadequate data to recommend for or against the use of antibiotics in the treatment of acute exacerbations
4. Drinking large amounts of water, high-dose mucolytics, antihistamines, chest physiotherapy, and sedation are all unproven treatments.[4]

Post discharge care

Patients discharged from the emergency department with systemic corticosteroids (a five- to 10-day nontapering course of 50- to 100-mg prednisone per day in adults) have decreased relapse of asthma symptoms, future hospitalizations, and use of short-

acting beta$_2$ agonists.[4] Allergen avoidance is routinely recommended .Regardless of the therapy chosen in the acute care setting, step-up therapy should be continued for several days to weeks after discharge.[4] Symptoms may be controlled quickly, but airway inflammation has been observed to be persist for two to three weeks. Scheduled dosing with inhaled beta$_2$ agonists should be continued until symptoms and PEF returns to baseline.[4] *(Castillo JR,et al)*

Prevention of exacerbations

Patient education, monitoring of symptoms and lung function, control of triggering factors and co-morbid conditions, and pharmacologic therapy are the cornerstones of prevention of exacerbations of asthma.The Expert Panel Report 3 (EPR-3) and Global Initiative for Asthma (GINA) describe a stepwise treatment approach and strategy to reduce impairments and prevent future risks like asthma exacerbations.[13,14]

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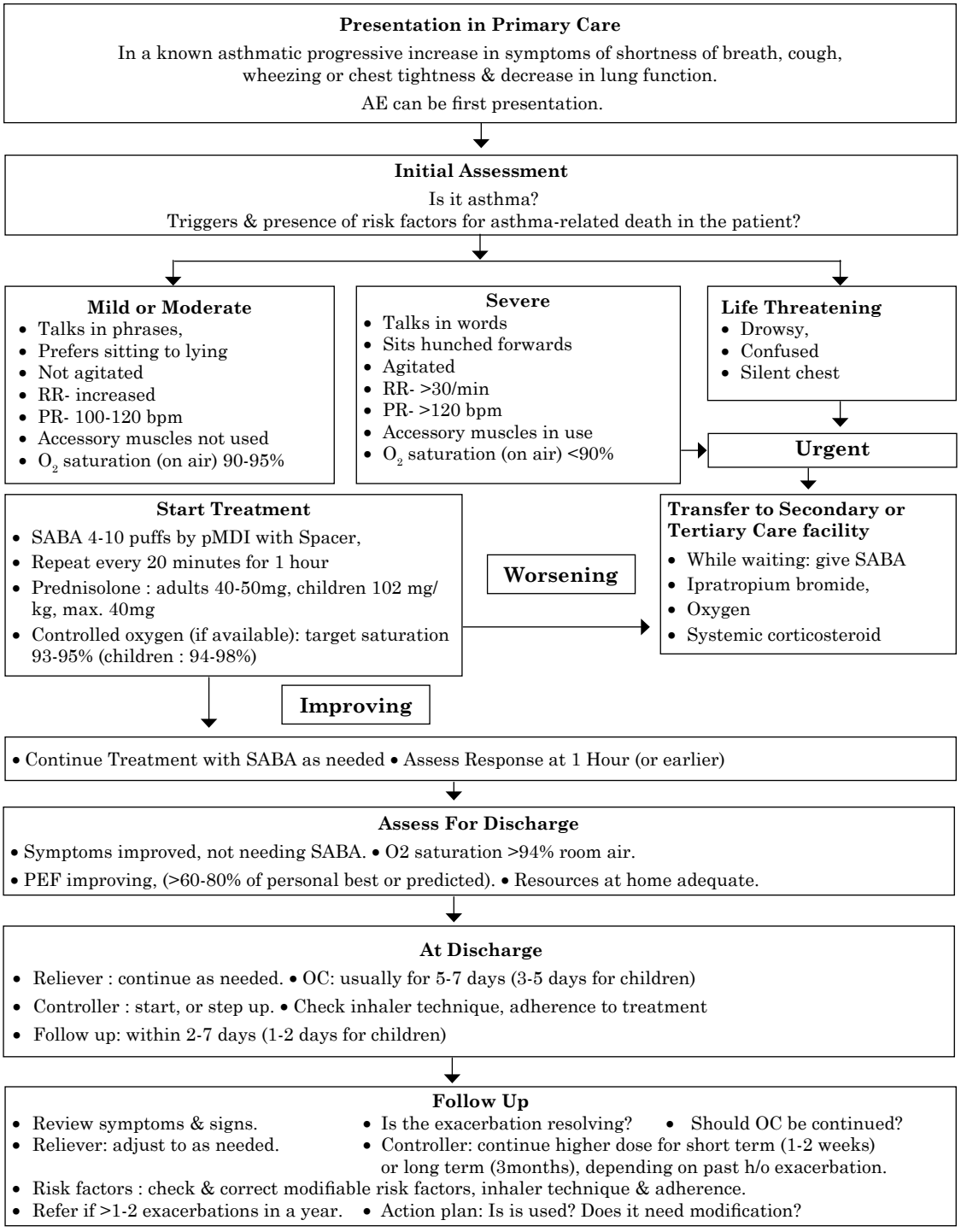

Abbreviation: AE - asthma exeserbation;RR-resp. rate;PR- pulse rate; O2 -Oxygen;PEF-Peak Expiratory Flow Rate; SABA Short Acting Beta 2 Agonist; pMDI-metered dose inhaler; OC-Oral Corticosteroids (modified GINA 2019).

Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Angira Dasgupta, Bodhisattwa Saha

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading contributors to global health expenditures with an estimated 3.2 million deaths per year and 2.6% of global disability-adjusted life years (DALYs) in a global disease burden survey.[1] Acute worsening or acute exacerbations of COPD (AECOPD) has long since been recognized as one of the main causes of COPD progression, poorer health-related quality of life and disease-associated mortality. Despite this, there are still areas of insufficient clarity so far as early identification, essential diagnostic procedures including biomarkers and disease-modifying treatments of AECOPD are concerned.[2]

The definitions of acute exacerbations of COPD remain somewhat arbitrary and qualitative. The current version of the Global Strategy for COPD (2) defines an exacerbation of COPD as an acute worsening of respiratory symptoms that result in additional therapy. This definition is based on the 2000 Aspen Lung Conference Consensus definition of respiratory exacerbations, as "a sustained worsening of the patient's respiratory condition, from the stable state and beyond normal day-to- day variations, that is acute in onset and may warrant a change in regular medication in a patient with underlying COPD"[3] and is by far the most used in clinical decision making or as an end-point in trials.

Acute exacerbations of COPD have been classified by Global Initiative for Chronic Obstructive Lung Disease (GOLD) according to the type of treatment it responds to: i) mild (treated with short acting bronchodilators only) ii) moderate (treated with short acting bronchodilators, antibiotics with or without oral corticosteroids) and iii) severe (patients need hospitalization or visit to emergency care) may be associated with respiratory failure.[2] Although, this might seem not to be very useful in clinical practice, it is important for COPD outcome studies.

This chapter will discuss briefly in four separate sections the etiologies, management, discharge and follow-up advice and prevention of acute exacerbations of COPD.

Section - A: Etiologies of acute exacerbation of COPD

The most common cause of an acute exacerbation of COPD across nations is due to infection by viruses or bacteria. Non-infectious agents may also trigger an acute exacerbation. However, in 30% individuals no specific cause can be ascertained.[4]

Infectious causes of AECOPD

The exact prevalence of infections as a cause for AECOPD is difficult to estimate as it depends on the definition of exacerbation used in a particular study.[5,6] In a systematic review involving the Asia-Pacific countries, the weighted mean prevalence of respiratory viral infections in AECOPD was 34%.[7]

Influenza virus was the most common virus in Asia, while ***picorna virus*** was more common in America, Australia and Europe.[7]

The prevalence of ***bacterial infection*** in acute exacerbation of COPD ranges from 26% to 81%.[4, 8-9] Surprisingly, similar bacteria are identified in various studies from most countries. These are *Pseudomonas aeruginosa, Klebsiella pneumonia, Haemophilus influenzae and Moraxella catarrhalis.*[10,11]

Frequently, co-infection by virus and bacteria at the time of AECOPD is seen, which ranges from 9% to 19%.[6]

Noninfectious causes of AECOPD

Amongst many, important noninfectious causes of AECOPD include ***air pollution*** (outdoors and indoors), meteorological effect and comorbidities of the patients such as pulmonary embolism, pulmonary edema and associated pleural diseases (pleural effusion and pneumothorax). Although well accepted, a causal relationship between air pollution and AECOPD is difficult to establish. An increase in air pollutants such as sulphur dioxide (SO_2),[12,13] nitrogen dioxide (NO_2),[12-15] ozone (O_3) [12,13] small-diameter particulate matter PM 2.5,[13-15] PM10[13] and coarse PM (2.5–10-µm aerodynamic diameter)[16] increases the risk of AECOPD and/or hospitalizations and even death. The harmful effects may occur immediately or after a time lag.

Second-hand smoking **and** ***exposure to biomass fuel combustion*** are of importance in indoor air pollution and exposure to second-hand smoke has been associated with increased risk of visits to emergency department and hospitalizations.[17,18]

A **lower ambient temperature**, as in winters, **low humidity** can lead to AECOPD and **hospital admissions.**[19,20] In fact, it has been shown that long-term humidification therapy (humidified, fully saturated air at 37 °C and flow rate of 20–25 L/min) can lead

to significant increase in exacerbation free days, increased time to first exacerbation and reduced exacerbation frequency for chronic airway diseases, including COPD.[21]

Recently, a lot of interest has been generated around lung **microbiome** and its role in COPD exacerbations.[22] Longitudinal studies which examined sputum in the pre exacerbation period, during exacerbations and also in the post exacerbation period seem to suggest that there is a shift in the microbiome taxonomic composition during exacerbations. It was observed that an increase in known pathogens such as *Haemophilus influenzae* during an exacerbation was accompanied by enrichment in the bacterial taxa closely related to it in the phylogenetic tree. On the other hand, the phylogenetically distant taxa declined. These raise the possibility of exacerbations being polymicrobial in nature. Further, the phylogenetic diversity following an exacerbation is influenced by the treatment received such as antibiotics and/or steroids.[23,24] The field of airway microbiome research is still in its infancy. The goal is to be able to identify potential therapeutic targets for preventing acute exacerbations and slowing down the disease progression.

Section - B : Management of acute exacerbations of COPD

A patient with acute exacerbations of COPD usually presents with acute onset worsening of respiratory **symptoms**, *dyspnoea, cough and/or sputum*, which is more than the usual day-to-day variations and requiring changes to their medication (2).

Diagnostic tests are directed at detecting:

- ***Inflammation-*** blood counts, sputum quantitative assay, CRP.
- ***Infection -*** sputum microscopy and culture, nasal swab for viral PCR, chest X-ray.
- ***Impaired gas exchange*** - pulse oximetry and arterial blood gas.
- ***Severity of airflow obstruction*** - spirometry, only if the patient is capable of performing a forced expiratory maneuver and
- ***Co-morbidities*** (ECG, Echocardiography).

The use of procalcitonin to identify bacterial infection has been a topic of much debate. A single RCT has demonstrated non-inferiority of the procalcitonin-guided strategy to the standard guideline-based approach, warranting further evidence (25). The choice of investigations depends on the availability and setting of treatment.

Depending on its severity, management of AECOPD may be possible in a primary care or an outpatient set up or, when severe, may require hospitalization and/or intensive care attention. About 80% exacerbations can be effectively managed as outpatients with bronchodilators, antibiotics and corticosteroids.

Indications for hospitalization includes:

- Severe symptoms (such as sudden worsening of resting dyspnea, increased respiratory rate, decreased oxygen saturation, confusion, drowsiness),
- Onset of new symptoms (peripheral edema, cyanosis),
- Failure to respond to initial treatment,
- Aacute respiratory failure,
- Serious comorbidities and
- Insufficient home support.[2]

According to the GOLD guidelines the need for ***intensive care or ICU care*** are indicated by:

- Failure to respond to initial treatment,
- Worsening hypoxia (arterial pH≤ 7.25 and/or partial arterial carbon dioxide concentration (PaCO2) ≥ 5.3 kPa or 40mmHg) despite oxygenation and non invasive ventilation
- Altered mental status (confusion, drowsiness or coma),
- Haemodynamic instability, such as need for inotropes and
- Need for invasive ventilation.

Pharmacologic management

Pharmacologic management of AECOPD mainly includes bronchodilators, corticosteroids, antibiotics and oxygen. Methylxanthenes are not recommended due to increase in their side-effect profiles.

Inhaled bronchodilators

Irrespective of the place of management, inhaled bronchodilator (short-acting ß2 agonists and short-acting muscarinic antagonists) is the immediate medication that is to be administered. Several methods of administration are available in the acute setting, including nebulizers and metered dose inhalers (MDI) with spacer device. Nebulizers and MDI with spacers have been demonstrated to have equal efficacy in relieving acute airflow obstruction[26] with no significant difference in length of hospital stay.[27] There are benefits and drawbacks of both methods. But overall, the familiarity of staff and patients and patient factors such as level of consciousness or severe dyspnoea are the determining factors for the method necessary in a particular clinical situation.

Corticosteroids

Systemic corticosteroid is used in the treatment of AECOPD as an anti-inflammatory agent.[28] Previously, it was thought that a prolonged course and high-dose systemic corticosteroids can give a longer and better anti-inflammatory effect. But, steroid use is associated with many adverse events, such as hyperglycemia, hypertension etc. There is currently no consensus on the standard regimen of systemic corticosteroids, in regard to dose, route and duration for AECOPD.

The GOLD guidelines recommend giving oral prednisolone 40mg/day for 5 days. The recent reduction in the Use of Corticosteroids in Exacerbated COPD (REDUCE) trial showed that a 5-day course of oral corticosteroids was not inferior to a 14-day course in terms of exacerbation recurrence but with a shorter length of hospital stay.[29] A Cochrane review suggested that a short course, 3 to 7 days, of systemic corticosteroids does not lead to increase in treatment failure or risk of relapse of AECOPD.[30] Further, the route of administration (intravenous vs oral) did not make any significant difference in outcomes.[28]

Antibiotics

Antibiotics are frequently used in the acute management of most patients (inpatients or outpatients). The choice of antibiotics to be used depends on local guidelines and microbial patterns. It is recommended for patients who experience at least two symptoms that are consistent with a greater likelihood of bacterial infection such as an increase in sputum purulence or volume and dyspnoea.[2]

Examples of commonly prescribed antibiotics include amoxycillin (with or without clavulanic acid), a macrolide or tetracycline, or a respiratory quinolone. The use of respiratory quinolones in tuberculosis endemic regions should be carefully decided. Oral antibiotics are preferred, although intravenous antibiotics can be used if the consciousness of the patient is impaired and there are chances of poor swallowing reflex or poor gastrointestinal absorption.

Oxygen

Supplementary oxygen is required in many patients of AECOPD. Oxygen should be titrated to target oxygen saturations of 88–92%.[31] The goal is to avoid both hypoxia and hyperoxia without causing carbon dioxide retention or worsened acidosis. Over-oxygenation can cause apnea in hypoxic COPD patients since hypoxia is the only drive for respiration in these patients. Hence, monitoring levels of oxygenation should be employed routinely either by arterial blood gas measurements or pulse oximetry, depending on availability. Importantly, patients with AECOPD should not be nebulised with oxygen. Air driven nebulisers should be used instead.

Non-Invasive Ventilation (NIV)

NIV or BiPAP is currently recommended by clinical guidelines as first-line treatment for acute hypercarbic respiratory failure.[2] The indications for initiation of NIV include i) respiratory acidosis (arterial pH≤ 7.35 and/or partial arterial carbon dioxide concentration ($PaCO_2$)≥ 6.0 kPa or 45mmHg), ii) persistent hypoxia despite supplemental oxygen, iii) severe dyspnoea with clinical signs of ensuing respiratory failure such as retraction of the intercostal spaces, high respiratory rate with use of respiratory accessory muscles and paradoxical respiration.[2] However, NIV is not indicated in patients who are drowsy, have confusion, have facial dysmorphisms, have excessive secretions and are haemodynamically unstable.

The mechanism by which NIV works in respiratory failure is by unloading the respiratory muscles, reducing the work of breathing and improves gas exchange. NIV also reduces intubation rate and related complications, duration of hospitalization and thereby reduces overall mortality. The inspiratory pressures used should ensure a volume of about 7 mL/kg by theoretical weight, and the expiratory pressures should be sufficient to reduce dynamic hyperinflation which is usually between 5 and 8 cm of H_2O.[32] Attempts with NIV should be abandoned if patient does not show signs of improvement by 1 hour of starting NIV.

Invasive Ventilation

Invasive ventilation is indicated in patients who do not respond to NIV and optimal pharmacotherapy.[2] Such situations include i) NIV failure ii) Post-respiratory or cardiac arrest iii) Diminished consciousness or psychomotor agitation despite sedation iv) Massive aspiration or Persistent vomiting v) Inability to remove respiratory secretions vi) Haemodynamic instability without response to fluids or vasoactive drugs vii) Severe cardiac arrhythmias and viii) Life threatening hypoxia on NIV.[33]

The choice of method and ventilatory parameters to be used must be specific for each patient's disease severity. Regarding the mode of ventilation, any of Volume-cycled ventilation (volume-controlled ventilation, VCV) or pressure-cycled ventilation (pressure-controlled ventilation, PCV) can be used in the initial phase. Two large controlled studies failed to demonstrate superiority of one of these methods over the other in COPD.[34,35] The only precaution is to avoid dynamic over inflation and consequent auto-PEEP generation. Other complications that require vigilance is volumetric trauma, barotrauma, atelectasis, and oxygen toxicity (with a fraction of inspired oxygen [FiO_2] >0.5).[32]

Co-morbidity management

Cardiovascular co-morbidity is common among COPD patients and includes arterial hypertension, chronic heart failure and ischaemic heart disease.[36] Other co morbidities are osteoporosis, depression/anxiety, obstructive sleep apnea and gastro esophageal reflux disease (GERD). Although, these do not directly contribute to an exacerbation, optimising their treatment is of paramount importance for holistic management of AECOPD.[2]

Section - C : Discharge from hospital and follow up

Adhering to a strict discharge and follow up plan is essential to avoid readmissions or emergency visits. A complete assessment of not only COPD but also the comorbidities is extremely important. At discharge, the patient should understand the medications (both maintenance and acute) and the inhaler technique should be re-explained. The need for home oxygen or home NIV should also be assessed and advised accordingly.[2] Early follow up (within one month of discharge) is recommended as this has lesser chances of exacerbation related readmissions.[37,38]

Importantly, non pharmacologic interventions such as pulmonary rehabilitation should be advised at discharge and follow up. A Cochrane review on peri-hospitalization and early post-hospitalization pulmonary rehabilitation showed wide-ranging benefits including a significantly reduced risk of readmission.[39] However, ensuring adherence to pulmonary rehabilitation schedule is a challenge, especially in the post discharge period. A common reason for nonparticipation in pulmonary rehabilitation is transport difficulties and ongoing breathlessness or weakness.[40]

Section - D : Prevention of acute exacerbation of COPD

Patients themselves and their care givers have an important role to play in preventing acute exacerbations of COPD especially post-hospital discharge. ***Inhaled long-acting β2 agonists***, alone or in combination with ***inhaled corticosteroids***, and ***inhaled long-acting muscarinic antagonists*** all reduce exacerbation rates.[41] The ***oral phosphodiesterase-4 inhibitor***, roflumilast, is associated with fewer exacerbations in COPD patients who are chronic phlegm producers and exacerbates frequently.[42] ***Oral mucolytic agents*** such as N-acetylcysteine also reduces acute exacerbations,[43] but is yet to find its place in the COPD guidelines. Apart from pharmacologic agents, pulmonary rehabilitation, smoking cessation and influenza and pneumococcal vaccination are important remedial factors that if adhered to reduce exacerbation rates.[44]

Recently, the role of **antibiotics** in AECOPD prevention has been demonstrated in clinical trials. With antibiotics in exacerbations of COPD, a prolonged time to the next exacerbation has been observed in patients who eradicate the bronchial pathogen after an exacerbation.[45] This suggests that in patients who effectively eradicate bacteria more time is needed to achieve the threshold of bacterial counts required for an exacerbation to occur, compared with patients who cure the exacerbation but in whom bacteria still persist after antibiotic treatment. The chronic use of *macrolides* in COPD has received attention in recent years where mechanisms other than antibacterial activity were explored. The main objective to the existing studies was to prevent exacerbations, either bacterial or viral, via mechanisms other than antibacterial activity.[46] In fact, two of these studies, of 3 months[47] and 1 year duration,[48] respectively, did not observe any changes in bronchial bacterial flora. However, the latter study using erythromycin 250 mg twice daily for 1 yr observed a significant reduction of 35% in the frequency of exacerbations compared with placebo.[49] Thus more robust evidence on long term antibiotics in AECOPD prevention is required before recommendations can be made.

Conclusion

Acute Exacerbation of COPD constitutes a major health and economic burden to any nation and to society at large. Infectious etiologies like bacteria and viruses, are the common causes of an acute exacerbation. Environmental factors including outdoor and indoor air pollution and meteorological effects also influence the rate of AECOPD. Diagnostic tests for AECOPD are directed usually at characterizing gas exchange, infection, inflammation and comorbidities. Management involves use of bronchodilators, antibiotics and systemic corticosteroids and, when severe, oxygen and mechanical ventilation (NIV or invasive mechanical ventilation). Comorbidities need to be addressed with care. Further studies are needed to assess the various pharmacologic and non pharmacologic strategies for preventing acute exacerbations of COPD.

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Acute Inhalation Lung Injuries

(Including tracheobronchial aspiration& drowning)

Govinda Narke, Sundeep Salvi

Abstract-Acute inhalation lung injuries are the injury to respiratory tract due to inhalation of toxic chemicals or gases. Type I gases are highly soluble and causes irritation and Type II gases are having low solubility and does not give warning sign of inhalation, reaches deeper into the respiratory tract and causes severe respiratory damage. Inhaled gases or chemicals may be absorbed systematically and causes inhalation injury and systemic toxicity. This is found commonly in carbon monoxide poisoning and in inhalation of pesticide fumes. In cases of burns, inhalation injury is the most common cause of death. Tracheobronchial aspiration and drowning also causes respiratory tract injury. Mechanical ventilation is required in most of the severe cases of inhalation injury, aspiration and drowning.

Introduction

Normal adult human inhales around 10000 liters of air every day in the lungs which is spread across a large surface area of 100 m.[2] Ideally pure air contains 78% of nitrogen, 21% of O_2 and remaining 1% is made up of argon, carbon dioxide, neon, methane, helium, krypton, hydrogen, xenon, ozone, nitrogen dioxide, iodine and trace amounts of carbon monoxide and ammonia. Human beings come across lot of toxic gases and chemicals in his day to day life.

Toxic exposures mainly occur via inhalation, direct contact with the skin or eyes and/or ingestion, for which inhalation with associated mortality is the most commonly reported. Gases and vapours are the commonly inhaled substances; liquids and solids can also be inhaled in the form of finely divided mists, aerosols, or dusts.

Inhaled substances may directly injure the pulmonary epithelium at various levels of the respiratory tract, leading to a wide range of disorders from tracheitis and bronchiolitis to pulmonary edema and acute respiratory distress syndrome. (ARDS).

Inhaled toxins or chemicals

Inhaled chemicals or gases may also be absorbed, resulting in systemic toxicity. Inhaled agents are also classified as airway irritants and systemic toxins. Inhalation injury is damage to the respiratory tract or lung tissue from heat, smoke or chemical irritants carried into the airway during inspiration. Among all the known causes of inhalation injury, smoke from fire and burns is the prime cause of death. Acute inhalational lung injury is caused by air pollutants like chemical gases, liquids including water (drowning) and aspiration of gastrointestinal contents.

Inhaled toxins or chemicals causing acute lung injury can be classified into *chemical irritants, asphyxiants* and *smoke inhalation* in burns.

1. Chemical Irritants

Irritant gases when inhaled dissolve in the water of the respiratory tract mucosa, releases acidic/alkaline radicals which causes an inflammatory response. Irritant gas exposures predominantly affect the airways, causing tracheitis, bronchitis, and bronchiolitis. Other inhaled agents may be directly toxic (e.g., cyanide, carbon monoxide) or cause harm by displacing O_2 and causing asphyxia (e.g., methane, carbon dioxide). The effect of inhaling irritant gases depends on the extent and duration of exposure. Chlorine, phosgene, sulphur dioxide, hydrogen chloride or sulphide, nitrogen dioxide, ozone and ammonia are among the most important irritant gases.

Table 1: Some chemical irritants causing acute inhalation injury: their characteristic's and sources of exposure

Agent	Characteristics	Source of Exposure	Toxic inhalational dose LTEL (8hr TWA) PPM / STEL (15 minute TWA) PPM
Ammonia	Highly water soluble;	Agriculture (mostly fertilizers); plastic manufacturing industries,	25/35ppm
Hydrogen chloride	Highly water soluble; colorless	Metal ore refining; meat wrappers	01/05ppm
Hydrogen sulfide	Slightly water soluble; colorless;	Decaying organic matter, in sewer and barns;	05/10ppm

Agent	Characteristics	Source of Exposure	Toxic inhalational dose LTEL (8hr TWA) PPM / STEL (15 minute TWA) PPM
Hydrogen fluoride	Highly water soluble; colorless;	Phosphate fertilizer, metal refining and	1.8/3ppm
Sulfur dioxide	Highly water soluble; colorless;	Airway pollution, burning of oil and coal,	Not known
Chlorine	Intermediate water solubility;	Household cleaners (household accidents	Not known/0.5ppm
Phosgene	Low water solubility; colorless;	Firefighters, welding, paint strippers, chemical	0.02/0.06ppm

(Threshold Limit Values (TLVs) are exposure guidelines developed by the American Conference of Governmental Industrial Hygienists (ACGIH). They are expressed as follows:-
TLV-TWA- Time-Weighted Average: The time-weighted average concentration for a normal 8 hour work day and a 40 hour work week, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.
TLV-STEL - Short Term Exposure Limit: a 15 minute time-weighted average exposure which should not be exceeded at any time during a work day even if the 8 hr TWA is within the TLV)

Acute exposure to high concentrations of toxic gas over a short time is characteristic of industrial accidents or occurring during gas transport. Large number of people are exposed and affected.

Bhopal Gas tragedy

It is the world's worst industrial disaster. It occurred on the night of 2–3 December 1984 at Union Carbide India Limited, pesticide plant in Bhopal, Madhya Pradesh. Over 500,000 people were exposed to methyl isocynate gas and other chemicals. The highly toxic substance spread rapidly around the towns located near the plant. Immediate toll of death was about 5000 and the cause was acute inhalation lung injury (AILI). Government in its official affidavit in 2006 stated that the Bhopal gas leak caused 558,125 injuries, including 38,478 temporary partial injuries and approximately 3,900 severely and permanently disabling injuries.

The initial effects of exposure to gas were coughing, severe eye irritation, feeling of suffocation, burning in the respiratory tract, breathlessness and vomiting. Owing to

their height, children and other people of shorter stature inhaled higher concentrations. Primary causes of deaths were asphyxia, circulatory failure and pulmonary oedema.

Findings during post-mortem revealed changes not only in the lungs but also brain, kidney and liver. The stillbirth rate increased by up to 300% and neonatal mortality rate by around 200% and congenital defects increased by many folds in and around Bhopal.(Bhopal gas disaster girl, the burial of one iconic victim of the gas leak, 4 December 1984)

Pathophysiology of acute inhalation lung injury

Respiratory damage is related to the concentration of the gas and its solubility. More water-soluble gases also classified as Type I (e.g., chlorine, ammonia, sulphur dioxide, hydrogen chloride) dissolve in the upper airway and immediately cause mucous membrane irritation, which may alert people to the need to escape the exposure.

Less soluble gases classified as Type II (e.g., nitrogen dioxide, phosgene and ozone) may not dissolve until they are well into the respiratory tract and reach up to the lower airways. These agents do not give early warning signs and are more likely to cause severe bronchiolitis and often have a delay of ≥ 12 hours before symptoms and complications like of pulmonary edema and ARDS develop.

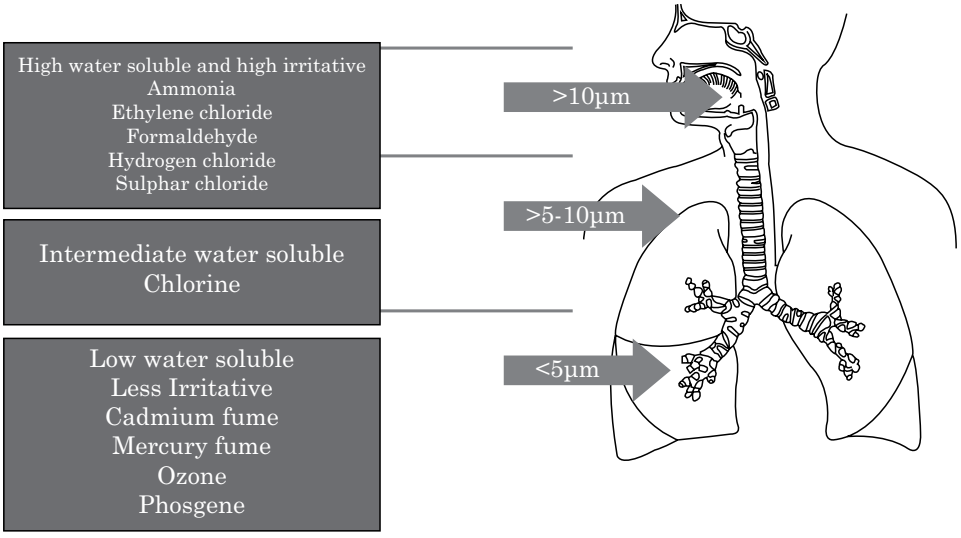


Fig. 1 : Distribution of inhaled gases and the site of injury in the respiratory tract according to particle size and water solubility

2. Asphyxiants

Based on the effects of chemicals, asphyxiants are of two types;

a) **Simple asphyxiants** mainly act by displacing oxygen from inspired air resulting in a reduced amount of inspired oxygen and subsequent hypoxemia.

b) **Chemical asphyxiants**, like carbon monoxide and hydrogen cyanide, which act by interfering with oxygen delivery or utilization. However, any gas in high concentration can act as an asphyxiant.

Carbon monoxide (CO) is a chemical asphyxiant and CO poisoning is very common in domestic setting. Gas geysers in bathrooms and use of fire especially coal in enclosed system in the house to keep the homes warm are the commonest causes CO exposure.

Mechanism of action: Carbon monoxide binds to haemoglobin 240 times more tightly than oxygen, forming a compound called carboxyhaemoglobin. To simplify, if both carbon monoxide and oxygen are inhaled, carbon monoxide will preferentially bind to haemoglobin. This reduces the amount of haemoglobin available to bind to oxygen, so the body and tissues become starved of oxygen. Carboxyhaemoglobin also act on the blood vessels and increases their permeability. This is more common in the brain, causing the brain edema, leading to unconsciousness and neurological damage.

Clinical features: A tension-type headache is the most common symptom of mild carbon monoxide poisoning. Other symptoms are dizziness, nausea, vomiting, tiredness, confusion shortness of breath and difficulty in breathing.

Breathing in high levels of carbon monoxide gas can cause more severe symptoms. These may include:

- *Impaired mental state and personality changes* **(intoxication).**
- *Vertigo* – the feeling that you or the environment around you is spinning.
- *Ataxia* – loss of physical co-ordination caused by underlying damage to the brain and nervous system.
- *Breathlessness and tachycardia* (a heart rate of more than 100 beats per minute).
- **Seizures** – an uncontrollable burst of electrical activity in the brain that causes muscle spasms.

- *Loss of consciousness* – in cases where there are very high levels of carbon monoxide, death may occur within minutes.

Management: High flow oxygen by mask or endotracheal tube is the front-line treatment for all cases of CO poisoning. When hyperbaric oxygen is not available, the administration of 100% normobaric oxygen can be recommended until COHb is normal (≤3%) and the clinical improvement of the patient, usually by 6 hours.

3. Burns and Smoke Inhalation

Exposure to heat, particulate matter and toxic gases during fire and burns are the important causes of acute inhalational lung injury. Closed-space fires are often the reason for inhalation injuries. Due to improvements in the treatment of burn, shock and sepsis, inhalation injury is the main cause of mortality in the burn patients.

Thermal injuries are limited to upper airways and below the vocal cords damage occur only with inhalation. The entire respiratory tract can be affected by smoke inhalation from fires. Smoke contains particulate matter which is formed from incomplete combustion of an organic material, usually less than 0.5 µm in size. Thus, small particles can easily reach the terminal bronchioles and here they can initiate an inflammatory reaction and respiratory damage.

What happens in the lungs due to smoke exposure? Sub mucosal edema and bronchoconstriction occurs as a part of inflammatory response. Pulmonary vascular resistance is significantly raised by 12 hours after smoke inhalation, indicating a circulating mediators' response. The increase in venous resistance increases micro vascular pressure and increases the capillary leakage. There is increase in alveolar fluid and collapse of alveoli as a result of lack of surfactant causing a more rapid alveolar collapse and atelectasis. Atelectasis is a common component of smoke injury.

Clinical features: Dyspnea, tachypnea, diffuse wheezing and rhonchi after the radiographic changes. X ray shows diffuse atelectasis, pulmonary edema or bronchopneumonia. Altered gas exchange is reflected in blood-gas analysis and the assessment of changes in sputum characteristics is a useful parameter to monitor.

4. Chemical warfare and riot control agents

Chemical Warfare and Riot Control Agents of the past were gases such as mustard gas, phosgene. Nowadays, chemical warfare armamentarium includes systemic toxins derived from organophosphate pesticides. Besides being highly lethal neurotoxins, they cause significant lung injury on exposure. Syria is in the news for chemical warfare. The Syrian military dropped chemical weapons (chlorine bombs) on the towns of Talmenes in April 2014 and Sarmin in March 2015. In December 2016, at least 53 people were killed in an apparent nerve gas attack in villages

near Uqairabat, marking the first major nerve gas attack. In April 2017, the Khan Shaykhun chemical attack by using sarinan organophosphrus group of chemical agent and nerve poison killed 75 and injured more than 500 people.

Tear gas used for crowd control aim to incapacitate persons via immediate mucous membrane irritation. Chloroacetophenone and orthochlorobenzamalonitrile are the most common agents worldwide. They have effect on mucus membranes and also cause respiratory tract injury. Zinc chloride, which is the primary component of smoke bombs, is a potent lower respiratory tract irritant and may cause severe pulmonary edema.

Clinical features of tear gas exposure: Irritation of mucous membranes in the eyes, nose, mouth and lungs, and causes crying, sneezing, coughing, difficulty breathing, pain in the eyes, and temporary blindness. With tear gas symptoms of irritation typically appear after 20–60 seconds of exposure and commonly resolve within 30 minutes of leaving.

Treatment: There is no specific antidote to common tear gases. Getting away from the exposure and into fresh air is the first line of action. Removing contaminated clothing, removing shoes, bathing is helpful to remove the particles. Eye wash with water is also helpful.

5. Pesticides & Chemicals Sprays to Kill Cockroaches & Insects:

Use of pesticides has increased rampantly all across the word. Mist formed by spraying of the insecticide spray is inhaled by the person who is spraying the insecticide. It may get absorbed in the blood and also causes acute inhalation injury. In October 2017, 30 farmers from Yavatmal district of Maharshtra died because of inhalation of insecticide *profefenos* used on the cotton. Enclosed homes after pest control causes acute exposure of the pesticides and inhalation injury sometimes found lethal. Chemical sprays used in the houses to kill the mosquitoes and cockroaches also get inhaled while spraying and cause inhalational injury like tracheobronchtis, bronchitis and rarely pneumonitis.

Table 2 : Type of toxicity based on the extent of exposure:

Acute	Sub chronic	Chronic
Occurring from a single incident of exposure (single short-term exposure)	Occurring from repeated incidents of exposure over several weeks or months (intermediate exposure, normally less than the lifetime of the exposed organism)	Occurring from repeated incidents of exposure for many months or years (repeated long-term exposure, sometimes lasting for the entire life of the exposed organism).

Table 3 : Types of acute toxicity measures

Categories	Inhalation mg/L
I—Highly toxic	0 to 0.2
II—Moderately toxic	0 0.2 to 2.0
III—Slightly toxic	0 2.0 to 20
IV—Relatively non-toxic	20+

Clinical features of acute inhalation lung injury

Initial exposure to type 1 agents causes sneezing, coughing, and few patients present with hoarseness, wheezing, and stridor. With a high dose of a type 1 agent, chest tightness or shortness of breath may subsequently develop as a result of pulmonary edema. With type 2 agents, symptoms and signs are usually delayed several hours after exposure. Patients initially complain of chest tightness or shortness of breath. Physical findings may be minimal except for wheeze. Time of onset is shorter with higher doses; development of breathlessness within 4 hours of exposure suggests a potentially lethal dose.

Diagnosis

Diagnosis is usually from the history. Chest x-ray and pulse oximetry is very important. Chest x-ray findings of patchy or confluent alveolar consolidation usually indicate pulmonary edema. Fibre optic bronchoscopy (FOB) is the standard technique used to assess the presence and severity of inhalation injury. FOB also have therapeutic role for removing thick secretions and slough from the dead tissue in the respiratory tract and helps to keep the airway clear.

For severe inhalation exposure or suspected pulmonary aspiration, chest radiography and arterial blood gas analysis are strictly recommended. The presence of hypoxemia despite a normal arterial partial pressure of oxygen suggests carbon monoxide toxicity. Lab investigations include arterial blood gas analysis with carboxyhemoglobin, methemoglobin and lactate levels in suspected CO poisoning; RBC cyanide levels can be done for persistent acidosis. Metabolic acidosis may indicate cyanide or hydrogen sulfide intoxication. Cyanide is released in fires subsequent to the combustion of acrylic, rubber and plastic materials should be at the back of the mind of treating physician.

Serum Carboxyhemoglobin levels should be tested for all fire and explosion victims.

Management

Management does not differ by specific inhaled agent but rather by symptoms. Patients should be moved into fresh air and given supplemental O2. Treatment is directed toward ensuring adequate oxygenation and alveolar ventilation. Bronchodilators and O2 therapy may be sufficient in mild cases. Severe cases may need Endotracheal intubation or tracheostomy and mechanical ventilation. With respect to lung support, the only ventilatory practice proven to be beneficial in a large randomised trial is reduction of tidal volume to 6 mL/kg predicted bodyweight (or lower if needed), to achieve a plateau pressure of less than 30 cm H_2O. This reduced tidal volume is coupled with use of the minimum FIO_2-PEEP combination that is sufficient to achieve a saturation of 88–95% or a corresponding PaO2.

The efficacy of corticosteroid therapy is unproved. Prophylactic antibiotics are not recommended.

Because of the risk of ARDS, any patient with respiratory tract symptoms after toxic inhalation should be observed for 24 hours in the hospital. After the acute phase has been managed, patients may develop reactive airways dysfunction syndrome, bronchiolitis obliterans with or without organized pneumonia, pulmonary fibrosis and delayed-onset ARDS. Prevention of hospital associated infection with good infection control practices is important to achieve the optimal outcome in all acute inhalational lung injuries.

Tracheobronchial aspiration

Aspiration is the inhalation of foreign material into the airways beyond the vocal cords. Aspiration pneumonia is an infection secondary to aspiration of gastric contents colonised with bacteria.

Aspiration of food and liquids is more common in:

- Patients with oropharyngeal dysphagia, especially when it is due to stroke or cervical spine surgery.
- Elderly patients.
- Patients on sedative medications.
- Patients being fed by a gastric tube.
- Critically ill patients.

Among critically ill patients, the major risk factors for aspiration include:

- History previous episode of aspiration.
- Decreased level of consciousness (Glasgow coma scale score <9 or a high level of sedation).
- Neuromuscular disease, or congenital or acquired structural abnormalities of the aero digestive tract.
- Endotracheal intubation.
- Vomiting.

Other risk factors include the presence of a Ryles tube, abdominal/thoracic surgery or trauma, delayed gastric emptying and malpositioning of the feeding tube. Certain drugs reduce the lower oesophageal sphincter pressure and cause gastro-oesophageal reflux in anaesthesia and disease states, and thereby increase the risk for aspiration. These drugs include atropine, glycopyrrolate, dopamine, sodium nitroprusside, tricyclic antidepressants, beta-adrenergic stimulants, halothane, enflurane, opioids and propofol.

Patients that aspirate may have a reduced level of consciousness and require close observation for at least 48 hours. Although some patients have dramatic signs and symptoms, many are asymptomatic. A high index of suspicion and prompt action are required if optimum outcomes are to be obtained. Chest X-ray and arterial blood gas analysis should be done in all cases of aspiration.

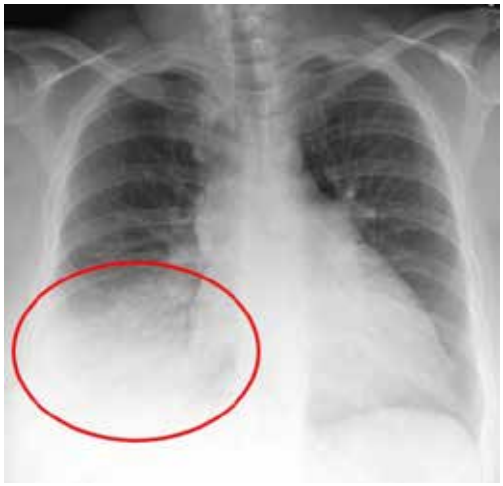
If you suspect aspiration by the patient, he/she should be immediately placed semi-prone position. Gentle oropharynx suction should be done with care to avoid a gag reflex which may worsen aspiration. Secure the airway by endotracheal intubation, if the patient is at risk of further aspiration because patient is unable to protect their own airway (regurgitation, poor cough reflex), or have signs of respiratory failure (tachypnoea, dyspnoea, confusion, cyanosis). Ryle's tube should be inserted to empty the stomach and 45° head-up position to prevent further aspiration.

Positive-pressure ventilation with positive end-expiratory pressure (PEEP) should be used in patients who are intubated for airway protection or respiratory failure. It helps to prevent atelectasis and improve the ventilation-perfusion ratio in patients who have aspirated gastric content. However endotracheal suctioning is performed before positive-pressure ventilation is started, to avoid forcing aspirated material deeper into the lungs. Respiratory secretions for cultures to be sent for all patients put on the ventilator support and antibiotics should be initiated immediately because of a high risk of developing ventilator-associated pneumonia. The antibiotics should be stopped or changed based on the culture results within 72 hours.

Aspiration pneumonia:

Clinical features suggestive of aspiration pneumonia include leukocytosis, fever and infiltrates on chest x-ray generally 48 hours after a confirmed or probable aspiration event. It is to be confirmed by repeat chest x-ray.

X-ray chest imaging can show infiltrates in gravity dependent lobes of the lung (inferior segment of right upper lobe or apical segment of lower lobe). Where the aspirate goes depends on the position of the patient (sitting up or supine)



Sputum and/or bronchoalveolar lavage culture and blood cultures should be obtained to guide antibiotic therapy as per institutional antibiotic policy.

Drowning

According to WHO, drowning is the 3rd leading cause of unintentional injury death worldwide, accounting for 7% of all injury-related deaths. There are an estimated 360 000 annual drowning deaths worldwide. Global estimates may underestimate the actual public health problem related to drowning. Children, males and individuals with increased access to water are most at risk of drowning. Drowning is the process of experiencing respiratory impairment from submersion/immersion in liquid. The drowning process begins with respiratory impairment as the person's airway goes below the surface of the liquid (submersion) or water splashes over the face (immersion). If the person is rescued at any time, the process of drowning is interrupted, which is termed a nonfatal drowning. If the person dies at any time as a result of drowning, this is termed a fatal drowning.

Pathophysiology of drowning: When a drowning individual cannot keep his or her airway clear, water entering the mouth is voluntarily spat out or swallowed. The next response is to hold one's breath, which may last no more than about a minute. When increased inspiratory drive, water is aspirated into the airways and coughing occurs as a reflex response. Laryngospasm may occur, but it is rapidly terminated due to brain hypoxia. If the person is not rescued, aspiration of water continues and hypoxemia leads to loss of consciousness and apnoea. Cardiac-rhythm deterioration occurs in the sequence of tachycardia followed by bradycardia, pulseless electrical activity and, finally, asystole. The whole drowning process, from submersion or immersion to cardiac arrest, usually occurs in seconds to a few minutes, Water in the alveoli causes surfactant dysfunction. Aspiration of salt water and aspiration of fresh water cause similar degrees of injury, even though their osmotic gradient is different. The combined effects of fluids in the lungs, loss of surfactant and increased permeability of the alveolar–capillary membrane causes decrease in lung compliance, increased regions of very low or zero ventilation to perfusion in the lungs, atelectasis and bronchospasm.

Management

Management of drowning starts from the rescue scene. If the victim is breathing, he or she should be placed on their side in the recovery position to prevent further aspiration. If the victim is not breathing and pulseless, begin cardiopulmonary resuscitation (CPR). This is one of the exceptions to the hands-only CPR guidelines. Rescue breathing needs to be initiated in a drowning victim. Hospital Care for the drowning patient depends on the situation surrounding the event and how they have responded to pre-hospital care. The initial approach is to stabilize vital signs by addressing the ABCs (airway, breathing and circulation.) Airway management may require intubation and mechanical ventilation. Injuries mainly cervical injuries, medical illnesses like seizers, MI which may be the cause of drowning needs to be addressed.

Prevention

Prevention of inhalation injury: Care in handling gases and chemicals are the most important preventive measure. Availability of adequate respiratory protection (eg, gas masks with a self-contained air supply) for workers as well for rescuers is very important in industries. Use of personal protective equipment by farmers while spraying pesticides, awareness about carbon monoxide poisoning due to gas geysers and fire in the house and ventilation is required at domestic level.

Prevention of drowning: Drowning can be prevented with few simple measures. Installing barriers (e.g. covering wells, using doorway barriers, fencing swimming pools

etc.) around water bodies to control access to water hazards, or removing water hazards entirely reduces water hazard exposure and risk. Supervised child care is important. Teaching school-age children basic swimming, water safety and safe rescue skills should be done. Setting and enforcing safe boating, shipping and ferry regulations is an important part of improving safety on the water and preventing drowning. Managing flood risks through better disaster preparedness planning and early warning systems can prevent drowning during flood disasters.

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Severe Pneumonia

Lalita Fernandes, Ashwini Pednekar, A.M.Mesquita.

Introduction

Pneumonia is a leading cause of morbidity and mortality worldwide. Pneumonia and influenza ranked as eighth leading cause of death in the United States in the year 2014.[1]With the advent of antibiotics, the number of deaths due to pneumonia has considerably reduced, however it continues to remain a major cause for concern. This is primarily due to improper diagnosis, delay in seeking treatment, improper or inadequate treatment and infections with drug resistant pathogens. There is a need to establish guidelines for the treatment and antibiotic selection in pneumonia in order to reduce pneumonia associated deaths as well as prevent injudicious use of drugs.

Definition

Pneumonia is defined as an inflammation of the lung parenchyma which is caused by an infectious agent. Pneumonitis refers to inflammation of the lung due to both infectious and non-infectious causes.

Types of Pneumonia

- Community Acquired Pneumonia (CAP)
- Nosocomial Pneumonia
  - Hospital Acquired Pneumonia (HAP)
  - Ventilator Associated Pneumonia (VAP)
  - Healthcare Associated Pneumonia (HCAP)

Community acquired pneumonia

CAP can be defined both on clinical and radiographic findings. In the absence of chest radiograph, CAP is defined as:

a) ***Symptoms of an acute lower respiratory tract illness*** (cough with or without expectoration, shortness of breath, pleuritic chest pain) for less than 1 week; and

b) ***At least one systemic feature*** (temperature >37.7°C, chills, and rigors, and/or severe malaise); and

c) ***New focal chest signs on examination*** (bronchial breath sounds and/or crackles); with

d) ***No other explanation for the illness***.[2]

When a *chest radiograph* is available, CAP is defined as: symptoms and signs as above with new radiographic shadowing for which there is no other explanation (not due to pulmonary edema or infarction). Radiographic shadowing may be seen in the form of a lobar or patchy consolidation, loss of a normal diaphragmatic, cardiac or mediastinal silhouette, interstitial infiltrates, or bilateral perihilar opacities, with no other obvious cause.

Nosocomial pneumonia

HAP is defined as pneumonia developing 48 hrs after admission to the hospital. It is caused by organisms which were neither present nor incubating at the time of admission to the hospital. VAP is defined as pneumonia that develops in patients after 48 hrs of endotracheal intubation. HCAP develops in non-hospitalised patients who have high risk of being colonised by nosocomial multidrug resistant pathogens.

It is seen in patients who had previous hospitalisation for 48 hours or more within the preceding 90 days, residence in a nursing home, recent intravenous antibiotic therapy, chemotherapy, home wound care within 30 days of infection, chronic dialysis, and contact with subjects colonised by multidrug resistant pathogens.

US studies suggest that HCAP is caused by MDR pathogens while European studies suggest that the etiology is similar to community acquired pneumonia. The IDSA 2016 guidelines on HAP/VAP have removed the concept of HCAP and consider it as HAP.

Epidemiology

Community acquired pneumonia (CAP) is a common disorder with an incidence of about 20% to 30% in developing countries compared to an incidence of 3% to 4 % in developed countries. The incidence varies markedly with age, being much higher in the very young and the elderly. It is estimated that India together with Bangladesh, Indonesia and Nepal account for 40% of global acute respiratory infection.[3] Pneumonia accounts for 16% of all deaths of children under 5 years old, killing 920 136 children in 2015.[4]

There were 56,832 deaths due to pneumonia and influenza in 2013, which combined were the eighth leading cause of death in the U.S; of which deaths due to pneumonia alone were 53,282.[5]

Microbiology

Table 1 : Common Microorganisms in pneumonia

Most common Causative organism causing Pneumonia (A & B)		
A. Community Acquired Pneumonia		**B. Hospital Acquired Pneumonia**
Bacterial • Streptococcus Pneumoniae • Haemophilus influenza • Staphylococcus aureus • Klebsiella pneumonia • Atypical organisms - • Mycoplasma pneumonia • Legionella pneumophila • Chlamydia pneumonia	**Viral** • Influenza A and B • Rhinovirus • Respiratory syncytial virus • Human metapneumovirus • Adenovirus 4 and 7 • Parainfluenza virus **Fungal** • Histoplasmosis • Blastomycosis • Coccidioidomycosis	• Pseudomonas aeruginosa • Escherichia coli • Klebsiella pneumoniae, • Acinetobacter • Methicillin-resistant Staph aureus

Pathology

Pneumonia has four stages –

Stage of exudation: Occurs in the initial 24 hours.The capillaries around the alveolar walls become inflamed and congested and cellular exudates containing neutrophils, lymphocytes and fibrin cross the capillary walls and fill the alveoli.

Stage of Red Hepatisation: Occurs after 48-72 hours. The affected part of the lung becomes hardened with the consistency of the liver. The capillaries are now engorged with blood and the alveoli are filled with fibrinous exudates containing RBCs, neutrophils, and fibrin.

Stage of Grey Hepatisation: Occurs over the next 2-3 days, lung appears gray brown to yellow because of fibrino-purulent exudate.

Stage of Resolution: Occurs after a week. There is phagocytosis of the organisms, resorption of exudates, re aeration of consolidated lung and return of the architecture to normal.

Clinical presentation

History

- Cough with or without expectoration
- Sputum production – It is important to inquire about the colour,consistency and amount of the sputum as this may give a clue to the causative organism.
  - Greenish in Pseudomonas infection
  - Red currant jelly in Klebsiella pneumonia
  - Rusty sputum in Pneumococcal pneumonia
- Dyspnoea
- Chest pain – Mostly pleuritic in nature, increases on coughing, deep inspiration.
- Haemoptysis
- Fever, chills, rigors
- Malaise

Examination

- Hyperthermia or hypothermia
- Tachypnea
- Reduced respiratory movements
- Impaired to dull note on percussion
- Decreased intensity of breath sounds, Tubular bronchial breath sounds, Whispering pectoriloquy, Egophony
- Adventitious breath sounds, such as crepitations and rhonchi
- Pleural friction rub

Investigations

- ***Blood counts*** –Haemoglobin, total and differential WBC count, platelet count
- ***Renal and liver function tests***
- ***Sputum gram stain and sputum culture and sensitivity tests***
- ***Blood culture***
- ***Arterial blood gases***

Radiology

Consolidation, Infiltrates, loss of diaphragmatic or mediastinal silhouette.

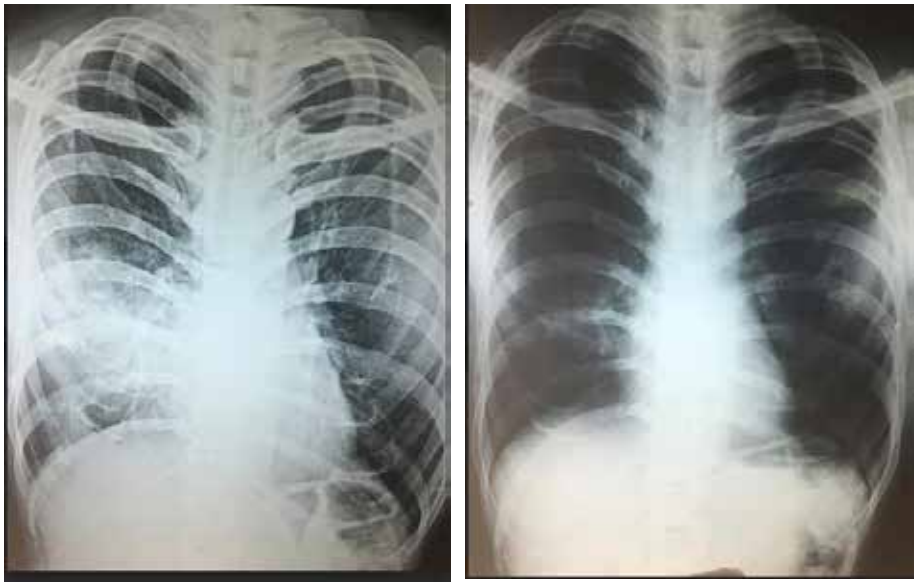

Fig.1 The radiograph to the left shows a right middle lobe pneumonia. The radiograph to the right is taken after antibiotic course and shows near total resolution of the consolidation.

Management

Salient features

- Early diagnosis and prompt treatment is essential in the management of pneumonia.
- Delay in the diagnosis and treatment can have serious consequences with resultant progression of pneumonia, development of sepsis and circulatory failure and respiratory, all of which can result in death.
- The initiation of antibiotic treatment should be as soon as possible. A loading dose may at times be necessary. This helps in limiting the spread of disease and development of complications.
- The clinician must be quick in deciding whether the patient requires inpatient/ intensive care management.

- While antibiotics are essential in the treatment of pneumonia it is also important to prevent antibiotic abuse. Prolonged duration of injectable antibiotics/ use of higher antibiotics when not indicated/use of inappropriate empirical antibiotic should be avoided. Preferably antibiotics should be given as per culture sensitivity reports, in the absence of which appropriate antibiotics may be given (as per recommended guidelines). Early shift to oral therapy in a clinically stable patient is encouraged.
- It is important that antibiotics should be given in the right doses and for the correct duration of time. This helps in reducing incidence of resistance. Also, routine monitoring is required to watch for any drug related toxicity.
- Measures like hand washing, regular disinfection, use of gloves, sterile techniques etc go a long way in preventing hospital acquired infections.

Management of pneumonia involves

- Diagnosis of pneumonia
- Assessment of severity of pneumonia using PORT/PSI or CURB65 score and decision to treat at either at outpatient level, in patient or ICU level.
- Selection of appropriate antibiotics based on the type and severity of pneumonia. Duration of therapy to be guided by response of the patient to antibiotics.
- Assessment to look for improvement or worsening in the form of complications like empyema, pyopneumothorax, meningitis and progression of pneumonic patch/ necrotising pneumonia.
- Suppotive Management

Assessment of Severity

Once the diagnosis of pneumonia has been made, it is important to classify the patients based on risk stratification. A number of scores are available to determine the severity of pneumonia, some of which are described below. The most widely used score is the PSI/PORT score. However it is cumbersome, time consuming and it may not possible to implement this scoring system at the outpatient level as laboratory findings also form part of the score. CRB 65 is a relatively easy scoring system which can be done at all out patient levels and does not require any laboratory investigations and can thus be used as an outpatient tool to determine the severity of disease.

Step 1. Use CURB65/CRB65 to decide about hospital admission. A score of 2 or more requires hospital admission. However, it is advisable to use one's clinical judgement to decide.

Step 2. Once admitted to the hospital, a decision needs to be taken as to whether the patient requires ICU care or not. Infectious Diseases Society of America/American

(Fig.10) Thoracic Society Guidelines for severe community-acquired pneumonia are used to indicate need for intensive care management (any one major criteria or more than three minor criteria positive)

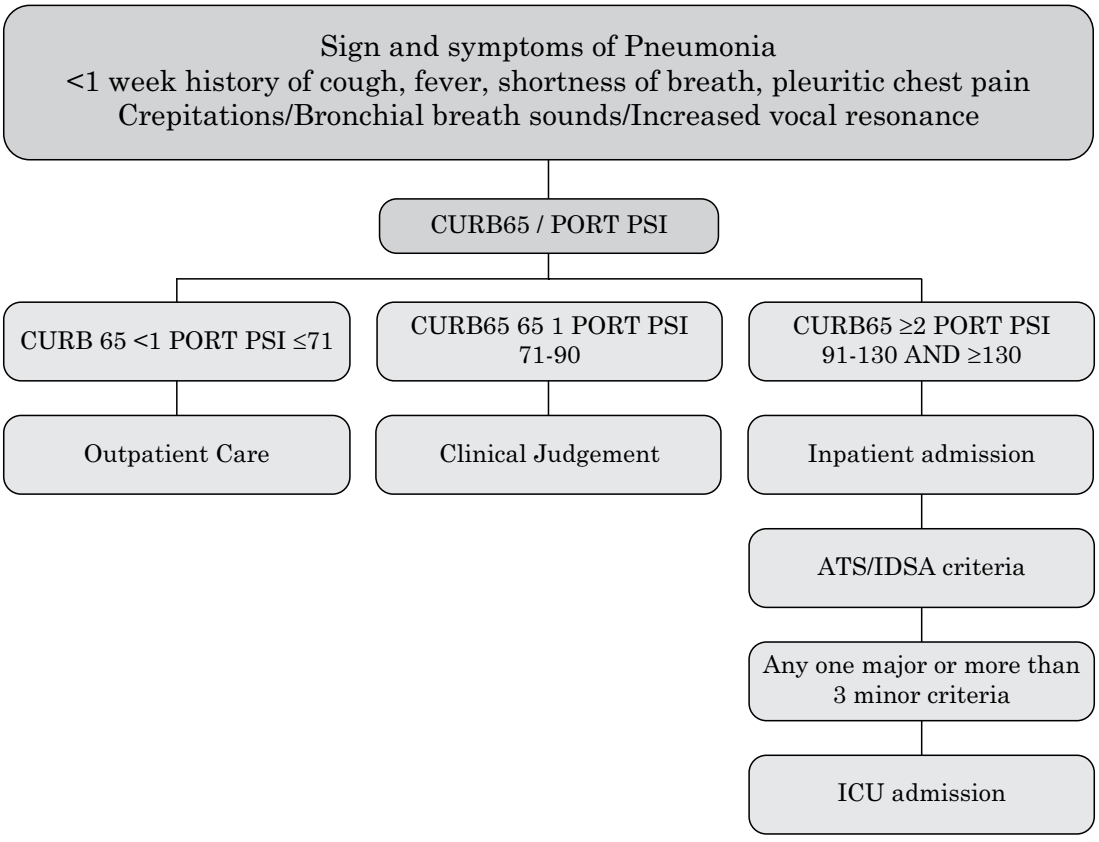

Table 2 : PORT/PSI scoring[6]

Patient Characteristics	Points
Demographics	
Age(years):	
Male: age —	Age(yr)
Female: age —	Age(yr) – 10
Nursing home resident	+10
Co-morbidities	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Examination findings	
Altered mental status	+20
Respiratory rate[3] 30/minute	+20
Systolic blood pressure 10.7 mmol/ L	+20
Temperature<38 deg C or >40 deg C	+15
Pulse rate >125/min	+10
Laboratory findings	
pH <7.35	+30
BUN >10.7 mmol/ L	+20
Sodium < 130 mEq/L	+20
Glucose >250mg/dl	+10
pO2 <60 mmHg	+10
Haematocrit < 30%	+10
Pleural effsuion	+10

Risk Class Score

Risk	Class	Score	Mortality
Low	I	<50	0.5%
Low	II	51-70	0.9%
Low	III	71-90	1.25%
Medium	IV	91-130	9%
High	V	>131	27.1%

- **CURB 65**[7]

  Confusion: new mental confusion

  Urea >7 mmol/L

  Respiratory rate >30 breaths per minute

  Blood pressure: diastolic BP <60 mm Hg or systolic blood pressure <90 mm Hg

  Age ≥65 y of age

  Group 1: 0 or 1 of the above;

  Mortality low – 1.5%.

  Likely suitable for treatment at home

  Group 2: 2 of the above;

  Mortality – 9.2%.

  Hospitalization for treatment

  Group 3: 3 or more of the above;

  Mortality – 22%.

  Likely requires admission to ICU

- **CRB 65** – Same as CURB65 but without Urea levels. Ideal for OPD evaluation.

- **SMART - COP**[8]

Systolic BP < 90mmHg	2 points
Multilobar involvement on CXR	1 point
Albumin < 3.5g/dl	1 point
Respiratory Rate >25 breaths/min	1 point
Tachycardia > 125 beats/min	1 point
Confusion	1 point
Oxygenation If patient is <50 years of age PaO2 less than 70 mm Hg, or O2 saturation 93% or less, or PaO2/FiO2less than 333 If the patient is >50 years of age PaO2 less than 60mm Hg, or O2 saturation 90% or less, or PaO2/FiO2less than 250	2 points
pH < 7.35	2 points

Interpretation of SMART-COP score

0 to 2 points—low risk of needing intensive respiratory or vasopressor support (IRVS)

3 to 4 points—moderate risk (1 in 8) of needing IRVS

5 to 6 points—high risk (1 in 3) of needing IRVS

7 or more points—very high risk (2 in 3) of needing IRVS

Severe CAP = a SMART-COP score of 5 or more points.

- **Infectious Diseases Society of America/American Thoracic Society Guidelines for Severe community-acquired pneumonia**

Antibiotic Selection (Based on ATS/IDSA guidelines)[9],[10]

Outpatient Department	
• Previously healthy and no risk factors for drug-resistant *S. pneumoniae* (DRSP) infection • Presence of comorbidities, such as chronic heart, lung,liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; use of antimicrobials within the previous 3 months (in which case an alternative from a different class should be selected); or other risks for DRSP infection:	• Macrolide (azithromycin, clarithromycin, orerythromycin) OR Doxycycline • A respiratory fluoroquinolone (moxifloxacin, gemifloxacin,or levofloxacin [750 mg]) or A b-lactam **plus** a macrolide (High-dose amoxicillin [e.g., 1 g 3 times daily] or amoxicillin-clavulanate [2 g 2times daily] is preferred; alternatives include cefpodoxime, and cefuroxime [500 mg 2times daily]; doxycycline is an alternative to the macrolide.)
In Patients • Inpatient, non-ICU treatment	• A respiratory fluoroquinolone or • A b-lactam **plus** a macrolide (cefotaxime, ceftriaxone, and ampicillin; ertapenem for selected patients; with doxycycline [level III evidence] as analternative to the macrolide. A respiratory fluoroquinolone should be used for penicillin-allergic patients.)

• Inpatient, ICU treatment	• A ß-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus either azithromycin or a fluoroquinolone • For *Pseudomonas* infection, use an antipseudomonal b-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either fluoroquinolone (ciprofloxacin or levofloxacin) or an aminoglycoside and azithromycin or an aminoglycoside plus fluoroquinolone • For community-acquired methicillin-resistant *Staphylococcus aureus*infection, add vancomycin or linezolid.

Hospital Acquired Pneumonia (Non VAP)

Not at High Risk of Mortality and no Factors Increasing the Likelihood of MRSA (any one)	Piperacillin-Tazobactam/ Cefepime/ Levofloxacin / Imipenem/Meropenem
Not at High Risk of Mortality but With Factors Increasing the Likelihood of MRSA	Piperacillin-Tazobactam/ Cefepime/ Levofloxacin / Ciprofloxacin/ Imipenem/ Meropenem/ Aztreonam Plus Vancomycin/Linezolid
High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d (Two drugs, avoid two ß-lactams)	Piperacillin – Tazobactam or Ceftazidime/ Cefepime or Imipenem/ Meropenem or Aztreonam Plus Ciprofloxacin/ Levofloxacin or Amikacin/ Gentamicin/Tobramycin Plus Vancomycin/Linezolid

Ventilator Associated Pneumonia

Empiric Treatment Options for Clinically Suspected Ventilator-Associated Pneumonia in Units Where Empiric Methicillin-ResistantStaphylococcus aureus Coverage and Double Antipseudomonal/Gram-Negative Coverage Are Appropriate – Choose one antibiotic from each column below :

Gram-Positive Antibiotics With MRSA Activity	Gram-Negative Antibiotics With Antipseudomonal Activity: ß-Lactam–Based Agents	Gram-Negative Antibiotics With Antipseudomonal Activity: Non-ß-Lactam–Based Agents
Vancomycin Or Linezolid	Piperacillin – Tazobbactam Or Ceftazidime/Cefepime Or Imipenem/Meropenem Or Aztreonam	Ciprofloxacin/Levofloxacin Or Amikacin/Gentamicin/ Tobramycin Or Colistin

Assessment

Patients are to be regularly assessed after initiation of antibiotics. In case of clinical deterioration, continuation of fever, new onset of radiological lesions; a change of therapy may be considered keeping in mind the onset of hospital acquired infection. Culture reports may aid in the choice of antibiotics. In case of good response, early shift to oral therapy within 48-72 hours is recommended. Injudicious use of antibiotics should be avoided.

Other Supportive Care

- Oxygen supplementation
- Intravenous fluids
- Analgesia and antipyretics
- Chest Physiotherapy and clearance of secretions
- Bronchodilators and N-acetylcysteine
- Non invasive ventilation/ Invasive ventilation

Differential Diagnosis

- Tuberculosis
- Pulmonary Embolism
- Malignancy and Post obstructive Pneumonia

Specific types of Pneumonia

Staphylococcal Pneumonia

Staphylococcus aureus is an important cause of pneumonia as it might cause rapidly progressing and severe disease. It is also an important cause ofhospital acquired pneumonia and thus it is important to choose antibiotics which cover this organism. With the emergence of drug resistant strains the treatment of Staphyloccal infection has become more difficult.

It is seen more often in diabetic patients, intravenous drug users, hemodialysis patients and surgical patients. Most hospital transmission is probably from the hands of healthcare workers who are transiently colonized by contact with infected patients or from their own reservoirs.

The chest radiograph may show localised infiltrates ormultiple rounded/patchy opacities which may at times be associated with cavitation. Sometimes thinwalled,air-containing cavities known as pneumatoceles appear. These are more common in young adults and children and resolve with adequate treatment but may sometimes rupture and cause pneumothorax.

Klebsiella Pneumonia

Klebsiella is the most common enteric Gram negative bacilli causing community acquired pneumonia and is also an important casue of hospital acquired pneumonia. K. pneumoniae is a commensal found in the oropharynx, more commonly seen in the presence of dental caries. It is believed to reach the lungs by aspiration and is therefore more commonly seen in alcoholics, diabetics, and intubated patients.

Klebsiellla pneumonia more commonly involves the posterior segments of the upper lobes and apical segments of the lower lobes. The affected area of lung becomes distended by viscid oedema fluid and this produces the characteristic bowed or bulging fissure sign seen on chest radiographs. Klebsiela pneumonia might also be associated with tissue necrosis and cavitation.

Pneumonia caused by Anaerobes

Anaerobes are found in the oropharynx as commensals. Their numbers are greatly increased in the presence of dental sepsis. Anaerobic pneumonia is the result of aspiration. Predisposing factors for aspiration are depressed cough reflex due to alcohol intake, sedation, strokes, general anaesthesia, etc. The main anaerobes are Bacteroides, Prevotella, Porpyromonas, Fusobbacterium and Peptostreptococcus.

Radiographic features suggestive of aspiration include unilateral or bilateral pneumonic infiltrates or abscess cavities, typically in the apical segments of either or both lower lobes or in the posterior segment of the right upper lobe, these being the segments most susceptible to aspiration by virtue of their dependent position in subjects who are lying supine. A complicatingpleural effusion or empyema may be present.

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Acute Exacerbation of Interstitial Lung Disease

Virendra Singh, Bharat Bhushan Sharma

What is ILD?

Interstitial lung disease (ILD) consists of a large group of more than 200 diseases characterized by involvement of lung parenchyma. There are different ways of categorization of ILD. ILD of unknown cause include idiopathic interstitial pneumonia (IIPs) mainly idiopathic pulmonary fibrosis (IPF) and fibrotic non-specific interstitial pneumonia (NSIP), granulomatous ILD including sarcoidosis and hypersensitivity pneumonitis (HP) and miscellaneous group. ILDs of known cause include drugs, and connective tissue disease related ILDs (CTD-ILD). In a recent prospective ILD registry from India, chronic HP, NSIP, IPF, CTD-ILD, sarcoidosis, cryptogenic organizing pneumonia (COP), occupational lung disease like silicosis and some other fibrotic lung diseases were identified as the most prominent causes of ILD in India.

What is acute exacerbation of ILD?

Clinical, radiological, histopathologic presentation and prognosis of patients with ILD varies significantly. Among all types of ILDs, the natural history of IPF has been described in a more comprehensive manner in the literature. Usually, the natural course of IPF takes a gradual decline with some stabilization of pulmonary function with the help of medications currently available. In a number of IPF patients, there is a sudden decline in lung function and overall worsening of disease. ILDs other than IPF, like CTD-ILD and idiopathic NSIP, are also seen to behave in a similar fashion. Since acute exacerbation of IPF (AE-IPF) has been described in greater detail in the literature, subsequent discussion on exacerbation of ILD will be mainly confined to AE-IPF.

Incidence of AE-IPF is largely unknown. In some retrospective studies conducted a decade earlier, the yearly incidence of AE-IPF varied between 5 to 20 %. More recent data based on randomized clinical trials conducted on IPF enrolling patients with mild to moderate disease showed that a number of total deaths occurred as an acute worsening of disease. In placebo-treated patients in these trials, AE-IPF were reported in 2–16%

over 6–14 months, while mortality ranged from 2.5–13.3% over about 6 months to 2 year period. Sub-acute deteriorations of disease were found to be even higher in these trials conducted on pirfenidone, N-acetylcysteine and variety of other drugs. Data are not available for true overall incidence and prevalence of AE- IPF in usual clinical or population setting. The most significant points to remember about AE-IPF are that we are unable to predict and prevent their occurrence and these are invariably associated with high mortality.

How to define AE-IPF?

AE-IPF is defined as an acute clinically significant deterioration of unidentifiable cause in patient with underlying IPF. Acute episodes of worsening of IPF initially found out in early 1990s by pathologists from Japan as diffuse alveolar damage superimposed on usual interstitial pneumonia (UIP) pattern. Japanese investigators subsequently started reporting acute exacerbations after pulmonary lobectomy and some other innocuous diagnostic procedures such as bronchoalveolar lavage (BAL). Ambiguity in the diagnosis of these acute episodes prevailed before identification of acute episodes of IPF in almost half of the cases randomized to placebo arm in clinical trial of interferon gamma.

Collard and other international experts in 2007 laid down criteria for diagnosis of AE-IPF based on data available from clinical trials. Recently in 2016 Collard HR and the international working group for AE-IPF have revised the definition and diagnostic criteria for AE-IPF. **(Table 1)**

Table 1 : Comparison of diagnostic criteria for AE-IPF

Criteria	Earlier diagnostic criteria Collard HR and IPF Clinical Trials Network (IPFnet), 2007	Revised diagnostic criteria Collard HR and the international working group for AE-IPF, 2016
1. Background	Previous or concurrent diagnosis of idiopathic pulmonary fibrosis.	Previous or concurrent diagnosis of idiopathic pulmonary fibrosis.
2. CT findings	High resolution CT with new bilateral ground glass opacities and/or consolidation superimposed on a background of reticulation or honeycombing consistent with UIP pattern.	Computed tomography with new bilateral ground-glass opacity and/or consolidation superimposed on a background pattern consistent with UIP.
3. Differential diagnosis	Exclusion of alternative causes like infection, PE, LVF, and identifiable cause of acute lung injury.	Deterioration of patient not fully explained by cardiac failure or fluid overload.
4. Clinical presentation	Unexplained worsening of development of dyspnoea within 30 days.	Acute worsening or development of dyspnoea typically less than 1 month duration.
5. Exclusion of infection	No evidence of pulmonary infection by endotracheal aspirate of bronchoalveolar lavage.	None
Revised definition 2017 **An acute, clinically significant respiratory deterioration characterized by new bilateral alveolar abnormality.** **Note : An AE- IPF that meets the definition given above but fails to meet all four diagnostic criteria due to missing CT scan data should be termed "suspected acute exacerbations"**		

It can be seen in the table that in the earlier diagnostic criteria it was essential to exclude alternative causes like infection, PE, and identifiable cause of acute lung injury. It also necessitated exclusion of evidence of pulmonary infection by endotracheal aspirate of bronchoalveolar lavage. It was not only difficult to perform diagnostic procedure on very sick patients with AE-IPF but also no yield could be obtained in a significant number of patients.

What is pathophysiology of AE-IPF?

AE-ILD resembles an acute lung injury (ALI) which on histopathology is seen as diffuse alveolar damage (DAD). DAD is found in autopsy series of patients with IPF and other ILDs including patients with CTD-ILD, NSIP, and HP. Besides pathology, AE-ILD and

ALI or ARDS have many clinical features in common, such as new bilateral infiltrates on radiographs (e.g., ground-glass opacification/consolidation) and an increased oxygen requirement that is refractory to usual management.

What are the risk factors responsible for AE-IPF?

Etiology of AE-IPF is still unknown but a variety of causes have been liked with it.

Infection

Acute exacerbation of bronchial asthma and COPD are frequently precipitated by infections. Similarly there is still a possibility of initial viral triggering of AE-IPF with disappearance of infection at the time of presentation. It has now been suggested that a detailed diagnostic workup for viral infections and atypical pathogens need to be done to exclude possibility of treatable infection as a trigger.

Lung surgery

In the studies that included surgery for lung cancer, ARDS was found in most of cases having underlying interstitial lung disease. It has also been proposed that high concentration oxygen supplementation and mechanical ventilation are risk for AE-IPF in this setting. Besides lung resection, surgical lung biopsy, cancer chemotherapy and even BAL has been identified to be associated with AE-IPF.

GERD

Gastroesophagael reflux and occult aspirations have also been suggested to be having a role in development of AE-IPF. Aspiration of gastric contents has been shown to produce diffuse alveolar damage.

Drug induced

Some studies from Japan have reported more frequent AE-IPF especially secondary to drugs like gefitinib. It is not clear whether this is due some genetic factors, ethnicity or reported by chance only.

What are clinical patterns of AE-IPF?

Presentation

Idiopathic pulmonary fibrosis is a disease with grave outcome with a median survival of 3-4 years. It is much more fatal than many a cancers. Initially, in AE-IPF, there is cough, fever and flu like symptoms. The most severe cases resemble ARDS where

the patient may be comatose because of severe hypoxemic and sometime hypercapnic respiratory failure. Severe hypoxemia may require immediate mechanical ventilation. Physical examination often reveals tachypnea, cyanosis, clubbing and bilateral basal inspiratory crackles. A previous chest x-ray or a high resolution CT (HRCT) may be of considerable help in establishing underlying disease and possible cause of present deterioration.

Imaging

In AE-IPF, HRCT shows new bilateral ground glass opacities (GGOs) or consolidations, frequently both, upon UIP pattern. Rapidly developing GGOs is not a feature of stable IPF, and any new development away from areas of fibrosis indicates DAD. Akira and colleagues have proposed a categorization of AE-IPF on the basis of GGOs/consolidation on HRCT that may have prognostic implications: a) peripheral, b) multifocal, and c) diff use, though this was not substantiated in further reports.

How to proceed for diagnostic workup of AE-IPF?

The present criteria for diagnosis of AE-IPF include both idiopathic exacerbations and those associated with suspected triggers (infection, post-procedural/postoperative, drug toxicity, and aspiration) as well. A proposed algorithm for workup of these patients is given in figure 1. Interestingly, this definition of AE-IPF parallels the Berlin criteria for acute respiratory distress syndrome (ARDS).

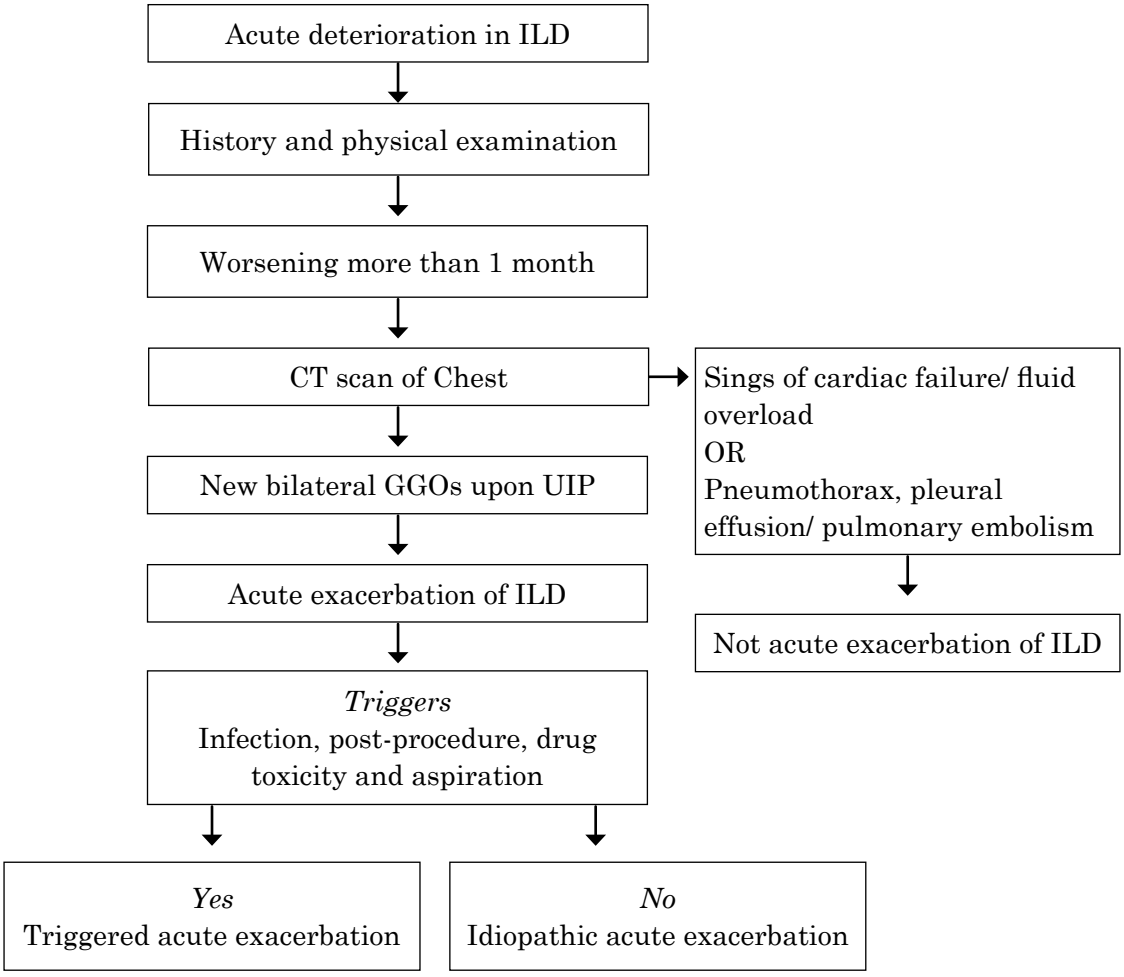

Figure 1 : Current diagnostic algorithm for AE-ILD

Biomarkers

KL-6, Neutrophil elastase, lactate dehydrogenase levels, and other serum markers have been studied for AE-IPF. A significantly higher serum levels of soluble ST2 protein in patients with AE-IPF was found. The levels of circulating fibrocytes have been found to be elevated in patients with stable IPF with a further increase in AE-IPF. Similarly, α-Defensin, ST-2 protein levels and antibody to annexin-1 have been shown to be significantly elevated in patient with AE-IPF. Antibody to annexin-1 has also been found to be elevated in BAL fluid from patients with AE-IPF. However, there is not enough data to justify routine use of these markers in diagnosis of AE-IPF.

How to treat AE-IPF?

In spite of advancement in current understanding of preventive and therapeutic measures used for IPF other ILDs the outcome of AE-IPF remains universally poor. Since no controlled clinical trial data for management of AE-IPF are available to date, the practical approach to management to AE-IPF is based on the fact that ALI/ARDS, acute interstitial pneumonia (AIP), and AE-IPF have common clinical, pathophysiological, and imaging features.

Overall approach to treatment of AE-IPF is based on careful decision-making. The need for mechanical ventilation and type of device should be judged carefully. Supportive care including palliation of symptoms and oxygen for hypoxemic patients has emerged as an important therapeutic strategy. A ventilation strategy employing low tidal volumes (4 to 6 mL/kg ideal body weight) used for patients with ARDS is advised by many experts. High positive end-expiratory pressure (PEEP) should not be used because of risk of over-inflation of intact lung units. And, for the same reason recruitment maneuvers or prone positioning is not effective. These patients require high-minute volume because of increased dead space therefore respiratory rate should be increased to the maximum acceptable rate.

Due to very high mortality associated with use of mechanical ventilation in respiratory failure, the international guidelines on the management of IPF make a weak recommendation against its use in this setting. In select group of patients, mechanical ventilation, or extra-corporal membrane oxygenation (ECMO) may be appropriate as a bridge to lung transplantation. Noninvasive ventilation (NIV), by decreasing work of breathing, may be considered as a potential palliative option that may help to reduce patient discomfort and permits management in less severe exacerbations. But, in most cases the excessive work of breathing associated with severe exacerbations cannot be managed effectively with NIV.

A proposed algorithm for management of AE-IPF based on expert opinion is given in Figure 2. Usual clinical practice is to treat AE-ILD with high-dose systemic corticosteroid and antibiotics like we do in exacerbations of COPD or asthma. There is weak recommendation in current guidelines on corticosteroids emphasizing that this recommendation is based on some low quality reports of benefit and overall mortality in AE-IPF remains high. Several observational studies on combination therapy of corticosteroids with other immunosuppressant drugs and monotherapies with cyclophosphamide, tacrolimus, sivelistat, rituximab, plasma exchange, intravenous immunoglobulin, polymyxin B-immoblilized fiber column perfusion showed mixed results and failed to demonstrate clear benefit for their use in AE-IPF. Therefore some intensivists prefer to stop immunosuppressive therapy at the beginning of treatment of AE-IPF and start anti-infective and other therapies based on results of diagnostic workup.

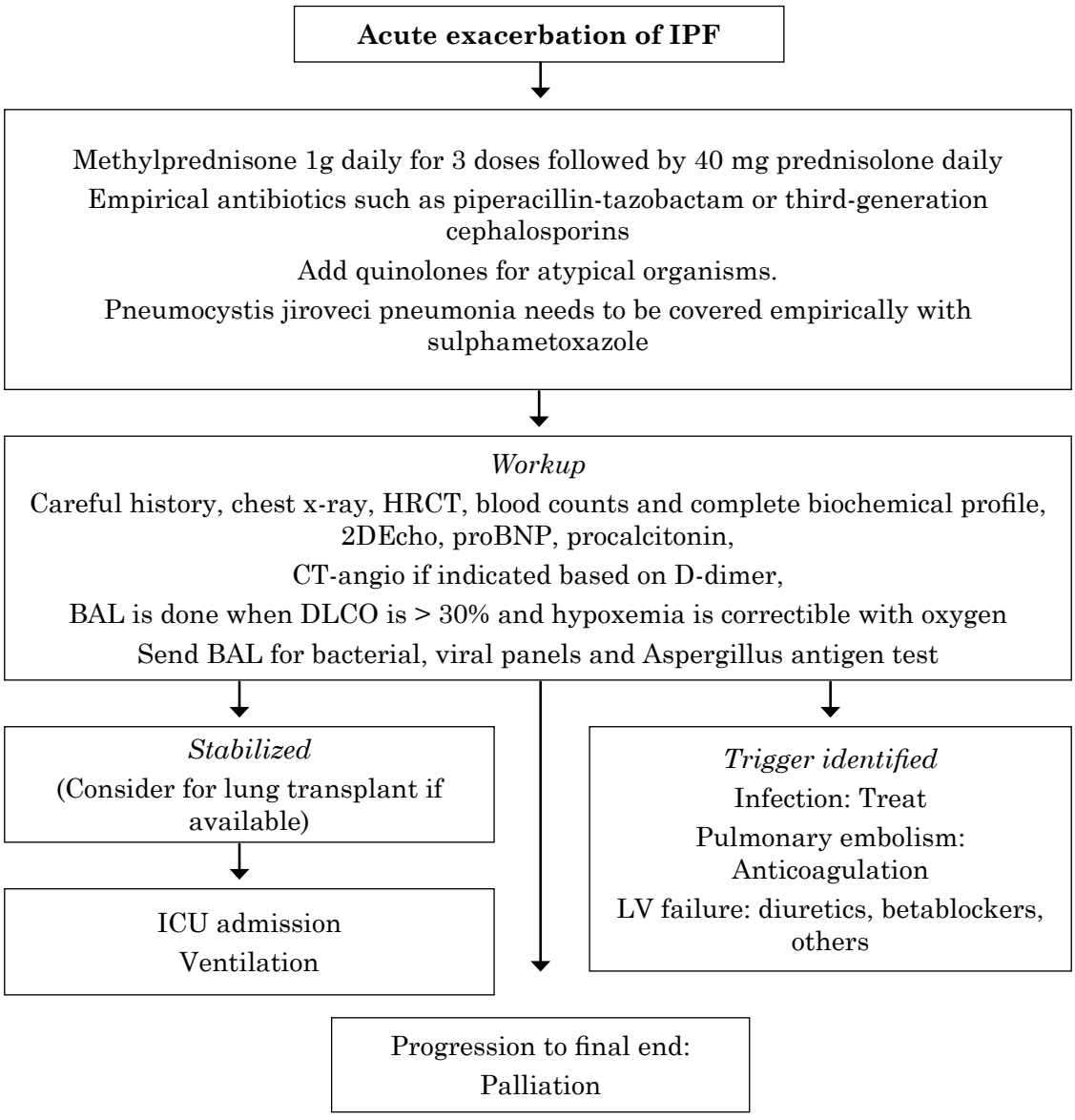

Figure 2 : A proposed management algorithm for AE-IPF

Reducing risk of exacerbations

In this context it is useful to remember that until a few years back the patients with IPF were being treated on triple therapy of prednisolone, azathioprine and N-acetylecysteine. Now there is paradigm shift in management of IPF after availability of two new effective anti-fibrotic drugs pirfenidone and nintedanib. The ASCEND and CAPACITY trials on pirfenidone showed that patients receiving pirfenidone had a lower risk for respiratory-related hospitalization compared to controls. Similarly, TOMORROW and INPULSIS trials on nintedanib showed a significant prolongation of the time to first AE in IPF. An important clue that has emerged from above is that these new drugs have potential to reduce the frequency of exacerbations and hopefully will alter the course of AE-IPF in due course of time, may be a decade later.

What is prognosis of AE-IPF?

The AE-IPF is universally associated with poor prognosis with the majority of patients dying within the first month and most of the rest within next 6 months. Severe disease at baseline, lower FVC and lower diffusion capacity are associated with high mortality. Presence of ground glass also indicates higher chance of death than scattered perihilar lesion.

Conclusions

ILDs consist of a large group of lung parenchymal diseases having varied presentations. Acute exacerbations have been identified with all ILDs but are described more extensively for IPF in the literature. Recently, new definition and diagnostic criteria for AE-IPF have been proposed in 2016. In spite of advancement in our current understanding for treatment of IPF and other ILDs, the outcome of AE-IPF remains universally poor even at the highest level of care.

Recommended reading

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Respiratory Emergencies in Tuberculosis

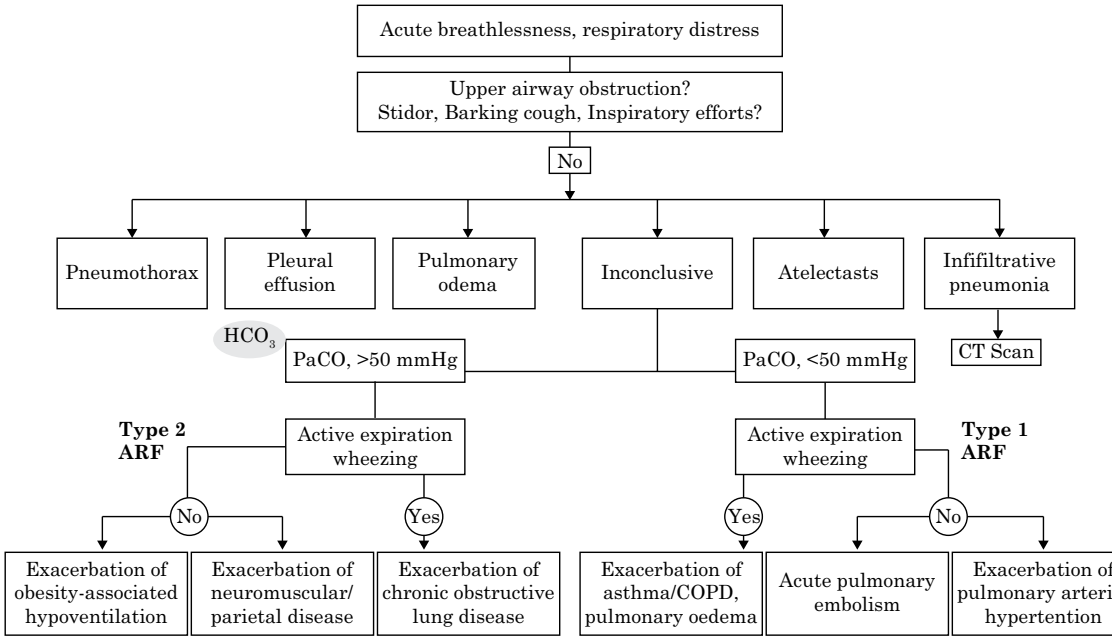
Dr. Suryakant Tripathi

Respiratory emergencies constitute a significant proportion of the workload in Emergency Room. Approximately 30-45% of all ER visits are due to respiratory causes only. Mortality is significantly high in these patients and is determined by the quality of care provided. Mortality rate may vary from 1% to >30% in various settings. There are various factors associated with mortality however the most important independent predictors of in-hospital mortality are respiratory rate and oxygen saturation, thereby suggesting that the respiratory system is involved either as a primary trigger or secondary manifestation of another organs acute dysfunction.

According to most pulmonologists, respiratory emergency is mainly the occurrence of acute respiratory failure either Hypoxic or Hypercapnic. Acute respiratory failure is defined by the patients inability to ventilate adequately or provide sufficient oxygen to the blood and systemic organs.[1]

Acute Hypoxic Respiratory Failure or Type 1 ARF is defined as PaO2<60 mm Hg or 8 kPa and Acute Hypercapnic RF or Type 2 ARF is defined as PaCo2>45 mm Hg or 5.99 kPa. However, this definition lacks a clinical point of view. Clinically, ARF is associated with dyspnea along with clinical signs of respiratory distress such as use of accessory muscles of respiration, nasal flaring and chest in-drawing, tachypnea, cyanosis, flapping tremors, encephalopathy in severe hypercapnia with respiratory acidosis along with signs of sympathetic overactivity (tachycardia, hypertension and sweating).

 # Flowchart 1: Approach to a patient with Respiratory Emergency



(Adopted from ERS Handbook – Adult Respiratory Medicine)[1]

Patients of Pulmonary Tuberculosis may present with respiratory emergency. Although exact data on the prevalence is unknown, but mostly the cases present more as complication of primary pulmonary tuberculosis. In this article we discuss four main ways in which a patient of TB may present to emergency.

1. Haemoptysis
2. Pneumothorax
3. Respiratory Failure
4. Massive Pleural Effusion

Haemoptysis

Haemoptysis is a common and potentially serious complication of PTB. The incidence of hemoptysis in patients of PTB is reported to range from 30-35%.[2,3,4] Haemoptysis may occur as initial manifestation of TB, during the course of the disease or post treatment. It can sometimes be massive and life-threatening. Massive hemoptysis may be associated with atelectasis.

Hemoptysis is considered life threating when there has been blood loss ranging from 100 ml up to or more than 1000 ml per day[5] OR 150ML of blood expectorated in a 24hr period or bleeding at a rate more than or equal to 100ml/hr.[6]

An important point to be kept in mind is to confirm whether it is really hemoptysis or hematemesis, as the management strategy differs widely in either situation.

 # Table 1 : Differentiation of Hemoptysis from Hematemesis

Hemoptysis	**Hematemesis**
There is usually a tingling sensation in the throat prior to the episode	Patient will usually complain of nausea and upset stomach
The blood is frothy and bright red	Blood is dark red, brown and non frothy
Blood is associated with sputum	Blood is associated with food particles
pH will be neutral to alkaline	Blood will give acidic pH
Stool examination for occult blood is negative	Stool is almost always positive for occult blood
History of lung disease is usually present	H/O gastrointestinal or liver disease is usually present
Not associated with malena	Associated with malena

Various etiologies are implicated for hemoptysis, which are described in the table below.

 # Table 2 : Etiology of Hemoptysis

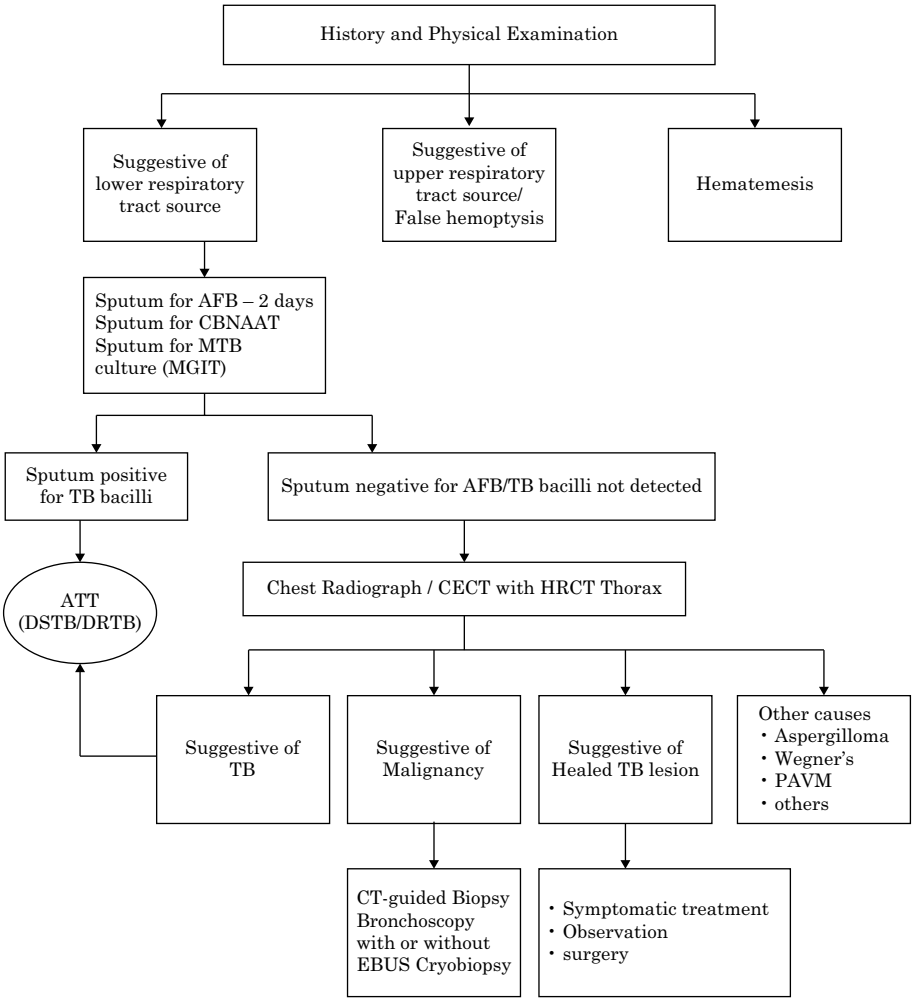
Infections	• Pulmonary tuberculosis • Post tuberculosis Rasmussen's aneurysm • Pneumonia • Lung abscess • Bronchiectasis • Fungal Infections • Broncholith
Neoplasms	• Bronchogenic carcinoma • Metastatic nodules • Carcinoid tumours • Bronchial adenoma • Hamartoma • Scar carcinoma

Cardiovascular Disorders	• mitral stenosis • pulmonary infarction from thromboembolism
Trauma	• Penetrating lung injury • Lung contusion
Hematologic disorders	• Blood dyscrasias
Autoimmune disorders	• Good pasture's syndrome • Wegener's granulomatosis • Small and medium vessel vasculitis
Metabolic disorders	• Uremia • Liver cirrhosis
Vascular disorders	• Pulmonary arteriovenous malformation • Osler-weber-Rendu syndrome

Some of the common causes of hemoptysis in Pulmonary TB are-

- Bleeding from cavity wall
- Rupture of Rasmussen's Aneurysm
- Tuberculous endobronchitis
- Post-Tuberculous Bronchiectasis
- Aspergilloma
- Broncholith
- Direct erosion of capillaries of arteries by inflammation
- Scar carcinoma

Flowchart 2 : ***Approach to a patient with Hemoptysis***



Early flexible bronchoscopy is the initial diagnostic procedure of choice in most patients with life threatening hemoptysis. It can be performed bedside in unstable patients and is successful most often in localizing the the site of bleeding.[7,8] It has therapeutic role also to prevent recurrence and control the current situation.

Initial management involves:

- Stabilizing the vitals of the patient
- Ensure adequate oxygenation and ventilation,
- Positioning the patient (lateral decubitus with suspected side down),

- Administration of antibiotics via intravenous access
- Hemostatic agents and
- Cough suppressant (Preferably codeine or its derivative based)
- Sedation of the patient

- If *intubation* is needed, a large bore endotracheal tube is used to facilitate interventional and diagnostic bronchoscopy. Management in most cases is dependent upon delineation of the cause and bed rest, sedation and resuscitative measures aimed at *restoring fluid balance and hemodynamic status* usually suffice. *Broad spectrum antibiotics* are also added to the armamentarium to treat superadded infection. *Anti-tubercular treatment* is indicated in patients with active TB.

- In case the bleeding is recurrent or massive or compromising the haemodynamic status of the patient *fiberoptic bronchoscopy* is indicated to localize the site of bleeding along with a CT Scan with contrast. The use of contrast may help to identify vascular abnormalities such as arteriovenous malformations or aneurysms.

- *Bronchoscopic treatment* includes performing *iced saline lavage*, *administration of topical vasoconstrictive agents, balloon tamponade, ablative therapies like use of laser therapy, electrocautery, argon plasma coagulation (APC)* to stop the bleeding from localized site. The prolonged use of balloon tamponade catheters should be avoided to prevent ischemic mucosal injury and post-obstructive pneumonia. *Endobronchial tamponade* should only be applied as a temporary measure until a more definitive therapeutic procedure can be deployed. Other methods that can be employed in a specialty center include *Bronchial artery embolization* and *surgery*.

Bronchial Artery Embolization

The immediate success rates for control of massive haemoptysis is excellent, ranging from 64% to 100%, although recurrent non-massive bleeding has been reported in 16–46% of patients.

Surgical Management

Surgery is considered for the management of localised lesions. Surgical mortality ranges from 1% to 50% in different series depending on selection criteria. Surgical resection is indicated when Bronchial Artery Embolization is unavailable or the bleeding is unlikely to be controlled by embolization. It remains the treatment of choice for the management of life threatening hemoptysis in bleeding aneurysm and cavitary lesions. The surgical treatment of aspergilloma is also associated with relatively high mortality rate that ranges from 7-23%.[9,10] surgical approach needs to be considered in those with massive hemoptysis and adequate pulmonary reserve.

Pneumothorax

Spontaneous pneumothorax has been reported in 5-15% of patients with pulmonary TB.[12,13] Pneumothorax is the most common respiratory emergency with patients presenting with acute onset of dyspnea and chest pain in the emergency department.

In country like ours where TB is a common problem, it is a common cause of pneumothorax thereby presenting as acute breathlessness. Spontaneous Pneumothorax may result from rupture of a subpleural TB cavity into the pleural space. Infection of pleural cavity results in pyopneumothorax.

Pneumothorax can also result from rupture of a bleb or bulla secondary to fibrosis and destruction of lung.[14]

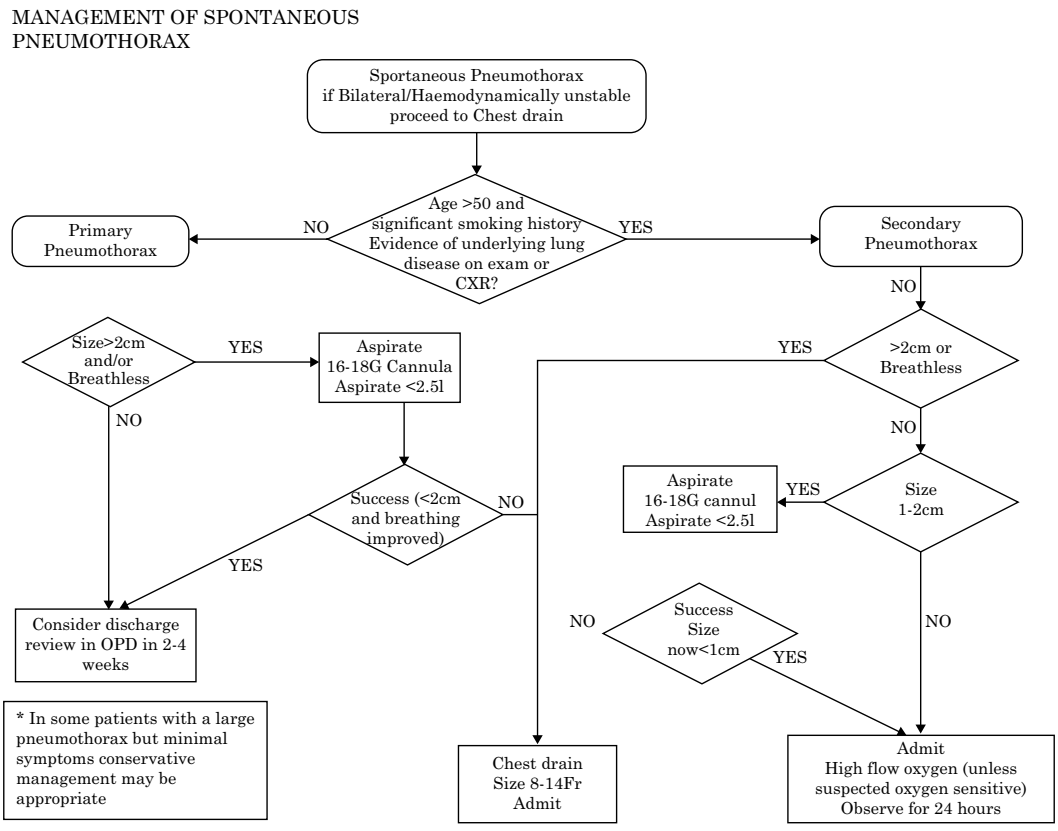
Diagnosis

Physical findings on examination include use of accessory muscle, or labored breathing, decreased chest movement on the affected side, diminished breath sounds, absent tactile or vocal fremitus with hyper resonant note on percussion. Rarely patients present with coexisting subcutaneous emphysema. Tracheal deviation and mediastinal shift is a late sign but always not indicative of tension pneumothorax.[17] Hemodynamic compromise (tachycardia, hypotension) or cardiopulmonary collapse is indicative of tension pneumothorax or underlying lung disease like COPD.[18] Oxygen desaturation is evident. Electrocardiographic findings are also nonspecific and may reveal a sinus tachycardia. A more serious rhythm disturbance (eg, bradycardia) may be associated with severe hypoxemia or indicate tension pneumothorax and impending cardiovascular collapse.

Management

Haemodynamically unstable patients and patients with severe respiratory distress are typically those with a large or tension pneumothorax, patients with extensive trauma, or patients with significant underlying lung disease. Such patients are resuscitated with the emphasis on stabilization of the airway, breathing, and circulation. Unstable patients should also concomitantly undergo rapid bedside imaging, usually with ultrasound, to confirm the diagnosis before undergoing emergent needle or chest tube thoracostomy. In the event that ultrasonography is unavailable or unhelpful, then an empiric decision to place a chest tube without confirmatory imaging should be made on clinical assessment alone.[16] Treatment of Primary spontaneous pneumothorax (PSP) include oxygen with observation, simple aspiration, and thoracostomy tube/ catheter. Patients with a large Secondary Spontaneous Pneumothorax (≥2 cm from the pleural line to the chest wall), prompt drainage by tube or catheter thoracostomy and subsequent hospitalization to treat the underlying cause are indicated because of the risk of respiratory impairment and need for definitive intervention.[15]

 # Flowchart 3: Management of Pneumothorax



(Adopted from BTS guidelines for management of pneumothorax)

Respiratory failure

Acute respiratory distress syndrome (ARDS) is known to be one of the complications of military TB and also in bronchogenic Pulmonary TB. Bronchogenic PTB is a less–recognized cause of acute respiratory failure, simulating an acute febrile illness or diffuse interstitial lung disease, with a short duration of symptoms.[19] Some decades ago, respiratory failure resulting from tuberculosis was reported mainly in cases of military tuberculosis. In 1977, the first case series of respiratory failure in 16 patients with tuberculosis and fibro cavitary disease was described.[26]

The incidence of this clinical situation was reported to be 1.5–1.9% in earlier studies.[20,21] Mortality was reported to be 75% in patients with symptoms for more than 2 weeks.[22]

Although ARDS is reported in active TB and military dissemination, many patients with confluent pulmonary infiltrates (non-military-PTB) or consolidation with atypical clinical features may present with acute respiratory failure. However, acute respiratory failure associated with PTB was reported to have a good prognosis with 67% survival when compared to 46% in patients presenting with ARDS[20]

Cause of hypoxemia in non-military PTB is a result of direct injury to alveolar epithelial cells from tubercular antigens through liquefied, caseous lesions. These effects may further be accentuated by bronchogenic spread. A small amount of bacillary antigen is enough to evoke an exudative response in the host and is an important determinant of direct injury.[23] The key factor in the above process is the activation of alveolar macrophage. Lipoarabinomannan (LAM), a tuberculous cell wall constituent, similar to the lipopolysaccharide in Gram-negative sepsis, activates macrophages that trigger the production of tumor necrosis factor (TNF)-alpha, interleukin (IL)-1beta, and mRNA from mononuclear phagocytes. Similarly, mycobacterial heat shock protiene-65 kD and *M. tuberculosis* culture filtrate may incite similar effects.[24]

In addition, *M. tuberculosis* makes endothelial cells more susceptible to the toxic effects of TNF-alpha and increases ICAM-1 expression on endothelial cells. Increased expression of this molecule may allow increased binding of neutrophils to the endothelium.[25] In later stages, the spread of infection into the blood may diffusely injure the vascular endothelium. This may cause similar effects seen in indirect injury from sepsis leading to ARDS.[26] A combination of these processes would ultimately affect the A□a O_2gradient leading to hypoxemia, thus manifesting as respiratory failure.

Diagnosis

Presentation as an acute infective episode or interstitial pneumonia simulating early ARDS or acute respiratory failure, or as an acute febrile illness, progressing to dyspnoea of less than 2 weeks, could be a reflection of hypoxemic respiratory failure. Few case reports also shows lobar consolidation and acute respiratory failure, simulating bacterial pneumonia, warranting mechanical ventilation.

ARDS can be diagnosed once cardiogenic pulmonary edema and alternative causes of acute hypoxemic respiratory failure and bilateral infiltrates have been excluded. The Berlin Definition of ARDS[27] requires that all of the following criteria be present for diagnosis:

- Respiratory symptoms must have begun within one week of a known clinical insult, or the patient must have new or worsening symptoms during the past week.
- Bilateral opacities must be present on a chest radiograph or computed tomographic (CT) scan. These opacities must not be fully explained by pleural effusions, lobar collapse, lung collapse, or pulmonary nodules.

- The patient's respiratory failure must not be fully explained by cardiac failure or fluid overload. An objective assessment (eg, echocardiography) to exclude hydrostatic pulmonary edema is required if no risk factors for ARDS are present.
- A moderate to severe impairment of oxygenation should be present, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2). The severity of the hypoxemia defines the severity of the ARDS:
  - Mild ARDS – The PaO_2/FiO_2 is >200 mmHg, but ≤300 mmHg, on PEEP or CPAP ≥5 cm H_2O.
  - Moderate ARDS – The PaO_2/FiO_2 is >100 mmHg, but ≤200 mmHg, on PEEP ≥5 cm H_2O.
  - Severe ARDS – The PaO_2/FiO_2 is ≤100 mmHg on PEEP ≥5 cm H_2O.

The most common radiological findings reported are reticular infiltrates and consolidation and cavitation which occurs in 27–50% of cases.[29] The most common laboratory findings are anaemia, leucopenia, leukocytosis, hypoalbuminemia.[28]

Clinical characteristics and chest X-ray and Sputum examination remain the main tools for the early diagnosis of active pulmonary tuberculosis.

Symptom duration longer than two weeks and the presence of micronodules or a cavitary pattern on chest X-ray were significantly associated with active pulmonary tuberculosis

Mycobacterial culture takes 6–8 weeks. Therefore, the treatment of intensive care unit (ICU) patients can rarely be based on culture results. In addition, obtaining material for mycobacterial analysis can be difficult, especially in patients with EPTB and in mechanically ventilated patients whose parameters preclude diagnostic procedures, such as diagnostic bronchoscopy. If the patient is mechanically ventilated, procurement of sample for proper testing is essential. Diagnostic bedside bronchoscopy is often used for this purpose. Broncoalveolar Lavage, Transbronchial Lung Biopsy are frequently done in these patients and samples are subjected to CBNAAT and MTB Culture (MGIT) for accurate detection of MTB as well as drug sensitivity pattern. Although antituberculosis treatment is potentially toxic, it is recommended in many cases that patients admitted to an ICU with tuberculosis symptoms start receiving the medications before the results of diagnostic tests are available, given that delayed treatment initiation can result in death. In immunocompromised patients the index of suspicion should be even higher.[29] Appropriate diagnostic investigation, as well as knowledge of the clinical and radiological presentations of severe tuberculosis, can contribute to earlier diagnosis and treatment initiation.

The introduction of new techniques, including early detection of the aetiological agent by PCR, can aid in diagnosis and contribute to early initiation of treatment. In addition, HRCT has been used in situations in which chest X-ray does not contribute to the diagnosis of active disease, such as in cases of minimal parenchymal changes and in the differentiation of old fibrotic lesions from those that are characteristic of bronchogenic dissemination.[31]

Management

Appropriate antituberculosis treatment is an important factor that can affect patient outcome. Higher mortality is found among patients who do not receive optimal treatment.

Evidence mandates a particular strategy of mechanical ventilatory support for ARDS.[32,33] Lower tidal volumes (6-8 ml/kg body wt.) are applied to prevent microscopic barotrauma to relatively normal alveoli, which can worsen the extent and/or severity of inflammatory pulmonary edema, an outcome sometimes described as *ventilator-induced lung injury*.

The other major aspect of mechanical ventilatory support concerns the use of positive end-expiratory pressure (PEEP). PEEP increases the amount of aerated lung, thereby improving oxygenation by decreasing the shunt fraction, allowing a lower FiO2 to be used. However, it can also be associated with barotrauma and depressed cardiovascular function.

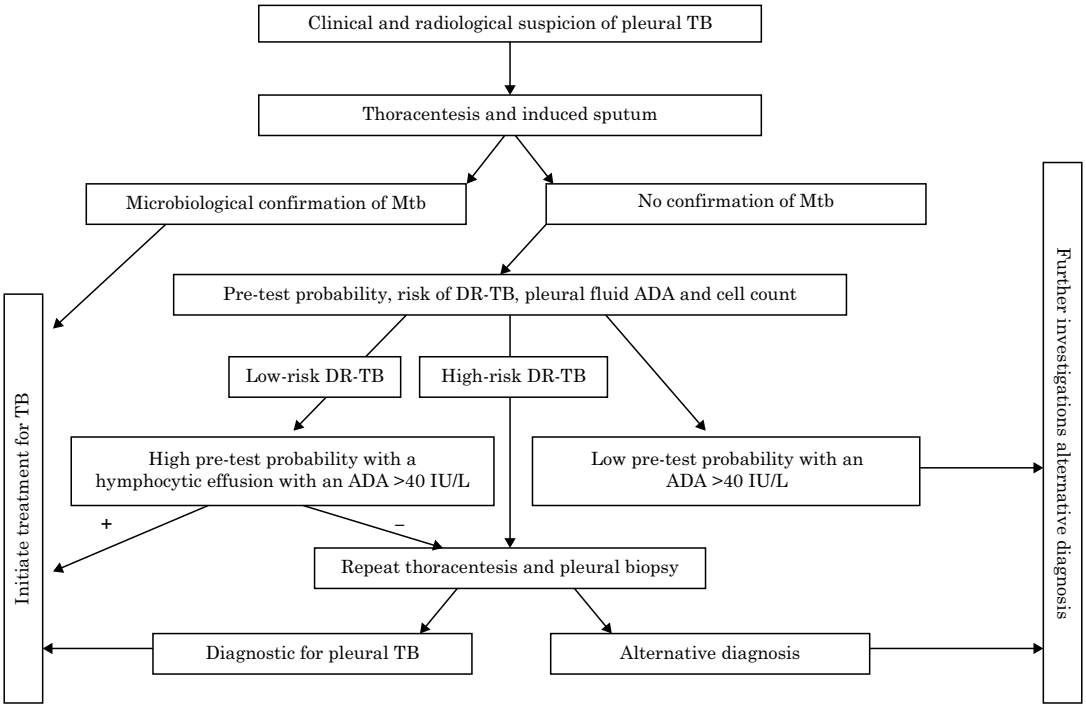
Other ventilation strategies can be used as "rescue" therapies when oxygenation is inadequate. These include prone ventilation, neuromuscular blockade and extracorporeal membrane oxygenation (ECMO).

Corticosteroids in the treatment of PTB with bronchogenic dissemination and respiratory failure may be beneficial as a non-specific anti-inflammatory therapy.[34]

Massive pleural effusion

Tubercular Pleural Effusion is one of the most common sites of extrapulmonary TB, with varying incidence in different regions. The incidence is proportionately higher in endemic regions as compared to non-endemic areas. Globally TB effusion is higher in younger patients. TB effusion typically present as acute to subacute illnesses characterized by unilateral pleuritic chest pain (-75%), cough (-70%), fever (-85%), night sweats (-50%), dyspnea (-50%) and weight loss (25-85%).[35,36]

#FlowChart 4: Approach to a patient of Pleural Effusion



Diagnosis

An often cited study by Valdes *et al* .reported that TB effusions occupied more than two-thirds of the hemithorax in 18.5% of patients, between one- and two-thirds of the hemithorax in 47.2% and less than one-third of the hemithorax in 34.2%. Another observational study reported that TB effusions accounted for 12% of all massive effusions (complete opacification of one hemithorax).[37,38]

Initial diagnostic modality includes chest radiograph, occasionally a chest CT is indicated. The typical CT scan of a patient with a TB pleural effusion shows diffuse thickening of both the visceral and parietal pleura, separated by fluid (the 'split pleura' sign).[39] In comparison to CXR, the rate of concomitant parenchymal disease found in cases with TB effusions is far higher on CT scan. The role of transthoracic ultrasound in tuberculous effusions is primarily to guide investigations and interventions, maximizing the yield and improving safety.

General pleural fluid analysis shows straw coloured lymphocytic exudate with elevated LDH. ADA levels above 40IU/L in pleural fluid carries a positive predictive value of 98% in high TB prevalence regions. Pleural fluid CBNAAT is the preferred modality in recent times for microbiological confirmation and detection of resistance.

Management

In large pleural effusions therapeutic thoracentesis relieves dyspnea rapidly. The recommended therapy is 6 months of standard anti-tuberculous treatment consisting of 2 months intensive phase with rifampicin, isoniazid, pyrazinamide and ethambutol (RHZE fixed-dose combination), followed by a 4-month continuation phase with RHE. Multiple thoracentesis may be needed if recurrent filling and dyspnea occurs for symptom control.

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Respiratory Emergencies in Covid–19

Dr. Rishabh Kochar, Dr. Sanjay Kumar Kochar

The novel coronavirus (named SARS-CoV-2) has emerged as one of the greatest challenges to the medical fraternity both because of rapidity of its spread and lack of a cure or vaccine at present. Genetic analysishas linked the SARS-CoV-2 to beta coronavirus genus of the Coronaviridae family and established it's relation to the SARS virus.The disease Covid-19 has had variable presentations and even after 4 months and more than 20 lakh cases the entire spectrum of the disease is not known.Another baffling thing about the disease is that huge number of cases have been considered to be asymptomatic with estimates ranging from 5-10% from China, 40% reported in Japan and in India; Indian Council for Medical Research (ICMR) reporting that up-to 80% patients may be asymptomatic or have mild symptoms only. These asymptomatic cases may act as Trojan horse and spread the disease in the community.[1, 2, 3]

Though considered as a primarily respiratory virus, there have been numerous case reports documenting associated diarrhea and gastrointestinal symptoms, acute kidney injury to the extent of patients requiring dialysis, transient hepatitis, myocarditis, neurological complications, coronary and cerebrovascular diseases to name just a few. The data regarding disease spread and symptomatology are highly variable and reports from different countries are providing different perspectives of the spectrum and its impact. In coming time more report with vast variations in different aspects of corona infection may come. This chapter will primarily be focused on respiratory emergencies and complications related to acute corona virus.

According to available data about the most common presenting symptoms are fever, cough and breathlessness with 15% patients having severe illness requiring oxygen therapy. It is estimated that up-to 5% patients may develop severe disease requiring intensive care and ventilation support. [1] The nature of severe diseases is commonly severe pneumonia, acute respiratory failure and ARDS which may be complicated by secondary bacterial infection and sepsis. For the purpose of understanding, the respiratory emergencies have been divided in two groups,

- Including the primary emergencies arising directly out of the Covid-19 disease such as acute respiratory failure, exacerbation of underlying obstructive lung diseases.
- The second group will encompass the complications and emergencies arising out of the patient management and involvement of other systems leading directly or indirectly to pulmonary involvement such as venous thromboembolism, pneumothorax and pulmonary edema secondary to cardiac failure.

Table -1 demonstrates the spectrum of emergencies in Covid-19. It is to note that the following table is based on the published data available at the time of writing this article and the list is bound to change as our understanding of disease increases

Table -1.Respiratory emergencies in Covid-19

Respiratory Emergencies in Covid - 19	
Primary **From direct pulmonary involvement**	**Secondary** **From local or systemic complications**
• Severe Pneumonia • Acute respiratory failure • Acute respiratory distress syndrome	• Pneumothorax • Pulmonary Embolism • Acute pulmonary Edema

Risk Factors

Multiple studies and case reports from around the world have firmly concluded that the disease is more severe in elderly with more adverse outcome than in young people. Apart from old age several other risk factors have been established and include cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer. Other than these factors active smoking and obesity have also been found to be associated with more severe disease. Also, males have been found to have a more severe disease pattern and a higher mortality rate than females and the cause for it is still unclear.

Risk factors for severe Covid -19 illness[1, 4]:

- Old age
- Cardiovascular diseases
- Diabetes
- Chronic respiratory diseases
- Hypertension
- Cancer
- Patients taking ACE inhibitors and angiotensin-receptor blockers (ARBs)[5]

Thus, a good medical history and knowledge of prior conditions may help identify the patients with high chances of developing a serious or complicated disease and institute early intensive measures. For example a patient with poorly controlled diabetes with mild Covid-19 pneumonia has a high risk of deterioration and should be observed more closely. Interaction between the virus and Angiotensin Converting Enzyme 2(ACE2) receptor has been touted as potential mode of entry into the cell and patients taking

ACE inhibitors and angiotensin-receptor blockers (ARBs) are theoretically at a higher risk but discontinuation of these drugs is not warranted.[5]

Just like the primary disease, the disease related complication has also been reported at a higher rate in the patient with pre-existing morbidities than in previously healthy subjects.

Primary Respiratory Emergencies

a. Severe Pneumonia

It is the most common diagnosis in severe Covid-19 patients. When complicated it may read to rapidly progressive respiratory failure and need for ventilator support. The frequency of severe pneumonia has been between 5-10% in various studies but these are just the initial data.A non-severe pneumonia is defined as pneumonia not requiring oxygen therapy and without the signs of severe infection as described below. Severe pneumonia has been defined in World Health Organization (WHO) guidelines as [1]

- For adolescent or adult: fever or suspected respiratory infection, plus one of:
  - Respiratory rate > 30 breaths/min
  - Severe respiratory distress; or
  - SpO2 ≤ 93% on room air
- For Children: Cough or difficulty in breathing, plus at least one of the following:
  - Central cyanosis or SpO2 < 90%;
  - Severe respiratory distress (e.g. grunting, very severe chest indrawing);
  - Signs of pneumonia with a general danger signs like inability to breastfeed or drink, lethargy or unconsciousness, or convulsions
  - Fast breathing (breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50 and 1–5 years: ≥ 40

The decision is made on the basis of clinical judgment but chest imaging may help in identifying or ruling out the complications. If mismanaged, severe pneumonia can get complicated with secondary bacterial infection or patient may end up needing ventilator support. The management of severe pneumonia is discussed later.

b. Acute Respiratory Failure

It is defined as a condition in which the lungs fail to perform one or both of their functions viz. oxygenation and carbon dioxide removal. Depending on the type of

function lost it may be classified as Type I respiratory failure with hypoxia PaO2 less than 60mmHg and a normal or low PaCO2 or type II respiratory failure PaCO2 more than 50 mmHg. The respiratory failure may be causedby the infection itself, as in pneumonia or acute respiratory distress syndrome (ARDS), or by exacerbation of pre-existing lung diseases like asthma, chronic obstructive pulmonary disease (COPD) or bronchiectasis.[6, 7]

The reason it is taken as separate from ARDS or severe pneumonia is the fact that many patients with long standing pulmonary diseases with Covid-19 infection may present as acute exacerbation/ acute respiratory failure and without all the common symptoms listed (fever, cough) and without radiographic evidence of pneumonia or ARDS. Such patients may be missed in screening for Covid-19 based purely on symptoms and radiological findings. Therefore maintaining a high level of suspicion for Covid-19 is necessary in patients having acute respiratory failure with lack of diagnostic clues.[6, 7, 8]

c. acute respiratory distress syndrome[1, 7, 8]

ARDS is one of the most serious forms of acute lung injury. Previously defined as the acute onset of respiratory failure, bilateral infiltrates on chest radiograph and hypoxemia in the absence of evidence of left atrial hypertension, the definition has now been revised as per the Berlin criteria which defines ARDS as follows[9]

- Timing- within 1 week of clinical insult or onset of respiratory symptoms
- Radiography- bilateral alveolar or interstitial infiltrate not fully explained by effusions, consolidation, or atelectasis
- Non cardiac origin of edema and absence of left atrial hypertension
- Severity- based on the PaO2/FiO2 ratio
  i. Mild (PaO2/FiO2 200-300)
  ii. Moderate (PaO2/FiO2 100-200)
  iii. Severe (PaO2/FiO2 ≤100)

It is one of the most disastrous manifestations of Covid-19 and development of ARDS is associated with very high mortality. The exact pathophysiological cascade leading to ARDS in SARS-CoV-2 infection has not been delineated though some differences in Covid-19 related ARD have been found. In such patient with ARDS there is discordance between the lung mechanics and the degree of hypoxia. The lung volumes and compliance have been found to be relatively high if compared to the severity of the hypoxemia. Possible mechanisms have been elucidated to be hypoxic vasoconstriction, shunting of blood and impaired regulation in pulmonary circulation.[10]With more reports we may

get a clearer insight into why the above differences are seen and if they are uniform across all patient spectrums.

Management severe acute respiratory illness when covid-19 is suspected

All patients where Covid-19 is suspected as a cause for acute respiratory illness should undergo rapid screening and sampling for the same along with complete blood counts, liver and kidney function tests, chest radiograph, electrocardiography (ECG) and ABG to establish the initial baseline characteristics. Strict infection prevention and control (IPC) measures should be applied and appropriate distancing and PPE usage should be mandatory. The patients should be kept is isolation and if not possible, should be clustered with others having same diagnosis. At present there is no definite cure or antidote available for Covid-19 and the management is guided by symptomatic care, empirical therapies and ongoing local clinical trials. The following treatment summary has been prepared from WHO guidelines, local guidelines and ongoing trials.[1, 7]

- *Symptomatic management*- mild cases can be managed symptomatically with antipyretics and supportive measures and can be discharged with careful explanation of warning signs of severe disease.
- *Empirical antimicrobial therapy*- All patients with SARI should receive empirical antibiotics as soon as possible after hospital admission. Choice of antibiotic is based on patient's condition, co-morbidities and local pathogens. Antibiotics can be de-escalated at later course. Rational use of antibiotics is recommended. Antivirals (neuraminidase inhibitors) can be added empirically if seasonal influenza is prevalent.
- *Past treatment*- Ongoing medications must be reviewed and only necessary drugs should be continued. Drugs which may have interaction with ongoing therapy or may affect treatment outcomes may need to be modified/ replaced or stopped.
- *Oxygen therapy*-It is the cornerstone of management of any acute respiratory illness. All patients with SpO2 < 94% should be given supplemental oxygen therapy either via prongs or masks. During acute stages the target should be >93% and once stabilized flow can be reduced to keep SpO2 above 90%.Patients with delirium, hemodynamic instability and multi-organ failure are poor candidates for high flow oxygen therapy.

  Early oxygen therapy may delay the need for intubation or entirely avoid it by reducing the work of breathing, improving oxygenation and reducing respiratory fatigue. That said, all patients on oxygen therapy should be continuously monitored for worsening of dyspnea, respiratory fatigue and desaturation and in case of deteriorating condition early intubation and mechanical ventilation should be done.

Non-invasive ventilation can be used in selected group of patients but they are associated with risk of aerosolization.

- *Invasive mechanical ventilation*-in presence of failing respiratory function and inadequate oxygenation despite all measures, early intubation provides the best chances of survival to the patient. Rapid sequence intubation using proper airborne precautions is preferred. The recommended settings for adults is tidal volume between 6-8 ml/kg with plateau pressure preferably <30cm H2O. In case of difficult ventilation or patient-ventilator dyssynchrony deep sedation and muscle relaxant use is recommended.

  In patient with moderate to severe ARDS 12-16 hours of prone ventilation with high PEEP is preferred instead of lower PEEP. As in ARDS due to other causes, fluid restricted strategy is preferred and corticosteroids have been found to have no role as of now.

- *Extra Corporeal Membrane Oxygenation (ECMO)*- ECMO had proven itself to be a useful tool during the H1N1 epidemic the same story may be repeated during this pandemic. Although many trials are ongoing and data regarding outcomes of Covid-19 patient on ECMO are not yet available, lack of data should not prevent the use of ECMO in such cases wherever deemed necessary. It is also important to remember that resources have already been stretched thin by the disease and resources should not be diverted from existing pool into setting up of new ECMO units. [11]

- *Miscellaneous*-Other therapies such as inotropic use, fluid and calorie management should be guided by patient's condition. Many patients develop acute kidney injury or volume overload severe enough to require dialysis and the facility for same should be available in a center treating severe Covid-19 patients.Management of sepsis, septic shock and hospital acquired infection should be according to pre-existing guidelines and apart from fluid restrictive resuscitation strategy no specific changes have been suggested so far. Strict infection control measures should be taken to prevent catheter related infections and cross-infection between patients.

  Patients should also be given adequate protection against pressure sores and stress ulcer in gastrointestinal tract. Corticosteroids, unless being used for specific indications or under trials, have shown no benefit at present and should not be used routinely. The need for venous thromboembolism prophylaxis in patients who are immobilized for long durations cannot be over-emphasized. Pulmonary embolism has emerged as one of the major secondary complications and its diagnosis is confounded by the fact that pedal edema and elevated D-dimer levels may be present in many patients without venous thrombosis and this reduces their predictive value.[1]

- *Emerging therapies*-The challenges posed by Covid-19 has led to a race to find a drug which can cure the disease and if not, at least reduce the severity and complications. Among these the front runner is hydroxychloroquine which has been found effective in lab studies and in-*vivo* studies. Though definite positive result is lacking but existing evidence lies in its favor and it has been recommended by Indian Council of Medical Research in prophylaxis and management of Covid-19.[12, 13]

  Apart from this use of convalescent plasma therapy from recovered Covid-19 patients has been undergoing vigorous research. Various old drugs like azithromycin, cholchicine, chloroquine, losartan, ritonavir and newer medications like remdesivir, interlukein-6 inhibitors, DAS 181 are under various phases of clinical trials and results will be available soon.Amongst the newer drugs Remdesivir is the front runner and has shown in-vitro antiviral action with reduction in viral load and better patient related indices.[14, 15]Till the time we find a magic bullet to kill this virus prevention is the best and only therapy we have.

Secondarycomplications

Pneumothorax

Pneumothorax may come as primary presentation or a complication of intubation and mechanical ventilation, but far more cases associated with latter have been reported then as a primary manifestation of disease. Delay in recognition and management of pneumothorax may lead to death and many case series evaluating Covid-19 patients have pneumothorax listed as a primary cause of death.

It usually presents as acute worsening of dyspnea, desaturation and unexplained sudden hemodynamic collapse in an otherwise stable ventilated patient. Although no preventive strategy is available, knowledge of patient's preexisting lung conditions and protective ventilation with low pressures may be helpful.

The fact that pneumothorax is very much treatable with almost completerecovery and failure to recognize it can lead to patient's death makes it imperative to keep a high level of suspicion. Pneumothorax should be kept as a possible cause in assessment of non-responding or rapidly deteriorating patients.[16]

Pulmonary Embolism

The prevention and management of Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) in critical care patients has been an unforgiving quest for doctors worldwide. Prolonged mechanical ventilation, immobilization and widespread activation of inflammation cascade acts as a petri dish for thromboembolic complications in patients with severe Covid-19 disease. Adding to that, the raised D-dimer levels in

severe disease precludes its use as a screening tool in such patients. Many case reports have confirmed frequent occurrence of pulmonary embolism complicating Covid-19 pneumonia.[17, 18]

Acute pulmonary embolism can lead to catastrophic respiratory and circulatory failure and sudden unexplained death. It can also aggravate the ventilation- perfusion mismatch in such patients who already have a poor reserve, further complicating the ventilation strategies.

Since many patients with pulmonary embolism may die without the diagnosis being made, under-reporting and downplaying its associated risk with Covid-19 is a possibility.

The presentation and management is similar to non Covid-19 patients with PE. The best strategy is prevention and all susceptible patients should be given adequate prophylaxis for DVT and PE prevention with available means.

Acute Pulmonary Edema

A myriad of etiologies can lead to pulmonary edema including, but not limited to- volume overload, myocarditis and congestive cardiac failure, acute kidney injury (AKI), sepsis, and even ARDS. All of these risks are a possibility and have been widely reported in association with severe Covid-19 disease, especially fulminant myocarditis and AKI.

While there is a lot of focus on ARDS, due to similar presentation and radiologic features, pulmonary edema may be missed and patient may continue to be treated as ARDS. Many patients who present with ARDS may later develop pulmonary edema due to AKI or systemic sepsis or viral myocarditis and show rapid deterioration after a span of stabilization. Though case reports of such a presentation have been few but a possible risk cannot be ruled out.[19, 20] Also, the actual incidence of pulmonary edema may be downplayed in favor of ARDS due to similarities in presentation and lack of adequate diagnostic and therapeutic facilities due to limited resources.

Though no preventive strategy can be said foolproof but getting regular ECG, monitoring renal function and volume status, worsening of indicators sepsis may help indicate impending risk and initiate counter-measures.

The data regarding the secondary complications is still coming in and many of these are expected to change in coming time. Unlike the primary complications of the disease which we can do nothing to prevent, the secondary complications can be prevented and even treated well with available means. The number of secondary emergencies can be reduced with proper preventive strategies, keen sense of observation and keeping a high index of suspicion for all possibilities.

Specific guidelines are not available at present but with more and more data being gathered, disease specific protocols may emerge in the near future.

Summary

The battle with coronavirus is going to be a long and hard with a protracted course. Although the literature on Covid-19 has grown extensively,a lot of information regarding the entire clinical spectrum, complications, underlying pathophysiological mechanism and outcomes is still not complete. As the data and research into the subject grows, we'll get a better understanding of the disease. There is no way to predict the risk of developing serious Covid-19 disease or cure the disease itself but the complications arising out of it and the secondary emergencies can be prevented and treated well with existing means. Proper prophylaxis and early intervention in some of these complications may help bring down the disease specific mortality.

At present there is no vaccine or a curative strategy available, but hope lies in the fact that more than 80 clinical trials on various drugs and procedures are ongoing and a few vaccines have been approved for test in healthy volunteers. Till these give a successful result, our best weapon against the virus is prevention.

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Author information

1. Dr. Rishabh Kochar
Senior Resident, Department of Medicine,
Lady Hardinge Medical College and Associated Hospitals,
New Delhi, 110001
Address for correspondence-
B-3, 94, Sudarshana Nagar, Bikaner, 334003 (Raj), India
E-mai- rishkochar@gmail.com
Ph- +91-9871215080

2. Dr. Sanjay Kumar Kochar
Senior Professor
Head: Respiratory Division & I/c Malaria Research Center,
Nodal officer: Medical Education Unit & Multidisciplinary Research Unit
Coordinator: COVID-19
Department of Medicine, S.P. Medical College, Bikaner - 334003 (Raj),India
Adress: B-3/94, Sudarshana Nagar, Bikaner - 334003 (Raj), India
E-mail- drskkochar@rediffmail.com
Ph - +91-151-2200456, +91-9460128222

Severe Haemoptysis

Amitesh Gupta, Parul Mrigpuri

Introduction

Haemoptysis is a common presenting respiratory symptom which brings the patient to a pulmonary physician.Severe haemoptysis may be life threatening, which requires appropriate treatment and investigations on priority basis. It may present as a fatal episode with a mortality rate of up to 50% - 100% in the absence of adequate and early management. Severe haemoptysis includes major or massive haemoptysis.

Definition

Severe haemoptysis has been defined in different literatures so far available. Expectoration of 200 to 600 ml of blood in a day is defined as “major” haemoptysis, while the amount above this level is generally accepted as “massive” haemoptysis. Any amount of haemoptysis which leads to hemodynamic instability may be considered as severe haemoptysis. Severe haemoptysis constitutes 1% - 1.5% of all haemoptysis cases. It can be life threatening either as a result of aspiration and compromised gas exchange or because of circulatory collapse secondary to acute blood loss.

Causes and Pathophysiology

Haemoptysis has multiple causes usually categorized under four headings (Table 1)

Table 1:Causes of Haemoptysis

Bleeding may originate from small or large lung vessels. Most common causes of hemoptysis include bronchiectasis, tuberculosis, fungal infections and cancer.

Two arterial systems supply blood to lungs. Pulmonary arteries provide 99% of the arterial blood to the lungs and are involved in the gas exchange. The bronchial arteries supply to the extra and intrapulmonary airway sand to the pulmonary arteries. They also supply mediastinal lymphnodes and nerves, visceral pleura, esophagus, vasa vasorum of the aorta, and pulmonary veins. Complex capillary anastomoses exist between the pulmonary arteries and the systemic bronchial arteries.Whenever pulmonary circulation is compromised; the bronchial supply gradually increases

causing a hyper flow in the anastomotic vessels, which then become hypertrophic and break into the alveoliand bronchi, giving rise to hemoptysis. In chronic inflammatory diseases, the release of growth factors promotes neovascularization and pulmonary vessel remodeling with engagement of collateral systemic vessels which are fragile and prone to rupture.

Incidence for two major causes mechanisms responsible for of haemoptysis are: the systemic arteries [bronchial arteries and non-bronchial systemic arteries (NBSA)] in 90% of cases and the pulmonary arteries in fewer than ~~under~~ 10% of cases. Identifying the origin of bronchial arteries before treatment is helpful because over 30% have an abnormal origin which may lead to endovascular treatment failure. Bronchial arteries commonly originate from the upper portion of the descending thoracic aorta. If the arteries arise from the descending aorta at the level of the vertebral bodies of T5–T6, the origin is defined as orthotopic. When the bronchial arteries originate at other levels, including aortic branches, they are defined as ectopic. Common ectopic origins include inferior aspect of the aortic arch, subclavian artery, brachiocephalic trunk, thyrocervical trunk, internal mammary artery, costocervical trunk, pericardiophrenic artery, inferior phrenic artery, abdominal aorta, and coronary arteries.

Diagnosis and Management

History and Physical Examination: history should focus on determining the anatomic origin of bleeding and to exclude hematemesis and causes of pseudo-hemoptysis.

Pseudo-hemoptysis is defined as spitting of blood that does not originate from lungs, ~~The origin of blood may be~~ from oral cavity, larynx, oesophagus or stomach. Once sources of bleeding other than the lower respiratory tract have been excluded, specific aetiologies can be considered (Table 1).

A detailed history of non-pulmonary symptoms suggestive of underlying disease should be taken e.g. history of orthopnoea, pedal oedema, paroxysmal nocturnal dyspnoea should be taken to exclude cardiac cause.

Physical examination should begin with determination of cardiopulmonary status and the need for resuscitation. Severe haemoptysis usually warrant admission. Criteria for admission to the intensive care unit or for referral to a specialty centre for expedited evaluation are defined. (Table 2). Hemodynamic instability, abnormal gas exchange, cardiopulmonary comorbidities, and lesions at high risk of massive bleeding require inpatient evaluation. Table 3 mentions the initial investigations to be done while evaluating a case of haemoptysis.

Table 2: Indications for admission to the intensive care unit or referral to speciality centre**.**

Table-3: Suggested initial tests in patients with massive haemoptysis.

The goals of management of haemoptysis include:

- Maintenance of airway,
- Localization of site of bleeding to control haemorrhage and
- Treatment of underlying cause.

- In patients of severe haemoptysis, efforts must be made to look for the etiological cause of haemoptysis.
- Chest imaging may provide insight about the aetiology, as well as guide further resuscitation and evaluation.
- Once the bleeding site has been determined, the patient should be placed in the lateral decubitus position with the affected lung down to prevent pooling of blood in the normal lung and airway.
- Rapid bleeding may require immediate airway control with rigid bronchoscopy or endotracheal intubation to maintain the airway.
- For stable patients with no identifiable lesion on chest radiography or bronchoscopy, chest CT (computed tomography) angiography and/or bronchial artery arteriography with or without embolization should be performed to guide treatment.
- Patients with active pulmonary tuberculosis should be started on anti- tubercular treatment.
- The cases with pyogenic lung infection should be managed with antibiotics.
- Blood transfusion may be given to maintain haemoglobin meanwhile the cause for haemoptysis is searched.
- Intravenous fluids may be given to maintain the hemodynamic status.

Role of bronchoscopy in severe haemoptysis: Bronchoscopy performed with either a rigid or flexible scope is helpful in diagnosis of haemoptysis and localization of bleeding site. Although rigid bronchoscopy has a better role in severe haemoptysis due to its ability to maintain airway, severe haemorrhage may interfere with the visualization of airway and use of scope may cause recurrent bleeding because of mucosal irritation. Bleeding site if identified, balloon inflation or laser coagulation may be used to control haemorrhage. Bronchoscopy also provides information regarding endobronchial lesions and allows sampling for tissue diagnosis and microbial cultures.

The use of CT angiography in severe haemoptysis: It is a non-invasive and highly useful radiological investigation and allows detailed evaluation of lung and vascular structures.

MDCTA (Multidetector Computed Tomographic Angiography) should be performed in deep inspiration if possible, failing which it should be performed in free respiration. Coverage should begin from the lung apices (C5-C6) to the hilum of the kidneys (L1-L2), from the supra-aortic vessels to the origin of the inferior diaphragmatic arteries. Signs of systemic bleeding in MDCTA are indirect, where as signs of pulmonary arterial involvement are direct.

When a MDCTA is requested for haemoptysis, bleeding from the pulmonary artery must firstly be excluded, looking for direct signs, although in some cases both mechanisms may be involved.

MDCTA allows a conclusion to be drawn that the haemoptysis has its origin in a systemic artery by excluding a pulmonary arterial mechanism. It visualizes the bronchial arteries (BA) and the non-bronchial systemic arteries responsible for the bleeding. It allows evaluation of distal airways beyond level of bronchoscope however it has limited role in characterization of endobronchial lesions.

MDCT helps in recognition of arterial supply before endovascular treatment and assists in selecting ectopic vessels amenable to embolization thus preventing recurrence of haemoptysis.

Embolization of systemic arteries (BA and NBSA): In majority of situations, the approach is via the right femoral artery after inserting a 5-F introducer. By referring to MDCTA findings, arteries feeding the bleeding area are catheterized and an angiography series is then performed.

Pulmonary artery vascular occlusion: In most situations, the approach via the right femoral vein is sufficient, using a 7- or 8-French introducer. In specific situations for anatomical reasons, such as a raised right hemidiaphragm and past history of right middle and lower lobe lobectomies, the internal jugular approach is preferred. The occlusion should be as close as possible to the pulmonary artery lesion responsible for the bleeding. Proximal occlusion is sufficient for a distal, acute rapid process or in cancer. Sandwich occlusion is preferred to avoid the recurrence of the bleeding through the systemic vessels in inflammatory and chronic infectious processes, particularly tuberculosis.

Bronchial artery embolization provides immediate control of haemoptysis in over 80% of cases (65 to 92%) depending on the underlying disease. Control is more effective with

cryptogenic haemoptysis, bronchiectasis or tuberculosis whereas this is less effective in aspergillosis or lung cancer. Early recurrence occurs in 10 to 20% of cases. The immediate response should be a further review of the MDCTA looking for other bronchial systemic arterial conditions, either of atypical origin, or ectopic, a NBSA supplying the territory responsible for the bleed or alternatively a pulmonary source which was not initially seen. Long-term recurrence after bronchial arterial embolization occurs in 10 to 60% of cases and is due either to recanalization of the embolized vessels or due to further hypervascularization when the cause for it remains. This is common in aspergilloma and cancer.

Role of surgery: Surgery is the management of choice in cases of iatrogenic pulmonary artery rupture, hydatid cyst, leaking aortic aneurysm and chest trauma. It is considered in management of localised lesions only. Its main limitation is that surgery cannot be performed in unstable patients with inadequate respiratory reserve.

Management of haemoptysis in different clinical settings is important, especially in case of severe bleeding, which represents a life-threatening condition. Imaging, especially MDCTA, has an important role in identification of a possible cause for bleeding. Systemic bronchial and non-bronchial arteries are identifiable on MDCTA and play a major role in massive bleeding. Knowledge of normal and variant anatomy of these arteries is crucial for the planning of endovascular embolization. Currently, arterial embolization is the most effective and minimally invasive procedure for treating massive and recurrent haemoptysis.

Recommended Reading

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Table 1 : Causes of Haemoptysis

Parenchymal source	Tracheobronchial source	Primary vascular source	Other rare causes
Tuberculosis and its Sequelae	Bronchiectasis	Arteriovenous malformation	Systemic coagulopathy oriatrogenic (anticoagulants / thrombolytic agents)
Pneumonia	Neoplasm	Pulmonary embolism	Catamenial haemoptysis (pulmonary endometriosis
Mycetoma ("fungus ball")	Bronchitis	Elevated pulmonary venous pressure	Dieulafoy`s disease of the bronchus
Lung abscess	Broncholithiasis	Pulmonary artery rupture	Cryptogenic haemoptysis
Lung contusion	Airway trauma		
Idiopathic pulmonary hemosiderosis	Foreign body		
Wegener granulomatosis			
Lupus pneumonitis			
Goodpasture syndrome			

Table 2 : Indications for admission to the intensive care unit or referral to speciality centre.

1. Aetiology with high risk of bleeding (e.g., aspergillosis, lesions with pulmonary artery involvement)
2. Gas-exchange abnormalities (respiratory rate > 30 breaths/minute, oxygen saturation < 88% in room air, or need for high flow oxygen [> 8 L/ per minute] or mechanical ventilation)
3. Hemodynamic instability (haemoglobin < 8 g /per dl or a decrease of more than 2 g/ per dl frombaseline, consumptive coagulopathy, or hypotension requiringfluid bolus or vasopressors)

4. Massive haemoptysis (> 200 mL in per 48 hours or > 50 mL/episode in patients with chronic pulmonary disease)
5. Respiratory comorbidities (e.g., previous pneumonectomy,chronic obstructive pulmonary disease, cystic fibrosis)
6. Other comorbidities (e.g., ischemic heart disease, need foranticoagulation)

Table 3 : Suggested initial tests in patients with massive haemoptysis.

Tests	Indications
Blood typing and crossmatch	For patients with hemodynamic instability from blood loss or in whom complete blood count reveals anaemia that warrants transfusion
Chest radiography	For all patients with haemoptysis; may help localize bleeding and identify aetiology; provides images for later comparison to evaluate resolution of disease
Coagulation studies	For patients with a history of coagulopathy or current anticoagulant use
Complete blood count	For all patients with haemoptysis to rule out thrombocytopenia and to evaluate for anaemia
Renal function testing	Should be obtained before imaging with edia and in patients with suspected vasculitis
Sputum testing (Gram stain, acid-fast bacilli smear, fungal cultures, cytology)	Should be obtained if massive haemoptysis or an infectious aetiology is suspected

Respiratory Failure in Non-COPD Patients

K. Sailaja

Though COPD is the leading cause of disease burden in a pulmonary unit, many other conditions pose a diagnostic and a management challenge when seen in the emergency or the critical care unit.

Definition

Respiratory failure is a condition in which the respiratory system fails in one or both of its gas exchanging functions

- Oxygenation of mixed venous blood
- Carbon dioxide elimination from mixed venous blood
- Mixed venous blood is carried through the pulmonary arteries

Classification

Depending upon the arterial partial pressure of oxygen and carbon dioxide levels, respiratory failure may be classified as ***hypercapnic*** or ***hypoxemic*** (Table - 1). In many cases, hypercapnic and hypoxemic respiratory failure coexists. Disorders that initially cause hypoxemia may be complicated by respiratory pump failure (see below) and hypercapnia. Conversely, diseases that produce respiratory pump failure are frequently complicated by hypoxemia due to secondary pulmonary parenchymal processes (e.g., pneumonia or atelectasis) or vascular disorders (e.g., pulmonary embolism).

Table 1 : Classification of respiratory failure

Respiratory failure	**Onset -** Acute or, Chronic
Hypoxemic Pa_{O2} < 55 mm of Hg. on FiO_2>0.6 or more	Acute - Develops in minutes to hours Chronic- Develops over several days or longer
Hypercapnic Pa_{CO2} > 45mm of Hg.	

Abbreviation: Pa_{CO2}- Arterial P_{CO2} ; Pa_{O2} - arterial P_{O2} ();FI_{O2} - Oxygen in inspired air () FiO_2

Pathophysiology

Respiratory failure can result from an abnormality in any of the "effector" components of the respiratory system listed below: –

Effector Components

- CNS efferent
- Peripheral nerves
- Respiratory muscles, chest wall
- Airways
- Alveoli
- Dead space ventilation (VE)
- Minute alveolar ventilation (VA)
- $PaO_{2,}$ $PaCO_2$
- Chemo-receptors
- Afferent integration in CNS

Central nervous system, peripheral nervous system, respiratory muscles and chest wall, and airways constitute 'respiratory pump.

Hypoxemic Respiratory Failure

In vide variety of diseases associated with hypoxemia, four pathophysiological mechanisms seems to be operating:

- Alveolar hypoventilation.
- Ventilation–perfusion mismatch,
- Shunt, and
- Diffusion limitation

Alveolar hypoventilation occurs in neuromuscular disorders that affect the respiratory system

In the absence of underlying pulmonary disease, the hypoxemia accompanying alveolar hypoventilation is characterized by a normal alveolar–arterial oxygen gradient.

On the contrary, disorders in which any of the other three mechanisms are operative are characterized by widening of the alveolar–arterial oxygen gradient, which is normally less than 20 mm Hg.

With ***ventilation–perfusion mismatching***, areas of low ventilation relative to perfusion contribute to the hypoxemia. Similarly, with ***shunt,*** intrapulmonary or intracardiac, deoxygenated mixed venous blood bypasses ventilated alveoli, resulting in "venous admixture."And in diseases associated with ***diffusion limitation***, there is impairment of oxygen transport across the alveolar-capillary membrane.

Hypercapnic Respiratory failure

At a constant rate of CO_2 production, $PaCO_2$ is determined by the level of alveolar ventilation. The relationship between alveolar ventilation, rate of CO_2 production and $PaCO_2$ is described by the equation:

$$\mathbf{PAO_2 - PaO_2 = [PIO_2 - PaCO_2/R] - PaCO_2}$$

Where

PAO_2 = alveolar PO_2

PaO_2 = arterial PO_2

PIO_2 = inspired PO_2

$PaCO_2$ = arterial PCO_2

R = respiratory exchange ratio

So according to the equation, it is ventilatory supply versus demand. There are clinical situation responsible for respiratory failure with different pathophysiological mechanisms leading to decrease ventilatory supply or increase ventilatory demand.

Table 2 : Factors that diminish ventilatory supply

Factor		Clinical Examples
Decreased respiratory muscle strength	Muscle Fatigue	• Recovery from acute respiratory failure, • High respiratory rates • Increase inspiratory time
	Disuse atrophy	• Prolonged mechanical ventilation, • Following phrenic nerve injury
Increased muscle energy requirement or decreased substrate supply	High elastic work of breathing	• Low lung or chest wall compliance • High respiratory rate
	High resistive work of breathing	• Airway obstruction
	Reduced diaphragm perfusion	• Shock • Anaemia
Decrease motor neuron function	Decreased phrenic nerve output	• Polyneuropathy, • Guillain-Barre syndrome • Phrenic nerve transaction or injury • Poliomyelitis
	Decreased neuromuscular transmission	• Myasthenia gravis • Use of paralyzing agents
Abnormal respiratory mechanics	Airflow limitation	• Bronchospasm • Upper airway obstruction • Excessive airway secretions
	Loss of lung volume	• After lung resection • Large pleural effusion
	Other restrictive defects	• Pain-limited inspiration • Tense abdominal distension due to ileus • Peritoneal dialysis fluid, or ascites
Malnutrition		• Protein-calorie starvation
Electrolyte abnormalities		• Low serum phosphate • Low potassium concentrations
Arterial blood gas abnormalities		• Low pH, - Llow PaO_2, - High PaO_2
Fatty infiltration of diaphragm		• Obesity
Unfavourable alternation in diaphragm length-tension relationship		• Flattened domes of diaphragm cause by hyperinflation

Modified: Source Data from Lanken PN. Pathophysiology of respiratory failure. In: GrippiMA.ed. Pulmonary Pathophysiology. Philadelphia. PA: JB Lippincott; 1995.

Table 3 : Factors that increase ventilatory supply

Factor	Clinical Examples
Increased V_D/V_T	Acute asthma, emphysema, late phase of acute respiratory distress syndrome, pulmonary emboli
Increased Vo_2	Fever, sepsis, trauma, shivering, increased work of breathing, massive obesity
Increased RQ	Excessive carbohydrate feeding
Decreased $PaCO_2$	Hypoxemia, metabolic acidosis, anxiety, sepsis, renal failure, hepatic failure
Abbreviations; V_D- dead space volume; V_T - tidal volume; Vo_2. rate of oxygen consumption;RQ-respiratory quotient (the respiratory exchange ratio in the steady state); $PaCO_2$. arterial PCO_2 *Source: Data from Lanken PN. Pathophysiology of respiratory failure. In: GrippiMA. ed. Pulmonary Pathophysiology. Philadelphia. PA: JB Lippincott; 1995.*	

Approach to the patient

- Begins with clinical suspicion of its presence
- Confirmation based on arterial blood gas analysis
- Evaluation of underlying cause
- Look for OTHER SIGNS
  - Abdominal pain in acute pancreatitis
  - Leg pain due to long bone fracture
  - Neurological symptoms like restlessness,anxiety,confusion, tremors
  - Cardiovascular signs like tachycardia,shock

A close clinical examination usually gives a clue to the cause of respiratory failure

Principles of Management

Principles of management in acute respiratory failure would include general and cause specific

1. Triage decisions –
   a. The first step is to determine the appropriate setting for the care.
   b. Admission to a standard inpatient medical floor(Intensive care),.
   c. Access for:

- acuity of respiratory failure,
- degree of hypoxaemia, hypercapnia, acidaemia,
- presence of comorbidities like cardiac failure or renal insufficiency

2. Airway Management–
   a. Assurance of an adequate airway is the key to manage a patient of acute respiratory failure. The decision to choose a specific method of support is taken in view of the diagnosis, the values of the blood gas and the acuity of the hypoxaemia.
   b. Endotracheal intubation and mechanical ventilation to be considered with severe hypoxaemia and hypercapnia
   c. NIV support may be considered in patients of COPD,pulmonary oedema,OSA when the respiratory failure is relativelyearly
3. Addressing the underlying cause – All the strategies are aimed at supporting the patient in the critical phase while the underlying cause is corrected.

Monitoring

The key to success of managing a patient of respiratory failure is to recognise and deal with deterioration or complications as early as possible.

Complications

These pertain to the underlying physiological abnormality as well as the interventions done to support the patient.

The management of acute respiratory failure is an art and many a time these patients also require a post-acute care. This care may translate into a domiciliary support, with long term oxygen or NIV. A careful discharge plan is warranted while sending the patient home.

Pulmonary	**Cardiovascular**
• Pulmonary emboli • Pulmonary barotrauma (interstitial emphysema, pneumothorax, subcutaneous emphysema, pneumoperitoneum, tension lung cyst, subpleural air cyst • Pulmonary fibrosis	• Hypotension • Arrhythmias • Decreased cardiac output • Myocardial infarction • Pulmonary hypertension

Related to Use of Mechanical Devices

- Complications of mechanical ventilation (infection, arterial desaturation, hypotension, barotrauma, others)
- Complications of insertion and maintenance of pulmonary artery catheter (pneumothorax, air embolism, arrhythmias, infection, thrombosis, pulmonary artery rupture)
- Complications of tracheal intubation
  - Related to prolonged intubation attempt (hypoxemic brain injury, cardiac arrest, seizures, others)
  - Related to right main bronchus intubation (hypoventilation, pneumothorax, atelectasis)
  - Self – or inadvertent extubation
  - Endotracheal tube dislodgment
  - Endotracheal tube cuff leak
  - Injury to pharynx, larynx, trachea
  - Complication of tracheotomy (pneumothorax, bleeding, tube dislodgment, tracheoinnominate fistula, tracheoesophageal fistula, tracheal stenosis)

Gastrointestinal	**Renal**
• Hemorrhage (including "stress" ulceration) • Ileus Diarrhea	• Acute renal failure Fluid retention
Infectious	**Nutritional**
• Nosocomial pneumonia • Bacteremia • Sepsis • Paranasal sinusitis	• Complications of underlying malnutrition (decreased respiratory muscle strength, immune suppression, others) • Complications of enteral feeding (pneumothorax, pleural effusion, sinusitis, aspiration, diarrhea) • Complications of parenteral feeding (pneumothorax, sepsis, hyperglycaemia, hyperosmolar coma, hypophosphatemia, liver function test abnormalities) • Complications of refeeding (hypercapnia)

Other

- Psychiatric (anxiety, depression, confusion, sleep dysfunction, psychosis)

Hematologic (anaemia, thrombocytopenia)

Suggested readings:

1. Fishman's Pulmonary Diseases & Disorders, 5th Edition
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Acute Respiratory Distress Syndrome

Vitull K. Gupta, Meghna Gupta, Varun Gupta

Acute respiratory distress syndrome (ARDS) is a relatively common, disabling, lethal or life threatening form of acute respiratory failure characterized by inflammatory pulmonary edema resulting in severe hypoxemia[1] initially described by Ashbaugh and colleagues in 1967.[2] Originally, it was known as adult respiratory distress syndrome and was later changed to acute respiratory distress syndrome. ARDS represents an acute response to diverse etiologies, risk and trigger factors, resulting in bilateral lung opacities on radiography and hypoxemia. In this chapter, we will discuss the key features of ARDS. ARDS is common, and is associated with significant morbidity with frequent mortality and represents an important public health problem.

Definition

ARDS was first defined in 1994 by the American-European Consensus Conference (AECC) as the acute onset of hypoxemia (arterial partial pressure of oxygen (PaO2) to fraction of inspired oxygen (FIO2) [$PaO_2/FIO_2 \leq 200$ mm Hg], acute lung injury (ALI) with bilateral infiltrates on chest radiograph, with no evidence of left atrial hypertension.[3] In 2011, a consensus Berlin definition of ARDS was developed by a panel of experts, an initiative of the European Society of Intensive Care Medicine endorsed by the American Thoracic Society and the Society of Critical Care Medicine.[4] Definitions of ARDS which have evolved over the years have retained the central features of the initial description by Ashbaugh and colleagues. All definitions are based on the clinical features and chest imaging because currently no validated diagnostic tools are available to measure lung permeability, edema, inflammation or diagnostic biomarkers.[5] American–European Consensus Conference (AECC),[3] Berlin[6] and Kigali[7] criteria for ARDS are discussed in table below.

Table 1 : American–European Consensus Conference (AECC), Berlin and Kigali criteria for ARDS

	AECC definition	Berlin criteria	Kigali modification of Berlin criteria
Timing	Acute onset	Within 1 week of a known clinical insult or new or worsening respiratory symptoms	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Oxygenation	P_{aO2}/F_{iO2} ≤200 mmHg (defined as acute lung injury if ≤300 mmHg)	***Mild*****:** P_{aO2}/F_{iO2} >200 mmHg but ≤300 mmHg ***Moderate:*** P_{aO2}/F_{iO2} >100 mmHg but ≤200 mmHg **Severe**: P_{aO2}/F_{iO2} ≤100 mmHg	S_{pO2}/F_{iO2} ≤315
PEEP requirement	None	Minimum 5 cm H_2O PEEP required by invasive mechanical ventilation (noninvasive acceptable for mild ARDS)	No PEEP requirement, consistent with AECC definition
Chest imaging	Bilateral infiltrates seen on frontal chest radiograph	Bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or CT	Bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or ultrasound
Origin of oedema	Pulmonary artery wedge pressure <18 mmHg when measured or no evidence of left atrial hypertension	Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment, such as echocardiography, to exclude hydrostatic oedema if no risk factor present)	Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment, such as echocardiography, to exclude hydrostatic oedema if no risk factor present)

(PEEP: positive end-expiratory pressure; P_{aO2}: arterial oxygen tension; F_{iO2}: inspiratory oxygen fraction; S_{pO2}: arterial oxygen saturation measured by pulse oximetry; CT: computed tomography.)

Compared with the AECC definition, the Berlin definition had a better prediction for mortality with increased percentage of mortality associated with increasing stages of ARDS: mild 27%, moderate 32%, and severe 45% with 95% CI.[6] The severity of ARDS

is classified according to the degree of hypoxemia (PaO2/FIO2 ratio), with mutually exclusive categories of mild (PaO2/FIO2, 201–300), moderate (PaO2/FIO2, 101–200), and severe (PaO2/FIO2 <100) (2).[6]

Epidemiologic Features

Population-based estimates of ARDS range from 10 to 86 cases per 100,000, with the highest rates reported in Australia and the United States. In low-income countries, ARDS is likely to be underreported because of limited resources to obtain chest radiographs and measure arterial blood gases.[8]

Pathogenesis

ARDS occurs as a consequence of an alveolar injury due to various causes producing diffuse alveolar damage causing release of pro-inflammatory cytokines (tumor necrosis factor, interleukin (IL)-1, IL-6, IL-8), which recruit neutrophils to the lungs, where they get activated and release toxic mediators (reactive oxygen species and proteases) that damage the capillary endothelium and alveolar epithelium leading to alveolar edema,[1] which eventually, leads to the impairment of gas exchange, decreased lung compliance and increased pulmonary arterial pressure. Injury response manifests in three phases:

- **Exudative phase** (acute phase 1–6 days): This phase represents lung's initial response to injury. It is characterized by innate immune cell–mediated damage of the alveolar endothelial and epithelial barriers and accumulation of protein-rich edema fluid within the interstitium and alveolus. Resident alveolar macrophages secrete proinflammatory cytokines, leading to neutrophil and monocyte or macrophage recruitment, as well as activation of alveolar epithelial cells and effector T cells, to promote and sustain inflammation and tissue injury.[9] Endothelial activation and microvascular injury also contribute to the barrier disruption in ARDS and are worsened by mechanical stretch leading to diffuse alveolar damage.
- **Proliferative phase** (subacute phase 7–14 days): The repair processes initiated during the proliferative phase is essential for host survival. It is characterized by resolution of pulmonary edema, attempts to repair by proliferation of type II alveolar cells, squamous metaplasia, interstitial infiltration by myofibroblasts and early deposition of collagen, the provisional matrix restores alveolar architecture and function. There may also be infiltration of fibroblasts and some evidence of collagen deposition.

- **Fibrotic phase** (chronic phase after 14 days): The final or fibrotic phase does not occur in all patients. Some patients progress to fibrotic phase, characterized by obliteration of normal lung architecture, diffuse fibrosis and cyst formation.[10]

There is resolution of the acute neutrophilic infiltrate (unless there has been superimposed nosocomial pneumonia) with more mononuclear cells and alveolar macrophages in the alveoli. In many patients, gradual resolution of the edema and acute inflammation takes place without fibrosis.

Risk Factors

ARDS is not a disease, but a clinical syndrome presenting with acute respiratory failure as a result of clearly determined pulmonary and nonpulmonary predisposing factors[11] [12] but there is insufficient awareness about environmental and individual risk factors. Chronic alcohol abuse and active or passive cigarette smoke have been associated with an increased incidence of ARDS.[13] The impact of environmental pollution on the incidence of ARDS has not been established. Role of vitamin D deficiency as a risk factor is debated.

Table 2 : Common risk factors for ARDS[1,10]

Direct	Indirect
Pneumonia	Non-pulmonary sepsis
Aspiration of gastric contents	Major trauma
Inhalation injury	Pancreatitis
Pulmonary contusion	Severe burns
Pulmonary vasculitis	Non-cardiogenic shock
Drowning	Drug overdose
	Multiple transfusions or transfusion associated acute lung injury (TRALI)

Genetic features and biomarkers

ARDS does not develop in the majority of patients with clinical risk factors, suggesting that other factors like genetic susceptibility play an important role in the pathogenesis of ARDS, which inturn is influenced by differences in coexisting conditions (e.g., pneumococcal pneumonia after splenectomy), virulence factors (e.g., H1N1 influenza) and environmental exposures (alcohol use or active smoking and injurious mechanical-ventilation practices).[14]

Genetic studies suggest that about 40 genes influence the development or outcome of ARDS, including the genes encoding interleukin 10 (*IL-10*), angiotensin-converting enzyme (*ACE*), vascular endothelial growth factor (*VEGF*), tumor necrosis factor (*TNF*) as well as *SOD3*, *MYLK*, *NFE2L2*, *NAMPT*, and *SFTPB*.[15]

Adverse outcomes of ARDS have been linked to increased levels of certain plasma biomarkers like markers for epithelial injury (receptor for advanced glycation end products and surfactant protein D), dysregulated coagulation (low protein C and high plasminogen activator inhibitor 1 levels), systemic inflammation (interleukin- 6 and interleukin-8) and endothelial injury (angiopoietin 2). Study of these biomarkers may help explain pathogenesis of ARDS and help in identifying treatment-responsive subtypes of ARDS.[5]

Prevention

ARDS takes about 2 days to develop after hospitalization, giving very little time for implementation of preventive strategies for ARDS.[16] [17] Studies suggest that strategies like efficient ICU care under intensivist, early volume resuscitation, antibiotics for sepsis, lower tidal volumes for all mechanically ventilated patients and restrictive use of blood products (to reduce the risk of transfusion-associated lung injury and volume overload) help prevent the development of nosocomial ARDS.[14]

Glucocorticoids, aspirin, statins and beta-agonists have failed in prevention trials, although inhaled beta-agonists prevented high-altitude pulmonary edema.

Results of a small study suggested that combination of beta-agonists and glucocorticoids prevented the development of ARDS, but failed to provide mortality benifits.[14]

Classification of the severity of ARDS and use of traditional clinical variables or severity-of-illness scores, such as the Acute Physiology, Age, and Chronic Health Evaluation (APACHE) III score, were not useful to identify treatment-responsive subtype of ARDS, where as assessment of plasma biomarkers was helpful to device treatment strategies.[5]

The timing of treatment remains a major challenge of ARDS prevention trials and current evidence suggests that ARDS may not preventable.[18]

Treatment

Treatment of ARDS is mainly supportive, focusing on limiting further injury to the lungs by lung-protective ventilation to prevent ventilator-associated lung injury[19] conservative fluid therapy to prevent or reabsorb edema of lung along with identification

and treatment of the underlying causes like sepsis-associated ARDS is treated with early resuscitation, appropriate antibiotic agents and control of source of infection.[20]

Lung protective ventilation

Invasive mechanical ventilation (IMV) with lung protective strategies is the mainstay of ARDS treatment. Lung-protective ventilation has reduced the mortality of ALI from 40% in 2000 to 25% in 2006.[21]

Current clinical practice guidelines by professional societies[22] recommend low tidal volume and air pressure IMV. ARDS Network trial has shown that IMV with lower tidal volumes (LTV) and airway pressures (tidal volume of 4–6 ml/kg predicted body weight and maintenance of plateau pressure between 25 and 30 cm H_2O) as compared to conventional approach of higher TV, resulted in an absolute reduction of mortality in ARDS.[23]

A PEEP of at least 5 cm of water is recommended, but a meta-analysis of trials in patients with moderate-to-severe ARDS suggests that mortality increases with relatively low PEEP, as compared to a higher PEEP (a mean initial PEEP of approximately 16 cm of water).[22] The optimal PEEP required is unclear.[24] A rational approach of adjusting PEEP or tidal volume in proportion to the patient's respiratory system compliance is suggested which minimizes the driving pressure (the difference between plateau airway pressure and PEEP), thus balancing the opening of the lung and preventing atelectrauma against overdistention (limiting volutrauma).[25]

But evidence also suggests that any level of tidal volume or airway pressure which may be safe in uninjured lung, may not be safe in ARDS or ALI patients and may cause volutrauma (regional over distention), atelectrauma (by repetitive opening and closing of alveoli) and biotrauma (injury to epithelial and endothelial) in injured lung further increasing the injury and inflammation.

Long-term intubation may carry a high rate of complications, such as ventilator-associated pneumonia (VAP), delirium and critical illness myopathy and neuropathy. The optimal approach to lung-protective ventilation is unknown.

Prone ventilation

Prone ventilation is presently recommended in cases of moderate-to-severe ARDS (Pao2/ Fio2 <120 mm Hg) as it is associated with improved oxygenation and reduced mortality.[22] Beneficial effect of prone position is because of decrease in trans-pulmonary pressure gradient helping in recruiting the collapsed areas of the lung without causing significant increase in the airway pressures and reducing the risk of ventilator associated lung injury through the combined effects of more uniform distribution of

ventilation and less compression of the left lower lobe by the heart.[26] Prone ventilation was found to be significantly effective in obese patients with ARDS than in non-obese patients.[27]

High-frequency oscillatory ventilation (HFOV)

HFOV seems to be ideal for lung protection in ARDS, but evidence suggests that it offers no advantage over conventional ventilation strategies and may be harmful. A study showed no 30-day survival or cost benefit of HFOW in patients[28] though a patient-level meta analysis has suggested a benefit when the Pao2:Fio2 ratio is less than 60mm Hg.[29] Another meta-analysis showed no improvement with HFOW in survival in ARDS patients, although there was no increase in the risk of barotrauma or hypotension and also reduced the risk of oxygenation failure.[30]

Airway pressure release ventilation

Airway pressure release ventilation (i.e., applied continuous positive airway pressure that at a set interval releases the applied pressure) may improve oxygenation and tolerance of mechanical ventilation but has not been proven to reduce mortality. Both these ventilation strategies may improve oxygenation by increasing the mean airway pressure, which may adversely affect hemodynamics.

Noninvasive ventilation (NIV)

NIV and continuous positive airway pressure (CPAP) is commonly used in mild ARDS, but its use in acute hypoxaemic respiratory failure is controversial and the choice of the interface device is still debated.[31] [32] NIV may increase the risk of death in patients with severe hypoxemia. Oxygen administration through high-flow nasal cannulae and NIV provided with a helmet may be effective alternatives to IMV in patients with less severe ARDS. Both approaches have the potential to reduce respiratory drive and the risk of ventilation-induced lung injury.[33] [34]

Neuromuscular blockage

Neuromuscular blocking agents (NMBAs) are commonly used in ARDS, but its use is controversial. Use of short term NMBAs in ARDS patients have shown a beneficial outcome mainly by decreasing the barotrauma and ventilator-induced lung injury in a meta-analysis.[35] [36] NMBAs have shown to improve outcomes in patients with moderate to-severe ARDS (Pao2:Fio2, <150 mm Hg) as compared to deep sedation alone, may be because neuromuscular blockage ensures patient–ventilator synchrony, reducing the risk of ventilator-associated lung injury.[37] Deep sedation when given alone may be associated with deleterious effects.

Fluid conservative therapy

Fluid conservative therapy has shown benefits in ARDS patients in shortening the duration of assisted ventilation, but doesn't improve survival[38] and the benefit appears to occur largely after reversal of shock.[39] In ARDS patients, due to increased alveolar vascular permeability, there is presence of alveolar edema, which may worsen as a consequence of fluid overload. Small randomized trials of diuretics and albumin after the shock reversal showed improved oxygenation and decreased duration of IMV,[40] but a larger trial did not show mortality reduction with the use of albumin in general ICU patients.[41] For nutritional support, aggressive early caloric supplementation with parenteral nutrition may be harmful.

Intravenous β-2 agonist in ARDS

A single center RCT, showed benefit of intravenous infusion of Salbutamol for 7 days in ARDS patients, by causing significant reductions in extravascular lung water and plateau airway pressures[42] but a multicenter RCT, showed no benefit of intravenous Salbutamol in ARDS patients and showed significant detrimental effects with increase in mortality.[43]

Corticosteroids in ARDS

Role of systemic glucocorticoids in ARDS patients is a debate for past decades. ARDS is considered to be an acute lung inflammatory disease as pulmonary and systemic inflammations play an important role in the pathogenesis and progression of ARDS[44] but corticosteroids with strong anti-inflammatory properties have not shown mortality benefits.

A meta-analysis and review of 8 RCTs and 10 cohort studies concluded that corticosteroids may be harmful in some patients and should not be routinely used in ARDS.[45] Consensus exists about initiation of glucocorticoids if needed, before 14 days of ARDS and in absence of large RCTs, a meta-analysis [46] reinforces the role of prolonged low dose and slowly tapered glucocorticoids in the management of ARDS.

Another study suggested that glucocorticoids may improve oxygenation and airway pressures and, in patients with pneumonia, may hasten radiographic improvement, but may not be associated with a consistent mortality benefit and are harmful if started 14 days or more after ARDS has been diagnosed.[47]

Extracorporeal membrane oxygenation (ECMO)

ECMO may be indicated in patients of very severe ARDS (Pao2:Fio2, <60 mm Hg) when no improvement in oxygenation is observed after adequate lung protective and fluid

restrictive therapy. One randomized trial suggested benefit with ECMO, but failed to show if the benefit was because of ECMO or good specialized care, since all referred patients were not treated with ECMO.[48]

Pharmacologic Therapy

A large number of pharmacologic therapies including glucocorticoids, surfactants, inhaled nitric oxide, antioxidants (procysteine [l-2-oxothiazolidine- 4-carboxylic acid]),, protease inhibitors, neutrophil elastase inhibition, anticoagulation, nonsteroidal anti-inflammatory agents (ketoconazole and lysofylline), statins, albuterol, and a variety of other anti-inflammatory treatments have been evaluated in trials for the treatment of ALI/ARDS, but none of these agents has been proven to be effective, although some of them may be effective in a subgroup of patients with specific causes of lung injury. Unfortunately, no pharmacologic therapy for ARDS has been shown to reduce either short-term or long-term mortality.[5]

A novel therapeutic approach in early clinical development involves intravenous delivery of mesenchymal stem cells, which interact with injured tissue through the release of multiple soluble bioactive factors.[49]

Table 3 : Management of ARDS

Measures	Procedure
Maintenance of Oxygen Levels	• Intubation/mechanical ventilation (most patients) • Noninvasive ventilation for mild ARDS or to ↓ intubation rates (helmet better than face mask)
Anti-inflammatory agents (corticosteroids)	• Low doses methylprednisolone (1 mg/kg/day) helps to resolve ARDS
Fluid management	• To maintain central venous pressure <4 mmHg or PAOP <8 mmHg to prevent pulmonary oedema
Prone position in bed	
Decrease oxygen consumption	• Antipyretics, light sedatives, analgesics etc
Increase oxygen delivery	• Inotropics to increase filling pressure (if no pulmonary oedema) • Restrict transfusions to maintain hemoglobin between 7–9 g • Inhaled vasodilators (nitric oxide, prostacyclin and prostaglandin E1) to improve V'/Q' matching

Measures	Procedure
Supportive care	• Sedation and analgesia • Neuromuscular blockade if severe ARDS • Haemodynamic monitoring/management *via* CVC • Nutritional support • Maintenance of Blood Glucose levelsontrol • VAP prevention and treatment • DVT prophylaxis • Gastrointestinal (stress ulcers) prophylaxis • Care of bladder, bowel & back

(PAOP: pulmonary arterial occlusion pressure; V'/Q': ventilation/perfusion; CVC: central venous catheter; VAP: ventilator-associated pneumonia; DVT: deep vein thrombosis.)

Conclusions

ARDS is a relatively common, disabling and lethal or life threatening form of acute respiratory failure characterized by inflammatory pulmonary edema resulting in severe hypoxemia. ARDS occurs as a consequence of an alveolar injury due to various pulmonary and nonpulmonary predisposing factors producing diffuse alveolar damage. ARDS does not develop in the majority of patients with clinical risk factors, suggesting that other factors like genetic susceptibility play an important role in the pathogenesis of ARDS, which inturn is influenced by differences in coexisting conditions. The timing of treatment remains to be a major challenge of ARDS prevention trials and current evidence suggests that ARDS may not preventable. Treatment of ARDS is mainly supportive focusing on limiting further injury to lungs by lung-protective ventilation to prevent ventilator-associated lung injury, conservative fluid therapy to prevent or reabsorb edema of lung along with identification and treatment of the underlying causes like sepsis-associated ARDS is treated with early resuscitation, appropriate antibiotic agents and control of source of infection. Although, there are no proven specific treatments for ARDS, there has been considerable progress in managing patients with ARDS by use of lung-protective ventilation strategies as well as conservative fluid management. Future directions of research should focus on identification of the mechanisms of susceptibility, primary prevention and early treatment, as well as on targeted pharmacological therapies for this devastating condition.

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Hyperventilation Syndrome

Dr Surendra Kumar

Hyperventilation syndrome (HVS) is defined as ventilation in excess of the metabolic needs of the body, eliminating more carbon dioxide than is produced, and, consequently, resulting in respiratory alkalosis and an elevated blood pH.[1]The hyperventilation syndrome is widely held to have a psychogenic etiology. This is not always the case. Identical patterns have been observed secondary to central nervous system disorders such as encephalitis and drug encephalopathies (e.g., salicylate intoxication).[2] Symptoms of HVS and panic disorder overlap considerably, though the two conditions remain distinct. Approximately 50% of patients with panic disorder and 60% of patients with agoraphobia manifest hyperventilation as a symptom, whereas 25% of patients with HVS manifest as panic disorder.

Pathophysiology and symptoms

The underlying mechanism by which some patients develop hyperventilation is unknown. One theory suggests that certain stressors provoke an exaggerated respiratory response. Several such stressors have been identified, including emotional distress, sodium lactate, caffeine, isoproterenol, cholecystokinin and carbon dioxide. Predisposition to HVS may also be rooted in childhood.

Patients with HVS tend to breathe by using the upper thorax rather than the diaphragm, and this results in chronic over inflation of the lungs. When stress induces a need to take a deep breath, the deep breathing is perceived as *dyspnea*. The sensation of dyspnea creates *anxiety*, which encourages more deep breathing and a vicious circle is created. In the brain, and probably in other organs, respiratory alkalosis is associated with greatly increased glycolysis with production of lactic and other acids.[3] The unimportance of renal compensation in humans has been confirmed by studies at high altitude. CSF compensation is also incomplete, CSF pH in humans showing only 50% compensation at the end of 26 hours of voluntary over breathing to a PaCO2 of 31 mm Hg.[4]

Proprioceptors in the lung and chest wall signal the brain with a *"suffocation alarm"* that triggers release of excitatory neurotransmitters that are responsible for many of the symptoms such as *palpitations, tremor, anxiety and diaphoresis*.

Painful tingling in the hands and feet, numbness and sweating of the hands, and cerebral symptoms following voluntary hyperventilation were first described by Haldane and

Poulton.[5] The first cases of spontaneous hyperventilation with *dizziness and tingling* leading to *tetany* were described in 1922 by Goldmanin patients with cholecystitis, abdominal distention, and hysteria.[6] and Burke[7] studied the neurophysiologic basis of the increase in neuronal excitability.

In normal subjects, *paresthesiae developed in the hands, face, and trunk when $PACO_2$ declined on average by 20 mm Hg*, and spontaneous electromyographic activity occurred when $PACO_2$ declined by a further 4 mm Hg.

Giddiness, paresthesiae, loss of consciousness, visual disturbances, headache, ataxia, tremor, and tinnitus, and more alarming symptoms such as hallucinationand unilateral somatic symptoms on the left more than the right have been described. These are often misdiagnosed as epilepsy, transient ischemic attacks, demyelination, or migraine. These symptoms probably arise from reduction in cerebral blood flow, described in many studies.[8] This reduction is probably due to change of pH rather than PCO2 and is associated with significant cerebral hypoxia. HVS occurs in acute and chronic forms.

Acute HVS accounts for only 1% of cases but is more easily diagnosed. Acute voluntary hyperventilation is associated with reduction in peripheral resistance and mean arterial blood pressure with an *increase in heart rate and cardiac output*.[9] Hyperventilation may mimic coronary disease by producing ST segment depression[10] and chest pain that maybe reproducibly precipitated by exertion. Chronic HVS can present with a myriad of respiratory, cardiac, neurologic or gastrointestinal (GI) symptoms without any clinically apparent over breathing by the patient. In the GI system, epigastric pain, a bloated feeling, and vomiting have been described.[11]Hypocapnia can be maintained without any overt change in the minute ventilation if the patient exhibits frequent sighs interspersed with normal respirations.

Epidemiology

The incidence of HVS is higher in first-degree relatives than in the general population, but no clear genetic factors have been identified.

It is thought that up to 6% of the general population exhibits aspects of HVS. The peak incidence is between the ages of 15 and 55 years, but cases have been reported in all age groups except infants. HVS has a strong female preponderance: the female-to-male ratio may be as high as 7:1.A postal survey indicated that 8% of adults without asthma have functional breathing problems (of which symptomatic hyperventilation is the most common).[12]

Diagnostic Considerations

Particular care must be exercised when a diagnosis of HVS is being considered in an elderly person or a person with co morbid disease.

In addition to the conditions listed in the differential diagnosis other problems to be considered include:

Acute respiratory distress syndrome (ARDS).

Chronic nasal congestion.

Reduced alar nasal muscle activity.

Differential Diagnoses:

- Acute Coronary Syndrome.
- Arrhythmias.
- Bacterial Pneumonia.
- Carbon Monoxide Toxicity.
- Central nervous system lesions.
- Diabetic Ketoacidosis.
- High altitude.
- Hypocalcemia.
- Metabolic Acidosis.
- Nasopharyngeal Stenosis.
- Panic Disorder.
- Pleural Effusion.
- Pulmonary Embolism.
- Sepsis.
- Sulfhemoglobinemia.
- Ventricular rupture.
- Anxiety Disorders.
- Asthma and COPD.
- Carbon Monoxide Toxicity.
- Cardiomyopathies.
- Chordae tendonae rupture.
- Heart Failure.
- Hyperthyroidism & Thyrotoxicosis.
- Interstitial lung diseases.
- Methemoglobinemia.
- Pain.
- Pericarditis.
- Pneumothorax.
- Pulmonary hypertension.
- Smoke Inhalation Injury.
- Venous Air Embolism.
- Withdrawal Syndromes.

Approach Considerations

Upon a first attack of acute HVS, the diagnosis depends on recognizing the typical constellation of signs and symptoms and ruling out the serious conditions that can cause the presenting symptoms.

Acute coronary syndrome (ACS) and pulmonary embolism (PE) are two of the most common serious entities that may present similarly to HVS. Usually, clinical assessment is sufficient to rule out these entities. Depending on that assessment, more specific testing is sometimes warranted. A standard workup for atypical chest pain, including pulse oximetry, chest radiography and electrocardiography (ECG), may still be warranted depending on the clinical picture.

Laboratory Studies

Patients with a history of HVS who have undergone an appropriate workup at some earlier time may not need any further laboratory evaluation in the setting of a recurrence. Recognition of the typical constellation of dyspnea, agitation, dizziness, atypical chest pain, tachypnea and hyperpnea, paresthesias, and carpopedal spasm in a young, otherwise healthy patient with an adequate prior evaluation is often sufficient to establish the diagnosis.

Arterial blood gas (ABG) and electrolyte measurement is indicated if any doubt exists as to the patient's underlying respiratory status. Arterial blood gas analyses may be helpful when HVS-induced alkalosis is suspected or when shunting or impaired pulmonary gas exchange is being considered.Serum sodium level falls slightly, both in the arterial and in the jugular venous blood. Hyperventilation has been reported to cause both hypokalemia and hyperkalemia.[13,14]

In chronic HVS, ABG sampling confirms a compensated respiratory alkalosis in a majority of cases. The pH is typically near normal, with a low $PaCO_2$ and a low measured serum bicarbonate level. ABG sampling is also useful in ruling out toxicity from carbon monoxide poisoning, methemoglobinemia, and sulfhemoglobinemia which may present similarly to HVS.

Drug toxicology screening is often indicated.Pulmonary function help to rule out other underlying lung conditions, such as asthma or pulmonary embolism.

If acute PE is being considered, a quantitative enzyme-linked immunosorbent assay (ELISA) D-dimer assay may be helpful in young patients who are free from comorbid illnesses.

ECG changes are common and may include the following:

- ST depression or elevation.
- Prolonged QT interval.
- T-wave inversion.
- Sinus tachycardia.

Hyperventilation syndrome can be clinically misdiagnosed as epileptic seizures. Therefore an electroencephalogram (EEG) may be required.[15] cerebral symptoms may require CT or MRI scan of the brain.

Imaging studies

Imaging studies are not indicated when the diagnosis of HVS is clear. In less obvious cases of HVS, imaging studies are typically normal. Chest radiographs may reveal hyperinflation.

Because PE can present with findings identical to those of HVS, a first-ever episode of acute HVS may warrant ventilation/perfusion scanning or computed tomography (CT) pulmonary angiography to rule out perfusion defects. Chest radiography is indicated for patients who are at high risk for cardiac or pulmonary pathology. Chest radiography is also indicated when the diagnosis is not clear.

Treatment

Because respiratory distress or chest pain has many potentially serious causes, the diagnosis of HVS should never be made in the field. Organic causes for the presenting symptoms should be excluded as a necessary first step to reassuring both patient and referring physician that potentially life threatening disorders that may contribute to misattribution are not present, and that hyperventilation contributes to the presenting symptoms. Even when a patient with these complaints carries a prior diagnosis of HVS, he or she must still be transported to a hospital for a more complete evaluation.

The next stage is to seek the causes of the hyperventilation. Disorders such as mild asthma contributing to excessive respiratory drive require aggressive treatment, but additional extensive explanation and reassurance, given with confidence and authority by a trained physician, is one of the keystones to successful management.

Many regimens have been developed for treatment of hyperventilation. In some patients, and especially those verging on panic, a regimen involving breathing exercises and diaphragmatic retraining may be of benefit.[16] Some believe that the effect of such training is nonspecific, but a recent study showed that guided breathing retraining improved cardiac symptoms and physiologic variables in a group of patients with hyperventilation.[17] However, other controlled studies suggest that these techniques have only limited effectiveness.[18]

Pharmacologic Therapy

Medications, including *benzodiazepines* and *selective serotonin reuptake inhibitors (SSRIs)* have been employed to reduce the frequency and severity of episodes of hyperventilation.

Benzodiazepines (e.g.lorazepam) are effective in reducing stress that may provoke HVS and are thought to reset the central nervous system (CNS) response to a variety of "panicogens."

Selective serotonin reuptake inhibitors (SSRIs)e,g. paroxetinehave been reported to reduce the frequency and the severity of episodes of hyperventilation.

Stress reduction therapy, administration of beta blockers, have all proved effective in reducing the intensity and the frequency of episodes of hyperventilation.

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Haemothorax

Neeraj Gupta, Akhilesh Verma

Haemothorax is the presence of a significant amount of blood in the pleural space, a potential space between the visceral and parietal pleura. Bleeding may arise from the chest wall, intercostal or internal mammary arteries, great vessels, mediastinum, myocardium, lung parenchyma, diaphragm, or abdomen.

Although pleural effusion is more common and has to be distinguished from haemorrhagic exudates and haemothorax, a content of 5% haematocrit makes the effusion indistinguishable from blood. A punctuate of at least 50% of the haematocrit in the patient's blood is postulated for the definition of haemothorax.[1,2] This criterion may not always be really helpful due to low erythrocyte count in supernatant liquid left after coagulation.

Pathophysiology

Bleeding into the hemithorax may arise from diaphragmatic, mediastinal, pulmonary, pleural, chest wall and abdominal injuries. Each hemithorax can hold 40% of a patient's circulating blood volume. Studies have shown that injury to intercostal vessels (e.g., internal mammary arteries and pulmonary vessels) lead to significant bleeding requiring invasive management.[3]

*Early physiologic response of a hemothorax has hemodynamic and respiratory components***.**

The severity of the pathophysiologic response depends on the location of the injury, the patient's functional reserve, the volume of blood, and the rate of accumulation in the hemithorax.[4,5,6] **In the early response, acute hypovolemia leads to a decrease in preload, left ventricular dysfunction and a decrease in cardiac output. Blood in the pleural space affects the functional vital capacity of the lung by creating alveolar hypoventilation, V/Q mismatch, and anatomic shunting. A large** hemothorax can lead to an increase in hydrostatic pressure which exerts pressure in the vena cava and pulmonary parenchyma causing impairment in preload and increase pulmonary vascular resistance. These mechanisms result in tension hemothorax physiology and cause hemodynamic instability, cardiovascular collapse, and even death.

Aetiology

Hemothorax is a frequent manifestation of traumatic injury (blunt or penetrating) to thoracic structures. Most cases of hemothorax arise from blunt mechanism with an overall mortality of 9.4%.[7] Non-traumatic causes are less common. Etiology of hemothorax can be subdivided into three main causes:

- Traumatic Haemothorax
- Iatrogenic Haemothorax
- Non traumatic Haemothorax

Traumatic Haemothorax

The most common mechanism of hemothorax is a blunt or penetrating injury to intrathoracic or extrathoracic structures that result in bleeding into the thorax.

Thoracic injuries occur in approximately 60% of multi-trauma cases and are responsible for 20 to 25% of trauma mortalities.[8] Trauma is the leading cause of mortality in the fourth decade of life.[9] Injury to thoracic structures may arise from direct impact or rapid deceleration forces. Thoracic skeletal fractures, lung contusion, and diaphragmatic injuries are common findings in blunt chest trauma.[10] Studies suggest that thirty to fifty percent of patients with severe blunt chest injury have a concomitant pulmonary contusion, pneumothorax, and hemothorax.[11,12] Pneumothorax, hemothorax, or hemopneumothorax were found in 72.3% of the cases of traumatic rib fractures, in a series by Sirmali et al.[10]

Iatrogenic Haemothorax

The most common causes of iatrogenic hemothorax are the perforation of a central vein by a percutaneously inserted catheter [13, 14,15] or leakage from the aorta after translumbar aortographic study.[16] Iatrogenic hemothorax can also follow thoracentesis or pleural biopsy.

Central venous catheterisation

The main cause of bleeding is puncture of the accompanying artery (carotid and subclavian). Although the incidence of arterial puncture (subclavian) following central venous catheterisation is reported to be around 5%, the reported incidence of hemothorax is less than 1%. Individuals on antiplatelet agents and other coagulation disorders are especially at higher risk.A non-self limiting haematoma can disrupt the mediastinal

pleura or the needle can perforate the artery and the pleura with direct bleeding into the pleural space.[17,18] Hemothorax may even develop during removal of central venous catheter. New onset or aggravated breathlessness following central venous catheterisation along with hypotension and unilateral haziness on chest radiograph must arouse suspicion of this complication.

CT guided biopsy

The main complications are pneumothorax and intraparenchymal bleeding with haemoptysis. The overall rate of complications is 30%. The risk of haemothorax is 1-3.5% ;between 6% to 10% of patients need intervention, mainly thoracic drainage.[19,20]

Thoracic Drainage

The rate of adverse events depends on the circumstances involved such as emergency of the procedure, expertise of the physician, method of insertion of chest tube, diameter of drainage tube and underlying disease, including coagulation disorders.[21,22] The use of large-bore trocar drainage bears the highest risk. Rapid drainage of pulsatile, dark red blood, shortness of breath, tachycardia and hypotension are signs and symptoms of this serious complication. The risk of hemothorax following thoracocentesis is less than 1%. Such an event may remain undetected unless patient develops signs of hypovolemia.

Non Traumatic Hemothorax

Nontraumatic hemothoraces are distinctly uncommon. The most common cause, not associated with pneumothorax, is metastatic malignant pleural disease. The most common tumours are schwanommas of von Recklinghausen disease and soft tissue tumours such as sarcomas, angiosarcomas, and hepatocellular carcinomas.

The second most common cause is a complication of anticoagulant therapy for pulmonary emboli, and the third leading cause is probably catamenial hemothorax.

Other causes of spontaneous hemothorax include a complicationof a bleeding disorder such as haemophilia or thrombocytopenia, a complication of spontaneous pneumothorax, ruptured thoracic aorta, pancreatic pseudocyst, rupture of a patent ductus arteriosus, rupture of a coarctation of the aorta, rupture of a splenic artery aneurysm through the diaphragm, rupture of a pulmonary arteriovenous fistula, hereditary hemorrhagic telangiectasia (Osler-Rendu-Weber syndrome), intrathoracic extramedullary haematopoiesis, chickenpox pneumonia, osteochondroma of the rib, and bronchopulmonary sequestration. In some patients, the cause of the hemothorax remains unknown despite exploratory thoracotomy.[23]

Diagnosis

Symptoms

Thorough and accurate gathering of history from the patient, witnesses, or prehospital providers may help in ascertaining the cause as well as suspicion of such complication. Important history components include chest pain, dyspnoea, mechanism of injury (fall, direction, and speed), drug/alcohol use, comorbidities, surgical history, and anticoagulation/antiplatelet therapies. If the effusion appears within 24 hours of a medical intervention then haemothorax is likely.

Physical findings

Clinical findings of hemothorax are broad and may overlap with pneumothorax; a cold white nose may be the first sign of loss of intravascular volume in some of the cases.

Symptoms and signs include respiratory distress, tachypnea, decreased or absent breath sounds, dullness to percussion, chest wall asymmetry, tracheal deviation, hypoxia, narrow pulse pressure, and hypotension.

Inspect the chest wall for signs of contusion, abrasions, "seat belt sign," penetrating injury, paradoxical movements ("flail chest"), ecchymosis, deformities, crepitus, and point tenderness. Distended neck veins may indicate concomitant presence of pneumothorax or pericardial tamponade but might be absent in the setting of hypovolemia. Increased respiratory rate, effort, and use of accessory muscles may be signs of impending respiratory failure.

Investigations

Initiate with a routine check-up with a chest radiograph and/or sonography. Point-of-care ultrasound in trauma has significantly impacted the evaluation and disposition of trauma patients. In addition to the four conventional views, the eFAST includes oblique views of both hemidiaphragm to evaluate for dependent fluid (hemothorax) and anterior views to evaluate for pneumothorax.

CT scan is indicated to identify the cause, extent and the source of bleeding which is important to plan further treatment.

Emergent angiography may reveal site and extend of rupture of subclavian artery.

Management

Tube Thoracostomy

The treatment of choice for patients with traumatic hemothorax is the immediate insertion of a chest tube. Obviously, if there is only a very small hemothorax, tube thoracostomy is not necessary. An occult hemothorax is one that is seen on CT scan but not apparent on the supine chest radiograph. Tube thoracostomy is not necessary for most patients with occult hemothorax.[23]

Tube thoracostomy is performed if either diaphragmatic domeis obscured or if the fluid is more than 2 cm inthickness on the lateral decubitus radiograph.[24] Most patients need tube thoracostomy for a relativelyshort period. Chest tubes should be removed as soon as they stop draining or cease to function because they can serve as conduits for pleural infection.Large-bore chest tubes (size 24 to 36 F) should be inserted in patients with hemothorax because the blood frequently clots.[23] Beall et al.[25] recommend inserting the chest tube high (fourth or fifth intercostal space) in the midaxillary line because the diaphragm may be elevated by the trauma.

Surgery

Primary surgical intervention is required to prevent sequelae and complications of moderate to massive hemothorax. Immediate thoracotomy or thoracoscopy is indicated for suspected cardiac tamponade, vascular injury, pleural contamination, debridement of devitalized tissue, sucking chest wounds, or major bronchial air leaks.[23] Vascular injury is suggested if the initial chest tube output is more than 1,500 mL.

There is no precise criterion for the amount of pleural bleeding that should serve as an indication for surgery, because each case must be considered individually[23]; however, if the bleeding is at a rate of more than 200 ml/hour and shows no signs of slowing, thoracotomy or VATS should be seriously considered. Surgical repair of bleeding subclavian artery may be considered.

An alternative approach to the patient with persistent bleeding is to perform a contrast-enhanced CT scan and then perform transcatheter arterial embolization in patients who exhibit contrast extravasation.

Secondary surgical treatment for residual pneumothorax or persistent hemothorax using VATS procedure may sometimes be required, preferably within one week. In patients who are not candidates for surgery, local application of fibrinolytic agents like streptokinase, urokinase or tissue plasminogen activator may be tried.

Interventional methods other than surgical treatment include balloon tamponade of bleeding artery, stent-graft placement, applications of coils in bleeding artery and percutaneous closure devices.

The efficacy of prophylactic antibiotics for the prevention of empyema in patients with tube thoracostomy for hemothorax is unclear. Maxwell et al.,[26] in a randomized, double-blind study, gave cefazolin for 24 hours, for the duration of tube thoracostomy or placebo to 224 patients. The use of antibiotics did not significantly affect the incidence of empyema or pneumonia. A longer durationof tube thoracostomy and a higher thoracic trauma score were associated with a higher incidence of empyema[26].

It appears that prehospital autotransfusion has a role in the management of life-threatening hemothorax. Barriot et al.[27] developed a system by which autotransfusions could be administered in ambulances.

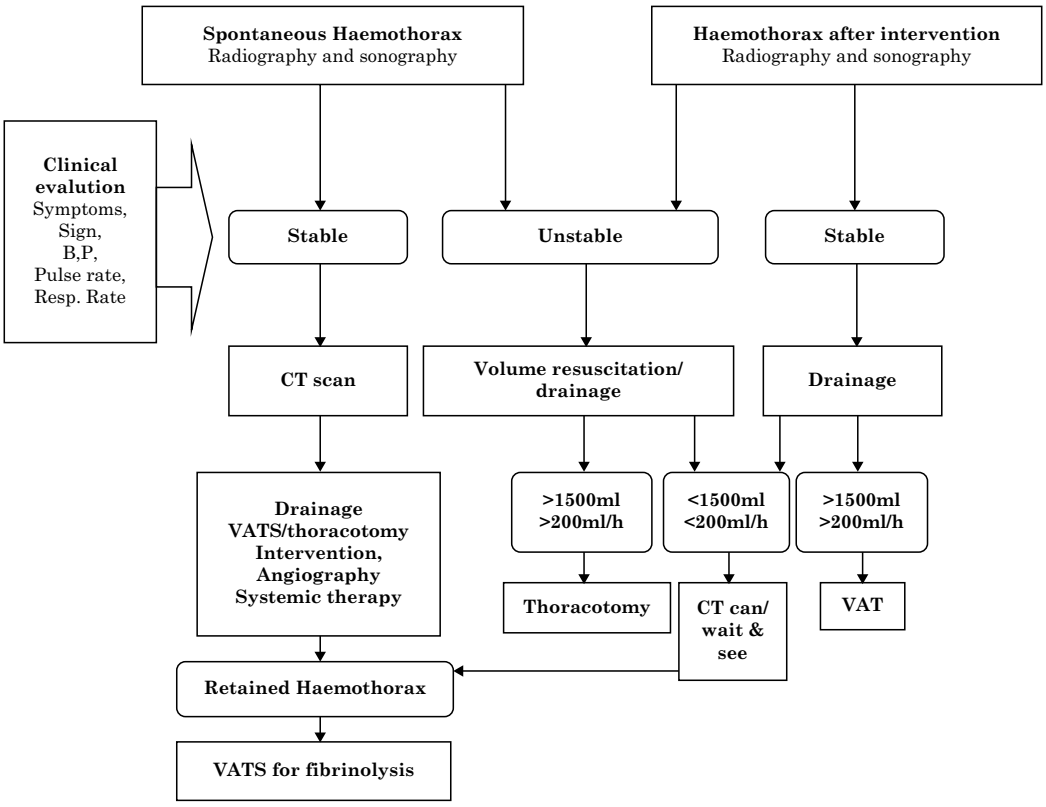
For hemothorax complicating anticoagulant therapy, immediate discontinuation of the anticoagulant therapy must be ensured and insertion of chest tubes should be considered.

Catamenial hemothoraxcan be treated by suppressing ovulation using oral contraceptives or progesterone or suppression of gonadotropins using danazol or gonadotropin-releasing hormone.[23] However, hormonal therapy frequently fails. In such instances, chemical pleurodesis can be performed, and if this measure fails, total hysterectomy with bilateral oophorectomy can be done.

Conclusion

Hemothorax, although a rare entity, is an emergency situation requiring immediate attention towards diagnosis and treatment. Conservative or surgical interventions are required depending on the underlying cause, volume of hemothorax and cardiorespiratory status of the patient. Thoracotomy should be used in unstable patients with unknown cause of bleeding. Early VATS is safe and effective treatment to manage most of the cases.

Haemothorax Treatment Algorithm



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Pneumothorax

Don Gregory Mascarenhas

Pneumothorax is air in pleural cavity. The pleural pressure remains negative as compared to atmospheric pressure throughout the respiratory cycle in a normal individual. The pressure difference between pulmonary alveoli and the pleural cavity (transpulmonary pressure) causes elastic recoil of lung. In pneumothorax, alveoli or airway becomes connected to pleural cavity, resulting in migration of air from the alveoli to the pleural cavity until the pressures of both areas are in equilibrium. This causes reduction in vital capacity and arterial oxygen tension leading to respiratory failure and sometimes death.

Classification

1) Etiological

Primary Spontaneous Pneumothorax (PSP)

Secondary Spontaneous Pneumothorax (SSP)

Traumatic Iatrogenic Pneumothorax (TIP)

Traumatic (Non Iatrogenic) Pneumothorax (TNIP)

2) Clinical

Open pneumothorax

Closed pneumothorax

Tension pneumothorax

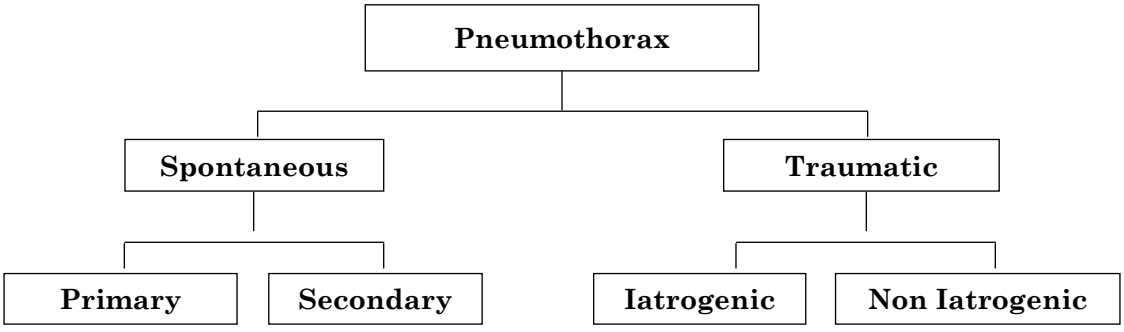


Figure 1 : Etiological classification of Pneumothorax

Primary Spontaneous Pneumothorax (PSP)

These occur without a history of trauma/underlying lung disorder.Most cases are due to rupture of subpleural bleb. Most patients are taller and thinner. In these patients, pressure gradient is greater from lung bases to apices.

Birt -Hogg -Dube syndrome: its due to mutation in folliculin gene mapped to chromosome 17p11.2. It is autosomal dominant. These patients have high incidence of PSP, benign skin tumours and renal tumours.

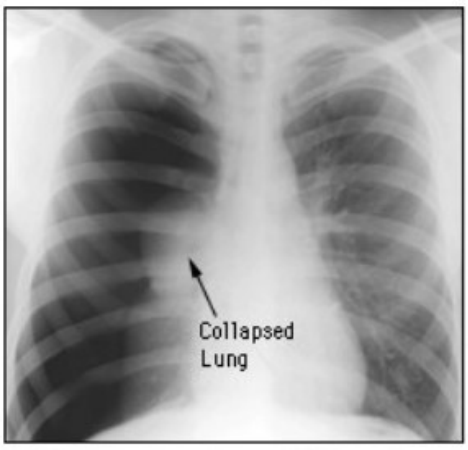
Clinical features

PSP is mostly seen in young individuals between 20 to 30 years. Patient presents with sudden chest pain and/or dyspnea, usually after lifting weights or strenuous exercise. It can rarely present as Horner's syndrome due to traction on the sympathetic ganglion produced by shift of mediastinum. Signs include tachypnoea, tachycardia. On examination of the chest, trachea is shifted to contralateral side, there is bulge on the affected side, with reduced movements, hyperresonant note on percussion and absent breath sounds on auscultation. ECG changes may be seen. Rightward shift of frontal QRS axis, reduced precordial r wave voltage, reduced QRS amplitude and precordial T wave inversion may be seen in a left sided pneumothorax. In a right sided pneumothorax, there may be prominent R wave voltage, with reduced S wave voltage in lead V2, mimicking posterior myocardial infarction.

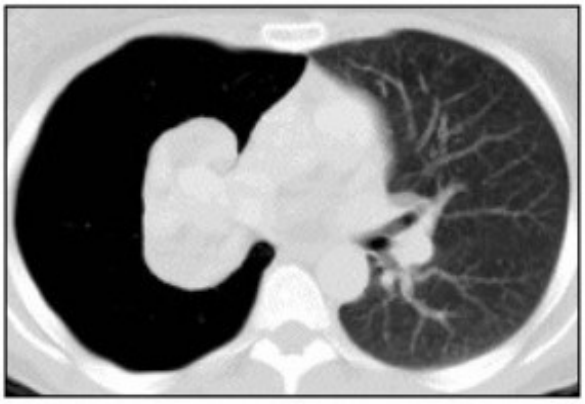
Diagnosis

Clinical features as described above.

Chest Xray shows a pleural line. It may be associated with pleural effusion which is usually eosinophilic.



X-Ray chest PA view showing
Right Lung Pneumothorax



CT chest showing
Right Lung Pneumothorax

Figure 2: X-ray chest & CT Chest of a patient of Right Lung Pneumothorax

Quantification of pneumothorax

a. Light's index

Percentage of pneumothorax =100 { 1- a^3/b^3}

Where a= diameter of collapsed lung, b= diameter of hemithorax

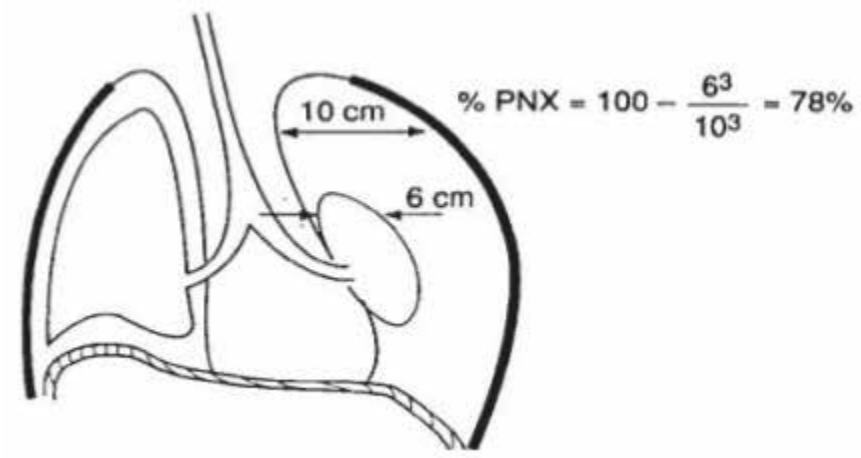


Figure 3 : Quantification of pneumothorax – Light's Index

b. Collin's method

Percentage of pneumothorax = 4.2 + { 4.7 x (A+B+C) }

Where A=distance(in centimeters) between the apex of partially collapsed lung and apex of the thoracic cavity

B &C = distance(in centimeters) between the midpoints of the upper and lower halves of the collapsed lung from the lateral chest wall respectively.

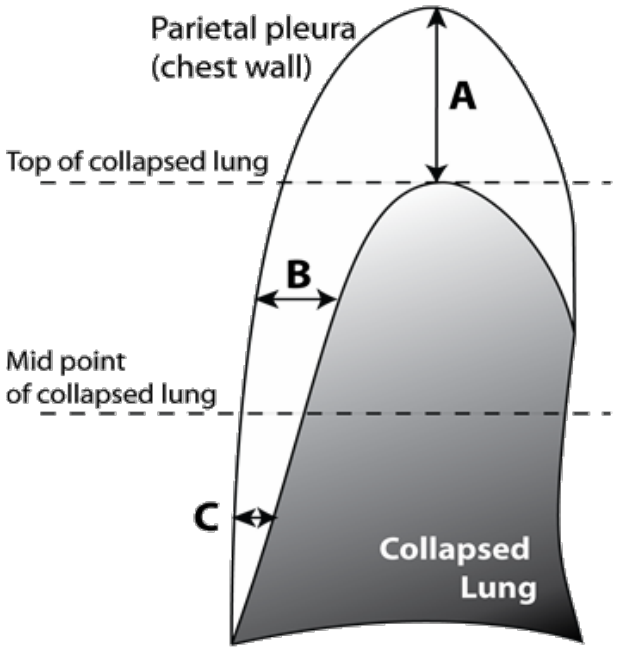


Figure 4 : Quantification of pneumothorax – Collin's Method

c. Rhea method

This method states that there is a 10% pneumothorax for every 1 centimeter distance of pleural line from thoracic wall as measured in a chest X-ray.

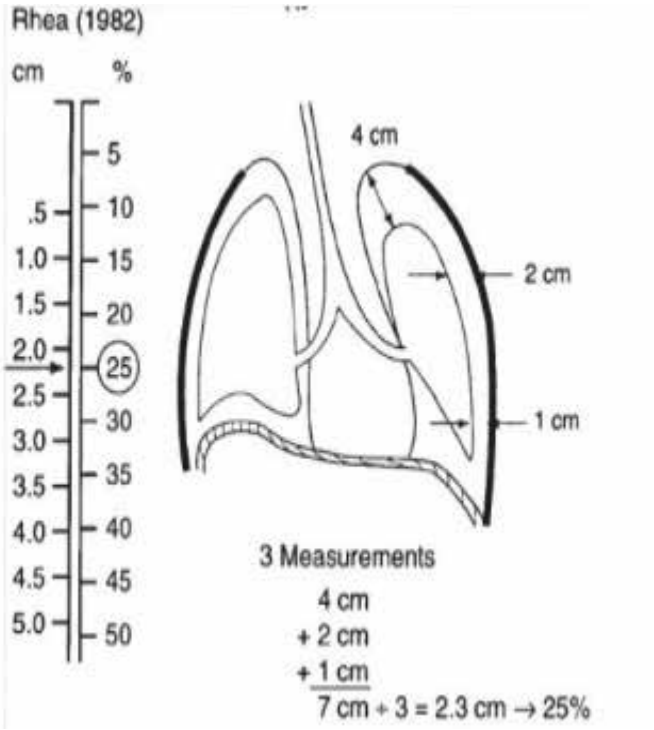


Figure 5 : Quantification of pneumothorax – Rhea Method

British Thoracic Society (BTS) semi-quantitation of pneumothorax

a ***Small Pneumothorax***: If rim of air between the pleural and chest wall is less than 2 centimeters at the level of hilum.

b ***Large Pneumothorax***:If rim of air between the pleural and chest wall is greater than 2 centimeters at the level of hilum.

American College of Chest Physicians (ACCP) semiquantitation of pneumothorax

a ***Small Pneumothorax***: apex to cupola distance is less than 3 centimeters.

b ***Large Pneumothorax***: apex to cupola distance is more than 3 centimeters.

Recurrence rate

Recurrence rates of ipsilateral pneumothorax has been between 52-54% and 16% on contralateral side as per studies by sadikot et al and Gobbel et al. Women have

more chances of recurrence than men. People who stop smoking have lesser chances of recurrence than those who continue to smoke.Recurrence rates are more in taller and light weighted individuals.

Treatment

***a. Observation*:** In a closed spontaneous pneumothorax of less than 15%, there will be spontaneous reabsorption, albeit at a slower rate of 1.25% per day.

b. Supplemental oxygen: Oxygen increases the rate of air absorption by almost 4 fold. Any patient of pneumothorax who is hospitalized, should be treated with high concentrations of supplemental oxygen.

***c. Simple Aspiration*:** any PSP of more than 50% should be aspirated using a 16 Guage needle under water seal, usually in 2^{nd} or 3^{rd} intercostal space in midclavicular line. A maximum of 4 litre of air can be aspirated. If there is no resistance felt beyond this point, it means that there is no complete expansion of lung/ there is a persistent air leak. Tube thoracostomy/VATS should be performed in such cases.
Simple aspiration reduces the duration of hospital stay. Recurrence rate is comparable to tube thoracostomy. Life threatening hemorrhage can occurs at 2^{nd} space due to injury to internal mammary artery, hence aspiration in anterior axillary line in 4^{th} or 5^{th} intercostal spaces is recommended by Light et al.

***d. Tube thoracostomy/ intercostal drain(ICD)* :** It should be done if patient is having severe dyspnoea, pneumothorax is more than 50% or if above mentioned treatment fails. It is generally done with a smaller sized tube, at the uppermost site with the tube positioned in the uppermost part of pleural space. The chest tube should remain in place for 24 hours after the lung expands and air leak stops (as indicated by bubbles in underwater seal). Clamping of tube is controversial and is not indicated. Pleurodesis can be tried using talc or tetracycline to prevent recurrences. If there is persistent air leak beyond 4 days, thoracoscopy/ thoracotomy is advised. Alternately 50ml of blood can be withdrawn from a vein and injected intrapleural through the chest tube to close the site of leak (due to action of fibrin in the blood).

d. Thoracoscopy: It is done using a thoracoscope when there is persistent air leak to look for any underlying causes.

f. Video Assisted Thoracoscopic Surgery (VATS) : It is an alternative to thoracoscopy. Its done by a thoracic surgeon. This procedure can treat the bullous disease via stapling of bullae and can also cause a pleurodesis.

g. Thoracotomy: Its done only if thoracoscopy/ VATS fails. Here the bullae are over sewn and pleura are scarified.

Secondary spontaneous pneumothorax (SSP)

These occur in patients who already have an underlying lung disorder. Most common causes include tuberculosis, COPD, lung malignancy, ILD, sarcoidosis and other pulmonary infections. Most studies in India show pulmonary tuberculosis super ceding COPD as the major cause of SSP.

Clinical Features

Most patients present with dyspnea and chest pain. Dyspnoea is out of proportion to the size of pneumothorax as the lung functioning is already compromised due to underlying disease process. On examination, patient may be hypotensive and cyanotic. Examination of chest may have similar findings as in PSP along with signs of underlying disease. Respiratory Failure is more frequent as compared to PSP.

Diagnosis

Chest x-ray : It shows pleural line along with collapsed lung. Patients with underlying COPD may have large bullae and/or emphysema in the opposite lung.

Ultrasound of the chest: it shows absence of gliding sign. Cysts/ pleural adhesions may be seen.

CT scan of the chest: It should be done to find out etiology when chest Xray is nondiagnostic.

Treatment

Management options are similar to PSP. However ICD insertion is preferred along with pleurodesis to prevent recurrence of pneumothorax.

Iatrogenic Pneumothorax

These are pneumothoraces induced due to an invasive procedure by a clinician. Most common causes include transthoracic needle aspiration, thoracocentesis of mild/ moderate pleural effusion, insertion of a central line, Positive pressure ventilation, pleural biopsy, transbronchial lung biopsy etc.

Clinical features

Most often patient deteriorates after the aforementioned procedures with dropping arterial saturation, hypotension, cyanosis. Examination of chest may reveal features

similar to PSP. Patients developing pneumothorax after mechanical ventilation may develop mediastinal emphysema.

Diagnosis is mainly done by the development of symptoms and signs of pneumothorax following the procedure. Chest Xray shows a pleural line.

Treatment

If patient is asymptomatic or has mild symptoms, observation/ high flow oxygen will suffice. If patient is having increased respiratory distress, aspiration of air has to be done. If patient has pneumothorax induced by mechanical ventilation or has severe respiratory distress, ICD is preferred. Pleurodesis is not done as recurrence rates are less.

Traumatic (Non-Iatrogenic) Pneumothorax

It can be due to a penetrating (gunshot/stab injuries) or non penetrating trauma. Clinical features resemble PSP. Tube thoracostomy is indicated. If haemo-pneumothorax is present, one chest tube is placed in superior part to drain air and one in lower part of chest to drain blood. Surgical repair may be needed if there is bronchial or oesophageal rupture.

Open Pneumothorax

Here there is constant air movement and atmospheric pressure is more than intrapleural pressure. It most often occurs in a SSP due to alveolo-pleural fistula. Amphoric breath sounds are heard on auscultation of affected side. ICD is usually indicated

Closed Pneumothorax

Here there is no communication between pleural cavity and atmosphere. Breath sounds will be reduced or absent on the affected side. Simple aspiration and supplemental oxygen will suffice.

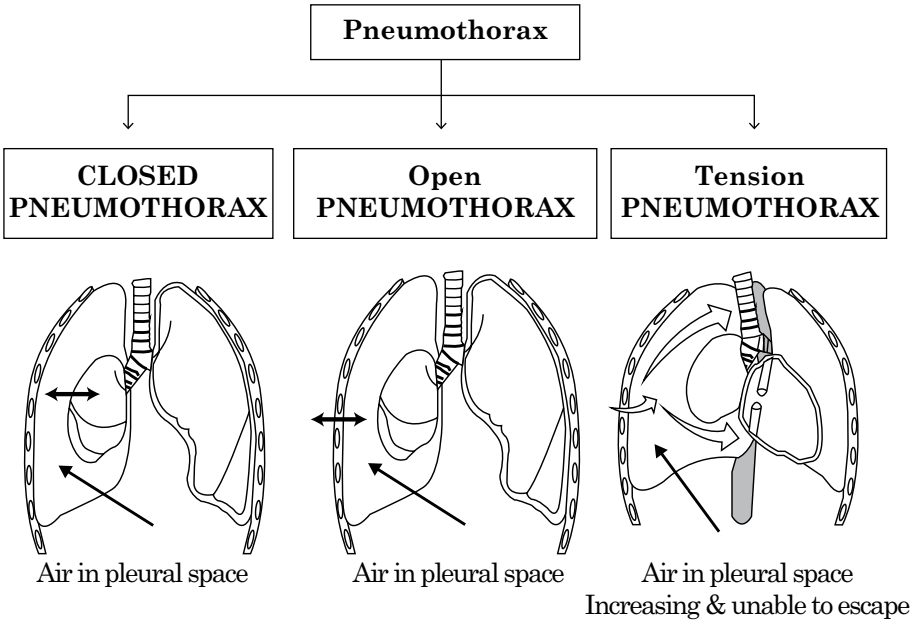


Figure 4 : Types of Traumatic (Non Iatrogenic) Pneumothorax

Tension Pneumothorax

Tension pneumothorax occurs when the intrapleural pressure exceeds atmospheric pressure in expiration and most often in inspiration too.Most often its due to Mechanical ventilation.Patient develops sudden onset of dyspnea. Clinically patient develops tachycardia, tachypnoea cyanosis, diaphoresis, hypotension. Neck veins may be distended. Trachea is deviated to opposite side. Affected Hemithorax is larger as compared to opposite side. ABG shows marked hypoxemia with respiratory acidosis.

Treatment include emergency drainage of air using a wide bore needle in 2nd intercostal tube connected to a water seal along with supplemental oxygen. Wide bore intercostal drain should be inserted later on if tension still persists.

Catemenial Pneumothorax

Here pneumothorax occurs in association with menstruation. Its usually recurrent and occurs between the day before and within 72 hours of menstruation. Most commonly due to pleural or diaphragmatic endometriosis., but sometimes due to diaphragmatic defects causing leakage of air from peritoneal cavity to pleural cavity. Surgical treatment is similar to PSP. Medical treatment included gonadotropin releasing hormone antagonists.

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Acute Pulmonary Embolism

Kumar Utsav Samaria, J.K. Samaria

Introduction

Pulmonary thromboembolic disease (PTE) refers to the condition in which blood clot(s) (thrombus or multiple thrombi) migrate from the systemic circulation to the pulmonary vasculature. Most of these thrombi arise from the deep veins of the lower and upper extremities (deep venous thrombosis [DVT]). Clinically, Pulmonary Embolism (PE) is extension of DVT. True incidence of PE is unknown. Silent PE is present in approximately 32% patients of DVT.[1]

Sources of Emboli

Most cases (80%–95%) of PE occur as a result of thrombus originating in the lower extremity. Thrombus often begins at a site where blood flow is turbulent, such as at a venous bifurcation, or behind a venous valve. Most embolus originates in the deep veins of calf, of which popliteal vein is the mostcommon source of Acute Pulmonary Embolism (APE).

Emboli may originate from sources like pelvic veins in cases such as in pregnancy, pelvic thrombophlebitis or pelvic infections, prostate disease, or recent pelvic surgery. Emboli may also originate from upper extremity thrombosis associated with central venous catheters or intravascular cardiac devices. Air embolism, amniotic fluid embolism, fat embolism are other commonly known source of embolism.

Predisposing Factors

There is interplay of genetic and acquired risk factors, & multiple mechanisms lead to development of DVT & PE, & that multiple factors can often be found in individual patients. Virchow's Triad of "Venous Stasis, Hypercoagulability & injury to venous wall (endothelium)" is helpful in stratifying patients according to the risk profile.(TABLE 1: Clinical States predisposing to Venous Thromboembolism)

Table 1 : Clinical States predisposing to Venous Thromboembolism.

Clinical States	Mechanism
Stasis	• Immobility • Bed Rest • Anesthesia • CHF/Cor Pulmonale • Prior Venous Thrombosis
Hypercoagulability	• Malignancy • Anticardiolipin • Antibody • Nephrotic Syndrome • Essential thrombocytosis • Estrogen Therapy • Heparin-induced thrombocytopenia • Inflammatory bowel disease • Paroxysmal nocturnal hemoglobinuria • Disseminated intravascular coagulation • Protein C and S deficiencies • Antithrombin III deficiency • Trouma • Surgery

Acquired risk factors

The risk imposed by a *major surgical procedure* is well recognized. Without prophylaxis, venous thrombosis occurs after approximately 20% of all major surgical procedures with associated embolism after 1% to 2%.[3] The incidence of thromboembolism without prophylaxis is even higher in orthopedic patients with over 50% of major orthopedic procedures complicated by venous thrombosis.[4]

Pregnancy is the most common cause of venous thromboembolism in women younger than 40 years old, and if untreated may account for 20% to 50% of all pregnancy-related deaths.[7] The incidence of v*enous obstruction from uterine compression* is estimated at 0.76 to 1.72 cases per 1000 pregnancies. 90% of all DVT cases are noted in the left leg.

Use of *oral contraceptive agents* (4-6-fold increased risk)[8] and *hormonal replacement therapy* (2-4 fold increase)[9] has also been associated with an increased risk of venous thromboembolism.[7,8]

Both *obesity* (BMI >29) & *metabolic syndrome* are associated with increased risk of atherosclerosis & venous thromboembolism.[10] Cancer is estimated to increase the risk of venous thromboembolism by 4-6 folds. [11, 12]

Various hematologic conditions such as *polycythemia vera, essential thrombocytosis,* and *acute leukemia* may increase the risk of venous thromboembolism by increasing blood viscosity (hyperviscosity syndromes) and through the release of procoagulants.[13]

Pathophysiology

Once detached from their point of origin, emboli travel via the systemic venous system, through the right chambers of the heart, and eventually reach the pulmonary arterial system. Physiological effects vary from asymptomatic disease to haemodynamic collapse & death. Major factors that determine the outcome include:

- Size and location of emboli;
- Coexisting cardiopulmonary diseases;
- Secondary humoral mediator release and vascular hypoxic responses; and
- The rate of resolution of emboli

Haemodynamic consequences

Obstruction of the pulmonary vascular bed by embolism acutely increases right ventricular after load. Compensatory mechanisms exist that allow up to 70% obstruction of the pulmonary vascular bed before right ventricular failure develops.[24-27] In the absence of pre-existing cardiopulmonary disease, obstruction of less than 20% of the pulmonary vascular bed results in minimal hemodynamic consequences as a result of recruitment and distention of pulmonary vessels.[24] When the degree of pulmonary vascular obstruction exceeds 30% to 40%, cardiac output is maintained by increase in heart rate & myocardial contractility.

Compensatory mechanisms begin to fail when degree of pulmonary artery obstruction exceeds 50% to 60%. With further acute obstruction, the right heart dilates, right ventricular wall tension increases, right ventricular ischemia may develop, the cardiac output falls, and systemic hypotension develops.. [27, 28]

Gas-Exchange abnormalities

Hypoxemia is the most common immediate physiologic consequence of PE. Obstruction of the pulmonary vasculature prevents systemic venous blood from reaching the pulmonary capillaries of the involved vessels and redirects the blood flow to other parts of the pulmonary vascular bed.

This results in an increase in ventilation–perfusion (V/Q) inequality, intrapulmonary shunting, and decreases in the mixed venous O2 level, thereby magnifying the effect of the normal venous admixture.[29,30] Further shunting and increase in alveolar dead space can also occur as a result of alveolar hemorrhage or to atelectasis related to loss of surfactant. Patients with PE often develop hypocapnia due to hyperventilation. One uncommon consequence of PE is pulmonary infarction (occurring in 20% patients with significant cardiac/Pulmonary) disease.

Diagnosis of pulmonary embolism

a. Clinical Presentation

The mainstay for the diagnosis of PE is a high index of suspicion; most patients with embolism have one or more factors predisposing them to the condition like advancing age, a period of bed rest, a prolonged air flight, or a minor traumatic injury.The presentation of acute PE can be categorized into one of the three clinical syndromes:

- Isolated dyspnea
- Pleuritic pain or hemoptysis; and
- Circulatory collapse.[31, 32]

Without history of prior cardiopulmonary disease, the syndrome of pleuritic pain or hemoptysis was found to be the most common mode of presentation, occurring in approximately 60% of patients. Isolated dyspnea occurred in approximately 25%, whereas circulatory collapse occurred in 10%. Complete anatomic resolution of PE appears to be uncommon. When there is sufficient residual pulmonary vascular obstruction, some patients may develop chronic thromboembolic pulmonary hypertension (CTEPH).[34, 35]

The most common presenting symptom of acute PE is the sudden onset of dyspnea, it may occur over minutes to hours. Other symptoms include pleuritic chest pain, cough, leg swelling or pain, and hemoptysis. The most common physical

finding is unexplained tachypnea (respiratory rate greater than 20/min) present in approximately 70% of patients with embolism. Less frequent physical findings include rales, tachycardia, and an increased pulmonic component of the second heart sound. Fever may develop in some for hours after event. [36]

b. Clinical Assessment

Wells et al. had prospectively tested a rapid seven-item bedside assessment to estimate the clinical pretest probability for PE it came to be called Well's Score for Pulmonary Embolism**.** [37]

Table 2 : Wells Clinical Prediction Score

Variable	**Points**
DVT symptoms/signs	3.0
PE likely or more likely than alternative diagnosis	3.0
Heart rate >100	1.5
Immobilization/surgery previous 4 weeks	1.5
Previous DVT or PE	1.5
Hemoptysis	1.0
Malignancy	1.0
Total Score	**Pretest Probability**
<2.0	Low
2.0-6.0	Moderate
>6.0	High
Dichotomized Score	
£4	PE unlikely
>4	PE likely

A similar scale is also being used called Geneva Clinical Prediction Score, it included Blood gas Abnormalities, & chest radiography findings, it was later revised to contain eight clinical variables without gas exchange or radiographic information was validated & published. [38]

Table 3 : Revised Geneva Clinical Prediction Score

Variable	Points
Age >65 y	1
Previous DVT or PE	3
Surgery (under general anesthesia) or lower limb fracture within 1 month	2
Active malignancy (currently active or considered cured <1 y)	2
Symptoms	
Unilateral lower limb pain, hemptysis	2
Clinical Signs	
Heart rate: 75-94 beats/min	3
Heart rate: >95 beats/min	5
Pain on lower limb deep venous palpation or unilateral edema	4
Total Score	Pretest Probability
0-3	Low
4-10	Moderate
>11	High

c. Laboratory Findings

Modest leucocytosis, hypoxemia (most common findings), hypocapnia, high $(A\text{-}a)_{O2}$ gradient. [39, 40, 41]

d. ECG findings

Findings in acute PE are generally tachycardia, nonspecific and include T-wave changes, ST-segment abnormalities, & left or right axis deviation.

Atrial arrhythmias more commonly occur in patients with underlying Cardio-pulmonary disease. The classical "S1Q3T3 pattern" is highly specific for PE patients is seen in minority of patients. Presence of an S1Q3T3 pattern, right bundle branch block, or T-wave inversion in leads V1 toV3 in a patient with PE should suggest the presence of right ventricular dysfunction. [42,43]

e. Chest Radiograph Findings

Most PE patients have nonspecific findings like Atelectasis, Pleural effusion, pulmonary infiltrates & mild elevation of hemidiaphragm. Classic findings of pulmonary infarction such as Hampton's Hump or decreased vascularity (westermark sign) are rarely found. Chest Xray are useful in PE mainly to rule out alternative diagnostic possibilities.[44]

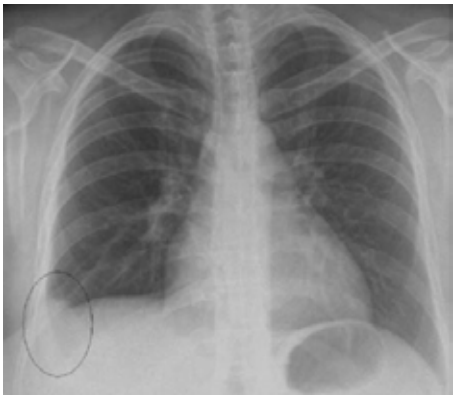

Image 1: Westermark Sign

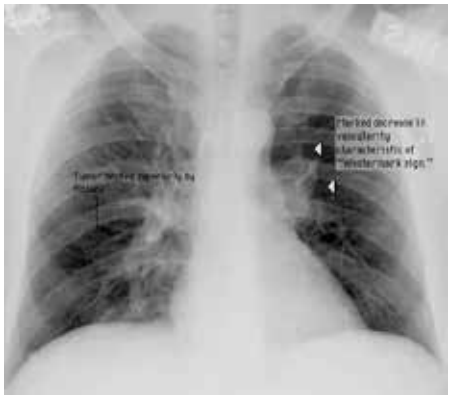

Image 2: Hampton's Hump

f. IMER levels

D-dimer is a highly sensitive but non-specific marker of PE. Increased levels are present in nearly all patients with venous thromboembolism but also in a wide range of other circumstances like advancing age, pregnancy, infections, inflammatory states & malignancy. Therefore, the role of D-dimer testing is limited to one of venous thromboembolism exclusion. [45, 46]

g. Ventilation-Perfusion Scanning

Previously considered the investigation of choice for pulmonary embolism, V/Q scans are largely replaced by CT imaging. As per the PIOPED Trial, a negative V/Q study is capable of ruling out the diagnosis of PE.[47] The positive predictive value of a "high probability" study (one characterized by multiple, segmental- sized, mismatched defects) approximates 88%; when coupled with a high clinical probability of embolism, the positive predictive value increased to 96%. In certain situations, like Contrast Allergy, Renal dysfunction or pregnancy, V/Q scans are still preferred over CT-PA because V/Q scan does not require IV contrast. [48]

h. Echocardiogram

Transthoracic echocardiography has emerged as a potentially important tool for risk assessment and treatment guidance in patients with acute PE. Overall sensitivity of transthoracic echocardiography in PE approximates 50%.[49] Properly performed transesophageal echocardiography has demonstrated sensitivity and specificity exceeding 90% in the detection of proximal emboli involving the pulmonary trunk and the right and left main pulmonary arteries. [50,51]

i. Lower Extremity Evaluation

Duplex Ultrasonography has a central role in the Non-Invasive diagnosis of symptomatic lower extremity DVT. Most reliable finding is "Non compressibility of a Venous Segment". As per a meta-analysis, USG is more useful in accurate detection of asymptomatic proximal DVT in Post-Operative Orthopedic patients. Approximately 30% to 40% of patients with PE will also have signs and/or symptoms of DVT & 60% to 80% will have evidence of proximal DVT when subject to duplex ultrasonography. [52, 53]

j. MRI

The sensitivity and specificity of MRA among patients with technically adequate scans was 78% and 99%, respectively Sensitivity for PE involving the main or lobar pulmonary arteries was only 79%. It's a reserve investigation for patients where avoidance of radiation is preferred (pregnancy) or there is IV contrast Allergy.[54]

k. Computed Tomography

CT-PA has become the first-line imaging test for PE. PIOPED II trial, demonstrated sensitivity for the diagnosis of PE of 83%, specificity of 96%, positive predictive value of 86%, and negative predictive value of 97%.[41,47] CT can be considered confirmatory in excluding embolism in patients with a low or intermediate likelihood of disease and confirming embolism in patients with intermediate or high probability of disease.

l. Conventional Pulmonary Angiography

Previously accepted "Gold Standard" for PE diagnosis is now less frequently done because of widespread availability & technical Superiority of CT-PA

Diagnostic Approach

For outpatients, the use of a clinical prediction rule coupled with D-dimer testing can substantially reduce the number of imaging studies performed. In patients with a

low or intermediate clinical likelihood of PE, a negative D-dimer study is sufficient to exclude the diagnosis, assuming a highly sensitive assay is used. An imaging study should be performed in all patients with a high probability of disease as well as those with a low or intermediate probability whose D-dimer tests are positive. Patients with signs or symptoms of lower extremity DVT should initially undergo lower extremity duplex ultrasonography, a positive lower extremity study, although not proving PE has occurred, has the same therapeutic implications. In patients without lower extremity symptoms or signs who have a high or intermediate clinical probability of PE, a positive CT- PA confirms the diagnosis. In patients with a low or intermediate clinical probability, a negative CT-PA excludes the diagnosis.

Treatment

Management of acute PE consists of a systematic approach that involves early intervention, patient risk stratification, selection of therapy, and determination of treatment duration.

When a diagnosis of venous thromboembolism is suspected, empiric treatment should be considered until the diagnosis is either objectively excluded or confirmed. An exception can be made in those patients with a low clinical likelihood of disease, adequate cardiopulmonary reserve, and a high risk of bleeding complications. Most physicians advocate a short period of hospitalization in patients with newly diagnosed acute PE. Hospitalization should be made mandatory include hypoxemia, hypotension, hemodynamic instability, or sufficient renal disease to contraindicate the use of LMWH or a factor Xa inhibitor.

a. Heparin

Anticoagulation with heparin remains the standard initial therapy. There are two main choices of Intravenous Unfractioned Heparin and subcutaneous LMWH preparations.

Standardized protocols for unfractionated heparin administration and monitoring have been recommended. One commonly employed dosing regimen using an initial intravenous bolus of 80 units of heparin per kilogram followed by a continuous infusion initiated at 18 U/kg/h has been demonstrated to reach therapeutic thresholds more quickly than regimens using fixed dosing.

The heparin drip is adjusted based on monitoring of the a PTT, drawn 6 hours after the initial bolus dose, then 6 hours after each dose adjustment, with a target aPTT ratio of 1.5 to 2.5. [55] More recently, an approach using a fixed dose of subcutaneous

unfractionated heparin without aPTT monitoring, administered as an initial dose of 333 U/kg followed by a dose of 250 U/kg every 12 hours. [55]

LMWH preparations are now anticoagulant of choice in uncomplicated venous thromboembolism including PE. Situations in which the use of UFH is appropriate include renal insufficiency, extremes of body weight, and circumstances in which a rapid adjustment or reversal of anticoagulation is needed, such as women in the late stage of pregnancy who may need Cesarean sections, patients with recent surgery or recent history of bleeding, and hemodynamically unstable patients with venous thromboembolism who may need surgical procedures such as emergency embolectomy. Advantages of LMWH compared with UFH include

- Longer half-life and ease of use;
- Ability to consistently achieve early therapeutic anticoagulation;
- No need to monitor anticoagulant effects; and
- Reduced incidence of major bleeding complications [57, 58]

b. Factor Xa Inhibitors

Fondaparinux, a synthetic pentasaccharide, represented the first in a new class of antithrombotic agents.[60] Fondaparinux has been approved for prophylaxis in patients undergoing hip, knee, and abdominal surgery as well as for treatment of DVT and PE in conjunction with warfarin. Rivaroxaban represents the first in a new generation of oral factor Xa inhibitors. [62, 63]

c. Thrombolytic Therapy:

Thrombolytic drugs cause direct lysis of thrombi by increasing plasmin production through plasminogen activation. Most used thrombolytics are Streptokinase, Alteplase (rt-PA), & urokinase.[65] The use of thrombolytic therapy in PE appears to be appropriate when an accelerated rate of thrombolysis may be considered lifesaving, specifically, present with hemodynamic compromise while on Heparin & those with Intracavitatory Right heart Thrombi. [26, 66]

d. Interventional Radiologic Techniques:

Interventional thrombus fragmentation represents a potential alternative to systemic thrombolysis or surgical embolectomy for treatment of PE.[67] If the bleeding risk is not exceedingly high, catheter fragmentation may be combined with local or systemic thrombolysis.

e. Vena Caval Filters

IVC Filters are indicated in those patients who have a contraindication to anticoagulation. Placement of an IVC filter is not a benign procedure and carries several possible risks.[73]

Long term management

Long-term management includes use of traditional anticoagulants, including warfarin and heparin, as well as a variety of new pharmacologic agents. In addition, insertion of devices in the inferior venacava to prevent additional embolic events has been employed.

Duration of therapy

A 3 month course of anticoagulation appears to be adequate in patients having Post-operative DVT. [68,69] Patients with idiopathic (unprovoked) thromboembolism have a substantially higher rate of recurrence, needs to be given to extended therapy.[70] Patients with antiphospholipid antibody syndrome, those with active cancer, and those with deficiencies of protein S, protein C and antithrombin III are at considerable risk for thromboembolic recurrence and should be candidates for life long therapy.[71,72]

Most cases of APE occur as a result of thrombus originating in the lower extremity. Symptoms are usually minimum or absent in embolism in a small segmental pulmonary branch, but sometimes absent even in patients with larger emboli. High levels of suspicion during clinical evaluation is critical for the the identification of patients requiring relevant diagnostic tests. LMW haparin therapy and thrombolysis offers satisfactory out comes in most cases but few cases may need other therapeutic options & interventions.

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Acute Right Heart Failure

Dr Mridul Mahanta, Dr Gurpreet S Wander

Introduction

The RV fails when it fails to maintain enough blood flow through the pulmonary circulation to achieve adequate left ventricular filling and is due to pressure or volume overload or myocardial disease. The commonest cause of RV failure is pulmonary hypertension and epidemiologically, the most frequent pathology for pulmonary hypertension development is LV failure.

Acute right heart failure can occur suddenly in a previously healthy heart due to massive pulmonary embolism or right-sided myocardial infarction, but many cases encountered in the intensive care unit involve worsening of compensated RV failure in the setting of chronic heart and lung disease.

Right heart failure (RHF) is regarded as the final common pathway of heart failure syndrome. But unfortunately, till today cardiologists are "LV centric" though circulation is a closed system and the RV plays an integral part in it.

Definition of RHF as a symptomatic and progressive disorder

RHF is defined as a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the right heart to fill or eject appropriately.1

The cardinal clinical manifestations of RHF are:

- Fluid retention manifested as peripheral edema or ascites;
- Decreased systolic reserve or low cardiac output syndrome, which may present as exercise intolerance, fatigue or altered mentation; and
- Atrial or ventricular tachyarrhythmias.

Etiology and pathophysiology of RHF

The right ventricle (RV) is regarded as a less important member of the contractile apparatus. This arose from the concept that the RV functions rather as a passive conduit and it pumps blood to only one organ, the lungs. However, the circulatory system is a closed one and both ventricles are interdependent, working together in an orchestrated complex pattern and failure of one ventricle deleteriously affects the performance of the other.

The RV is triangular in side section and crescent-like in cross-section and is made up of superficial circular and deeper longitudinal fibres. The superficial fibres encircle the heart and are continuous with the subepicardial fibres of the LV. The deep longitudinal fibres run from the apex to the base of the heart.

The RV contracts in three ways:

- The inward motion of the RV free wall,
- Shortening of longitudinal fibres pulling the apex towards the base of the heart, and
- Traction by LV contraction.

The contraction of longitudinal fibers contributes most to the systolic performance of the RV, whilst the LV traction component contributes about 20-40% of RV cardiac output.

The RV ejects the same stroke volume as the LV but against a much lower resistance of the pulmonary vasculature. The RV can withstand volume overload for years but cannot handle a pressure overload similarly. However, to maintain cardiac output in the face of an acute rise of pulmonary pressure, the RV augments its force of contraction and failure to adapt acutely results in rapid RV dilatation and dysfunction.Usually, RV function is maintained until late stages of the disease. Eventually, the RV fails, becomes more spherical, tricuspid regurgitation ensues causing more right heart failure and a vicious circle develops ending in venous system congestion.Time and again it has been shown to be the most important indicator of poor prognosis in heart failure. Right heart failure as the primary presentation of acute decompensated HF and cause of hospitalisation accounted for 2.2% of HF admissions in the CHARITEM registry;[2] however,it was present as secondary to acute LV failure in more than one fifth of the cases.In Egyptian Heart Failure-LT registry, 4.5% of patients with acute heart failure presented with RHF as opposed to 3% in other ESC regions.[3]

Several factors may contribute to progression of RV failure after initial stress

- The timing of myocardial stress (adult period > pediatric),
- Type of stressor (pressure overload > volume overload), and
- Myocardial ischemia, as well as
- Neuro-hormonal and immunologic activation.4,5
- Switch in contractile protein isoforms,
- Alteration in cardiac metabolism,
- Alterations in enzymes and ion channels involved in myocyte excitation-contraction coupling,
- Matrix remodeling and neurohormonal and cytokine activation.6-13

Recent studies also demonstrate that specific pathways may be selectively involved in RV remodeling. The differentially expressed genes were involved in the Wnt signaling pathway, apoptosis, migration of actin polymerization and processing of the ubiquitin system.14 The different embryological origin of the RV and LV and their different physiological environments may explain for this.15,16

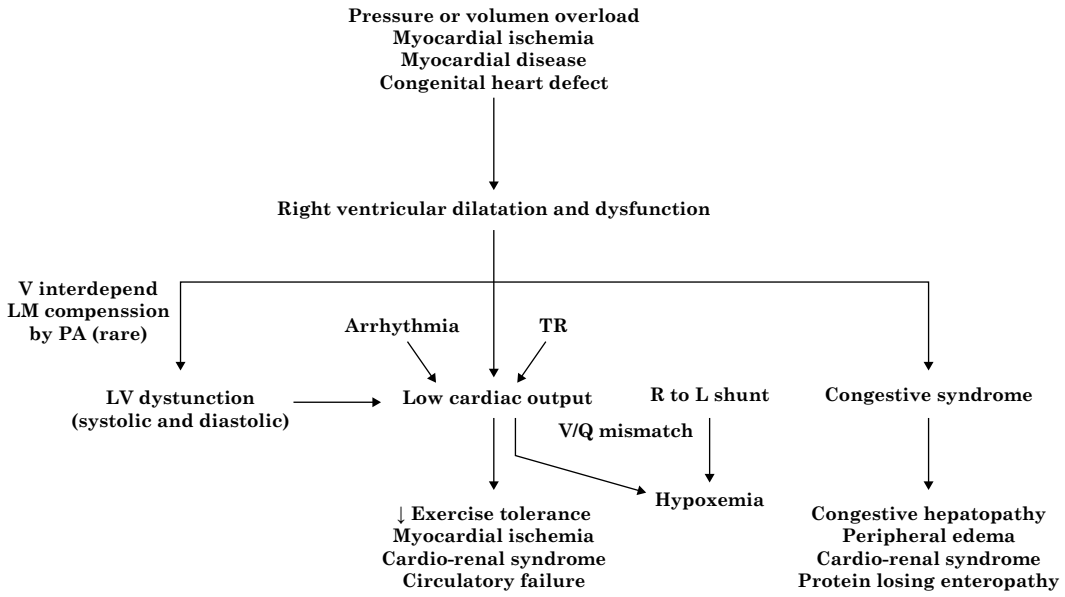

Figure 1 - Pathophysiology of right heart failure. Adapted from Haddad et al.4

Diagnostic evaluation of patients with RHF

The history is very much important in the evaluation of RHF.The presence of coronary artery disease, emphysema/chronic bronchitis, history of deep venous thrombosis, recurrent abortions, autoimmune diseases especially scleroderma and systemic lupus erythematosus (SLE), and infections, e.g., HIV, tuberculosis and schistosomiasis and family history of PAH should be thoroughly sought.

Symptoms of right heart failure are mainly due to systemic venous congestion and/ or low cardiac output. This includes exertional dyspnoea, fatigue, dizziness, ankle swelling, epigastric fullness and right upper abdominal discomfort or pain.

Signs: raised jugular venous pulse (JVP), left parasternal lift, an accentuated second pulmonary sound, right ventricular gallop, usually a pansystolic murmur over the tricuspid area which increases with inspiration, and sometimes diastolic murmur of pulmonary insufficiency; also, an enlarged tender liver, ascites frequently present as well as ankle oedema. Raised JVP is a specific sign of right heart failure and is a prognostic marker. It correlates with mortality and a risk of heart failure hospitalisation in LVF(SOLVD study).[17] Kussmaul sign, which is an increase of JVP on inspiration, can help in pointing to the cause of RHF.

The goals of the initial evaluation of patients with RHF are to better characterize its etiology, severity and functional status, the presence and extent of end organ

damage (renal dysfunction, liver dysfunction) and the presence of associated conditions.

Echocardiography plays a key role in the diagnosis of right heart disease. Signs of right heart disease on an echocardiogram can include

- RV enlargement,
- RV systolic dysfunction(e.g.TAPSE)
- Tricuspid regurgitation,
- Pulmonary hypertension,
- Congenital heart defects,
- Valvular heart disease, or
- Left heart disease.

Magnetic resonance imaging (MRI) is becoming the gold standard for evaluating right heart structure and function and is particularly useful in

- Complex congenital heart defects (eg, Ebstein's anomaly, hypoplasic RV),
- Precise quantification of valvular regurgitation and
- Planning of a complex surgery

Angiography by MRI, computed tomography-angiography or heart catheterization

may be of particular value in excluding chronic thromboembolic pulmonary disease, in assessing complex arterio-venous malformations or congenital heart defects.

Right heart catheterization is an important part of the evaluation of right heart

disease. Indications for right heart catheterization include assessment of pulmonary vascular resistance or impedance, pulmonary pressures, cardiac output shunt fraction, and pulmonary vasoreactivity.

Exercise testing is also very useful in objectively assessing clinical deterioration in patients with PAH or congenital heart disease. Caution is, however, advised in performing maximal exercise testing in patients with severe pulmonary vascular disease.[18]

Obtaining baseline renal and liver function tests, albumin, uric acid levels as well as B-type natriuretic peptide levels may be of particular interest in determining prognosis of right heart disease.[19-25]

Electrocardiography is part of the routine evaluation and allows assessment of cardiac rhythm, QRS duration or the presence of atrio-ventricular conduction block.

Other studies should be individualized depending upon the suspected etiology of RHF.

Lung or heart biopsy is rarely indicated in patients with isolated right heart disease.

Genetic counseling should be pursued in patients with congenital heart disease or arrhythmogenic right ventricular dysplasia (ARVD).

Management of RHF

The management of RHF is not well supported by randomized controlled trials. Furthermore, clinical trials in patients with RHF have not been powered for mortality endpoints. Among patients with RHF, the evidence is best established for patients with PAH.[1,26]

Circulation and RV

The pulmonary circulation is a low-pressure circuit both at rest and during exercise. The lung can recruit partially collapsed or unused vessels as cardiac output increases and there is relatively low degree of vascular motor tone in the proximal pulmonary vascular bed.The more compliant RV is better suited to accommodate large increases in right-sided venous return but tolerates acute increases in afterload poorly.[27-29] As RV afterload increases, the RV begins to dilate limiting its ability to increase contractility. An enlarging RV begins to impede LV filling by moving the interventricular septum toward the LV in a process known as interventricular dependence("D" sign in echo).LV filling in this setting is often refractory to intravascular volume expansion, as raising central venous pressure only increases the difference between RV end diastolic pressure and LV end-diastolic pressure, and further compromises LV filling.

A normal tricuspid annular plane systolic excursion is about 2.4–2.7 cm,[30,31] whereas a value below 1.8 cm has been shown to have an 87% accuracy at predicting a stroke volume index less than 29 ml/m2.

The most important aspect of managing RHF is tailoring therapy to its specific cause. In managing patients with RHF, it is also useful to divide the syndrome into 4 clinical categories:

- Biventricular failure,
- Systemic RV failure,
- Predominant sub-pulmonary RV failure, and
- Hypoplasic RV syndrome.

Causes of acute RV failure can be divided into three main categories:

- Excessive preload;
- Excessive afterload; and
- Insufficient myocardial contractility.

In most cases, acute RV failure is a combination of established pulmonary vascular disease complicated by acute derangements in one or more of these three main categories.In these situations, the conditions responsible for chronic RV failure cannot be reversed, and management should be directed toward optimizing RV function while reducing the cause of RV failure. At other times, acute RV failure is the result of a sudden increase in RV afterload, such as occurs with massive pulmonary embolism.In this situation, the first priority should be relieving the increase in afterload.

The physiological goals of RHF treatment include

- Optimization of preload, afterload and contractility.
- Sodium and fluid restriction and judicious use of diuretics all help optimize RV preload.

General Preventive Measures

- Referral to a congenital heart disease or pulmonary hypertension specialist when appropriate.
- Prevention or early recognition of RHF decompensation is key in managing RHF. Factors that may lead to volume overload include noncompliance with sodium (<2 g daily) or fluid restriction, non-compliance with medications or useof nonsteroidal anti-inflammatory drugs or nondihydropyridine calcium channel blockers.
- Patients with significant PAH or severe RHF should also be advised against pregnancy, as it is associated with increased maternal and fetal mortality rate.
- Prevention of infection with influenza and pneumococcal vaccination is also recommended, as is prophylaxis against bacterial endocarditis in patients with mechanical valves, previous infectious endocarditis or in patients with complex cyanotic CHD.

Reversing cause of acute RHF

- Biventricular failure is managed following the guidelines of the AHA/ACC or ESC for managing patients with chronic HF.Patients with biventricularfailure benefit from beta blockade and ACE inhibition or angiotensin receptor blockers.
- In patients with ST elevation myocardial infarction involving the right ventricle, early reperfusion should be achieved as early as possible.31 Maintenance of atrioventricular synchrony, correction of bradycardia and maintenance of hemodynamic stability with appropriate volume loading or inotropic support are also recommended.31
- In patients with acute hemodynamically compromising pulmonary embolism evidence supports the use of thrombolytic agents (alteplase).[32,33]
- In cor pulmonale we should try to avoid acute exacerbation,recurrent infection being the most common cause.As the pulmonary disease cannot be reversed treatment goal aims at oxygen therapy,NIV and preventing and managing intercurrent infections.
- Treatment of the other chronic cardiopulmonary conditions after acute control of the situations

RV Preload

Proper fluid management is critical for successful management of RV failure.
The causes of fall in intravascular volume in a critically ill RHF patient can be:

- Bleeding,
- Increased vascular permeability, and
- Insensible losses
- Sedatives and analgesics blunting sympathetic vasoconstriction of the systemic venous circulation, leading to decreased venous tone and reduced right-sided return
- Positive pressure ventilation can also impede RV preload by increasing intrathoracic pressure and reducing RV transmural filling pressure.

Adequate right sided filling pressure is essential in maintaining cardiac output in patients with acute RV failure 34. If low intravascular volume is suspected, volume resuscitation should be instituted as quickly as possible. However, RV preload requirements differ substantially based on whether afterload is normal or increased.

When RV failure occurs in the setting of normal pulmonary vascular resistance, such as in right-sided myocardial infarction, RV end-diastolic pressure often needs to be increased above normal levels to maintain cardiac output. However, when RV failure occurs in the setting of increased RV afterload, volume loading can result in displacement of the interventricular septum toward the LV and impaired LV diastolic filling.To complicate the matter, RV dilation increases free wall tension, resulting in increased oxygen demand and decreased RV perfusion. In this setting, intravascular volume may need to be decreased.

Optimal right-sided filling pressure may vary considerably between individual patients based on RV contractility and afterload. In general, preload goals should be to keep RV transmural filling pressures in a moderately elevated range, typically 8–12 mm Hg, and then adjusted from there to optimize RV function and cardiac output.

RV Afterload

Excessive afterload plays some role in nearly all cases of acute RV failure, and decreasing it is usually the most effective way of improving RV function. Unfortunately, many cases of acute RV failure are associated with chronic heart or lung diseases that cannot easily be reversed. In these situations, efforts should be focused on removing any factors that can contribute to increased pulmonary vascular tone followed by the judicious use of selective pulmonary vasodilators.

The causes of acute RHF due to increased afterload are

- Acute pulmonary thromboembolism causes acute RHF in the setting of acute submissive or massive PE.
- In critically ill patients, hypoxic pulmonary vasoconstriction can occur in response to decreases in oxygen tension in the alveoli, pulmonary arterial blood, or bronchial arterial blood, and is enhanced by hypercapnea or acedemia [35,36]
- High or low lung volume can worsen RV afterload, because pulmonary vascular resistance tends to be lowest when the lung is near functional residual capacity.37
- Several vasoactive factors such as endothelin and thromboxane, are elevated during sepsis, and have been shown to correlate inversely with cardiac output. Serotonin and IL-6 are also upregulated in sepsis and the acute respiratory distress syndrome.
- Decreased production of nitric oxide in the lung contributes to increased pulmonary vascular resistance in sepsis,38 and endotoxin can increase pulmonary vascular resistance via suppression of nitric oxide synthesis.
- Any injury that damages the pulmonary vascular endothelium can precipitate thrombosis in situ and raise pulmonary vascular resistance further.

Interventions aimed at reducing RV afterload should begin with correction of hypercapnea, acidemia, and alveolar hypoxia.

- Ideally, SaO2 should be kept above 92%, and ventilator settings should be adjusted to achieve a lung volume near functional residual capacity and a PCO2 and pH that are as close to normal as possible.
- Considering low-volume ventilation
- In case of acute submassive or massive PE systemic thrombolysis or pharmaco mechanical CDT has important role in reducing afterload.
- When adjustment of preload and afterload do not achieve satisfactory improvement in RV function, administration of *pulmonary vasodilators* may be appropriate. The drugs have systemic as well as pulmonary vasorelaxant properties, and is capable of causing hypotension. Furthermore, systemic administration can worsen gas exchange by blunting hypoxic pulmonary vasoconstriction and impairing V :=Q matching.[39,40]

Inhaled nitric oxide is a potent pulmonary vasodilator[41-43] with a rapid onset of action and an extremely short half-life, making it an ideal agent for attempting to unload the

RV in the intensive care unit. Furthermore, its greater effect on blood vessels in well ventilated lung can improve oxygenation by stealing blood flow away from areas of very low V:=Q or shunt. Inhaled nitric oxide has been shown to improve improve pulmonary hemodynamics and mixed venous oxygen saturation in patients with acute RV failure.

Three *prostacyclin derivatives* are currently available for treatment of pulmonary arterial hypertension. They exert their vasodilator effects by increasing intracellular cAMP levels, and, thus, may also provide inotropic effects on cardiac function. *Phosphodiesterase (PDE) 5 inhibitors* inhibit the metabolism of cGMP, the second messenger that mediates the vasodilatory effects of nitric oxide and the natriuretic peptides. In animal studies, PDE5 inhibitors increase contractility in hypertrophied RV, but not in normal RV.[44] Thus, these agents may improve RV function in patients with chronic pulmonary hypertension who develop acute RV failure.

The use of other currently available pulmonary vasodilators, such as the *endothelin receptor antagonists* and the recently approved soluble *guanylate cyclase stimulator, riociguat*, should probably be avoided in acute RV failure. *Calcium channel blockers* should also be avoided, because they have negative inotropic effects, and have been shown to increase RV stroke work index.[45]

Insufficient RV Contractility

Increases in RV preload and/or afterload increases free wall tension and O2 demand, while impeding LV filling, reducing LV output, and decreasing coronary artery pressure. Metabolic derangements from a variety of insults, including acid/base disturbances, generation of reactive oxygen species, and inflammatory cytokines, impair oxygen utilization and contribute to RV failure in critically ill patients.[46] At the same time, sepsis and other critical illnesses associated with increased metabolic demand result in the need for increased oxygen delivery, and may exceed the ability of the RV to maintain adequate cardiac output. Perfusion of the RV free wall is determined by the difference in RV free wall tension and coronary artery pressure.[47]

Coronary perfusion of the RV decreases during systole in patients with pulmonary arterial hypertension and normal systemic pressures, and a similar impairment is likely to occur when acute RV failure occurs in the setting of systemic hypotension. Fluid resuscitation that results in ventricular enlargement and increases in RV free wall tension without improving systemic arterial pressure can actually decrease RV perfusion.[48] Patients with acute RV failure associated with chronic pulmonary vascular disease may have RV systolic pressures that approach or exceed systemic pressure. In this situation, the first goal of vasopressor therapy is to restore systemic blood pressure to levels above RV systolic pressure. Drugs that increase myocardial contractility should be withheld until this first goal is achieved.

Vasopressors

Several vasoactive drugs have been used to manage RV failure in the intensive care unit. The ideal vasopressor for use in acute RV failure would be an agent that increases systemic arterial pressure and RV contractility without raising pulmonary vascular resistance. *Norepinephrine* is the most reasonable agent in hypotensive patients with acute RV failure and is often the initial pressor used in our institution for this purpose.

Inotropes

Low-dose dopamine is a reasonable option to improve RV contractility in patients with RV failure. At doses below 16 mg/kg/min, dopamine increases cardiac output without compromising pulmonary vascular resistance.[49] *Dobutamine* at low doses (5–10 mg/ kg/ min), dobutamine improves pulmonary artery/RV coupling in animal studies and improves myocardial contractility and pulmonary vascular resistance in patients with left heart failure.[50] *Milrinone,* a selective PDE-3 inhibitor can improve inotropy and pulmonary vasodilatation.[51,52] Milrinone is frequently the agent of choice in patients with pulmonary hypertension from biventricular failure, and in those recovering after ventricular assist or cardiac transplantation.53

Inotropes increase the risk of tachyarrhythmias, and should generally be considered only when there is evidence of inadequate oxygen delivery despite the correction of abnormalities in RV preload, afterload, and ischemia.

Calcium sensitizers, such as *levosimendan,* that enhance myocardial contractility without increasing cytosolic calcium and oxygen demand, have been used to increase cardiac contractility in heart failure. Randomized placebo-controlled studies have shown improvement in RV systolic and diastolic function in patients with left heart failure, and recent reports describe improved RV function in response to levosimendan in patients with RV failure associated with chronic thromboembolic pulmonary hypertension and heart transplantation.54

Mechanical Support

When medical therapy for acute RV failure in the intensive care unit is ineffective mechanical support may be considered. Extracorporeal life support, specifically veno-venous and veno-arterial extracorporeal membrane oxygenation, has been used

successfully in patients with RV failure due to massive pulmonary embolus, chronic thromboembolic pulmonary hypertension, and pulmonary arterial hypertension, usually as a bridge to endarterectomy or lung transplantation.[55] Unlike veno-venous extracorporeal membrane oxygenation that oxygenates venous blood, but requires the RV to pump the entire cardiac output through the

pulmonary circulation, veno-arterial extracorporeal membrane oxygenation pumps enough blood from the venous to the arterial circulation to unload the RV while maintaining systemic oxygenation. Veno-arterial extracorporeal membrane oxygenation improves RV function and oxygen delivery, and has been used successfully in awake, spontaneously breathing patients.[57]

More recently, pumpless lung-assist devices have been developed that connect the pulmonary artery to the left atrium with a low-resistance membrane oxygenator. Pulmonary blood flow through the low resistance circuit unloads the RV and enhances LV filling.[58] There is no role of IABP in the setting of acute RHF.

Conclusion

Acute RHF is an important cause of hemodynamic deterioration and hospital admission and mortality. The evaluation and management targets finding and treating any reversible cardiopulmonary factors. If acute and chronic conditions are not reversible management aims to optimize right ventricular preload, afterload and improving myocardial contractility. Role of ECMO is there in medically refractory acute RHF.

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Respiratory Emergencies in Neuromuscular Disorders

Rohit Bhatia, Nishita Singh

Introduction

Various acute and chronic neuromuscular disorders can lead to dysfunction of respiratory and/or bulbar muscles which in turn lead to type II respiratory failure, lower respiratory tract infections and eventually, death. Disorders of anterior horn cell, peripheral nerves, neuromuscular junction and muscles, can all cause respiratory dysfunction and mortality. Thus, it is essential to have a basic understanding of anatomy and physiology of neurological control of respiratory function and to know subtle symptoms and signs on history and examination to pick up respiratory involvement. This article reviews these basics along with initial evaluation and management of these respiratory emergencies in neuromuscular disorders.

Basic anatomy and physiology

Diaphragm, which is the main inspiratory muscle, responsible for more than half of ventilatory effort at rest, is innervated by phrenic nerve (C3-C5 root). It is highly resistant to fatigue due to high perfusion and composition with both high and low oxidative muscle fibers. Accessory muscles of inspiration like external intercostals, scalene and sternocleidomastoid act only when the work of breathing is increased. Normal expiration is a passive process; however, forceful expiration requires active contraction of internal intercostals and abdominal wall muscles.

Co-existing morbidities like airway disease (e.g.- obstructive airway disease), reduced lung compliance (due to scoliosis, pulmonary fibrosis or obesity), inadequate clearing of secretions due to bulbar weakness or mucus plugging due to restricted mobility can all contribute further to respiratory failure in these patients.

Pathophysiology

Respiratory muscle weakness along with reduction in airflow leads to decrease in functional residual capacity and ventilation/perfusion mismatch due to lower lung

volumes which in turn affects gas exchange and thus compromises the respiratory reserve. Once this has occurred, any increase in respiratory load in the form of increase in respiratory rate (e.g.- fever), decrease in lung compliance (e.g.- consolidation, atelectasis) and abdominal distension may lead to diaphragmatic fatigue and respiratory failure.

Following are the various mechanisms that can cause respiratory insufficiency in patients with neuro-muscular disorders:

- ***Upper airway problems***: weakness of oropharyngeal muscles and tongue can lead to increased risk of aspiration due to impaired swallowing. In addition, vocal cord paralysis further leads to partial upper airway obstruction.
- ***Inspiratory and expiratory muscle problems***: Weakness of diaphragm, intercostals and sternocleidomastoid leads to abnormal sigh, decreased lung expansion due to atelectasis and ventilation-perfusion mismatch which further causes hypoxemia. Progressive weakness of inspiratory muscles leads to decreased tidal volume and compensatory increase in respiratory rate to maintain minute ventilation. Persistent tachypnea with increased work of breathing leads to increased CO2 retention, hypoxemia and eventual respiratory failure. Weakness of muscles of expiration (external intercostals and abdominal muscles) leads to impairment of cough which causes pooling of secretions leading to mucus plugging and pneumonia.
- ***Associated cardiac disease:*** Many patients with neuromuscular disorders have associated cardiac muscle involvement leading to cardiomyopathy and congestive heart failure. The latter, leads to further decline in lung compliance and increase in workload of already weak respiratory muscles. Prolonged immobilization carries an additional risk of deep vein thrombosis and subsequent pulmonary embolism.
- ***Central mechanisms:*** In addition to these peripheral mechanisms, the adequacy of central respiratory drive is also important. In rapid eye movement sleep (REM) there is hypotonia of accessory muscles of respiration and airway along with transient reduction in respiratory drive which can lead to hypoxemia, hypercarbia and desaturation.(**1**)"container-title":"Intensive Care Medicine","page":"1876-1891","volume":"33","issue":"11","source":"PubMed","abstract":"OBJECTIVE: To determine the prevalence, risk factors, and outcomes of critical illness neuromuscular abnormalities (CINMA These may be early signs of respiratory failure especially in patients with sub acute to chronic neuromuscular disease.

Initial diagnostic evaluation

A detailed history and a thorough clinical examination with detailed evaluation of respiratory and bulbar muscles is a pre-requisite in all patients with neuromuscular

disease. Figure -1 demonstrates various mechanisms of respiratory dysfunction in these disorders. It is important to look for presence of concurrent lung disease, dysautonomia, systemic infection and malnutrition.

1. History

- Symptoms of respiratory muscle weakness depend upon the disease onset and evolution.
- In acute to sub-acute conditions like GuillainBarre Syndrome (GBS), predominant symptoms are of orthopnea, dyspnea and at times respiratory distress. These may or may not be accompanied by bulbar weakness.
- In chronic disorders like muscular dystrophies, the symptoms first begin in sleep in the form of nocturnal desaturation, nightmares, daytime somnolence, fatigue and early morning headaches.
- Thus, in general, faster progression of weakness leads to faster onset of respiratory failure and need for assisted ventilation.
- To know the etiological diagnosis, additional history like
  - onset of weakness (ascending type in GBS, ocular or bulbar in myasthenia gravis or botulism), - pattern (progressive or fluctuating),
  - associated autonomic disturbances (botulism or LEMS),
  - associated sensory symptoms,
  - family history of similar illness need to be asked.

  Table 2,3, 4 and 5 summarize the details of clinical history, examination findings and treatment of patients with neuropathy, neuromuscular junction disorder anterior horn cell disease and myopathies respectively, which can have respiratory failure.

2. Signs

- A patient with severe respiratory illness may be severely breathless and may not be able to speak in full sentences. He or she may not be able to count numbers up to 15 in a single breath and there may be associated paradoxical breathing; a sign of diaphragmatic failure and need for ventilatory assistance.
- There can be tachycardia, diaphoresis and use of accessory muscles of respiration.
- Alteration of consciousness and /or drowsiness may result from hypoxemia and / or hypercarbia.

- There may be pooling of secretions with decreased palatal movements and absent gag reflex suggestive of bulbar weakness with or without neck drop suggestive of neck muscle weakness.

  Box 1. gives clues on examination findings depending upon site of lesion. Table 1. gives list of disorders which can cause respiratory failure as per site of lesion.

  The examination should then be completed with assessment of extra ocular, facial, masticatory and appendicular muscles. Some important clues to the etiology of the disorder that should be looked for:

  - a *tall, thin face* (congenitalmyopathy, myotonic dystrophy),
  - *ptosis or ophthalmoparesis* (mitochondrial disorder, myasthenia),
  - f*asciculations* (motor neuron disease),
  - *paraspinal muscle wasting* (acid maltase deficiency),
  - *skin rash* (dermatomyositis) etc.

3. Laboratory Investigations

A complete assessment of respiratory function involves chest x-ray, arterial blood gases and bedside pulmonary function tests. Following are the tests routinely done in patients with neuromuscular weakness:

- ***Vital capacity (VC):*** This is a simple test and normal values can be calculated from patients' age, height and gender. Decline in VC by 15-20% on lying down is specific for diaphragmatic weakness. A normal VC with no fall on lying down rules out neuromuscular cause of respiratory failure. In patients with facial weakness there may difficulty in holding the mouth-piece tight near the mouth which may lead to false results. In a retrospective questionnaire study, vital capacity had the strongest co-relation with number of chest infections and days of antibiotic treatment in the preceding year. It has also found to be predictive of sleep disordered breathing, day time respiratory failure and survival from various studies. (2),(3)respiratory muscle function and peak cough flows had been obtained. Data were related to: (1

- ***Mouth pressures:*** These can be used to calculate maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) which are a measure of inspiratory and expiratory muscle strength respectively. Sniff nasal inspiratory pressure (SNIP) can be used when MIP is low and the higher of the two values is chosen. In an adult male, an MIP of less than 80 cm H2O (female: 70 cm H2O) or a SNIP of less than 70 cm H2O (female: 60 cm H2O) indicates significant respiratory

muscle. The British Thoracic Society guidelines state that VC is a valuable predictor of susceptibility to infection, however measures like MIP, MEP or SNIP provide little or no additional information as compared to vital capacity.(level of evidence 2)[4]

- ***Arterial blood gases:*** These may remain normal despite presence of respiratory weakness due to compensatory mechanisms. Slight elevation in pH and bicarbonate with normal PaO2 and PaCO2may be an indication of nocturnal hypoventilation. Those with recognized respiratory failure secondary to neuromuscular weakness will show hypoxemia and a compensated respiratory acidosis (raised PaCO2 and bicarbonate with a normal or mildly reduced pH). A daytime PCO2>45 mm of Hg predicts nocturnal hypoventilation with a sensitivity of 91% and specificity of 75%.[5] usually preceding daytime respiratory failure. Appropriate scheduling of polysomnography and the introduction of noninvasive ventilation (NIV)

- ***Chest X ray:*** This is a simple and convenient investigation which can give vital information about presence or absence of pneumonia, lung collapse, scoliosis and diaphragmatic palsy. Confirmation of diaphragmatic palsy requires fluoroscopy.

- ***Overnight monitoring:*** The most clear-cut overnight investigation in a patient suspected to have alveolar hypoventilation is oximetry. Apolysomnography (PSG), if available, can give additional information about heart rate, airflow, eye movements and stage of sleep at the time of desaturation. Box 2 gives the list of indications of PSG in various neuromuscular disorders. There are no studies that indicate the frequency required to perform sleep studies. The American Thoracic Society Consensus Statement for DMD recommends annual assessment(6). It may be done more frequently in those with faster clinical deterioration or in those whose disease progression is not known.

  However, it should be remembered that these tests are *only supplementary* to clinical examination and have their own drawbacks. Beside spirometry is effort dependent and require careful coaching prior to actual tests. Aggressive coaching before test can also cause fatigue resulting in false positive results. Poor mouth sealing and presence of secretions can also alter test results. FVC and pressures can be interpreted consistently only when taken in same body position. Any major discrepancies between volume and pressure measurements are usually due to inadequate measurements. Pre-existing lung or airway disease can also alter the results.

- ***Specific tests for neuromuscular disorders:*** Specific tests are then required to find etiology of the neuromuscular disease. These include:

– *Nerve conduction studies and electromyography* (EMG; including testing of thephrenic nerve and the diaphragm and repetitive nerve stimulation),

– *Blood tests* (chemistry panel, creatine kinaseand aldolase, antibodies for MG (acetylcholine receptor antibody (AchRAb, muscle specific kinase (MusKAb), antibodies for Lambert-Eaton myasthenic syndrome, serologies for infectious agents, antiganglioside antibodies for GBS as deemed pertinent),

- *Lumbar puncture*, and

- *Biopsy of nerve and muscle.*

Some important acute neuromuscular disorders and respiratory dysfunction

1. Guillain-Barre Syndrome (GBS)

Also commonly known as acute inflammatory demyelinating radiculoneuropathy (AIDP) is an important cause of acute neuromuscular weakness and is the prototype of this disorder. Other variants of GBS are now well recognized including acute motor sensory axonal neuropathy (AMSAN). Around 25% of patients with GBS develop respiratory failure. Features that have been found to predict need for ventilation are:[7,8,9,10]

- Time interval of <7 days from onset to hospitalization,
- Bulbar weakness,
- Facial weakness,
- Rapid progression,
- Inability to stand or lift head or elbow off bed,
- Associated dysautonomia,
- Vital capacity <20 ml/kg, MIP<30 cm H2O, MEP<40 cm H2O, serial decline of the vital capacity, MIP or MEP by >30% (20-30-40 rule),
- Presence of demyelination on neurophysiological testing and
- Raised liver enzymes.

Another study by Paul and colleagues(10)done in 138 patients with GBS showed following were predictors of mechanical ventilation:

- Simultaneous weakness in upper and lower limbs,
- Presence of neck and bulbar weakness,
- Power in upper limbs <3/5,

- Bilateral facial weakness and
- Shorter duration from onset to bulbar weakness while preserved DTR's in upper limbs at nadir was significantly associated with no requirement of mechanical ventilation.
- Thus, detailed assessment of clinical features can give important clues in patients with acute neurological disorders.
- Non-invasive ventilation is not a preferred option as these patients may not improve for several days and many of them have associated autonomic dysfunction.
- Use of succinylcholine should be avoided during intubation to avoid risk of hyperkalemia.
- Use of neuromuscular blocking agents should be best avoided for risk of worsening weakness. It is very essential to maintain pulmonary toileting, adequate nutrition, frequent body turning and gastric protection. As these patients are conscious but paralyzed, it is important to timely reassure them and avoid sedation. The mortality rate in GBS due to respiratory failure can reach up to 5-10%(11).

2. Myasthenic crisis

- Myasthenic crisis is defined by respiratory failure and need for invasive/ non-invasive ventilation. Most common triggers are infections, surgery, non-compliance and use of other drugs which trigger MG.(12) Box 4 gives a list of medications which can exacerbate myasthenia.

- Signs which indicate impending respiratory failure are inability to count 1 to 20 in a single breath and paradoxical breathing.

- Cholinergic crisis need to be differentiated from myasthenic crisis clinically by presence of increased salivation, lacrimation, diarrhea, bradycardia and fasciculations. Anti-MuSK antibodies are found in 8-10% cases and these present more commonly with bulbar weakness and respiratory failure.

- Management of myasthenic crisis involves prompt initiation of immunotherapy and securing airway with non-invasive/ invasive ventilation. Initiation of bilevel positive airway pressure (BiPAP) earlier in course may prevent endotracheal intubation. Even those with bulbar weakness can tolerate non-invasive ventilation.

- It has also been shown that those with BiPAP have lower rates of pulmonary complications.(13)Rochester, Minnesota.\nMAIN OUTCOME MEASURES: Collected information included patients' demographic data, immunotherapy, medical complications, mechanical ventilation duration, and hospital lengths of stay, as well as baseline and preventilation measurements of forced vital

capacity, maximal inspiratory and expiratory pressures, and arterial blood gases.\nRESULTS: We identified 60 episodes of MC in 52 patients. BiPAP was the initial method of ventilatory support in 24 episodes and ET-MV was performed in 36 episodes. There were no differences in patient demographics or in baseline respiratory variables and arterial gases between the groups of episodes initially treated using BiPAP vs ET-MV. In 14 episodes treated using BiPAP, intubation was avoided. The mean duration of BiPAP in these patients was 4.3 days. The only predictor of BiPAP failure (ie, requirement for intubation Cholinesterase inhibitors, most commonly pyridostigmine, is used for symptomatic treatment. These tend to increase airway secretions; dose modification of these medications may be done appropriately. Immunosuppressive treatment with steroids is started after exclusion of active infection and preferably started at low doses and escalated gradually to a target dose of 1mg/kg to prevent risk of initial worsening of neuromuscular weakness in some patients. Standard long term therapy with steroid sparing agents and steroid tapering is followed.

3. **Critical illness neuromyopathy**

- Critically ill patients can develop severe weakness of limb and respiratory muscles due to axonal neuropathy and/or myopathy. These disorders usually occur in conjunction and hence the use of term neuromyopathy(14).These can be seen in up to 50% patients admitted with multi-organ failure, sepsis and who are ventilator-dependent for more than 72 hours, making it one of the common causes of difficult weaning in these critically ill patients(1)"container-title":"Intensive Care Medicine","page":"1876-1891","volume":"33","issue":"11","source":"PubMed","abstract":"OBJECTIVE: To determine the prevalence, risk factors, and outcomes of critical illness neuromuscular abnormalities (CINMA.

- Other risk factors include hyperglycemia, prolonged use of neuromuscular blockade, use of high dose steroids and immobility(15). On examination, all limbs are symmetrically flaccid and immobile with diminished and/or normal reflexes depending on whether there is involvement of peripheral nerves. Sensory examination is difficult and diaphragmatic weakness is common.

- Nerve conduction studies (NCS) and electromyography (EMG) are usually not very informative as they can be confounded by peripheral edema or un-cooperative patient.

- Critical illness neuropathy shows reduced amplitude of sensory and motor potentials with normal or diminished conduction velocities.

- EMG may show myopathic pattern with prolongation of CMAP duration as the earliest finding(16)"container-title":"Muscle & Nerve","page":"1040-1042","volume":"40","issue":"6","source":"PubMed","abstract":"Critical illness myopathy (CIM.
- Creatine kinase may be normal or only mildly elevated.
- Muscle biopsy in neuropathy will show atrophy of type 1 and 2 fibers with grouped atrophy seen in advanced cases.
- Nerve biopsy will show axonal loss.
- There is no specific therapy for these disorders and patient may continue to remain weak, weeks after discharge.

Chronic neuromuscular disorders and respiratory dysfunction

Patients with chronic neuromuscular diseases like motor neuron disease, muscular dystrophies, congenital myopathies, spinal muscular atrophy, and mitochondrial myopathies etc. can develop respiratory failure in late stages which may present as early daytime somnolence, fatigue and nightmares. Rarely, it may present as acute respiratory failure precipitated usually by infection. A serial recording of vital capacity or MIP may help early pick-up of respiratory involvement and fall in these parameters is an indication to start non-invasive ventilation.

Long-term management of respiratory failure in neuromuscular disorders

- Patients with chronic neuromuscular disorders prone to develop respiratory weakness should be referred to respiratory physician. Treatment should include assisted cough techniques, respiratory muscle training, chest physiotherapy, non-invasive ventilation based on nature of underlying disease, its progression and its impact on patients' quality of life.
- Box 3 gives information about the indications of starting NIV.
- Home based care plays a vital role in management of these patients as it helps in reducing infections, hospital admissions, cost burden and helps in maintaining adequate lung function thus prolonging survival of these patients.

Airway Clearance

- Various airway clearing techniques include standard chest physiotherapy, incentive spirometry, high frequency chest wall oscillations and intrapulmonary percussive ventilation which help in removal of tenacious secretions especially in children.

Respiratory muscle training

- These involve performing repetitive maximal or near- maximal, inspiratory and/ or expiratory techniques with closed glottis or by using a nearly occluded resistor valve. These help in improvement in respiratory muscle strength and increasing endurance of the same. However, there are no studies in children or adults which have assessed clinically important outcomes of ventilatory function.

Home based ventilation

- Home based ventilation is yet another aspect in management of these patients as it has shown to prolong life and decrease frequency of hospital admissions.
- There is a wide range of home ventilators available for use. The two main types are pressure and volume targeted. Some more expensive hybrid machines can operate in both modes.
- There are no long-term studies comparing clinically relevant outcomes for different modes of ventilation. Box 3. gives list of indications of NIV in these patients.
- Leaks, skin abrasions, mid face hypoplasia are few adverse effects of NIV.
- Home ventilation via tracheostomy may be considered in patients with severe bulbar dysfunction, in patients not maintaining saturation on NIV or when there is a need for NIV for more than 16 hours per day.

Psychological and mental health issues

- There are reports of behavioral and mental problems in children and young adults with chronic neuromuscular disorders. It is important to acknowledge these factors and address issues like anxiety, depression and poor social adjustment.

Conclusion

Many acute and chronic neuromuscular disorders are associated with respiratory disturbances and ventilator assistance may be required either acutely or on long term with chronic progressive disorders. Multidisciplinary approach is critical to prevent mortality and morbidity and also improve quality of life for chronic disorders.

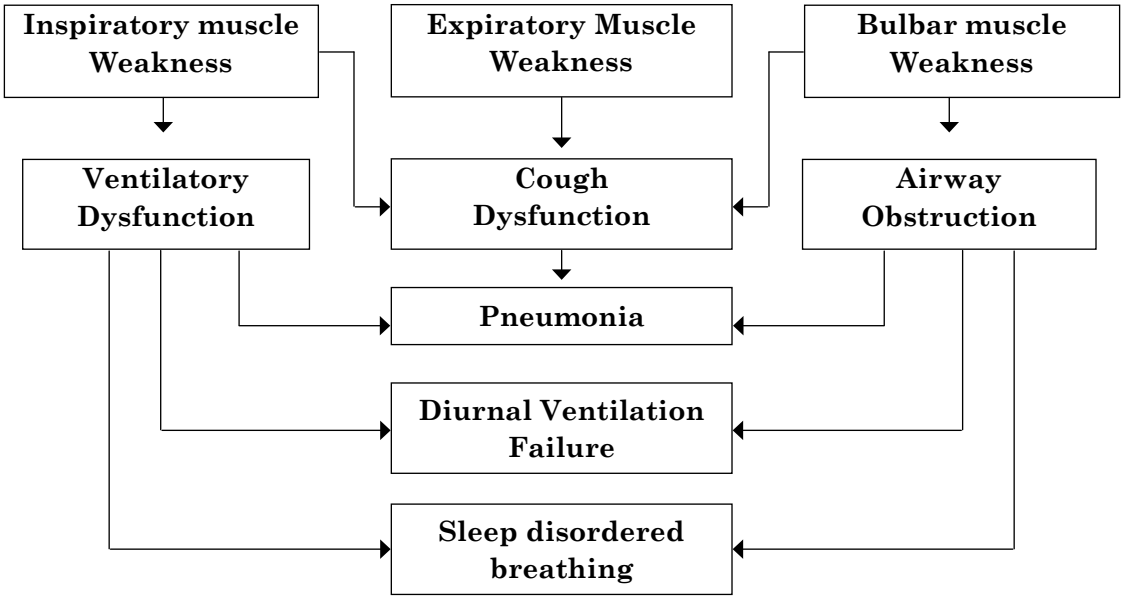

Figure 1 : Symptoms due to respiratory muscle weakness

Table 1 : Site of lesion with specific disorders likely to cause respiratory distress

Site of lesion & Specific disorders			
Anterior horn cell	**Peripheral nerve (& / or nerve roots)**	**Neuromuscular junction**	**Muscle**
• Motor neuron disease • Spinal muscular atrophy • Poliomyelitis & post-polio syndrome • Kennedy's disease • West Nile virus	• Guillain-Barre syndrome • Acute onset of CIDP • Critical illness polyneuropathy • Porphyria • Paraneoplastic • Phrenic nerve injury	• Botulism • Myasthenia gravis • Lambert-Eaton myasthenic syndrome • Organophosphate poisoning • Tick paralysis	• Inflammatory myopathy • Critical illness myopathy • Duchenne muscular dystrophy • Acid maltase deficiency • Congenital myopathy • Congenital muscular dystrophy • Limb girdle muscular dystrophy (especially LGMD 2C-2F, 2I) • Myotonic dystrophy (DM1) • Mitochondrial myopathy • Rhabdomyolysis

Table 2 : Neuropathies which are particularly likely to cause respiratory muscle weakness

Type of neuropathy	Clinical features	Laboratory features	Treatment
Acute inflammatory demyelinating radiculoneuropathy (AIDP) (GBS)	Proximal > distal weakness Less than 4 weeks Bifacial & bulbar involvement, Dysautonomia h/o vaccination or infection	NCS: Demyelinating type May have conduction blocks High CSF protein, Albumino- cytologic dissociation	IVIG PLEX
Chronic inflammatory demyelinating radiculoneuropathy (CIDP)	Proximal & distal weakness Proximal and distal sensory impairment, Progressive course >2 mo, Cranial neuropathy (uncommon)	EMG: demyelinating features High CSF protein Albuminocytologic dissociation	Steroids IVIg Immune suppressants
Polyneuropathy, Organomegaly, Endocrinopathy, M band, Skin changes (POEMS)	Polyneuropathy Organomegaly Endocrinopathy (diabetes, hypothyroidism, gynecomastia) Skin lesions (edema, clubbing, hypertrichosis, hyper pigmentation	EMG: severe, primarily demyelinating neuropathy, but axonal loss always present, M spike serum VEGF elevated Multiorgan failure, ascites, pleural effusion,	Irradiation or resection of plasmacytoma Melphalan, dexamethasone, IVIG Bortezomib, thalidomide
Vasculitis & collagen vascular disease	Multifocal neuropathy which becomes confluent Neuropathic pain Systemic vasculitis may be present	EMG: axonal polyneuropathy or, mononeuropathy multiplex Positive serology (ANCA, ANA, SSA, SSB, others) Nerve and muscle biopsy	Steroids, Immunosuppr-essants
Acute intermittent & variegate porphyria	Abdominal pain, followed by progressive weakness Motor /sensory, respiratory failure, bulbar and facial muscle weakness, Seizures, Psychiatric features Dysautonomia	EMG: axonal, predominantly motor neuropathy Elevated Urinary porphobilinogen Delta aminolevulinic acid	Intravenous glucose and haeme therapy

Type of neuropathy	Clinical features	Laboratory features	Treatment
Diphtheria	Polyneuropathy -15%, Respiratoryfailure-20% Onset: weeks after the onset of infection Bulbar weakness universal Ocular motor weakness Sensory and autonomic impairment:100% Cardiomyopathy (often fatal	EMG: prolonged distal motor latencies, slow motor conduction velocities CSF: high protein, mildly increased cells, albuminocytological dissociation Positive throat culture for Corynebacterium diphtheriae	Diphtheria antitoxin within the first 2 days of onset

IVIG: intravenous immunoglobulin therapy. PLEX: plasma exchange. VEGF: vascular endothelial growth factor. ANA: antinuclear antibody. ANCA: antineutrophilc cytoplasmic antibody. EMG: electromyography. NCS: nerve conduction study

Table 3 : Neuromuscular junction disorders which cause respiratory failure:

Disorder	Clinical features	Treatment
LEMS	Muscle weakness (especially proximal lower extremity) Ptosis: rare, Hyporeflexia, Dysautonomia, Muscle pain Association with small cell lung cancer in two-thirds of patients. Antibodies to P/Q voltage gated calcium channels in 90% of patients	Treatment of small cell lung cancer 3,4-DAP PE or IVIG
Botulism	Abdominal pain, nausea, or vomiting, diarrhea preceding weakness. Bulbar and ocular motor involvement. Respiratory failure: 20%–30% Dysautonomia Recent intake of canned food, soft tissue trauma, and infected wounds	Botulism anti-toxin
Organophosphorus poisoning	Suicidal attempt or accidental exposure. Respiratory failure, bulbar weakness, quadriparesis, fasciculations, cramps, miosis	Intravenous atropine and pralidoxime
Snake bite	Progressive bulbar paralysis and respiratory failure, ptosis, and ophthalmoparesis	Anti-snake venom
Neuromuscular blockade	Underlying kidney or liver failure, hypermagnesemia, medication interaction (e.g., sevoflurane), cholinesterase or pseudocholinesterase deficiency Use of a neuromuscular blocker (e.g., mivacurium, rapacuronium) Generalized weakness, ophthalmoparesis, ptosis, failure to wean	

Table 4 : Anterior horn cell disorders which cause respiratory failure:

Disease	Clinical features	Treatment
Poliomyelitis	Asymmetrical paralysis, bulbar & respiratory muscle weakness, dysautonomia EMG: increased CMAP amplitudes, denervation in multiple myotomes	Supportive care
West Nile encephalitis	Motor neuronopathy (similar to poliomyelitis) Asymmetrical weakness Diaphragm weakness, facial weakness: common Meningoencephalitis (headaches, ataxia, seizures) Test:IgM titer in serum and CSF	Supportive care
Tetanus	Risk factors: lack of adequate vaccination, puncture wounds, tongue piercing, poor hygiene childbirth (for the neonatal form) Severe, painful muscle spasms that may last seconds to minutes Generalized form: opisthotonus, generalized spasms, respiratory failure, dysautonomia, rhabdomyolysis and renal failure Milder, local forms: trismus, face muscle spasms (risus sardonicus), dysphagia, neck stiffness, and local limb spasms EMG: continuous high-frequency motor unit discharges during periods of spasms Wound culture positive in 30%–50%	Human tetanus immunoglobulin administration Antispasmodics Wound care

Table 5 : Myopathies which cause respiratory failure:

Disease	Clinical features	Laboratory features	Treatment
Inflammatory myopathy	Proximal /distal limb weakness Respiratory failure Skin rash in dermatomyositis Cardiomyopathy, ILD	EMG: myopathies, with spontaneous activity Raised CPK, Muscle biopsy Underlying malignancy should be excluded in polymyositis	Steroids IVIG PLEX
Rhabdomyolysis	Proximal/distal weakness, and myalgia And respiratory failure	Markedlyraised CPK Myoglobinuria, kidney dysfunction	Monitor renal function, IV hydration, alkalinize urine. Specific antivenom immunoglobulin in the case of envenomation

Disease	Clinical features	Laboratory features	Treatment
Acid maltase deficiency	Diaphragmatic weakness and respiratory failure common in the adult form: proximal/distal weakness, paraspinal atrophy, winging scapula Sleep-disordered breathing common	EMG: myopathic units, fibrillations, myotonic discharges, especially in the paraspinal muscles CPK: normal to markedly high, urine hexose tetra saccharide elevated Muscle biopsy or assessment of aglucosidase activity in blood or skin fibroblasts	BIPAP Long-term IV enzyme replacement

Box 1 : Examination findings as per clinical localization of lesion	
Examination findings as per clinical localization of lesion	
lesion	**Examination findings as per clinical localization**
Motor neuronopathy	• Muscle atrophy • Fasciculations • Frequent involvement of bulbar muscles • Lack of sensory signs and symptoms • DTRs: decreased or increased pathologic reflexes • Lack of ocular motor involvement until late in the course
Polyradiculopathy andneuropathy	• Loss of deep tendon reflexes • Motor and sensory impairment • Ocular motor involvement • Autonomic involvement
Neuromuscular junction disorder	• Significant ocular motor involvement • Frequent involvement of bulbar muscles • Proximal/distal limb weakness • Fatiguability • Muscle atrophy usually not present • DTRs: normal or decreased
Myopathy	• Proximal/distal limb weakness • Differential muscle weakness in dystrophies • DTRs: normal or decreased • Myalgia • Rhabdomyolysis

Box 2 : Indications of PSG in neuromuscular disorders
• Vital capacity <60% predicted • Loss of ambulation because of progressive weakness, or children who never attain the ability to walk • Infants with weakness • Children with symptoms of obstructive sleep apnoea or hypoventilation • Children with diaphragmatic weakness • Children with rigid spine syndrome

Box 3 : Disorder Sleep abnormality in various neuromuscular disorders	
Neuromuscular disorders	**Sleep abnormalities**
Duchenne muscular dystrophy	Obstructive sleep apnoea (younger patients) Hypoventilation (older patients)
Spinal muscular atrophy	Hypoventilation Apnoea/hypopnea
Myotonic dystrophy	Hypoventilation Apnoea /hypopnea Periodic limb movements Excessive daytime sleepiness
Peripheral neuropathies (eg,Charcot Marie Tooth dis.)	Hypoventilation Frequent arousals

Box 4 : Indications of starting NIV in neuromuscular disorders:
• To prevent respiratory decompensation • To alter chest wall/lung growth characteristics • During intercurrent chest infections • For perioperative period/gastric tube placement • During pregnancy • To rest respiratory muscles • To control nocturnal hypoventilation with or without symptoms • To treat established hypercapnic ventilatory failure • To palliate symptoms/end-of-life care

Box 5 : Drugs that exacerbate myasthenia gravis
• Antibiotics: aminoglycosides, colistin, polymyxin, macrolides, quinolones, imipenem, tetracyclines • Antiarrhythmics: procainamide, quinidine, lidocaine, trimethorphan • Neuromuscular junction blockers (succinylcholine, vecuronium), Quinine, Phenytoin • Immunosuppressants: steroids, cyclosporine • Antirheumatics: chloroquine, D-penicillamine • Psychotropics: lithium, chlorpromazine • Calcium channel blockers • Beta-Blockers • Magnesium • Iodinated contrast

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Chest Injuries-What Every Physician Must Know!

Dr. S.P. Chouhan, Dr. Vamshi Krishna Gone

Introduction

Thoracic injury account 25% of all severe injuries. In a further 25% it may be significant contributor to the subsequent death of the patient. Chest trauma, in comparison to other injured anatomic areas is unique in that it poses the double threat of hypoxia and hypovolemia both are rapidly lethal.

Most common cause of death in chest injury is Hemorrhage. The great majority of chest trauma do not require major surgical intervention. Mode of treatment is early physiological resuscitation, followed by correct diagnosis.

Many of these deaths can be prevented by prompt diagnosis and treatment. As in most of the emergency set ups physician is the first doctor to attend the emergency, he should have basic awareness about the management of trauma as a whole. In this chapter attempt will be made to discuss briefly the basic facts about management of chest injuries.

Types of Chest Injury:

- *Blunt Chest Injury (Closed Chest Injury)*

  Mostly by road side accidents (RTA), fall, crush injury; are usually associated with multiple injuries (head, limb, abdomen)
- *Penetrating Chest Injury (Open Chest Injury)*

  Mostly by assault, usually associated with chest wall damage, open pneumothorax and organ injury.

Pathophysiological sequance

Clinical presentation & the prognosis with thoracic trauma are related to the disruption of respiration, circulation, or both. Respiratory compromise can occur due to direct injury to the airway or lungs leading to interference in the mechanics of breathing. Depending

upon chest trauma there may be laceration of lung, intrapulmonary bleeding, and alveolar collapse, leading to decreased ventilation, ventilation-perfusion mismatch and reduced lung compliance ultimately causing hypoxia.

Circulatory compromise occurs usually because of significant blood loss, decreased venous return, decreased cardiac output as a result of direct cardiac or lung injury leading to intrathoracic bleeding, commonly manifests as hemothorax in both blunt and penetrating chest trauma. Massive hemothorax can lead to hypotension and hemodynamic shock. The ultimate development is metabolic and respiratory acidosis contributing to fatal outcome as shown in algorithm (Fig.1).

In patients who are recovering from trauma, there may be chest infection, especially amongst patients who had penetrating injuries. It may further add to development of shock.

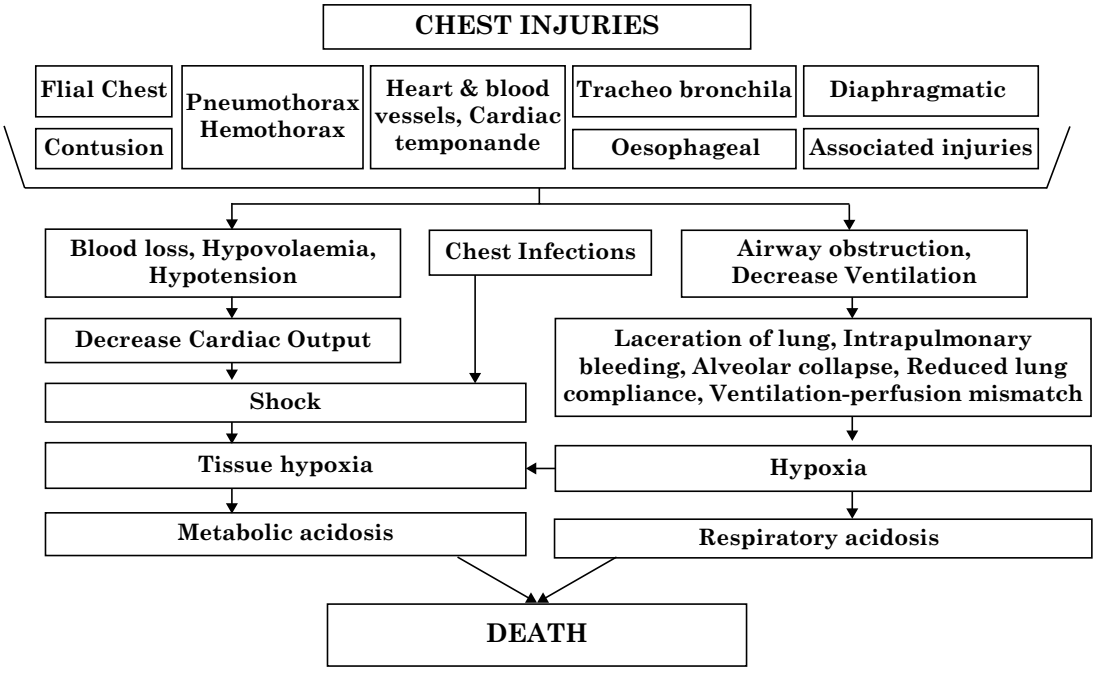

Figure 1 : Outlines of pathophysiological sequence of chest Injury.

Management of chest injuries

Broadly the initial evaluation of a trauma patient is based on the Advance trauma life support (ATLS) protocol. This begins with an assessment of the patient's airway, breathing, and circulation (ABCs) during the primary survey, typically in that order.

Quick decision and early interventions are key factors for better management and survival of the patients having chest injury. Management of chest trauma can be divided into three distinct levels of care;

- Pre-hospital life support (primary care),
- In-hospital e.g. in emergency room/ casualty/trauma centre life support (Secondary care and
- Surgical Management (tertiary care).

Chest injuries creates life threatening clinical situations which needs immediate attention and appropriate management. Such patients should be managed as early as possible in primary care or secondary care where ever the facilities and trained medical attendance is available. Some of these are:

- Airway obstruction
- Tension pneumothorax
- Pericardial tamponade
- Open pneumothorax (sucking chest wound)
- Massive hemothorax
- Flail chest
- Respiratory failure & shock

After stabilizing immediate life-threatening situations patient should be evaluated for life threatening injuries responsible for the potentially life-threatening situations e.g.

- Thoracic aortic disruption
- Tracheobronchial injury
- Blunt myocardial injury
- Diaphragmatic injury
- Oesophageal injury
- Pulmonary contusion/Laceration.

Most of these conditions need immediate surgical intervention and care under thoracic surgeon.

Management of immediate life threatening situations

- **Airway Obstruction**

  Blunt and penetrating laryngotracheal trauma, hematomas in neck or chalking of always with blood from traumatized airways or lungs are some of the causes of airway obstruction observed in chest injuries. Early intubation is very important, especially in case of neck hematoma before it increases in size and may cause airway oedema. Delayed intubation is more difficulty due to development of laryngotracheal oedema. In suach cases tracheostomy may be an alternative.

- **Tension Pneumothorax**

  It is developed when a oneway valve is created and air leak occurs either from the lung or through the chest wall. Features are lung compression and collapse, mediastinum displaced to the opposite side, decreasing venous return and compressing opposite lung.

  Most common causes are penetrating trauma, blunt chest trauma with a parenchymal injury and air leak that did not spontaneously close.

  Clinical presentation is restless with tachypnoea, dyspnoea and distended neck veins, tracheal deviation is late finding. There will also be hyper resonance and decreased or absent breath sounds over the affected hemithorax.

  treatment of tension pneumothorax is immediate decompression, initially large bore cannula into 2^{nd} intercostal space in mid clavicular line followed by insertion of chest tube through 5^{th} intercostal space in the anterior axillary line.

- **Pericardial Tamponade**

  Accumulation of relatively small amount of blood into the non distensible pericardial sac can produce compression of heart and obstruction of the venous return, leading to decreased filling of the cardiac chamber during diastole.

  Pericardial Tamponade is commonly seen in penetrating chest trauma. Injury in or around cardiac region with shock always consider cardiac injury until proven otherwise.

  Classic presentation is elevated central venous pressure, decline arterial pressure with tachycardia and muffled heart sounds. eFAST (extended focused assessment with sonography for trauma) showing fluid in pericardial sac. Chest radiography shows enlarged heart shadow.

Needle pericardiocentasis has been suggested in penetrating injury to heart. There is usually a substantial clot in the pericardium.

Pericardiocentasis has high potential for iatrogenic injury to the heart. The correct immediate treatment of tamponade is operative, either via a subxiphoid window or by open surgery (sternotomy or left thoracotomy)

- **Open Pneumothorax (Sucking chest wound)**

  It is usually because of large open defect in chest (> 3cm.), leading to immediate equalization between intrathoracic and atmospheric pressure. Air accumulates in the hemithorax (rather than in the lung) with each inspiration, leading to profound hypoventilation on the affected side and hypoxia.

  Initial management is promptly closing the defect with sterile plastic dressing (opposite) taped on three sides to act as a flutter type valve. A chest tube is inserted as soon as possible in situ remote from the injury site.

- **Massive Hemothorax**

  Most common cause of massive hemothorax is blunt injury. Commonly Bleeding from the torn intercostal vessels or occasionally from the internal mammary artery secondary to fractures of the ribs are responsible for the hemothorax. Accumulation of blood can significantly compromise respiratory effort, compressing lung and preventing adequate ventilation.

  Present as haemorrhagic shock, flat neck veins, unilateral absence of breath sounds and dullness on percussion.

  Initially treat hypovolemic shock and insert intercostals underwater closed drainage. Depending upon the amount of blood collected initial drainage of 100- to 1500 ml., and/ or 200 ml. of blood per hour over 3-4 hours may be done. Urgent thoracotomy is indicated. Physiotherapy and active mobilization should begin as soon as possible.

- **Flail Chest**

  Usually caused by blunt trauma of chest, associated with multiple rib fractures - 3 or more fractured in 2 or more locations, can also produces an underlying pulmonary contusion. Diagnosis can be made by observation of paradoxical movement of the chest wall segment on inspiration. The loose segment of chest wall is displaced inwards and less air moves into the lungs. On expiration, the segment moves outwards. Patient develops hypoxia. High risk patient may have pneumothorax or hemothorax.

CT scan with contrast and 3 D reconstruction of the chest wall is the gold standard for diagnosis of this condition. Mechanical ventilation is used but with the risk of ICU and ventilator related complications, morbidity and mortality.

These patients are treated with oxygen administration, adequate analgesia and physiotherapy. Ventilatory support is required, if respiratory failure persist in spite of initial therapy of adequate analgesia and oxygen. Surgery to stabilize flail segment using internal fixation of ribs may be useful. For severe pain persist, intercostal block may be useful.

- **Respiratory failure & shock**

  Depending on the vital parameters, clinical condition of the patient and available resources, respiratory failure and shock are managed by, standard protocol using Ambu Bag, endotracheal intubation, ventilatory support, IV fluids and blood replacement.

Management of potentially life threating injuries

- **Thoracic Aortic Disruption**

  Disruption of thoracic aorta is the common cause of sudden death after auto mobile collision or fall from a great height. The shear forces from sudden impact disrupt the intima and media. If the adventitia is intact the patient may remain haemodynamically stable.

  Aortic disruption should be clinically suspected in patients with gross asymmetry in systolic pressure (between the 2 upper limbs, or between upper and lower limb), widened pulse pressure and chest wall contusion. Erect chest radiography can also suggest thoracic aortic disruption. The most common radiological finding is widened mediastinum.

  Diagnosis confirmed by CT scan of the mediastinum. Trans-oesophageal echocardiography is an alternative diagnostic tool for unstable patients who cannot be moved to the scanner.

  Initial management consists of control of the systolic arterial blood pressure and maintaining vital parameters. There after endovascular intra aortic stent can be placed or the tear can be operatively repaired by direct repair or excision and grafting using Dacron graft.

- **Tracheobronchial Injury**

  Severe subcutaneous emphysema with respiratory compromise can suggest tracheobronchial disruption.

  Bronchoscopy is diagnostic. Treatment involves intubation of the unaffected bronchus followed by operative repair.

- **Blunt Myocardial Injury**

  Blunt injury to maycardium is a rare injury that causes hemodynamic instability. Patient develops early ECG abnormalities. Two-Dimensional echocardiography may show wall motion abnormalities. A trans-oesophageal echocardiography may also be helpful. There is very little evidence that enzyme estimation have any place in diagnosis. It may develop conduction abnormality with risk of developing sudden dysarrythemias and should be closely monitored.

- **Diaphragmatic Injuries**

  Any penetrating injury below 5^{th} inter costal space should rise suspicious of diaphragmatic injury. Blunt injury to the diaphragm is usually caused by compressive force applied to the pelvic and abdomen.

  The diaphragmatic rupture is usually large, with herniation of abdominal contents into the chest.

  Most of diaphragmatic injuries are silent and the presenting features are those of injury to surrounding organs. Chest radiography after placement of nasogastric tube may be helpful.

  Contrast study of the upper and lower GI track, CT scan, ultrasound and diagnostic peritoneal lavage all lack positive and negative predictive value. Most accurate VATS or laparoscopy operative repair is recommended in all cases. All penetrating diaphragmatic injury must be repaired via the abdomen and not the chest, to avoid penetrating hallow viscus injury.

- **Oesophageal Injury**

  Most injury result from penetrating trauma. Blunt injuries are rare. The patient can present with odynothagia (pain on swallowing saliva, food or fluids) subcutaneous or mediastinal emphysema, pleural effusion, air in perioesophageal space and unexplained fever.

  A combination of oesophagogram in the decubitus position and oesophagoscopy confirm the diagnosis in the great majority of cases.

The treatment is operative repair of any defect and drainage.

- **Pulmonary Contusion**

  More common in blunt trauma usually associated with a flail segment or fracture ribs. Potentially lethal injury and the major cause of hypoxaemia after blunt trauma.

  The natural progression of pulmonary contusion is worsening hypoxaemia for the first 24-48 hrs. Chest radiographic finding are delayed. Contrast CT chest is confirmatory. Hemoptysis or blood in the endotracheal tube is a sign of pulmonary contusion.

  In mild contusion, oxygen administration, pulmonary toilet and adequate analgesia. More severe cases mechanical ventilation is necessary.

Conclusions

Trauma is the leading cause of death worldwide. Approximately 2/3 of the trauma patients have a chest trauma with varying severity from a simple rib fracture to penetrating injury of the heart or tracheobronchial disruption. Blunt chest trauma is most common with 90% incidence, of which less than 10% require surgical intervention of any kind. Mortality is second highest after head injury, which underlines the importance of initial management. Many of these deaths can be prevented by prompt diagnosis and treatment

A dedicated, integrated thoracic trauma team consisting of multidisciplinary medical professionals could remarkably improve the clinical outcome.

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Flail Chest

Dr. Nitin Jain, Dr Nirmal Kumar Jain

Clinical Presentation

Flail Chest is one of the worst subset of severe blunt injury to the chest with increased morbidity and mortality.

Flail Chest is a severe consequence of blunt trauma to the chest wall. It happens when three or more ribs are broken in multiple places, causing a segment of bone to detach from chest wall. This causes serious breathing difficulties in a person as due to injury, the affected area loses its structure and leaves less space for lungs to expand.

The most common cause of flail chest is the blunt trauma caused by road traffic accident, blast, crush injuries or a fall. In rare cases it can also be caused by bone deterioration or disease.

The trauma can result in anything from minor bruising to rib fracture. Rib fractures may also cause other injuries such as puncturing a lung (pneumothorax) or damaging surrounding blood vessels and tissues.

Signs and Symptoms

Depends on severity of flail chest, most common being severe chest pain, tenderness, breathing difficulties, inflammation, bruising, telltale marking from a seat belt and most important being uneven chest rise when breathing.

Diagnosis

Physical examination is of utmost importance where uneven chest rise and paradoxical movement of a injured portion of chest wall is seen. Paradoxical movement is an obvious sign that the injured portion of the chest wall is not consistent with the breathing function.

Pulmonary contusion and/ or laceration, telltale marking from a seat belt are seen. Tenderness is present.

Chest Xray is diagnostic which predicts rib fractures, pneumothorax/ hemothorax / hemopneumothorax and pneumonia.

Multiple skigrams are needed sometimes to establish diagnosis. Chest Xray is less sensitive than CT scans.

Treatment

Principle aim of treatment is to protect underlying lungs and to improve breathing.

Face masks oxygen supplementation, CPAP, analgesics (mainly opioid analgesic), lidocaine patch, intercostal tube drainage and chest physiotherapy.

Surgical stabilization, compression osteosynthesis, rib fracture fixation is surgical modality for flail chest.

Mechanical Ventilation to achieve chest cavity stabilisation is the standard treatment for both flail chest and damaged lungs. The less complicated cases with less involvement of underlying lungs it is considered unnecessary.

Treatment goal for emergency personnel is to stabilize the chest wall,followed by identification and treatment of all injuries in and around the chest.

Complications

Flail chest can be life threatening and has high risk of complications such as respiratory failure or pneumonia. In extreme cases a stove in chest can occur, where the likelihood of surviving a stove in chest is rare. Long term disability in patients sustaining flail chest involving persistent chest wall pain, deformity, dyspnea on exertion.

Outcome And Prognosis

Persons with flail chest have a 5-10% reported mortality if they reach the hospital alive.Patient who does not need mechanical ventilation do better statistically and overall mortality seems to increase with increasing severity, age and number of total rib fractures.

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Airway Management

Mohammed Yunus Khilji, Sadik Mohammed

Abstract

Always be prepared for a difficult airway as no single airway assessment tool is sufficiently sensitive or specific to reliably predict or rule out a difficult airway. Intubation is rarely so urgent that airway assessment is not possible. Basic airway management is the foundation upon which advanced airway skills are based. Correct positioning of the head and neck is essential to ensure the best airway, but care must be taken in suspected cervical spine injury. Airway manoeuvres may also be needed to open the airway. Airway adjuncts such as oro- and nasopharyngeal airways are useful in supporting the airway. Assisted ventilation is required when respiratory efforts are inadequate; this may be achieved with a bag-mask or anaesthetic breathing system. Intubation is always preceded by basic airway care and supplemental oxygen. Immediate intubation is required if basic techniques cannot provide adequate oxygenation. Thorough preparation before undertaking RSI and tracheal intubation will minimize unexpected problems and facilitate a smooth and successful procedure. Failure to intubate must be followed by re-oxygenation/ventilation, and a reassessment of the need and urgency for intubation. Continued failure to oxygenate mandates rapid checks for remediable causes. If oxygenation continues to deteriorate, a surgical airway is indicated. The method chosen will depend on patient and practitioner factors.

Introduction

Compromise of the airway or ventilation is the most urgent of all emergencies as it requires a prompt and skilled response. Recognizing such compromise, knowing how and when to intervene and possessing the skills to do so, form a potentially life-saving combination. Fully trained anaesthetists possess these skills, but patients with airway or ventilation problems are frequently seen by doctors who are not trained anaesthetists. Furthermore, location for emergency airway management is usually outside the relatively controlled environment of an operating room (OR), most commonly in the resuscitation area of an emergency room (ER) where one has to work under conditions of stress and uncertainty. Apart from that the problems intrinsic to patients in ER, such as an unstable cervical spine, poor cardio respiratory reserve or profound metabolic dysfunction, must be anticipated and surmounted. All these factors make the airway

management difficult and challenging in ER. It is imperative that doctors working in ER can recognize the problem and initiate an appropriate and safe response. This chapter is therefore focused principally for emergency and acute physicians.

Evaluation and Prediction of a Difficult Airway

The incidence of difficult airway during elective anaesthesia is estimated to occur in 0.01–0.03% of cases. However, the characteristics of patients requiring intubation or assisted ventilation outside the OR are different to those undergoing elective surgical procedures, and the incidence of difficult intubation is significantly higher in ER. More importantly, a failed airway may occur at least ten times more frequently inthe emergency setting. So, difficulties with the airway must be expected in all emergency patients, and appropriate preparation should be undertaken. Some features may indicate a particularly high likelihood of airway difficulties, and in these cases modification of practice may reduce complications and improve outcome.

If time permits, thorough history including current medication and allergies, previous medical and surgical problems, last oral intake, and details of the patient's current condition should be obtained. Previous medical records can be invaluable. Airway management consists of mask ventilation followed by intubation or surgical airway. Difficulty can arise at any level and we should know the predictors of difficulty in managing airway and be prepared to manage them before we start.

- **Difficult mask ventilation**

  Difficult mask ventilation occurs when the patient's anatomy or injuries make it impossible to maintain adequate ventilation and oxygenation with a facemask and simple airway adjuncts alone.A poor seal between face and mask impedes bag–valve–mask ventilation. Six risk factors for difficult mask ventilation have been defined: beard, age > 57, snoring, BMI > 26, Mallampati III/IV, limited mandibular protrusion. A commonly used mnemonic for a quick assessment of ventilation difficulty is **BONES** (**B**-Beard; **O**-Obesity; **N**-No teeth; **E**-Elderly; **S**-Stiffness).

- **Difficult intubation**

  Difficult intubation has been defined as occurring when an experienced laryngoscopist, using direct laryngoscopy, requires more than two attempts with the same blade or; a change in the blade or an adjunct to a direct laryngoscope (e.g. bougie) or; use of an alternative device or technique following failed intubation with direct laryngoscopy. The following section reviews the commonly used clinical tests and examination to predict difficult laryngoscopy.

The **LEMON** mnemonic can be used as a reminder:

L-Look externally: gestalt view—trauma, trismus, obesity

E-Evaluate 3:3:2 rule (see below)

M-Mallampati score (see below)

O-Obstruction

N-Neck immobility: cervical collar, rheumatoid arthritis, surgery

3:3:2 rule

- Inter- incisor distance (3 fingers) – Measure with the mouth fully open and head extended. Less than 3 fingerbreadths imply more difficulty with intubation. – Average adult values are 3.5–4.5 cm.
- Hyo- mental distance (3 fingers) – Measure accurately from mental process to the hyoid bone with the head extended. As a general rule a thyro- mental distance (mental process to thyroid cartilage)…. Average adult values are 6-6.5 cms.

Thyro- hyoid distance (2 fingers) – Measure from the thyroid cartilage to hyoid bone (or base of mouth) with neck extended. Average adult values are 4.0- 5.0 cms.

Mallampati examination (Table 1)

This examination is performed with the patient sitting upright, head neutral, mouth fully opened, tongue extended and not talking (i.e. we can rarely ascertain a true Mallampati score in an ED patient requiring intubation but it can often be done prior to procedural sedation). It was originally described with three classes and later modified by Samson and Young into four classes:

Table 1 : Malampatti Classification (Modified by Samson and Young)

Class I	Soft palate, fauces, uvula, anterior and posterior pillars
Class II	Soft palate, fauces, uvula
Class III	Soft palate, base of uvula
Class IV	Hard palate

3 Difficult surgical airway

Look for factors which may obscure surgical landmarks. These can be remembered using the mnemonic:

SHORT: **S-**Surgery/Scar, **H-** Haematoma, **O-**Obesity, **R-** Radiation, **T** -Trauma/ Tumor.

4 **The MACOCHA score**: This score considers not only patient-related anatomical difficulty but also physiological factors and operator experience. The score has a maximum of 12 points, with zero predicting an easy intubation and 12 points predicting a very difficult one. This test has a sensitivity of 73% and has not been validated for video laryngoscopy.

Table 2 : The MACOCHA Score

FACTOR	POINTS
Mallampati score III or IV	5
Apnoea syndrome (obstructive)	2
Cervical spine limitation	1
Opening mouth 3 cm	1
Coma	1
Hypoxia	1
Anesthesiologist non-trained)	1

HAVNOT: A simple reminder for assessing predictors of a difficult airway is:

H- History – including previous airway problems

A -Anatomy – features of the face, mouth and teeth that may suggest intubation will be difficult

V- Visual clues – obesity, facial hair, age

N- Neck mobility and accessibility, including the presence of in-line stabilization

O- Opening of the mouth – less than three fingers' breadth suggests potential difficulty with intubation

T- Trauma – the possibility of anatomical disruption and blood in the airway

Equipments for Airway Cart

An emergency airway cart should be kept ready in every ICU and ER. This saves time and makes airway management easier and safer by allowing us to apply alternative methods of intubation as per protocol.

The contents of the airway cart may be modified according the need and availability of resources.

- ***For oxygenation and Ventilation***: Self-inflating ventilating bag with a reservoir bag attached /Bain's anesthesia circuit (for positive pressure ventilation), Face masks of various sizes, Oropharyngeal and nasopharyngeal airways.
- ***Suction catheter and suction machine.***
- ***Laryngoscopes*** with fully charged batteries for endo/naso tracheal Intubation and all sizes of blades including *large blade* (both Miller and Macintosh blades),
- ***Endotracheal tube*** of appropriately sized (at least 2) size 7.5–8.5 in adult males and 6.57.5 in adult females.
- ***Lignocaine jelly***, 10 ml syringe for inflating tube cuff,
- ***Stylet***
- ***Magill's forceps,***
- ***Ventilating Bougie,***
- ***Tube fixator/tapes and ties***.
- ***End-tidal CO2 monitor to confirm intubation***
- ***Drugs:*** Induction *agents and muscle relaxants, Topical anaesthetics and vasoconstrictors, Vasopressors* to treat hypotension.
- ***Fiber optic Bronchoscope, Video laryngoscope.***
- ***Rescue Airway Equipments***— *LMA/ILMA, cricothyroidotomy set and percutaneous tracheostomy set.*

Initial assessment and management

- First of all, check whether the airway is patent and protected, threatened, or partially or completely obstructed.
- Airway patency should be the first priority and protection from aspiration comes only after we have secured breathing and circulation.
- Observe for the diminished or absent airflow in the presence of continued respiratory effort.
- Also observe and listen for air movement and the rate and depth of respirations (at the mouth and nose, movement of the chest wall, presence of tracheal tug), listen for abnormal or noisy breath sounds (also auscultate the chest), assess the sound, quality of voice, feel for air flow Snoring, gurgling sound, paradoxical movement of the chest wall and abdomen and inadequate/absent chest rise during ventilation may suggest upper airway obstruction.

- Open the airway by head-tilt/chin-lift maneuver or byjaw-thrust if injury to cervical spine is suspected.
- After opening the airway look for any foreign body, blood or vomitus in the oropharynx. Clear the airway by suctioning or by manually removing foreign body.
- Maintain the patency of airway by inserting oropharyngeal or nasopharyngeal airway of appropriate size (length equivalent to distance from the tip of the nose/ angle of the mouth to the tragus).
- Nasopharyngeal airway diameter should be less than the patient's nostril. It should be avoided if the patient has risk of nasal trauma/bleeding or cerebrospinal fluid rhinorrhea.
- Perform bag-mask ventilation with a reservoir bag attached if the patient is not breathing adequately even with open airway.
- Effective assisted ventilation requires a good mask seal to minimize leakage.
- Look for adequate chest rise.
- Avoid high airway pressures; this reduces the possibility of gastric inflation, with subsequent regurgitation and aspiration.
- Cricoid pressure may be applied to reduce this risk, but is difficult to maintain for a long time.
- Partial airway obstruction can cause high airway pressures; therefore a two-person technique is recommended, especially for inexperienced practitioners. This technique enables one practitioner to use both hands to open the airway and hold the mask firmly on the face whilst a second practitioner compresses the bag.
- Meanwhile attach essential monitoring, secure intravenous (IV) lines and prepare for endotracheal intubation.

Endotracheal Intubation

- The decision to intubate or not is often the key first decision in treating a critically ill or injured patient.
- Tracheal intubation with a cuffed tube secures the airway and enables oxygenation and ventilation of the lungs.
- It protects the lungs from aspiration of blood or vomit and enables sedation to be safely given without risk of respiratory compromise.

There are four clinical situations in which intubation may be indicated:

- Apnoeic patient in respiratory arrest;
- A patient with obstructed/partially obstructed airway where basic airway care is ineffective;
- Patient requiring invasive respiratory support for oxygenation or ventilator failure and;
- Patient in whom basic airway care is effective, but whose predicted clinical course includes a high probability of airway obstruction, aspiration or ventilator failure.

CHECKLIST

- Fasting status,
- Oxygen,
- Airway cart,
- Suction,
- Monitoring and
- Patent IV line.

Preload the patient with 500 ml crystalloid in the absence of cardiogenic pulmonary oedema, keep all the drugs filled syringes ready, ensure availability of help in case of difficult airway and keep ventilator ready if mechanical ventilation is required.

Positioning and Pre-Oxygenation:

- Bring the patient's head near edge of the bed and adjust height of the bed according to your convenience.
- To optimize air-flow the head, neck and torso must be positioned to align the oral, pharyngeal and laryngeal axes.
- In an adult patient the airway axes are better aligned when the neck is flexed on the torso and the head is extended on the neck: the so-called **'sniffing the morning air'** position.
- Place a pillow or sheet of 10 cm height below the occiput which makes approximately 35-degree flexion of the lower cervical spine and an 85-degree to 90-degree head extension at the atlanto-occipital joint.
- Elevation beyond the sniffing position may improve the view in cases of difficult laryngoscopy. The lower cervical spine portion can be maintained in a flexed position by using a pillow under the head.

- Atlanto-occipital joint extension is achieved by pressure on the top of the head and/ or upward traction on the upper teeth or gums. In obese patients, considerable shoulders and head elevation may be necessary so that an imaginary horizontal line connects the patient's sternal notch with the external auditory meatus.
- This will align oral, pharyngeal and laryngeal axes making airway from lips to glottis in a nearly straight line.
- Sniffing position should be avoided in case of cervical injuries where manual in line cervical stabilization with head in neutral position is done.
- Cervical collar should be used all the time. If the head cannot be positioned optimally, e.g. when cervical stabilization isrequired after trauma, backwards upwards and rightwards laryngeal pressure (theBURP manoeuvre) may help to align the axes.
- Pre-oxygenation replaces the nitrogen in the alveoli with oxygen, which increases the oxygen reserve in the lung.
- Pre-oxygenation maximizes the time before desaturation occurs following the onset of apnoea.
- This provides more time for intubation to be attempted before having to stop to re-oxygenate the patient's lungs.
- Whenever possible, give 100% oxygen for three minutes before attempt.
- A patient who is breathing inadequately may not achieve enough alveolar ventilation to replace nitrogen in the lungs with oxygen.These patients may therefore require assisted ventilation to achieve adequate pre-oxygenation before intubation.
- If possible, use non-invasive ventilation with a pressure support ventilation level between 5 and 15 cm H_2O to obtain an expiratory tidal volume between 6 and 8 mL/ kg and PEEP of 5 cm H_2O (nasal cannula with an oxygen flow of 15 L/min may be used in addition when there is a mask leak) or High Flow Nasal Cannula with 70 L/ min of oxygen flow should be used.
- Patients in ER usually require rapid sequence induction of anaesthesia (RSI) which involves injecting an anaesthetic induction drug to achieve hypnosis, rapidly followed by a neuromuscular blocking drug to produce complete paralysis.
- To prevent inflation of the stomach, the lungs are not usually ventilated between induction and intubation, and the airway is protected by applying cricoids pressure to prevent regurgitation of gastric contents. The time from loss of consciousness to securing the airway is minimized because the patient's stomach is assumed to be full.

Medications

Thiopentone, Propofol, Ketamine, Fentanyl, Midazolam or Etomidate may be used for sedation depending on patient's haemodynamic status, associated comorbidities and expected difficulty in intubation.

Succinylcholine, Rocuroniun and Vecuronium for muscle relaxation may be used if required, keeping their advantages and disadvantages in mind (Table:1).

Drugs should be injected slowly and titrated until effect. Usually small doses are required in most of the sick patients and full calculated doses should not be given.

Table : 1 Medications used in airway management to facilitate intubation.

Drug	Dose	Important Effects
Midazolam	0.02–0.2 mg/ kg	Relatively cardiostable Optimum intubation condition may not be obtained when used alone Better amnesia Sedation
Fentanyl	0.05–0.4 mg	Fast-acting Optimum intubation condition may not be obtained when used alone Relatively cardiostable Analgesia Cough suppression Useful in combination with midazolam
Ketamine	1–2 mg/kg	Cardiostable Increased intracranial/ introcular pressure Bronchodilator Does not suppress airway re fl exes Potent analgesic Hypertension and tachycardia Safe induction of anesthesia
Propofol	1–2.5 mg /kg	Bronchodilatation useful in COPD/asthma, Can cause profound hypotension and bradycardia, Suppression of airway re fl exes, Reduces ICP
Thiopentone sodium	3-5 mg/kg	Rapid induction, Hypotension, Reduces ICP, Can precipitate laryngospasm and bronchospasm.
Etomidate	0.2–0.6 mg/kg	Cardiostable, may cause adrenal suppression in seriously ill patients.

Drug	Dose	Important Effects
Succinylcholine	0.5-1.0 mg/kg	Rapid action (1 min) and short duration (up to 10 min) hence ideal for RSI, Hyperkalemia and cardiac arrest, Contraindicated in severe acidosis, acute or chronic neuromuscular disease, burn patients and cervical spine trauma (upto 6 months),lower motor neuron disease, Malignant hyperthermia
Rocuronium bromide	0.4-1.0 mg/kg	Rapid action (60–90 s) hence ideal for RSI Long acting (30–90 min), No complications associated with Scoline
Atracuriumbesylate	0.4-0.5 mg/kg	Not metabolized by liver or kidney, Long acting (20–30 min), Delayed action, Histamine release, Hypotension

Laryngoscopy and intubation

- Hold the laryngoscope handle in the gloved left hand.
- Moistening or lubricating the blade will facilitate insertion if the mouth is dry.
- In case the chest impinges on the handle, making it difficult to insert the blade, we can use a short handle, the blade may be inserted sideways, or the blade may be inserted and then attached to the handle.
- Use fingers of the right hand to open the mouth and spread the lips.
- In patients with dentition, the optimum opening of the mouth is often achieved with a thumb-over-index-finger approach (***Scissor technique***), with the index finger on the upper maxillary teeth and the thumb placed on the lower teeth.
- Insert the blade at the right side of the mouth. This reduces the chances of damage to incisor teeth and helps to push the tongue to the left.
- Advance the blade along the side of the tongue toward the right tonsillar fossa so that the tongue lies on the left side of the blade.
- Use the right hand to keep the lips from getting caught between the teeth or gums and the blade. If the tongue is slippery, placing tape on the lingual blade surface may be helpful.
- When the right tonsillar fossa is visualized, move the blade tip toward the midline. Advance the blade behind the base of the tongue, elevating it, until the epiglottis comes into view.

- After the epiglottis is visualized, advance the blade until the tip fits into the vallecula.
- Apply traction along the handle at right angles to the blade to move the base of the tongue and the epiglottis forward.
- The glottis should come into view. Do not pull backward the end of the handle opposite the blade. This will cause the tip to push the larynx upward and out of sight and could cause damage to the teeth or gums.
- Once glottis is visualized, insert the tube into the right corner of the mouth and direct toward the glottis with the bevel parallel to the vocal cords.
- If there is cord movement, insert the tube during maximum abduction. Even with correct technique, the larynx will not always be visualized.
- Displacing the larynx by BURP maneuver on the thyroid cartilage may improve visualization of the glottis. Use of stylet in ETT or bougie (a thin long plastic/rubber cylinder with a benttip that is passed through the partially visible glottic opening and then the ETT is guided over it), or other airway adjunct can aid oral intubation.

For nasal intubation, use prior nasal mucosal vasoconstrictors (Xylometazoline or phenylephrine nasal drops) and lubrication. Magill's forceps may be used to guide the tube into the trachea. – Optimal external laryngeal manipulation **(OELM)** with the right hand or by an assistant by quickly pressing in both cephalad and posterior direction over the thyroid, cricoids or hyoid cartilage may be used to further optimize laryngoscopic view.

RSI (Rapid Sequence Intubation) is employed to induce unconsciousness and muscular paralysis to provide optimal intubating conditions, to avoid aspiration from a probable full stomach and to protect against reflex bradycardia and raised intracranial pressure due to manipulation of the airway. It is contraindicated if 'difficult' intubation is predicted and successful bag–valve–mask ventilation is considered unlikely. This will depend on the patient, the equipment and assistance available and the skill of the operator.

Confirm tracheal tube placement

- Proper tube positioning (ideally 2.5–4 cm above carina) must be confirmed clinically by auscultation over lungs and stomach (5 point auscultation).
- Gold standard is End Tidal CO_2 with a portable capnograph.
- Using depth of tube insertion (i.e. tube fixation at 20 cm. mark for females and 22 cm. mark for males at the incisor level) is most commonly used method to determine proper tube position in adults.

- When all above 3 methods are combined, the sensitivity is 100% and the specificity is 95%. Make a note of the exact distance of the ETT at the lips/nose on the case notes and ICU chart. This position should be noted daily during every nursing shift.
- Fix the tube with two adhesive tapes and/or a tie. Commercially available tube fixators may be used.

Post-intubation check

- The patient should be reassessed, with specific evaluation of the airway, ventilation and circulation.
- Use a suction catheter to clear material from the lower airways
- Check the monitors for heart rate, SpO2, blood pressure, end tidal CO2 and peak inspiratory pressure.
- Request a chest X-ray: it is the responsibility of the intubating clinician to examine the chest film, check the position of the tube and to withdraw or advance the tracheal tube as required.

Management of difficult airway

Unanticipated difficult airway: At the conclusion of a planned RSI in a patient with an adequate circulation, failure to detect expired CO2 indicates incorrect placement of the tracheal tube under these circumstances the tube must be removed.

Failure to place a tracheal tube correctly after an RSI is not a disaster, but failure to recognize incorrect placement, or to allow the patient to become injured during further attempts to secure an airway, are indefensible.

A systematic approach or algorithm must be followed for securing the airway (fig 1).

Anticipated difficult airway: Ensure expert help is readily available. If mask ventilation is difficult, avoid using muscle relaxants. Awake fiberoptic oral or nasal intubation should be the first option when available in case of availability. Other options like vedio laryngoscopes, ILMA etc should be kept ready with Airway Cart.

Complications of endotracheal intubation

- **During intubation**.
  1. Laryngospasm.
  2. Laceration.

3. Bruising of lips or tongue.
4. Damage to teeth.
5. Aspiration.
6. End bronchial or esophageal intubation.
7. Perforation of oropharynx, trachea, or esophagus.
8. Epistaxis.

- **Post-extubation.**
  1. Laryngospasm, sore throat, hoarseness, stridor, glottic or subglottic edema.
  2. Long-term intubation may result in tracheal stenosis, tracheomalacia, and tracheal mucosal ulceration.

Extubation

- Should be done in the patient who is fully awake and can protect his airway.
- Oropharyngeal secretions should be suctioned, head of the bed should be elevated, and endotracheal tube should be removed after a cuff leak test.
- In patients with a known difficult airway, extubation using an airway exchange catheter should be considered.
- Supplemental oxygen should be provided, and the patient should be observed in a monitored setting.
- Emergency airway equipment should be available to manage post extubation problems.

Summary

Tracheal intubation (TI) is a routine procedure in the Intensive Care Unit (ICU) and is often life-saving. In contrast to the controlled conditions in the operating room, critically ill patients with respiratory failure and shock are physiologically unstable. TI in the ICU is a potentially hazardous procedure, most commonly due to failing oxygenation and unstable haemodynamics during emergency intubations. It needs stepwise approach, adequate supervision, good pre-oxygenation with ready to use ventilatory support. Every emergency room and ICU set up should have intubation protocol, intubation aids, rescue devices; and adequately trained medical personnel.

Aidaa 2016 Guidelines for Tracheal Intubation in the Intensive Care Unit

Step 1: Preoxygenation and induction of anaesthesia

- Two persons (one experienced)
- Optimise preoxygenation with one of the following:
  - Noninvasive ventilation with 100% O_2, pressure support of 5-15 cm H2O for 3 minutes (nasal cannula with O_2 flow at 15 L/min)
  - HFNC O2 therapy
- Induction - Etomidate or Ketamine with Succinylcholine (if not contraindicated) or Rocuronium
- Use cricoid pressure
- IPPV with bag-valve mask with reservoir bag (use external PEEP valve set to 5-10 cm H_2O if available) / IPPV wih PEEP using the ventilator

Face mask ventilation unsuccessful

Face mask ventilation successful

Single attempt at tracheal intubation only if $Spo_2 \geq 95\%$

Step 2: Laryngoscopy and tracheal intubation

- Continue nasal oxygen using O_2 flow at 15 L/min OR HFNC O_2
- Direct/video laryngoscopy
- Maximum two attempts (repeat attempts only if SpO_2>95%
- Mask ventilation between attempts
- Optimise position, use external laryngeal manipulation, release cricoid pressure, use bougie/stylet if required
- Consider changing device/technique/operator between attempts
- Maintain depth of anaesthesia

Succeed → Confirm tracheal intubation using Capnography

Failed Intubation

CALL FOR HELP

Step 3: Insert SAD to maintain oxygenation

- Continue nasal oxygen using O_2 flow at 15 L/min OR HFNC O_2
- Preferably use second generation SAD
- Maximum two attempts (only if SpO2>95%)
- Mask ventilation between attempts
- Consider changing size or type of SAD
- Maintain depth of anaesthesia

Succeed → **Consider one of the following options:**
1. Percutaneous or surgical tracheostomy
2. Intubate through the SAD using a FOB only. provided expertise is available

Failed ventilation through SAD

Step 4: Rescue face mask ventilation

- Continue nasal oxygen using O_2 flow at 15 L/min OR HFNC O_2
- Ensure neuromuscular blockade
- Final attempt at face mask ventilation using optimal technique and adjuncts

Succeed → Surgical or Percutaneous tracheostomy

Complete Ventilation Failure → **CALL FOR ADDITIONAL HELP**

Step 5: Emergency cricothyroidotomy

- Continue nasal oxygen using O_2 flow at 15 L/min OR HFNC O_2 and efforts at rescue face mask ventilation
- Perform one of the following rechniques
  - Surgicval cricothyroidotomy
  - Wide bore cannula cricothyroidotomy
  - Needle cricothyroidotomy (use pressure requlated jet ventilation and attempt to keep the uppper airway patent)

Succeed → Convert to a tracheostomy at the earliest

This flow chart should be used in conjunction with the text

FOB=Fibreoptic bronchoscope
HFNC = High flow nasal cannula
IPPV = Intermittent positive pressure ventilation
PEEP = Positive end-expiratory pressure
SAD = Supraglottic airway device
SpO2 = Oxygen saturation

Post - procedure plan
1. Future airway management plan
2. Treat airway oedema if suspected
3. Monitor for complications
4. Counselling and documentation

Suggested readings

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Mechanical Ventilation

Dhruva Chaudhry, Mansi Gupta, Brijesh Prajapat

Introduction

Mechanical ventilation (MV) is a commonly used short-term life support modality worldwide in a diverse spectrum of indications including acute respiratory failure, to scheduled surgical procedures (planned trauma), trauma, infections, toxins etc. In a recent epidemiological study by Mehta AB et al, approximately 310 persons per 100,000 adults underwent invasive mechanical ventilation (IMV) for nonsurgical indications in the United States. The first description of endotracheal intubation and artificial ventilation was provided by Andreas Vesalius in the16th century. Bjorn Ibsen, an anesthesiologist recommended tracheostomy and positive-pressure ventilation to treat patients with paralytic poliomyelitis leading to drastic reduction in mortality of these patients from 87% to 40%. The first efficient mechanicalventilators were developed by Claus Bang, a Danish physician, and Carl-Gunnar Engström, a Swedish anesthesiologist which paved the path for effective positive pressure ventilation.

The next major step in the evolution of MV was the use of positive end-expiratory pressure (PEEP), mainly encouraged by the identification of adult (acute) respiratory distress syndrome (ARDS) by Ashbaugh et al. PEEP was first incorporated in ventilators in 1972, and the servo valves controlling flow allowed the introduction of new modes of ventilation such as pressure-controlled ventilation (PCV) and pressure support ventilation (PSV) later. In the recent times, ventilators have progressively become more compact, intelligent, user-friendly, and electronically based than the pneumatic-based, with incorporation of number of modes of ventilation and advanced monitoring capabilities.

Principles of mechanical ventilation

Mechanical ventilators display breath in real time by flow (F), volume (V) and pressure (P) curves, both as a function of time and loop. Assisted ventilation can be total, partial or absent, depending on respiratory muscles' ability to generate pressure applied to the respiratory system (Prs). Prs of ventilated patient is described by the equation of motion:

Prs = Paw + Pmus = (flow x resistance) + (volume (V)/compliance(C)) + k

k is a constant representing the alveolar end expiratory pressure. The term V/C corresponds to the pressure that must be applied to overcome elastic forces (Pel). Thus, a single breath is the expression of three known variables (pressure, flow and volume) and three related factors (Resistance, Compliance and k), as described by the equation of motion. In spontaneous mode Paw= 0 but in controlled ventilation mode Pmus= 0

Cardio-Pulmonary Interactions During Positive Pressure Ventilation (Table 1)

During inspiration, the mechanical ventilator applies positive pressure to the upper airways, which is higher than that in the alveoli, generating a flow of air into the lungs across the pressure gradient which is in contrast to airflow during inspiration in spontaneously breathing subjects. During expiration a drop of pressure in the upper airways generates a flow of air out of the lungs. The applied positive pressure to the alveoli is known as trans-pulmonary pressure and is determined by intra–alveolar pressure minus extra–alveolar pressure.

Mechanical ventilation causes an inspiratory rise in positive intra–thoracic pressure opposite to negative pressure breathing during a normal human breath leading to increase right atrial pressure (RAP) which leads to drop of pressure gradient resulting in a decrease in venous return. Pulmonary vascular resistance (PVR), the major determinant of RV afterload, is minimal near FRC and related to lung volume in a bimodal fashion. Atelectatic alveoli compress extra–alveolar vessels while alveolar over distension compresses intra–alveolar vessels, both resulting in an increase in PVR. Trans-pulmonary pressure is the main determinant of PVR and thus RV afterload. Increase in PVR and decrease in venous return thereby leads to decrease in left ventricular(LV) filling. Additionally, interventricular interdependence leads to shift of septum to left thereby encroaching left ventricle cavity, further reducing LV filling.

Variables of mechanical ventilator breaths (Table 2.) (Figure1.):- Variables are the set of factors that describe a mechanical ventilator breath.Various phases of a single breath are:

- Change from expiration to inspiration (triggering)
- Inspiration
- Change from inspiration to expiration(cycling)
- Expiration

Modes of ventilation (Table-3)

Mode in essence refers to the manner in which ventilator breath is described by set of variables (trigger, limit and cycle). Based on these variables, various modes have been designed that are broadly classified as assist control ventilation (ACMV) (volume or pressure controlled), intermittent mandatory ventilation (IMMV), pressure support ventilation (PSV).

- ***Volume controlled mode (VCV):-*** The controlled variable is volume while pressure varies throughout the respiratory cycle as depicted in the below waveforms. Volume time waveforms shows delivery of fixed volume (preset). Flow waveforms shows constant flow and pressure waveform shows increasing pressure with inspiration and reaches maximum pressure (PIP) followed by plateau pressure (Pplat) when airflow ceases during inspiration and then returns to baseline or PEEP level (Figure 5.).

- ***Pressure control mode (PCV):-***In PCV, the physician only indirectly controls the tidal volume and a certain pressure limit is set. During a ventilator delivered inspiration, as air is driven into the lungs, airway pressure rises, rapidly reaching the preset pressure control level. This pressure is maintained for the duration of inspiration. The pressure limit, the respiratory frequency (rate), and the inspiratory time are set by the physician. The advantage of PCV is the guarantee that Ppeak will remain at and never exceed the set pressure limit. The risk of barotrauma and of other adverse events related to high intrathoracic pressures is, thus, minimized. The major disadvantage of PCV is that in a patient with unstable or changing lung mechanics, any significant fluctuation in the lung compliance or airway resistance will directly affect the delivered tidal volumes. Tidal volumes can vary substantially with changes in compliance or resistance, producing undesirable changes in minute ventilation (Figure 6.).

- ***Pressure support/assist mode (PSV):-*** Here, the ventilator augments the inspiratory effort of the patient with positive pressure support, that means, breath is patient triggered. Since the level of the pressure support is preset, given a constant strength of inspiratory effort on the part of the patient, the tidal volumes can be made to rise or fall by varying the level of the pressure support. In other words, the level of pressure support determines the tidal volumes. Inspiration to expiration is cycled by flow (usually set at 25% of inspiratory flow (Figure 7.).

- ***Synchronized mode (SIMV):-*** In this mode, mandatory breaths are delivered in synchrony with the patient's inspiratory efforts at a frequency determined by the operator. If the patient fails to fails to start a breath, the ventilator delivers a fixed

volume breath and reset the internal timer for the next inspiratory cycle. SIMV allows patients with an intact respiratory drive to use their inspiratory muscles between assisted breaths. So, it is useful in both supporting and weaning intubated patients.

Ventilator waveforms

Scalars are waveform representations of pressure, flow or volume on the y axis vs time on the x axis. There are three types of scalar waveforms:

- **Flow vs Time scalar graph (Figure 2.)**- It includes the inspiratory as well as expiratory flow waveforms. Different types of inspiratory waveforms include constant (square) flow waveform, sine wave flow, accelerating flow, decelerating flow. In sinusoidal and ascending ramp flow, the initial flow rates are slow and cause dys-synchrony or flow starvation and thus should not be used in assist modes. Descending ramp and Square wave flows are usually the preferred flow as the initial flow rate meets the flow demand of the patient and thus decreases air hunger. In square flows,inspiratory time is shortest leading to highest peak inspiratory pressures but low mean inspiratory pressure thereby causing better venous return and cardiacoutput. In descending ramp flow, low peak inspiratory pressure but high mean airway pressure occurs leading to better lung inflation and oxygenation. The expiratory flow waveform is passive and determined by respiratory compliance and resistance of airways. It is equally important to look and analyse airway resistance, auto peep and airway secretions which can be easily picked up with help of expiratory waveforms.

- **Pressure vs time waveform(Figure 3.)-**Peak inspiratory pressure (PIP) is the maximum pressure recorded during ventilator driven breath. While the Plateau pressure (Pplat) is the end-inspiratory alveolar pressure and depends upon the compliance of lungs. Difference between the PIP and Pplat is the resistive force and increases with increase in resistance to flow like bronchoconstriction, secretion in the airways, kinking of tube, small size endotracheal tube etc. Plateau pressure is inversely proportional to the lung compliance and increases with main stem intubation, congestive heart failure, ARDS, abdominal distension, chest wall oedema/obesity, atelectasis, consolidation, fibrosis, thoracic deformity, tension pneumothorax & pleural effusion.

Ppeak – P plat = Flow x Resistance

Ppeak is increased by:

- Increasing resistance: Bronchospasm, Mucus plugging/secretions, ET block, biting the ET tube, tube kinking, clogged HME filter.
- Increasing flow: Increasing tidal volume, Increasing Inspiratory pause, Increasing I:E ratio

Pplat – PEEP = Tidal volume/ Compliance

P plateau is increased by:

- Decreasing compliance of lung: Pulmonary edema, ARDS, Atelectasis, Pneumonia.
- Decreasing compliance of the chest wall: Morbid obesity, ascites, stiff chest wall.
- Increasing Tidal volume
- Patient ventilator dys-synchrony

- **Volume vs time waveform (Figure 4.)-** Tidal volume is plotted on y axis and time is plotted on x axis. In volume control mode, fixed volume is delivered while in pressure control volume is variable depending on the limit of pressure which can be identified by studying the volume /time waveform.This waveform can also identify break in circuit, leak in circuit, ET cuff leak in which expiratory limb fails to return to x axis. During active expiration expiratory limb dips beyond the baseline while during auto PEEP expiratory limb fails to reach the baseline.

Indications & ventilatory strategies in specific disease states (table 4,5)

Mechanical ventilation is required for assisting and replacing spontaneous breathing. The most common indications for initiating the mechanical ventilation are acute hypoxemic RF (type I) accounting for around 65% of cases while hypercapnic RF accounts for the rest. The common reasons for initiating patients on invasive ventilatory support have been enlisted in Table 3.

The ultimate goal of mechanical ventilation is to provide adequate gas exchange while preventing ventilator induced lung injury (VILI) due to volutrauma, barotrauma, and atelectrauma. This often involves several trade-offs which are usually balanced out after clinical judgment of various critical clinical thresholds like pH, oxygenation (PEEP, FiO_2), stretch injury to lungs etc. The current recommendations for ventilatory management of various diseases using the low tidal volumes are guided by the concept of Lung Protective Ventilation (LPV). This strategy has consistently been proven to reduce mortality rates in ARDS (acute respiratory distress syndrome). Moreover, recent trials suggest that patients without ARDS but having a risk for lung injury should also

be ventilated with low tidal volumes (4-6 ml/kg PBW), however, those having no risk may be ventilated with tidal volumes up to 10 ml/kg. The ventilatory protocols for ARDS and acute exacerbation of airway diseases have been summarized in Table 4.

Weaning from mechanical ventilation

Weaning (process of discontinuing ventilatory support) should be attempted as soon as the primary cause of ARF starts stabilising or reversing. In a patient with preserved sensorium and hemodynamics, when minimal settings are required for oxygenation (FiO_2<40% and PEEP <8cm H2O) with adequate ventilation, perform spontaneous breathing trial (SBT) using T-piece or low pressure support (5-8 cm H2O).Many parameters can be helpful in deciding the readiness to wean from the ventilator such as the respiratory rate (RR), minute ventilation (MV), maximal inspiratory pressure (MIP), and the rapid shallow breathing index (RSBI, also known as Tobin's Index). RSBI greater than 105 is useful in predicting failure to wean (>90%). Around 5-10% of the patients on IMV in any ICU will become ventilator dependent. Failure to wean the patient occurs due to interdependent dysfunction of multiple organs including lungs, heart, brain, and neuro-musculature. Other factors like overuse of sedatives,metabolic derangements, prolonged immobilisation, malnutrition, and unresolved infections also play an important role. After 2-3 weeks of IMV despite disease stabilisation or reversal, these patients may require prolonged IMV via tracheostomy and a gradual weaning process over weeks to months.

Noninvasive ventilation

Noninvasive ventilation (NIV) refers to provision of ventilatory support to a patient through artificial means without the need to bypass the upper airway. Currently, noninvasive positive pressure ventilation (NPPV) is the most preferred mode of NIV being used in acute care setting as well as for domiciliary usage. There is an increasing tilt towards use of NIV in managing patients of acute respiratory failure in ICUs due to its several advantages over invasive mechanical ventilation. The use of NIV not only prevents the hazards associated with IMV (Table 7.) but also facilitates early weaning, shortens ICU and hospital stay, and reduces resource utilization and cost of health-care burden. However, NIV should not be considered as a replacement of IMV. The successful use of NIV is dependent on various factors like adequately trained staff, appropriate selection of the patient and location, choice of right interface and ventilatory settings, and finally a good monitoring for timely action in case of NIV failure.

NIV should be administered in an ICU or a high dependency unit (HDU) under close monitoring of an experienced personnel. The most crucial step in optimizing success

of NIV and providing maximum benefit is appropriate selection of the patients. This requires careful identification of patients having favorable clinical diagnosis supporting the use of NIV. It is very important to rule out possible contraindications for NIV use to minimize complications and risk of failure. The most robust evidence supporting the use of NIV as an upfront therapy in ARF has been in acute hypercapnic failure (COPD exacerbation) and hypoxemic failure (cardiogenic pulmonary edema and in immuno-compromised patients). The currently established indications, predictors of NIV failure and contraindications for its use in ARF are highlighted in Table 6.

After selecting the right candidate, it is equally important to choose the right ventilator mode and interface for patient. The choice of ventilator depends upon availability, patient need, and physician preferences. Most patients receive NIV with specially designed micro-processor controlled critical care ventilators. These ventilators offer advantages in terms of minimizing re-breathing, leak compensation, presence of in-built oxygen blenders, accurate tracking of various parameters, and ease of use for IMV as well. The presentation of a patient in ARF warrants the use of interfaces suited for mandatory mouth breathing, which include oro-nasal masks, full face-masks, and helmet mask. While oro-nasal mask is the best interface for use in acute care setting in terms of cost-effectiveness, availability, and physician familiarity, the newer assortments like helmet and full face masks are aimed at improving patient comfort, ease of feeding, preventing injury to facial structures and enhancing interface performance.

Each ventilation mode has its theoretic advantages and limitations. In hypoxemic ARF, CPAP alone may be sufficient to improve oxygenation however, addition of Pressure support (PS) helps in respiratory muscle unloading and improving dyspnoea and gas exchange parameters. A majority of patients in ARF can be managed with Pressure support (PS) mode (setting PEEP/ EPAP and PS above PEEP/IPAP, with the difference between the two providing the required ventilatory assistance). The applied PEEP/ EPAP also helps in counteracting the intrinsic PEEP due to dynamic hyperinflation in COPD patients. Other modes available for managing a subset of patients with ARF are Pressure controlled NIV (with back up rate), Average volume-assured pressure support (AVAPS), Proportional assist ventilation (PAV), etc. These modes can be potentially advantageous in ventilating patients with severe hypoventilation and enhancing patient comfort and patient ventilator synchrony.

While setting up NIV with pressure-targetted modes, it is recommended to initiate with low pressures for improving patient tolerance. Both the PEEP/EPAP as well as PS/IPAP should be gradually up titrated to obtain best tolerance, synchronization, respiratory rate (RR), and minute ventilation while reducing dyspnoea and anxiety. Oxygen should be supplemented to achieve saturation at or above 92%. Also, the triggering and cycling

criteria are of paramount importance in achieving maximum physiological and clinical benefit. Flow triggering reduces patient effort and provides for better patient-ventilator synchronization. The cycling criteria should be set according to patient's requirement for prolonged expiration and achieving the best patient ventilator synchrony.

Patients receiving NIV needs continuous monitoring aimed at identifying early signs of NIV failure, assessing for patient comfort and good patient-ventilator interactions, and determining whether initial goals like symptomatic relief, reduced work of breathing and improved blood gases, are being achieved. This includes monitoring of subjective responses like pain, comfort, dyspnoea, claustrophobia; vital signs, gas exchange parameters, air leaks, synchronization, and development of complications.

Although successful in most patients, the failure rates with NIV in ARF as seen in different studies are in the range of 30-40%. Like any other modality, use of NIV is not devoid of adverse effects and complications. It is of utmost significance to know about the potential complications (Table 7.) and to try and minimize them for better overall patient outcomes and more efficient utilization of ICU resources.

Newer advances

With evolution of ventilators with time, **'the feedback or servo control mechanism'** is capable of monitoring the conditional variables and automatically switches between various modes and also adjusts inspiratory time, flow, pressure, and even FiO_2. The examples of such modes are **(Automode, Smartcare PS, Intellivent, ATC (Automated Tube Compensation).** Another major challenge with IMV is to improve patient–ventilator interaction to match ventilatory support with patient demand. This has been attempted by adjusting the level of machine support in proportion to the estimated patient's effort **(PAV-Proportional Assist Ventilation).** Diaphragmatic electrical activity can also provide a means to give continuously ventilatory assist in proportion to the neural drive, both within breath and between breaths, and is referred to as **NAVA (Neurally Adjusted Ventilatory Assist)**.Additionally, in spite of the best ventilatory strategy, there is a failure to maintain oxygenation and ventilation in severe ARDS. In these patients, **Extracorporeal Membrane Oxygenation (ECMO),** is an alternative treatment. But, ECMO is a highly invasive treatment with significant risk and complications, with the mortality of 50–60%. It is assumed less invasive to use **Arteriovenous Extracorporeal Membrane CO_2 removal (AVECCO2R)** than ECMO, but its usage is limited by poor quality of evidence in support of this modality.

Conclusion

Mechanical ventilation has revolutionized the era of intensive care units (ICUs). These have become the indispensable part of all kinds and types of ICUs and are the most commonly used modality for short term organ support. Continuous efforts and research have led to the developments of compact and high end ventilators with servo (feedback) mechanism, compact modes (ASV, intellivent) and neurally triggered modes (NAVA). The major indications for use of IMV are acute hypoxemic respiratory failure (e.g. ARDS) and hypercapnic respiratory failure (e.g. acute exacerbation of COPD). However, use of mechanical ventilators should not be unnecessarily prolonged and patients should be actively screened for weaning during recovery to prevent the deleterious effects of the mechanical ventilation.

Suggested reading

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Figures & tables

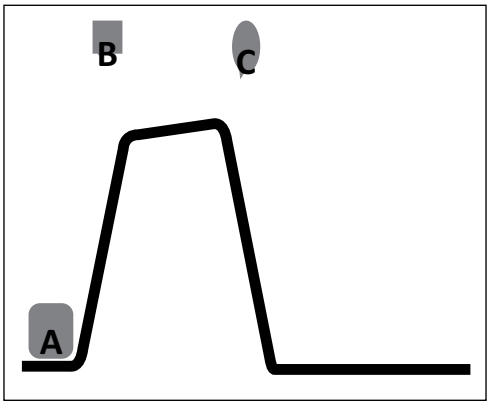

Figure 1 : Pictorial representation of variables. Point A represents trigger, Point B depicts limit and point C represents cycling.

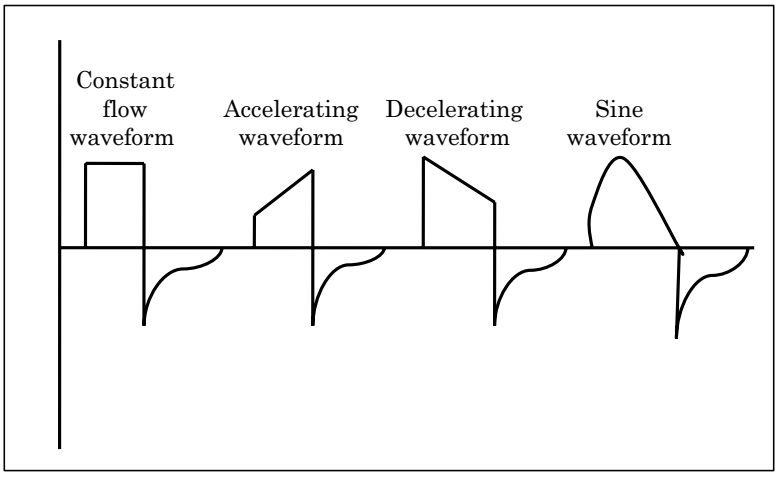

Figure 2 : Different types of flow waveforms used in mechanical ventilation

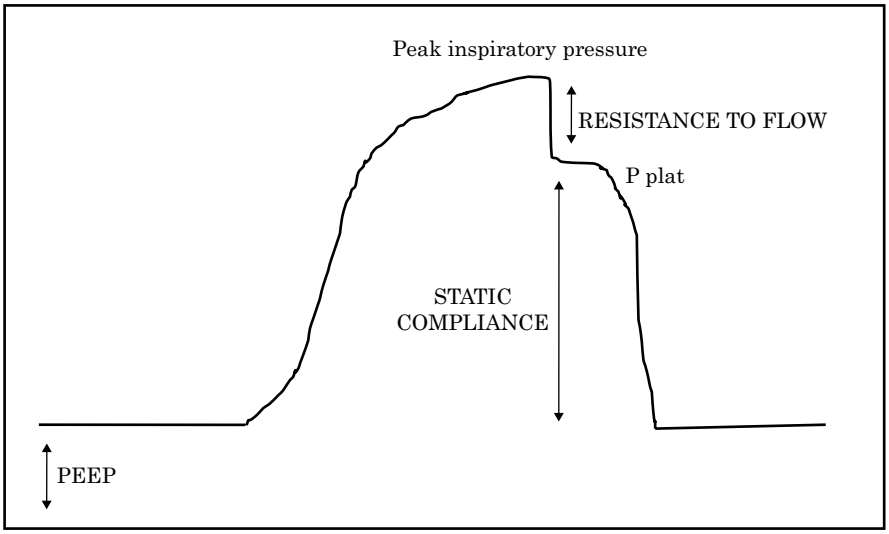

Figure 3 : Pressure vs time waveform during volume controlled mode (VC)

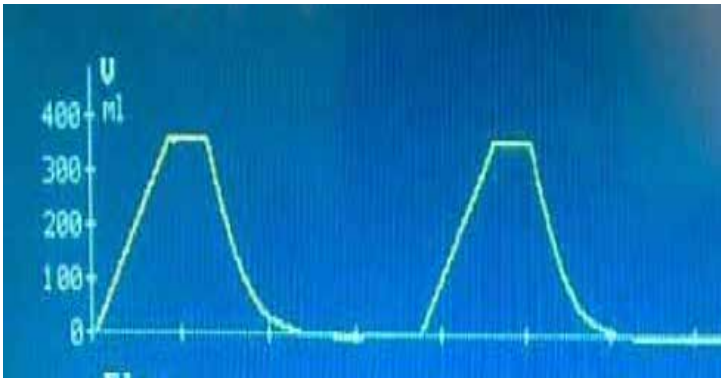

Figure4 : Volume vs time scalar during volume controlled ventilation (VC)

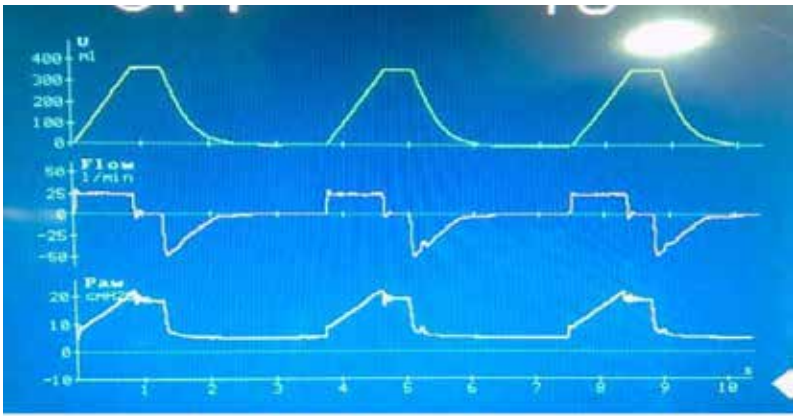

Figure 5 : Volume, pressure and flow scalars in volume controlled ventilation (VC)

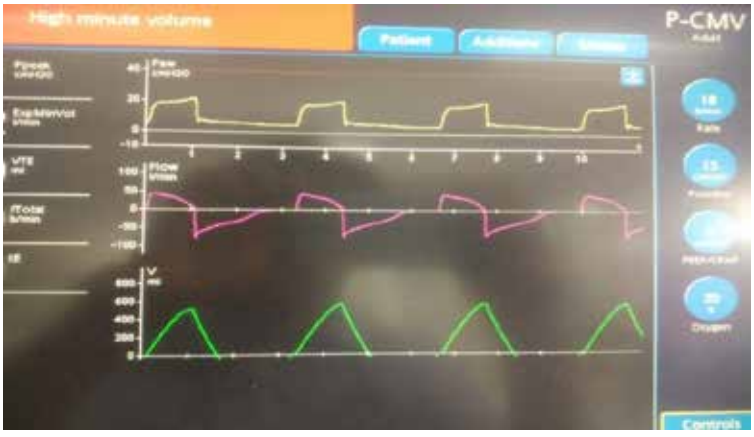

Figure 6 : Pressure, volume and flow scalars in pressure controlled ventilation (PCV)

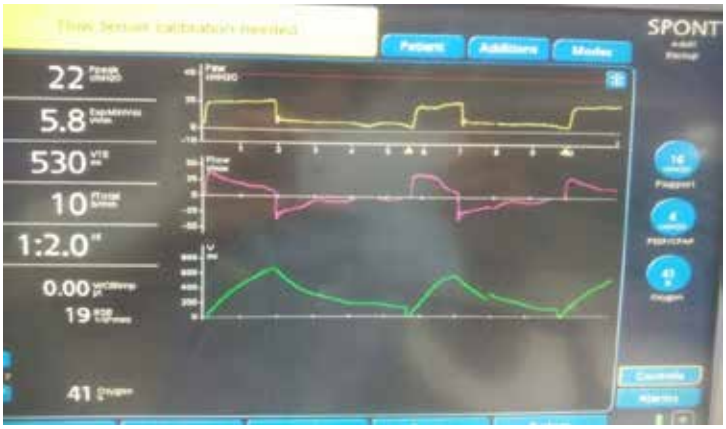

Figure 7 : Pressure, flow and volume scalars in pressure support ventilation

Table 1 : Variables of mechanical ventilator breaths

Trigger- (What causes the breath to begin?)	Flow (Assist breath) Pressure (Assist Breath) Time (Control Breath) Newer variables (Volume, Shape signal, neural)
Limit- What regulates gas flow during the breath?	Flow (Volume Control modes) Pressure (Pressure Control modes)
Cycle - What causes the breath to end?	Volume (Volume control) Time (Pressure control) Flow (pressure Support) Pressure (Safety cycling variable)

Table 2 : Different modes of ventilation and their characteristics

Mode of ventilation	Independent variables	Dependent variables	Waveforms that will be helpful	Waveforms remain unchanged
Volume control/ Assist-control	Tidal volume, RR, flow rate, PEEP, I/E ratio	Airway pressure (Paw)	Pressure time scalar- changes in PIP and Pplat Flow-time- expiratory limb for resistance	Volume-time

Pressure control	Paw, Inspiratory time, PEEP, I/E ratio	Tidal volume, flow	Volume –time and flow time scalars	Pressure time scalar
Pressure support/ CPAP	PS and PEEP	Tidal volume, RR, flow, I/E ratio	Volume –time and flow-time	

Table 3 : Physiological Effects of Mechanical Ventilation

Reverse of normal

- Inspiration: Positive pressure
- Expiration: Passive

Cardiovascular effects: Secondary to positive intrathoracic pressure

- Cardiac filling in expiration
- Increased Rt. Ventricular after load more with PEEP
- Ventricular interdependence, Decreased LV output
- Hypotension

Table 4 : Indications for Invasive Mechanical Ventilation

- Acute hypoxemic respiratory failure with cardiac/ respiratory arrest/ severe tachypnea with fatigue or impending arrest
- Acute hypoxemic respiratory failure with refractory hypoxemia (when the PaO2 <60 mm Hg even with FiO2 at 100%)
- Acute hypercapnic respiratory failure
- Acute illness with cardio-vascular instability requiring high dose of vasopressor or inotropes
- Inability to protect the airway associated with depressed levels of consciousness (GCS<8)
- Decreased ventilatory drive
- Inability to clear secretions with impaired gas exchange or excessive respiratory work
- Neuromuscular disease with respiratory muscle involvement (vital capacity <10-15ml/kg)
- Short term adjunct in management of acutely increased intracranial pressure (ICP)

Table 5 : Ventilation in specific disease states

	Mechanical Ventilation in ARDS (Acute respiratory distress syndrome)	Mechanical Ventilation in Exacerbation of Obstructive Airway diseases
Goal	• To optimize oxygenation and ventilation • To recruit stiff, non-compliant lung units with impaired gas exchange • To provide rest to fatigued respiratory muscles • To avoid injury to healthy lungs	• To optimally maintain gas exchange • To provide rest to fatigued respiratory muscles • To minimize dynamic hyperinflation and its consequences (barotrauma, pneumothorax, hypotension, and cardiac arrest) • To avoid injury to healthy lungs
Basic Principles	• Preferred mode: Assist control (VACV/PACV); IRV (Inverse ratio ventilation) may be needed • Decelerating flow pattern preferred • Tidal volume: close to 6ml/kg predicted ideal body weight (4-8 ml/kg) • Respiratory frequency: up to 35/min to optimize minute ventilation • Allow permissive hypercapnia • Preventing lung injury by keeping plateau pressure from exceeding 30cm H_2O • FiO2: Using the lowest possible to keep SaO2 at ≥88% (PaO2 ≥55 mmHg) • PEEP: adjusted to maintain alveolar recruitment while avoiding VILI and hemodynamic instability (as per ARDS Net Trial) • Prone positioning	• Preferred mode: Assist control (VACV/PACV); dual mode like PRVC • Constant high inspiratory flows • Tidal volume (6-8 ml/kg); decide by ventilator requirement • Respiratory frequency (10-14/min) to reduce intrinsic PEEP (PEEPi) • Preventing lung injury by keeping plateau pressure from exceeding 30cm H_2O • FiO2: Using the lowest possible to keep SaO2 at ≥88% (PaO2 ≥55 mmHg) • Provide longer expiratory times (I:E - 1:2.5-4) to promote lung emptying
Alternative strategies	• ECMO (Extracorporeal membrane oxygenation)	• Ventilation with helium-oxygen (Heliox) • ECCO2R (Extra corporeal CO2 Removal)
Adjunctive supportive measures	• Adequate sedation and paralysis (especially in first 48 hours) • Keep the lungs dry by avoiding fluid overload • Prevent infections Hospital Acquired Infections • Early weaning and mobilisation	• Adequate sedation with paralysis in first 24-36 hours (especially in status asthmaticus) • Reduce airway inflammation and bronchoconstriction with adequate doses of steroids, bronchodilators, etc. • Avoid post-hypercapnic metabolic alkalosis • Prevent patient-ventilator dys-synchrony • Early weaning on NIV (Noninvasive ventilation) in COPD patients

Table 6 : NIV in Acute Respiratory Failure (ARF)

Indications for NIV	Contraindications to NIV	Predictors of NIV Failure
Strong recommendation: • COPD exacerbations Prevent IMV Facilitate early weaning Extubation Failure • Cardiogenic pulmonary edema • Immunocompromised host with acute respiratory failure **Supported by weaker evidence for cautious use:** • Exacerbation of obstructive airway diseases other than COPD (Asthma, Bronchiectasis) • Mild-Moderate ARDS • Severe Community acquired pneumonia Post-operative acute respiratory failure • Respiratory failure due to Trauma • Acute decompensation of Chest wall and Neuromuscular diseases,Obesity hypoventilation syndrome **Others:** • Bronchoscopy in high risk patients • Pre-oxygenation before intubation • Do-not intubate patients/ palliative care	• Agitated, uncooperative patient • GCS <10 or inability to protect the airway or clear respiratory secretions (impaired cough/ swallowing) • Severe neurological disturbance, coma, seizures • Unable to apply mask due to burns, trauma, facial surgery, deformity, etc. • Upper airway obstruction • Excessive secretions/ vomitting • Upper gastrointestinal (GI) bleed • Hemodynamic instability requiring Vasopressors/ Inotropic support • Undrained pneumothorax • Recent upper GI surgery • Multi-organ dysfunction	• Inability to cooperate or coordinate with ventilator or effectively use the interface • Severe dyspnoea with RR> 30/min, accessory muscle use with paradoxical breathing • Greater severity of illness indicated by APACHE II (>29), SAPS II (>34), etc. • Hypercapnic respiratory failure with very low arterial pH at baseline (<7.10) • Hypoxemic respiratory failure with severe ARDS / community acquired pneumonia • Presence of multi-organ dysfunction or cardio-vascular instability • Lack of improvement in pH, RR, oxygenation, blood gases at 1 hour

Table 7. Complications of Mechanical Ventilation

Invasive Mechanical Ventilation	Noninvasive Mechanical ventilation
Complications related to intubation • Need for sedation and paralysis • Trauma to oral cavity, hypo-pharynx, larynx, trachea • Loss of upper airway protective mechanisms • Right main-stem bronchus intubation • Accidental esophageal intubation • Potential risk of vomiting and aspiration • Nasal necrosis and sinusitis with nasal intubation	**Complications related to interface** • Anxiety and discomfort • Claustrophobia • Skin irritation, ulceration, necrosis • Difficulty in feeding
Complications related to mechanical ventilation • Cardiovascular and hemodynamic instability • Ventilator induced lung injury (Barotrauma, atelectrauma, etc.) • Risk of ventilator associated pneumonia • Suction trauma (necrosis, bleed) to trachea-bronchial mucosa • Ventilator induced diaphragmatic dysfunction • Immobilization, risk of venous thrombo-embolism, critical illness myo-neuropathy • Psychological effects like psychosis, delirium, anxiety-depression, etc.	**Complications related to ventilation** • Nasal dryness, sinusitis • Conjunctivitis • Gastric distension • Re-breathing • Air leaks • Patient-ventilator asynchrony • Disturbed sleep • Psychological effects
Complications post-extubation • Glottic oedema • Tracheal injury • Laryngo-spasm • Vocal cord dysfunction • Tracheal stenosis & tracheomalacia • Prolonged mechanical ventilation and tracheostomy	**Others** • Aspiration • Retained secretions • Respiratory arrest

Oxygen Therapy

Sanjay Kumar Kochar

Introduction

Oxygen therapy is the administration of oxygen as a medical intervention and is among the most commonly used therapies worldwide. Normal air is composed of 20.947% oxygen by volume. Oxygen is essential for the cell metabolism, and thus, tissue oxygenation is essential for all normal physiological functions. Oxygen, as a therapeutic agent, has been introduced several decades ago, but much has been learned regarding the detrimental effects of hypoxemia and the beneficial impact of oxygen therapy. Oxygen saturation, "the fifth vital sign", should be checked by pulse oximetry in all breathless and acutely ill patients (supplemented by blood gases when necessary) and the inspired oxygen concentration should be recorded on the observation chart with the oximetry result.[1, 2]

While it is one of the most commonly used interventions, it is also one of the least taught subjects in medical school. Though cheap, easily available and a pillar of medical therapeutics, importance of teaching methods of oxygen delivery, their proper use and problems is frequently underplayed. To say that oxygen therapy for a breathless patient is like intravenous fluid therapy for a dehydrated patient is not entirely true, but serves as a useful analogy to understand the gaps in our knowledge. While there are piles upon piles of studies and books on fluid management, the same on oxygen use are hard to find. Due to its relatively easy availability and gaps in knowledge, oxygen is prone to indiscriminate use and evidence is emerging that liberal and unwarranted use may have adverse consequences like worsening carbon dioxide retention and increased oxidant injury.

The large numbers of patients receiving supplemental oxygen as treatment and the high costs incurred in providing oxygen therapy necessitate the practitioner to know the indications for short duration and long-term oxygen therapy (LTOT) as well its effects on survival, pulmonary hemodynamics, sleep, and exercise capacity.

Systemic effects of hypoxia

Hypoxia is a state where the supply of oxygen is inadequate to meet the normal metabolic requirements and if sustained, it may be incompatible with life. Generally 4 types of hypoxia are described:[3]

- Hypoxic Hypoxia –Partial pressure of oxygen (PaO2)in the arterial blood is low (<60mmHg)or saturation (Sao2) <90%.
- Anemic Hypoxia - Amount of hemoglobinto carry oxygen is low
- Stagnant or Ischemic Hypoxia- Blood flow to the tissue is low
- Histotoxic Hypoxia — Tissue can't utilize oxygen

Oxygen therapy is most effective in management of hypoxic hypoxia and the terms hypoxia or hypoxemia used further in the article is to be considered synonymous with hypoxic hypoxia. Hypoxemia causes various alterations in the physiology both in short and long term.[3, 4]

- Hypoxemia causes peripheral vasodilation, which induces a compensatory tachycardia and a subsequent increase in cardiac output to improve oxygen delivery.
- On a cellular level, mitochondrial function declines, anaerobic glycolysis occurs, and lactate/pyruvate ratioincreases.
- Alveolar hypoxia causes pulmonary vasoconstriction in an effort to match ventilation and perfusion and thus pulmonary hypertension.
- Hypoxia can activate renin-angiotensin axis which increases the risk of acute tubular necrosis.
- Cerebral hypoxia leads to impaired judgment at low levels of oxygen, with progressive loss of cognitive and motor functions, and eventually loss of consciousness as severe hypoxemiaensues.[5]
- Long term effect of pulmonary hypertension causes signs of right ventricular failure (cor-pulmonale) such as elevated jugular venous pressure (JVP), pedal edema, and hepatomegalyand ascites.[6]
- Sustained hypoxia leads to increase in erythropoietin secretion leading to erythrocytosis and thereby, increasing oxygen carrying capacity. These compensatory mechanisms are useful in short term but have cause detrimental long-term effects, such as polycythemia.
- Hypoxia can lead to myocardial ischemia/infarction, ischemia/infarction of other critically perfused organs, hypotension, and arrhythmias.
- Other nonspecific symptoms like headache, breathlessness, restlessness and tremors can be found in patients with hypoxemia.

Table 1 Systemic effects of Hypoxia

System	Effects
Central nervous system	Confusion, drowsiness, hypoxic-ischemic encephalopathy, infarction, intracranial haemorrhage, seizures, cerebral oedema, hypotonia, hypertonia
Cardiovascular	Myocardial ischemia, poor contractility, myocardial stunning, hypotension
Pulmonary	Pulmonary hypertension, pulmonary haemorrhage, respiratory distress
Renal	acute tubular or cortical necrosis
Gastrointestinal	Anorexia, nausea, perforation, ulceration with haemorrhage, necrosis
Metabolic	Metabolic acidosis, inappropriate secretion of antidiuretic hormone, hyponatremia, hypoglycaemia, hypocalcaemia
Integument	Subcutaneous fat necrosis
Haematology	Polycythemia

Oxygen sources and storage

Oxygen can be separated by a number of methods, including chemical reaction and fractional distillation, and then either used immediately or stored for future use. The common sources are-[7]

1. **Liquid storage**- Liquid oxygen is stored in chilled tanks until required, and then allowed to boil to release oxygen as a gas.

2. **Compressed gas storage**- The oxygen gas is compressed in a gas cylinder which provides a convenient storage. It does not require refrigeration as needed with liquid storage.

3. **Instant usage-** The use of an electrically powered oxygen concentrator or a chemical reaction based unit can create sufficient oxygen for a patient to use immediately. Thee system have the advantage of providing continuous supply without the need for bulky cylinders, but these cannot reach very high flow rates.

Oxygen delivery systems

Various devices are used for administration of oxygen. In most cases, the oxygen will first pass through a pressure regulator, used to reduce the high pressure of oxygen delivered from a cylinder (or other source) to a lower pressure. Thereafter the rate offlow is controlled by a flow-meterwhich measuresthe flow in liters per minute (Lpm). Based on delivery system design these are divided into many subtypes such low flow and high flow systems and based on the change in fraction of inhaled oxygen (FiO2) into fixed vs. variable flow systems.

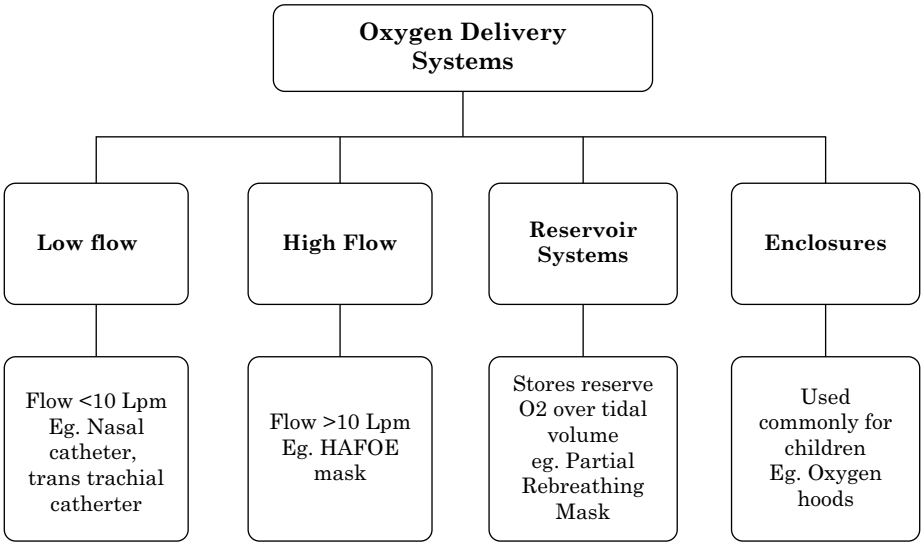

Figure 1 : Types of oxygen delivery systems based on design

Division based on performance

This division is based on the predictability and consistency of FiO2 provided by the inhalational system. These are of two types-[7, 8, 9]

- **Variable Performance Devices**

  In such devices, the FiO2 of the inhaled air change with patient's ventilator pattern. These devices are either low flow devices like nasal cannula or reservoir systems like partial or non-rebreathing masks. If the reservoir volume is more than tidal volume, the reservoir systems can also provide fixed FiO2.

- **Fixed Performance Devices**

  In these systems a fixed amount of FiO2 is provided to the patient irrespective of the breathing pattern. Such a performance is seen in high flow devices like High Air Flow Oxygen Enrichment (HAFOE) or Venturi masks.

Common oxygen delivery devices

- **Low flow devices**[8]

  Many patients require only a supplementary level of oxygen in the room air they are breathing, rather than pure or near pure oxygen. This can be delivered through a number of devices dependent on the situation. These are usually low flow devices with variable FiO2. Some devices can be used with both high and low flow systems like non rebreathing masks and venturi masks.[9]

  – **Nasal cannula (NC):** It is a thin tube with two small nozzles that protrude into the nostrils. These have benefitof being comfortable to use and don't hamper activities (like eating). It can oxygen at low flow rates, 2–6 liters per minute (Lpm), delivering concentration of 24–40%. FiO2 is variable and changes with patient's breathing

  – **Simple face mask:** It often used at between 5 and 8 Lpm, with a concentration of oxygen to the patient of between 28% and 50% depending on oxygen flow rate.

  – **Partial rebreathing mask:** It is based on a simple mask, but features a reservoir bag, which increases the provided oxygen concentration to 40–70% oxygen at flow rates of 5 to 15 Lpm. Some amount of rebreathing is allowed and may lead to CO2 accumulation.

  – **Non-rebreather mask**: draws oxygen from attached reservoir bags, with one-way valves that direct exhaled air out of the mask. When properly fitted and used at flow rates of 8-10 Lpm or higher, they deliver close to 100% oxygen. This type of mask is indicated for acute medical emergencies.

  – **Demand oxygen delivery systems (DODS)**: also called oxygen resuscitators deliver oxygen only when the person inhales, or, in the case of a non-breathing people, the caregiver presses a button on the mask. These systems greatly conserve oxygen compared to steady-flow masks, which is useful in emergency situations when a limited supply of oxygen is available.

- **High flow oxygen delivery** [8, 9, 10]

  These are used in cases where the patient requires a high concentration of up to 100% oxygen; a number of devices are available:

  – ***Non-rebreather mask:***when used at high flow rates of oxygen at >10 Lpm, it provides close to 100% FiO2

  – ***Venturi mask:*** It is more controlled air-entrainment mask, which can accurately deliver a predetermined and fixed oxygen concentration.

  – ***Humidified high flow nasal cannula:*** which enables flows exceeding a patient's peak inspiratory flow demand to be delivered via nasal cannula. Although practically appealing, it is wasteful as a lot of oxygen just disperses in the environment.

  – ***Trans-tracheal oxygen:*** Oxygen is delivered via a catheter inserted percutaneously between the second and third tracheal rings.

  – ***Positive pressure ventilation delivery mask:***these masks can deliver high flow rates of oxygen along with a postitive respiratory support. Such masks are used with BiPAP.

  – ***Filtered oxygen masks:*** These masks have the ability to prevent exhaled, potentially infectious particles from being released into the surrounding environment. These are normally of a closed design such that leaks are minimized and breathing of room air is controlled through a series of one-way valves.

Medical uses of oxygen therapy

Oxygen as a medical treatment can be used in hospital, pre-hospital or entirely out of hospital, dependent on the needs of the patient. The need for oxygen may be acute and for short duration such as in patients with pneumonia or myocardial infarction or it may be chronic and persistent as seen in patients of Chronic Obstructive Pulmonary Disease (COPD) and other chronic lung diseases.

Indication of short-term oxygen therapy[8, 9, 11]

Any patient presenting with hypoxia and signs and symptoms of respiratory distress irrespective of underlying cause should be given oxygen. In cases where hypoxia cannot be documented but patient is in distress, it is better to give oxygen than to withhold it. Some indications of oxygen therapy in emergency are as follows.[8, 9, 11]

- **Acute Pulmonary diseases**
  - *Pneumonia*- not all cases of pneumonia require oxygen but it supplementation helps alleviate the anxiety and has placebo effect.
  - *Asthma*- oxygen is needed only during acute attacks if the saturation falls below 94%
  - Acute heart failure and acute pulmonary edema- these conditions are associated with ventilation perfusion mismatch and sluggish pulmonary flow. Supplemental oxygen reduces hypoxic vasoconstriction in pulmonary vessels and reduce V/Q mismatch
  - *Pulmonary Embolism (PE)*- acute PE is associated with significant drop in blood flow to certain areas of lung and hypoxemia due V/Q mismatch. If PE is suspected and hypoxia is not corrected by oxygen, possibility of intra-cardiac shunting should be considered.
  - *Exacerbation of chronic lung diseases such as COPD or bronchiectasis* – such patients need controlled oxygen to keep Spo2 between 88-92%. This to prevent the loss of hypoxic drive
- **Systemic diseases needing oxygen therapy**[11]
  - *Shock*-circulatory shock of any kind is associated with impairment of pulmonary and systemic blood flow. Supportive oxygen helps to reduce hypoxia and anaerobic metabolism
  - *Major trauma*- patients with major trauma frequently have chest wall or airway injuries and possible obstructions. Even significant pain may lead to limitation of respiratory movements.
  - *Severe sepsis*- it is associated with impaired peripheral circulation and metabolic acidosis. Correction of hypoxia may lead to improvement in acidosis.
  - *Cardiac arrest and during resuscitation*
- **Indication of oxygen therapy in other conditions**
  - Oxygen can be prescribed in advanced cancer or neurodegenerative disease, despite having relatively normal blood oxygen levels.
  - High concentration oxygen is used as home therapy to abort cluster headache attacks, due to its vaso-constrictive effects.[12]

- It is also used in resuscitation, major trauma, anaphylaxis, major hemorrhage, shock, active convulsions and hypothermia.[11]
- It may also be indicated for any other patient where their injury or illness has caused hypoxemia, although in this case oxygen flow should be moderated to achieve target oxygen saturation levels, based on pulse oximetry (with a target level of 94–98% in most patients, or 88–92% in COPD patients).

- **Supplemental oxygen therapy in non-hypoxemic patients**
  - Oxygen therapy is useful in carbon monoxide poisoning, specially hyperbaric therapy
  - Hyperoxiais also be used to accelerate the resolution of pneumothorax in patients who do not require a chest drain.[13]
  - Short-term postoperative oxygen therapy, for 2 hours, has beenshown to reduce the risk of surgical wound infections indouble blind trials of patients having bowel surgery but not in general surgery.[14, 15]
  - Hyperbaric oxygen reduced the risk of amputation in patients with chronic diabetic foot ulcers and may improve the chance of healing over 1 year, but definite evidence is absent. It is not known if conventional oxygen therapy has any effect on wound healing.[16, 17]

Patients who are receiving oxygen therapy for hypoxemia following an acute illness or hospitalization should not routinely have a prescription for continued oxygen therapy without a physician's re-assessment of the patient's condition. If the person has recovered from the illness, then the hypoxemia is expected to resolve and additional care would be unnecessary and a waste of resources

Indication of long-term oxygen therapy (LTOT)

LTOT is defined as long term oxygen use outside of the hospital settings. It is usually prescribed in patient suffering from chronic pulmonary diseases such as COPD or ILD with advanced disease, poor reserve and persistent hypoxia. Chronic hypoxemia leading to the development of cor-pulmonale portends a poor prognosis. Oxygen therapy in such cases is associated with improvement in quality of life and increased survival.[18, 19, 20] The duration of oxygen use per day depends on patient's condition and can vary from few hours to round the clock. Few indications are:[18, 19]

- **Chronic obstructive pulmonary disease (COPD)**
  - Patients with stable chronic obstructive pulmonary disease (COPD) and a resting PaO_2 ≤7.3 kPa should be assessed for long-term oxygen therapy (LTOT).LTOT in such patients offers survival benefit and improves pulmonary hemodynamic.
  - LTOT should be ordered for patients with stable COPD with a resting PaO_2≤8 kPa with evidenceof peripheral edema, polycythemia (hematocrit ≥55%) or pulmonary hypertension.
  - LTOT reduces the mortality and incidence of corpulmonale while improving quality of life and exercise capacity in such patients.[21,22]
- **Interstitial lung disease (ILD) with**
  - Resting PaO_2≤7.3 kPa or ≤8 kPa in the presence ofperipheral edema, polycythemia (hematocrit≥55%) or evidence of pulmonary hypertension.
- **Cystic fibrosis with**
  - Resting PaO_2 ≤7.3 kPa or ≤8 kPa in the presence of peripheral edema, polycythemia (hematocrit ≥55%) or evidence of pulmonary hypertension.
- **Pulmonary hypertension**
  - LTOT should be ordered for patients with pulmonary hypertension, including idiopathic pulmonary hypertension, when the PaO_2 is ≤8 kPa.
- **Neuromuscular or chest wall disorders**
  - Non-invasive ventilation (NIV) should be the treatment of choice for patients with chest wall or neuromuscular disease causing type 2 respiratory failure. Additional LTOT may be required in case of hypoxemia not corrected with NIV.
- **Advanced cardiac failure with**
  - Resting PaO_2 ≤7.3 kPa or ≤8 kPa in the presence of peripheral edema, polycythemia (hematocrit ≥55%) or evidence of pulmonary hypertension on ECG or echocardiograph.

Adverse effect of oxygen supplementation

- The most significant effect of excess oxygen on the respiratory system is hypercapnic respiratory failure in a population of vulnerable patients especially in COPD patients. This does not occur in the absence of significant pulmonary disease or musculoskeletal disease affecting the thorax, and it occurs while the PaO_2 is still within the normal range or slightly below normal. There are at least five mechanisms responsible for this:
  - V/Q mismatch
  - Decreased ventilatory drive
  - Haldane effect
  - Absorption atelectasis
  - Higher density of oxygen compared with air.
- Rebound hypoxemia following sudden cessation of supplementary oxygen therapy
- Coronary and cerebral vasoconstriction
- Reduced cardiac output
- Damage from oxygen free radicals
- Increased systemic vascular resistance
- Delay in recognition of physiological deterioration[7]
- High levels of oxygen given to premature infants causes blindness by promoting overgrowth of new blood vessels in the eye obstructing sight, the disorder is called retinopathy of prematurity (ROP).
- In rare instances, hyperbaric oxygen therapy patients have had seizures
- Fire risk: Oxygen itself is not flammable, but the addition of concentrated oxygen to a fire greatly increases its intensity[7]

Conclusion

Using a reservoir mask for patient on LTOT and using a nasal cannula in a patient of severe pneumonia are both recipes for certain doom. Though both the methods are delivering oxygen but they are still not fulfilling their purpose to the patient. A well-informed doctor who knows proper use of oxygen therapy can mean the difference

between life and death of a patient.The same oxygen if used in wrong way or with incorrect equipment will only lead to wasteful consumption of resources, additional financial burden and a wrong sense of satisfaction without any benefit to the patient. Proper knowledge of the means of oxygen delivery and being able to choose appropriate method for every situation is very important.

More important than knowing where to use oxygen is where not to use it. With betterment in our knowledge various complications associated with wrongful oxygen use are coming to light. We are slowly learning that although oxygen is life and source of all the life on our planet, too much of oxygen is not good. As a Sanskrit proverb says:

"अतिसर्वत्रवर्जयेत्"

"Excess is always prohibited"

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Extracorporeal Membrane Oxygenation in Adults

Rishabh Kochar, Sanjay Kumar Kochar

Historical perspective

One of the very first human attempts to artificially oxygenate blood was met with futility as it involved a simple mixing of gas and blood but without any anti-coagulation. With the discovery of heparin in 1916, the task became a little easier but the basic design was still the same i.e. gas was allowed to bubble up in the blood and mix with it. These circuits were designed with special attention to bubble sizes to ensure adequate oxygenation and needed traps to prevent them from entering the patient's blood. Improvement in design and mechanics lead to a mechanical extracorporeal oxygenator being used in first intra-cardiac surgery under direct vision in 1953. It was two decades before it could be used medically when in 1972 first adult patient was reported to have survived on ECMO. [1]

The initial results fueled a trial on extracorporeal support, which was published in 1979 with a disappointing outcome of only 10% survival. It was realized that ECMO was not a treatment modality but only a support system till the patient's own lungs improve or an alternate treatment is found. Another understanding developed that positive pressure ventilation was doing more harm than previously thought and was preventing the recovery of damaged lungs. Clinicians responded and protective ventilation strategies were developed, and ECMO was combined with them to facilitate carbon dioxide removal.[1]

All this time, as the ECMO struggled to make a mark in adult patients; the pediatricians continued to use ECMO andhad data which supported that ECMO was saving lives in the pediatric population. During the 2009 influenza epidemic, ECMO was used to nurse many adult patients back to health and showed improved survival. This lead to resurgence of interest in adult ECMO and paved the path for its future. Simultaneous to the so called "Pulmonary ECMO", another version of ECMO developed which was capable of supporting both the cardiac and pulmonary. It was similar to the cardiopulmonary bypass machine and could be used for both acute and chronic conditions. The modern ECMO can support failing lungs or both the lungs and the heart

An Ideal Ecmo Unit

An ECMO unit, when run under ideal conditions is resource and personnel intensive and translates into high running costs. Thus, an ECMO unit is only feasible when established in a large center with high patient turnover and access to multiple super-specialties like pulmonary medicine, cardiology, palliative care, neurology, nephrology, cardiothoracic surgery and advanced imaging to name just a few. Following listed members are needed to run an ECMO group:[1]

- A team of clinicians headed by anexpert and assisted by other clinicians and surgeons
- A team of perfusionists well equipped in ECMO knowledge and expert in managing extracorporeal circuits
- Leading doctors from other specialties like hematology, microbiologists and many others
- A team of Nursing staff specially trained for ECMO unit supported by a team of regular nurses for day to day care
- Coordinators for ECMO to coordinate referrals and patient transfers, review the ECMO team and develop protocols
- Supporting staff such as physiotherapists, pharmacists, dieticians, porters who have knowledge and training on handling of a patient on ECMO.

Along with the above, the ECMO unit should have on-site facilities for[1] -

- Endoscopy, vascular surgery, interventional cardiology, plastic surgery, 24 hour running operation theatre
- Radiology-CT, Ultrasound, portable X-ray, Echocardiography
- Round the clock essential biochemistry and hematology service
- Transfusion services, hemofiltration, plasmapheresis, hemodialysis
- Organ donation services
- Facilities for isolation many patients maybe suffering from communicable diseases like H1N1

An ideal ECMO care also requires many high end medical and electrical devices such as heaters/ coolers, monitoring devices, infusion pumps, ventilators, pulse oxy-meters, bedside ECG, DVT pumps in addition to those used conventionally in the ICU.

Patient Considerations

As said before, it cannot be emphasized more that the ECMO is a supportive therapy used to buy time. In cases where ECMO is used in incurable diseases, it can be used to support the patient till cardiac and/or pulmonary transplant is available. In case of patients who have failed on existing treatment protocols and in whom transplant is not feasible, putting on ECMO will only prolong the suffering and have more complications then benefits.

Criteria that determine when to put the patient on ecmo

There are no definite criteria that determine when to put the patient on ECMO or if the patient even needs ECMO. The decision of putting a patient on ECMO is guided by clinical experience backed by scientific data from patients treated so far. The most important factor to put in consideration will be the potential reversibility of the underlying disease process and chances of recovery. The factors which should be considered are:[1, 2, 3]

- **Reversibility of the underlying disease** : There is no definite method or scores to determine the reversibility of the underlying disease, especially in patients with diseases such as ILD, COPD, bronchiectasis. It is left on the clinician's judgment to decide the potential for reversibility. In many cases such as an exacerbation of COPD or pneumonia in a patient of ILD, the precipitating cause can be treated and patient may return to his prior functioning.

- **Failure of conventional therapy** : ECMO should not be used as a last resort as previously considered. It is now understood exhausting all clinical options before referring a patient for ECMO is detrimental. If a patient needs ECMO, he should be referred without delaying in anticipation for conventional therapies to work.

- **Co-morbid conditions** : Previous studies have identified patients with multiple co-morbidities to have poorer outcomes on ECMO. Although data are variable but more the number of co-morbidities more likely are the complications. Brain injury was considered as a contraindication but such patients have been supported on anti-coagulation free veno-venous ECMO.

- **Advanced age** : Advanced age is associated with frailty, an erratic response to physiological stresses and a prolonged recovery from illness. The same is corroborated in poor outcome on ECMO in patients aged more than 65 years. Age more than 65 years was previously considered a contraindication. Though it is not so anymore, but prognosis in such patients must be guarded.

- **Prolonged mechanical ventilation** : Patients on mechanical ventilation for more than 7 days before being shifted to ECMO have dismal outcomes. Thus, it is imperative to shift the patient on ECMO swiftly once a consensus has been reached
- **Cost** : The economic impact of the therapy on the patient is a factor to consider in our settings. The cost of installation alone isvery expensive and adding the cost of daily running, maintenance and additional tests needed specifically for ECMO add a significant recurring expense(ending in millions of rupees). These expensesmaybe difficult for the patient to bear and he/she may forego ECMO for less effective but also significantly less costly conventional therapies.

After above considerations, the following patients may be taken up for ECMO support

ECMO for Respiratory Support-[1]

All potentially reversible cause of acute respiratory failure merit ECMO use

- *Acute respiratory distress syndrome-* severe bacterial or viral pneumonia, aspiration syndromes
- *ECMO to relieve lung stress-* toxic inhalations, airway obstruction
- *Lung trauma*
- *Lung transplant-* as a bridge to transplant, graft failure
- *Pulmonary hemorrhage syndromes*

ECMO for Cardiac or both Cardio-respiratory support-[1, 2, 4] Classical indications are refractory hypotension despite adequate volume and high dose inotropes and/or intra-aortic balloon pump (IABP), refractory low cardiac output-<2L/min/m^2

- All indications of ECMO for respiratory support with associated *severe cardiac dysfunction*
- *Cardiogenic shock or severe cardiac failure-* acute coronary syndromes, refractory arrhythmias, pulmonary embolism, drug overdose(local anesthetic, anti-depressants), myocarditis, pulmonary embolism, sepsis with severe cardiac dysfunction, acute mechanical defect like papillary muscle rupture
- *Inability to wean from cardio-pulmonary bypass after cardiac surgery*
- *Cardiac transplant-* as a bridge to transplant or VAD support, graft failure after cardiac or combined heart and lung transplant
- *Chronic cardiomyopathy* patient awaiting definitive treatment

- *Post cardiac arrest* as a part of ECMO assisted CPR or eCPR- ECMO assisted CPR has higher survival rates if instituted early. Beyond 10 minutes of conventional CPR, the delay in ECMO use reflected reduced chance of survival at the rate of 1% every minute more of CPR.
- *Cardio-respiratory failure of unknown etiology*- to buy time for diagnosis and appropriate therapy
- *ECMO as a bridge to organ donation* to ensure organ perfusion till retrieval

Contraindications for using ECMO[1, 2, 3]

- Futile treatment without any hope for recovery or without any exit strategy as in patients of disseminated malignancy, prolonged CPR with poor tissue perfusion, severe brain injury.
- Peripheral vascular disease precludes the use of peripheral veno-arterial ECMO.
- Contraindication for systemic anti-coagulation
- Immunosuppression with absolute neutrophil count<400/mm^3

It is important to note that some previous criteria such as advanced age and obesity are not considered as contraindications anymore. Also, cerebral hemorrhage which was previously a contraindication for ECMO is not an absolute contraindication now as many such patients have been supported to recovery on anti-coagulation free veno-venous circuits for long times and with little complications.

Inclusion and exclusion criteria

In spite of clearly mentioned indications, patient selection for ECMO may still be difficult. No unified criteria have been developed for patient selection but the criterionused for CESAR (Conventional Versus ECMO for Severe Adult Respiratory Failure) Trial have given positive results and may serve as a useful guide for patient selection[5]

Inclusion

- Reversibility
- 18–65 years of age
- Murray score (discussed below) ≥3
- Non-compensated hypercapnia with pH <7.2

Exclusion

- Ventilated with fraction of inspired oxygen (FiO2) >80% or peak airway pressure >30 cmH_2O for more than 7 days

  Severe trauma within last 24 h, intracranial bleeding and any other contraindication to systemic anti-coagulation
- Moribund and any contraindication to continuing active treatment

Table 1 : Murray score for acute lung injury

a. **Chest X-ray**	
No alveolar consolidation	0
Alveolar consolidation confined to one quadrant	1
Alveolar consolidation confined to two	2
Alveolar consolidation confined to three quadrants	3
Alveolar consolidation confined to four quadrants	4
b. **Hypoxaemia**	
PaO2/FiO2 ≥300 mmHg	0
PaO2/FiO2 225–299 mmHg	1
PaO2/FiO2 175–224 mmHg	2
PaO2/FiO2 100–174 mmHg	3
PaO2/FiO2 <100 mmHg	4
c. **PEEP**	
PEEP ≤5 cmH2O	0
PEEP 6–8 cmH2O	1
PEEP 9–11 cmH2O	2
PEEP 12–14 cmH2O	3
PEEP ≥15 cmH2O	4
d. **Respiratory system compliance**	
Compliance ≥80 mL/cmH2O	0
Compliance 60–79 mL/cmH2O	1
Compliance 40–59 mL/cmH2O	2
Compliance 20–39 mL/cmH2O	3
Compliance <19 mL/cmH2O	4

The total score is attained by dividing the values obtained from the initial analysis by the number ofelements used for the analysis. A score of zero indicates no lung injury, 0.1-2.5 is suggestive of mild to moderate lung injury and >2.5 is suggestive of severe lung injury.

The Ecmo Unit

ECMO is a circuit which takes blood from body, oxygenates it and pumps it back into the body. There are two predominant types of ECMO unit available based on where in the body the oxygenated blood is pumped back viz. a systemic vein or the arterial system.

- **Veno-venous ECMO or Respiratory ECMO:[1, 2] (Figure 1)**

  Blood is taken from one or more systemic veins and returned back via a vein close to the heart. Draining veins are usually inferior or superior vena cava, femoral veins, and blood is returned via internal jugular vein in a close proximity to right atrium. Also called Respiratory ECMO, this circuit is used when lungsare diseased but the heart is functioning normally, as in ARDS. The ECMO removes carbon dioxide and oxygenates the blood which is pumped back and mixes with the deoxygenated blood from rest of the body and is circulated via the heart. It supports carbon dioxide removal and oxygenation of blood but not circulation.

  New access systems allow for insertion of a double lumen catheter in which prevents insertion of multiple lines and lesser chances of procedure relate complications

  This type of ECMO circuit allows the use of lung protective ventilation and promotes lung recovery by reducing the damage from positive pressure ventilation.It supports only gas exchange while circulation is maintained by heart.

- **Veno-Arterial ECMO or Cardiac ECMO: [2, 4](Figure 2)**

  Blood is taken from large systemic veins and after passing through the oxygenator, pumped back into one of the systemic arteries. The draining veins are the same but the blood is returned to the body via the arteries. The veno-arterial circuits can support both the heart and lungs and useful in conditions with cardiac or combined cardio-respiratory failure as discussed above.

  The arteries in such circuit may be large peripheral arteries like the femoral, axillary or carotid artery accessed via skin or the central artery like aorta which is accessed by thoracotomy. If the peripheral arteries are used, the blood from the ECMO circuit flows against the patient's circulation which puts more pressure on failing heart and is detrimental to cardiac recovery.

  Also in such cases, the limb distal to the site of cannulation has reduced blood flow and may become ischemic. To avoid such a complication a separate reperfusion line is used to ensure blood flow to the distal limb

  Using the ascending aorta as return conduit, ECMO pumps in the same direction

as the native circulation and supports cardiac recovery. In veno-arterial ECMO the blood flows to systemic circulation mostly via the ECMO pump which significantly reduces the blood flow through right heart and pulmonary circulation predisposing to thrombosis.Also, the pressure generated by ECMO when using peripheral artery may reduce the left heart output causing ventricle distension and clot formation.

- **Arterio-venous circuit:**[1]

  Any veno-arterial circuit without a flow pump will have the blood flowing through the artery into the vein using the heart as the pump. These circuits have limited flow and used rarely when only carbon dioxide removal is needed as blood flow rate of as less as 0.5 L/min/m^2 can do the desired work

EXTRACORPOREAL CIRCUIT[1, 6] (Figure 3)

- **Oxygenator**

  Also called Membrane lung or artificial lung is the chief component of the ECMO circuit. It is made of multiple hollow fibers with thin walls. Common materials used for membrane are silicon rubber or polymethyl pentane which allows better gas exchange, less reactions and less hemolysis. The gas exchange through the oxygenator depends on blood flow, gas flow (sweep gas) and the composition of gas used. The oxygenator can be immersed in a bath which allows for heating/ cooling a needed for thermoregulation.

  Increasing the blood flow increases the utilization of oxygenator fibers and the increases surface area available for gas exchange, thus; improving the oxygenation. The removal of Carbon dioxideis directly proportional to the flow rate of sweep gas. Increasing the sweep gas flow increases Carbon dioxide removal.

  If the entire circuit is functioning properly and oxygenation is still inadequate, a second oxygenator can be added in parallel but it is rarely needed. In case of clot formation within the oxygenator, it may need to be changed.

- **Sweep Gas**

  it is the gas passing through the oxygenator. Usual composition is 100% oxygen, though a mixture of 95% oxygen and 5% carbon dioxide (carbogen) is also used. The flow rate of sweep gas determines the rate of carbon dioxide removal.Sweep gas is started at a flow rate equal to that of bloodin a ratio of 1:1 which is changed depending on the amount of carbon dioxide that is to be removed. Sweep gas pressure should be lower than the pressure of blood in the membrane or it may lead to air embolism.

- **Pump And Blood Flow Rates**

  The pump is placed after the inflow line and before the oxygenator. Pump selection is determined by its type, amount of blood flow or pressure needed and various pump designs are available like modified roller, centrifugalpump and peristaltic pump. Centrifugal pumps are most preferred because they have lesser heat and particle generation, less hemolysis and require less anti-coagulation. The flow is determined by the RPM of the pump, preload and afterload. Keeping the RPM of the pump constant, increase in preload increases the blood flowing through ECMO and increase in afterload decreases the blood flow.

  A minimum amount of blood (at least 2 liters per minute) must continue to flow through the circuit to avoid stasis and clot formation. For veno-arterial ECMO blood flow is needed is around 3L/min/m^2 or 60ml/kg/min in adults. For veno-venous circuits desired blood flow ranges from 60-80ml/kg/min. if only carbon dioxide removal is planned, flow rates should be 10-25% of cardiac output. The pressure at inflow should not be more negative than -300mmHg (to prevent hemolysis) and the pressure at the arterial side should not be more than 400mmHg.

- **Tubing**

  It is made of polyvinyl chloride and coated with heparin. Tubing is transparent to allow easy visualization of blood color and any thrombus that forms. The tube commonly used in adults has internal diameter of $3/8^{th}$ of an inch. A 1 meter long tube of this diameter ($3/8^{th}$ inch) at pressure gradient of 100mmHg allows blood flow at 5L/min which is sufficient for smooth operation.

  The tube connecting to the ECMO has various side ports which allow for sampling, drug injections and connection to additional machines such as renal replacement therapy. These side port, though useful, are prone to blood stasis and thrombosis and should be used as less as possible. There is a bridging tube between venous and arterial side of the circuit to allow recirculation of blood within the machine. This port is used when patient is being weaned from the ECMO, to remove any air that may have entered the circuit, or to improve oxygenation. When not in use, bridge should be flushed and no stagnant blood should remain in it to avoid thrombosis.

- **Ecmo Cannula**

  ECMO cannulas are made of mostly of biocompatible, heparin coated polyurethane with or without wire reinforced walls to prevent kinking and collapse. The venous

cannula has larger lumen and many side holes that allows more flow at lower pressures compared to arterial cannula which have narrower lumen and diffuser tips. Peripheral arterial cannulas have reperfusion line which is inserted in the vessel distal to the main cannula and small amount of oxygenated blood from outflow is diverted through it.

For veno-venous ECMO, double lumen cannula can be used which reduce the risk associated with procedure but have a more chances of recirculation of blood. This happens if the inflow and outflow ends are placed close together or if the outflow is directed towards inflow cannula.

- **Heat Exchanger**

  It is required to maintain the blood and patient temperature. A water bath I most commonly used heat exchanger where hot or cold water is circulated as desired to optimize temperature control. Since the water circulating in heat exchanger may get contaminated, periodic cleaning is needed.

- **Priming the circuit-**after assembly, the circuit is primed with isotonic balanced fluid. Some centers prefer to add human albumin to the circuit (12-25 grams) before exposure to blood. Priming helps to remove any air from the circuit, ensure circuit continuity and detect any leakage.

- **Monitoring The Machine**

  Multiple devices and fail-safes are given all across the circuit to prevent any mishap and raise alarm in case of malfunction or abnormality

  – **Blood flow monitoring**- As discussed, blood flow is a major determinant of arterial oxygenation and continuous monitoring is needed to determine any drop in flow. It is done using ultrasonic detectors connected over the return tubing to the patient.A minimum blood flow at 2-2.5L/min should be maintained to avoid thrombus formation.

  – **Pressure monitors-** undue negative or positive pressure can lead to hemolysis, damage the microfiber membrane and undue increase pressure may reflect block within the circuit or failing of oxygenator. For this purpose, three monitors are commonly used. First one in the venous line before the pump to determine inflow pressure and to avoid excessive negative pressure. Second monitor is after the pump and before the oxygenator where any obstruction in the oxygenator will cause rise in pressure. The third site is after the oxygenator to determine the pressure drop across membrane lung (by comparing with pre-oxygenator

pressure) and outflow pressure to the body.Increased drop in trans-membrane pressure is suggestive of thrombus in oxygenator.

- **Pre and post oxygenator O2 saturation measurements-** Venous oxyhemoglobin saturation helps to determine the O2 utilization of the patient while post oxygenator saturation determines the functioning of membrane lung. Post oxygenator oxyhemoglobin saturation should be 100% and any drop suggests membrane dysfunction.
- Bubble detectors on the blood return line and temperature monitors can be used if desired.

- **Monitoring The Patient**

  Monitoring the patient involves both the general condition- heart rate, O2 saturation, ECG, blood pressure, temperature, input-output balance, chest x-rays and the blood investigations. The general monitoring is same as non-ECMO patients.

  - **Plasma**- free hemoglobin measurement- to assess hemolysis
  - **Arterial blood gas monitoring**- it is needed periodically to ensure adequate CO2 removal and oxygenation

Anti-Coagulation and hematologic monitoring

The most difficult task after starting the circuit is to keep the patient in a very narrow range of equilibrium where anti-coagulation is just adequate to avoid thrombosis and not so much that it causes bleeding; while at the same time being on the lookout for hemolysis and thrombocytopenia. Anti-coagulation is needed to avoid thrombosis within the or in the patient's own circulation.

Thrombosis can lead to obstruction of the extra-corporeal circuit causing reduction in flow, impaired oxygenation and CO2 removal and even embolism into patient's circulation. Under extreme conditions with contraindication to anti-coagulation (eg. intracranial bleed) veno-venous circuits can be run for days without anti-coagulation using high flow rates (>2.5L/min). This is possible because the lungs act as a filter and may remove any small clots that may have formed. On the contrary, in veno-arterial circuits, any thrombus that forms will directly enter systemic circulation and may have drastic effects. Consequently, veno-arterial circuits should never be run without anti-coagulation.

Choice of anti-coagulant

Unfractionated heparin is the anti-coagulant of choice. This is due to its immediate onset of action, short half-life (30-90 min) and available antidote (protamine) in case of overdose. Low molecular weight heparin and fondparinux are less preferred because of long half-lives and their complete reversal is not possible. In case of any contra-indication to heparin or heparin induced thrombocytopenia, direct thrombin inhibitors with short half-lives, like argatroban and bivalirudin are preferred. Even for heparin, the established standards of dosing may have unpredictable response in a patient on ECMO and regular monitoring is needed.

Monitoring anti-coagulation

Multiple parameters are available to monitor the efficacy of anti-coagulation with their own pros and cons.

- **Activated coagulation time (ACT)**- it is a measure of heparin effect rather than heparin level. The test is simple, gives quick results and can be done at bedside. If needed it can be repeated hourly or even more. Target of anti-coagulation is to keep ACT at 1.5 times of normal for the ACT measuring system. The drawback is that are no set standards and the result must be validated initially with aPTT or anti- Xa levels to establish uniformity.[1, 2, 6]

- **Activated Prothrombin Time (aPTT)-** like ACT it also measures heparin effect, not heparin level. Ratio of patient's value of aPTT divided by the mean of normal aPTT range gives a ratio called activated prothrombin time ratio or APR and target APR is 1.5-2.5. The drawback of this test is that it does not measure heparin levels and needs to be correlated with anti-Xa levels.[1, 2, 6]

- **Anti- Xa levels-** It is considered as a gold standard test for measurement of heparin levels. The target level is between 0.3-0.5 IU/ml. The drawback is that factors other than heparin can also affect blood clotting and it cannot measure inhibition of other clotting factors. [1, 2, 6]

- **Thromboelastography-** The process uses a device to assess the entire clotting system and measure the clot forming ability of whole blood. The device measures the time to formation and density of clots and evaluates the function of platelets, clotting factors and fibrinolytic pathway together.

  Above discussed modalities should not be used alone as each gives information only about a specific parameter. A combination of methods assessing different pathways should be used and titration done accordingly.[2, 6]

Thrombocytopenia

Aapart from drug induced thrombocytopenia, ECMO patients can have unexplained thrombocytopenia without any other manifestations. Such patients who are not bleeding or undergoing intervention may need not to be treated if platelet count is above 20,000 but difference of opinion exists. Treatment in such cases is platelet transfusion as required.

Hemolysis

Variable amount of hemolysis occurs in all patients on ECMO. it may be due to shear stress by pump, oxygenator or immune mediated or thrombus related. Degree of hemolysis is measured by examining blood films, lactate dehydrogenase and plasma free hemoglobin. Management includes transfusion if hemoglobin level falls too low and avoiding excessive negative pressure, frequent transfusions, adequate anticoagulation and change of oxygenator if suspecting thrombotic occlusion. [1, 2]

Patient Management on ECMO

- **Cannulation**

  It is the first step of shifting the patient on extracorporeal support. The cannula can be placed by multiple methods viz. cut down, by Seldinger technique (used commonly for insertion of central venous lines), and cannulation of aorta or right atrium under direct vision after thoracotomy. The per-cutaneous insertion can be done at bedside in ICU itself, but ideally the process should be done in operating room under the guidance of vascular surgeon. Insertion of aortic cannula requires thoracotomy and is not possible outside the operating room. All cannulation should be preceded by systemic heparinization (50-100U/kg bolus).

- **Decannulation**

  The removal of cannula, just like placement is a complicated process and should ideally be done in OR. Prior to decannulation heparin should be discontinued for 30-60 mins. Percutaneous cannula can be removed directly followed by sustained local pressure, while surgically inserted lines should be removed in OR. Air embolism during the removal of venous cannula can be prevented by asking the conscious patient to perform Valsalva maneuver or by positive pressure ventilation if unconscious.

- **Ventilation on ECMO**

  The very purpose of ECMO is to allow for lung protective ventilation strategies and decreasing the damage from positive pressure ventilation. ECMOis initiated at maximal flow and ventilator setting changed to minimal pressure and volume that are maximally effective.In case of less than predicted response or excess CO2 washout, ECMO flow and configuration can be changed rather than tampering with the ventilator. Cooling the body, adding more drainage lines or second oxygenator may be helpful.

  If the patient is conscious and breathing spontaneously it is possible to stop ventilator support and continue only on ECMO. Such patient can be kept awake on ECMO with only oxygen support being needed. If restrictions are not there, patient can be allowed to move and resume some form of physical activity while connected to ECMO.[1]

- **Hemodynamics**

  Patients who need ECMO are usually critically ill and often have need for high doses of inotropes. This should not be seen as a need for Cardiac ECMO over Respiratory ECMO. After ruling out cardiac dysfunction, such patient can be started on veno-venous circuits and show rapid and sustained improvement in hemodynamic parameters with just adequate oxygenation. [1, 2]

- **Fluid Balance, Transfusion and Nutrition**

  The goal is to return extracellular volume and hematocrit to normal and fluid overload should definitely be avoided. Any volume overload worsens pulmonary edema and cardiac failure. Initial volume loading may be needed in first 24 hours due to machine related inflammation nut thereafter diuresis and fluid restriction is preferred. Hemodialysis or hemofiltration can be used if diuresis is not adequate.

  For transfusion strategy, there is no unified consensus with an ongoing argument for both restrictive and liberal transfusion strategies. Transfusion is justified to replenish the lost blood, increases the oxygen carrying capacity and to increase oncotic pressure. Higher oxygen carrying capacity translated to lower flow requirement and overall benefit goes in favor of high hemoglobin content rather than higher flow rates.

  There is no need for caloric restriction during ECMO and patient should be given his daily recommended intake. Enteral feeding is preferred as parenteral feeding is associated with unnecessary volume and components such as lipids in parenteral feeds may interfere with oxygenator.[1, 2]

- **Sedation, Position and Temperature**

  During the initiation and first 12-24 hours patient should be kept in sedation and anesthesia to avoid accidental decannulation or extubation and to help in deciding the optimum strategies. Thereafter the management I similar to a ventilator patient with intermittent drug holidays and if patient is found comfortable, complete tapering of sedation can be done.

  Temperature is maintained as close to normal as possible with little exceptions. Hypothermia (32- 34°)can be allowed where medically indicated (post- CPR,to avoid hypoxic brain injury)

  Patient should be kept mobile rather than a continuous fixed position. Frequent posture change and physiotherapy is advised. If the patient is conscious he can be allowed to move around in bed.[1, 2]

- **Management Of Heparin Induced Thrombocytopenia (Hit) And Abnormal Bleeding**

  – **Heparin induced thrombocytopenia or HIT** is characterized by consumptive thrombocytopenia with platelet count persistently below 10,000/μL and multiple arterial thrombi. Patient on extracorporeal support have thrombocytopenia due to various causes other than HIT and they should be ruled out. After establishing the diagnosis the patient can be treated by withholding heparin and using direct thrombin inhibitors.

    In cases of major internal bleeding with HIT or strong contra-indication to anti-coagulation heparin free veno-venous ECMO can be considered. In spite of best management the prognosis of patients who develop HIT on ECMO is usually poor. [1, 2]

  – **Bleeding complications-** Bleeding is the most common complication during ECMO due to anti-coagulation, thrombocytopenia and widespread inflammation. Even the simplest of procedures such as venous sampling, catheter insertion, suctioning of ET tube or finger pricks can cause profound bleeding and care should be taken during all such procedures. Some procedures like lumbar puncture, intramuscular injections are contraindicated.

    Minor bleeding such as from mucosal surfaces can be controlled with anti-fibrinolytics and local measures such as pressure and local packing where-ever possible.

Major bleeds such as gastrointestinal, pulmonary and intracranial hemorrhage are less common but have more serious consequences. Management of such patients involves local measures, such as endoscopy in GI bleed, neurosurgical intervention in intracranial bleed along with reduction of anti-coagulation and returning the coagulation status to normal by using fresh plasma, platelet transfusion and anti-fibrinolytics. In case everything else fails anti-coagulation should be stopped while EMCO is continued till coagulation returns to normal or ECMO should be stopped and patient shifted entirely on ventilator.[1, 2]

Weaning from ECMO[1, 2, 6]

Weaning a patient on extracorporeal support is easier in veno-venous ECMO compared to veno-arterial ECMO. This is because patients on veno-venous ECMO need only respiratory support and are self-sufficient in blood circulation, thus, only one system needs assessment. In veno-arterial ECMO both the pulmonary and cardiac functions need to be assessed repeatedly and both should be optimal before stopping support. This becomes even more difficult when peripheral arterial line is used and the ECMO circulates blood against the patient's native circulation and hampers the cardiac recovery.

- **Weaning from Veno-venous ECMO-** patients should be assessed daily for lung recovery and weaning with serial radiological assessment, lung compliance, gas exchange, and biochemical parameters. Lung function recovery can be simply assessed by switching off the sweep gas which shifts the entire gas exchange over to the lungs. Once this trial is satisfactory, the sweep gas flow is gradually decreased while maintaining target saturation 95%. If saturation is persistently over 95% and PaCO2 less than 50, sweep is discontinued and patient taken off ECMO. When in doubt about patient's condition, access cannula can be left in place for up to 24hrs in case there is a need to put back on support.

  In some cases oxygenation improves before CO2 clearance and patient is not able to clear CO2 adequately. Such patients can be shifted to selective CO2 clearance mode and may take weeks to recover fully.[1, 2]

- **Weaning from Veno-arterial ECMO-**[2, 4, 6] weaning from veno-arterial ECMO is difficult and no universal protocol exists for it. Patient's cardiac output and aortic pulsatility is monitored with echocardiography and inotropic support is gradually reduced. ECMO flow is gradually reduced to 25% of cardiac output and oxygen delivery and hemodynamic status monitored. If patient maintains adequate circulation, ECMO circuit is clamped for a trial period of 30min to 4 hours. If general

condition still stays good with adequate oxygenation and requirement of inotropes is less than maximum then decannulation can be planned. If patient cannot be weaned off, extracorporeal support can be continued as bridge to VAD or transplant if possible. [1, 4]

Future Course

Extracorporeal support is a budding branch in India. It is still not widely available, for both doctors and patients, and wherever it is available the costs of running are too high to be in everyone's reach or allow its frequent use. There is also a lack of clinical and patient data from India and studies comparing it to conventional management have been very few. As long as it is not made widely accessible and used frequently, a sense of skepticism and a shadow of doubt regarding ECMO will continue to linger and both the treating and the treated will keep preferring the time tested conventional methods over ECMO. To break this cycle we need to establish dedicated ECMO units and give a minimum basic training and hands-on in ECMO to all clinicians. ECMO has shown promising results all over the world but we won't know it unless we see the positive results firsthand. Studies have shown us the ability of ECMO to save lives; we only need to embrace it to realize its true potential.

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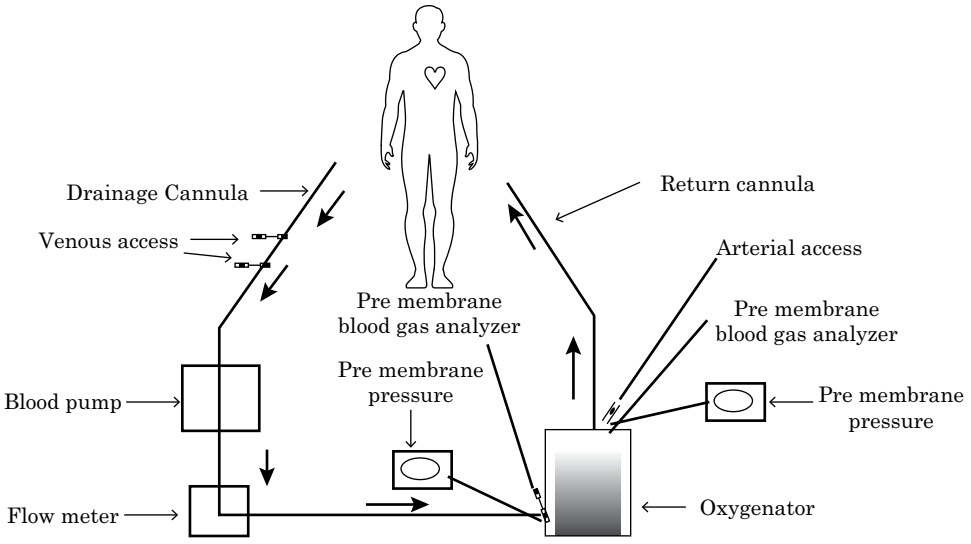

Figure 1 : ECMO circuit

ECMO circuit - diagram shows venous blood is removed from the patient through a drainage cannula & is pumped to the oxygenator, from there it goes back either to an artery (Veno-arterial ECMI) or a vein (veno-venous ECMO). There are access routes located along the extracorporeal membrane oxygenation circuit (venous &arterial access points) for infusion of medications and fluids and collection of laboratory tests, in addition topre-membrane& post-membrane pressure sensors & flow sensors.

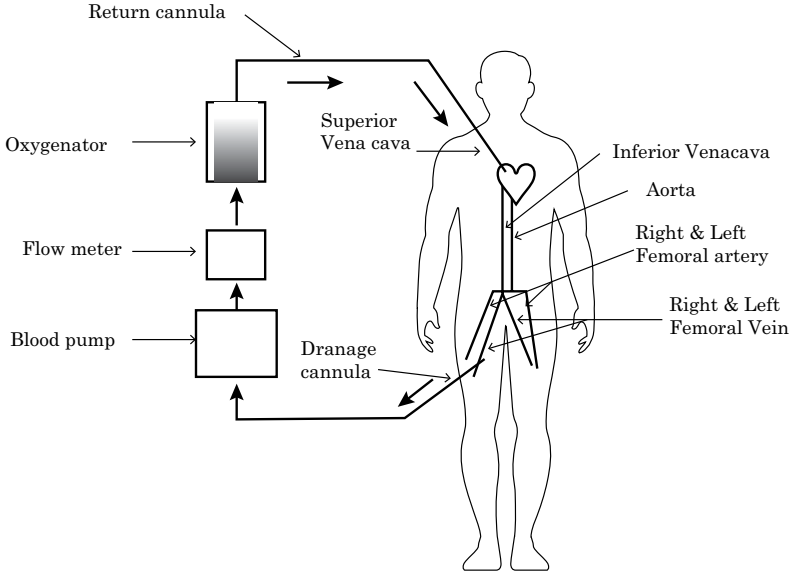

Figure 2 : Veno-venous ECMO

In veno-venous ECMO circuit blood from the inferior vena cava is drained through a cannula in the right femoral vein. Then, the blood passes through the propulsion pump and the oxygenation membrane, returning to the venous system of the patient through the right internal jugular vein.

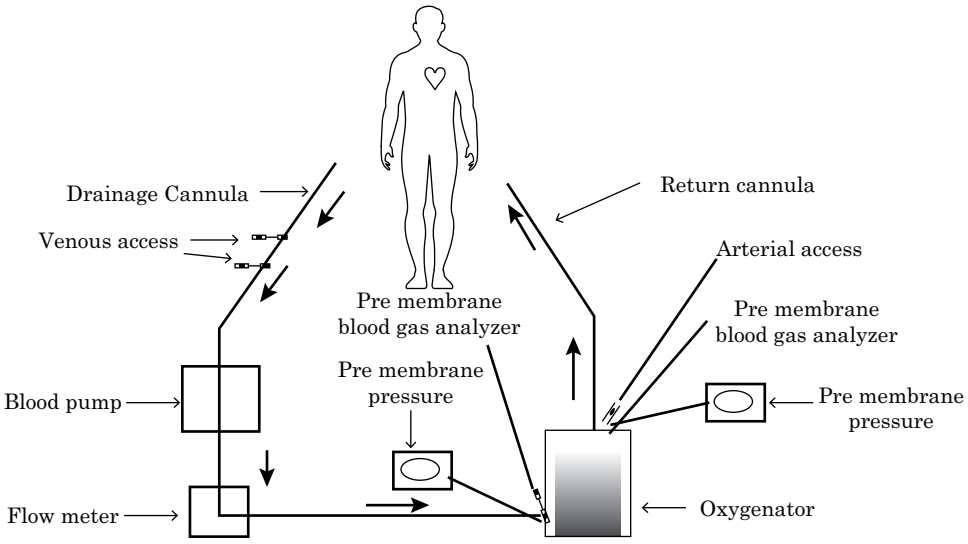

Figure 3 : Veno arterial ECMO

In veno- arterial ECMO circuit blood from the inferior vena cava is drained through a cannula in the right femoral vein. Then, the blood passes through the propulsion pump and the oxygenation membrane, returning to the arterial system of the patient through the left femoral artery.

Chest Tube Drainage

(INTERCOSTAL TUBE DRAINAGE)

Dr. V.K. Jain

Introduction

Chest tube drainage also known as Intercostal Tube Drainage (ICD) or Tube Thoracostomy is a important commonly used minor surgical procedure which can be used as emergency or elective in various clinical settings to remove fluid or air from the pleural space. Doctors of most specialties should be capable to put safe insertion and future management. In emergency ICD usually required for tension Pneumothorax and in trauma cases. Before insertion of a chest tube drain, all person should have been adequately trained. Technique and Management have been described in BTS guidelines[1] and otgers. [2-9]

Definition

Chest tube insertion is a commonly used therapeutic procedure to remove abnormal collection of air, fluid or both by insertion of intercostal tube in the pleural cavity & connected to the underwater seal bag/bottle.

Indications

- Pneumothorax
  - Tension Pneumothorax
  - Open pneumothorax (with BPF) usually persists or recurrent after initial relief
  - Closed Pneumothorax large or patient symptomatic
  - In Ventilated Patient
- Traumatic Haemo-pneumothorax
- Penetrating Chest Trauma
- Malignant Pleural Effusion
- Empyema
- Chylothorax

- Drainage of Pleural Effusion
- BPF with Pyo/Hydro/Pneumothotrax
- Preventive- Post Operative Cardiothoracic Surgery

Pre- ICD risk assessment

- Careful radiological assessment to rule out the bullous disease/pneumatocoele/large cyst vs pneumothorax, presence of collapse/unilateral white out vs effusion.
- Rule out the coagulopathy/platelet defect/risk of haemorrhage and to be corrected before ICD. Measurement of platelet count and prothrombin time are only recommended in patient with known risk factors.
- For elective chest drain insertion warfarin, should be stopped and time allowed to resolve of its effect.
- Drainage in case of Post-pneumonectomy space should be carried out by or after consultation with a Cardiothoracic surgeon.
- Lung densely adherent to chest wall throughout the hemithorax is an absolute contraindication to ICD.
- Verbal and Informed consent to be taken after explaining fully about the ICD procedure & risk associated to the patient & relatives.

Instrument/Equipments & Materials

All the following are required for ICD insertion and to be sterilized and follow antiseptic technique.

- Sterile Gloves/Gown/Drapes/Gauze/Swabs
- Antiseptic solutions- iodine/chlorhexidine in alcohol
- Sterile Tray to keep- Syringes/Needles/ Scalpel/Blades /Scissor/Curved Clamps & artery forceps etc.
- Suture
- Drugs- Lignocaine, epinephrine, fentanyl, midazolam, atropine
- Intercostal tubes(Different size) & connecting tube
- Underwater seal bag/bottle
- Guidewire with dilators
- Dressing material

Practical points to keep in mind managing the ICD

- Premedicate patient for pain control and anxiety and assess need for further medication during and after procedure.
- Monitor the Cardiovascular status and oxygen saturation before, during and after procedure
- Take care of Vaso-vagal attack during procedure.
- Prophylactic antibiotics should be given in trauma patients.
- Local infiltration of anesthetic solution & insertion of ICD tube to be put in the intercostals space away from the inferior border of the rib, to avoid the injury to intercostal vessels.
- Incision through the skin & subcutaneous tissue should be 2-3 cm transversely (not vertical).
- Before inserting the tube always check air or fluid through anesthetic needle & syring by aspiration from the pleural cavity. If not choose other site or use the Image guidence. Insertion of tube to be done gently without any substaintial force to avoid any injury.
- Patient with ICD tube should manage in ward by trained staff.
- Chest XRay should be available at the time of ICD insertion routinely except in tension pneumothorax & preferably after ICD insertion.
- Icd bag/bottle must be kept below the insertion site & also ensure the adequate water to cover the end of the tube to maintain the underwater seal.
- Daily assessment & record of functioning of the ICD tube to be done carefully & record amount of fluid, severity of bubbling of air (BPF) & column movement (Respiratory swings)
- Repeated chest XRay to be done for the assessment as required.
- Chest tube should not clamp if bubbling of air is present or in case of pneumothorax unless lung is expanded with no BPF or air leak. If chest tube is needed to clamped it should be closely monitor by pulmonary physician/surgeon to watch any breathlessness or developing subcutaneous emphysema, if show immediately unclamped the tube.
- In case of massive pleural effusion, draining should be done in controlled manner to prevent the complication of re-expansion pulmonary oedema.

Standard method for chest tube insertion

Patient's Position:- The preferred position for drain insertion is on the bed, slightly rotated, with the arm on the side of the lesion behind the patient's head to expose the axillary area.[9] An alternative is for the patient to sit upright leaning over an adjacent table with a pillow or in the lateral decubitus position.[10]

Insertion Site of tube drainage:- Most commonly use site of insertion of tube is mid axiallry line in "safe triangle" usually in 4th or 5th intercostals space. This is the triangle bordered by the anterior border of the latissimus dorsi, the lateral border of the pectoralis major muscle, a line superior to the horizontal level of the nipple, and an apex below the axilla (Figure 1).

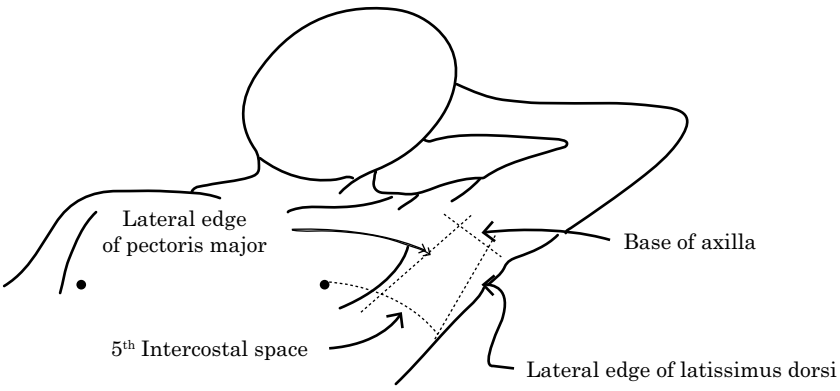

Figure 1

The tip of the tube should be as high and anteriorly for pneumothorax and if fluid of any type the tube usually inserted posteriorly and laterally.Do not direct the tube towards the mediastinum because of contralateral pneumothorax may occur. The diaphragm, liver or spleen can be lacerated if patient is not properly positioned or tube inserted too low. Sometimes mid clavicular line in 2nd intercosalspace required but not commonly used.[1,2]

Size of insertion tube:- Small bore tube(8-14F) are usually inserted with the help of image guidance with a guidewire and not required blunt dissection. Usually prefered in pneumothorax, effusion, loculated empyema.Medium bore tube ranging 16-24F can be inserted by help of guidewire or blunt dissection. Large bore tube of more than 24F is usually inserted after blunt dissection and in this incision should be similar as diameter of the tube.[1,11]

Complications

- Injury to lung, heart & great vessels
- Diaphragmatic perforation
- Sub-diaphragmatic placement of the tube
- Tension or open pneumothorax
- Subcutaneous emphysema
- Unexplained or persistent air leak
- Hemorrhage
- Recurrent pneumothorax
- Infection & empyema
- Cardiogenic or vasovagal shock
- Re-expansion pulmonary oedema

Conclusion

Intercostal tube drainage is a commonly required minor surgical elective/emergency procedure to remove the air and or fluid. The procedure should be always done by trained physician/surgon and managed by the trained staff in ward under supervision of experts.

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Bronchoscopy in Respiratory Emergencies

Valliappan Muthu, Ritesh Agarwal, Digambar Behera

Introduction

Respiratory diseases occupy a major burden in the emergency departments worldwide. Up to 50% or more of the emergency visits are for medical complaints including dyspnoea, chest pain, and hemoptysis.[1] Apart from the medical causes of respiratory symptoms; polytrauma patients also experience a wide range of pulmonary problems such as pneumothorax, hemothorax, lung contusion, tracheal rupture amongst several others. Of the emergency admissions (excluding injuries) to the hospitals in the United Kingdom, respiratory emergencies accounted for 13%.[2] The common respiratory emergencies are acute respiratory failure (due to pneumonia, chronic obstructive pulmonary disease, asthma, pulmonary embolism, massive pleural effusion, pneumothorax,or trauma), lung collapse (foreign body aspiration, lung cancer) and hemoptysis.

Chest radiograph and computed tomography (CT) of the thorax are the initial investigations in evaluating individuals with respiratory complaints. Though they provide a clue to the etiology and guide management in several instances, direct inspection of the airway becomes essential in some cases. Bronchoscopy involves the direct visualization of the tracheo bronchial tree using an instrument, generally introduced through the nose or mouth. Bronchoscopy can be performed for a variety of diagnostic or therapeutic indications.[3,4] In the current review, we describe the types of bronchoscopy, their indications, contraindications, procedure, and utility in respiratory emergencies.

Types of bronchoscopy

Bronchoscopy can be either flexible or rigid bronchoscopy. The choice of procedure depends on the patient's general condition, indication (diagnostic or therapeutic), availability and expertise (Table 1). A flexiblebronchoscope (FB) is a thin flexible instrument introduced through the nose or mouth of a subject who is generally awake or under conscious sedation. It is primarily employed for diagnostic purposes.[5] Where as, rigid bronchoscopy (Figures 1 and 2) is mostly reserved for therapeutic indications and is

usually performed in the operating room under general anesthesia. Rigid bronchoscope provides better control of airway and is the procedure of choice in unstable patients. Both flexible and rigid bronchoscopy are complementary to each other. In fact, both the bronchoscopies may be performed together in several subjects. Rigid bronchoscopy is often preceded byFB to plan the therapeutic strategy. Also, the distal airways can be accessed using a FB introduced through the lumen of the rigid bronchoscope.

Indications

Massive Hemoptysis

Massive hemoptysis has been variably defined as expectoration of 100 to 600 mL blood over a period of 24 hours or hemoptysis accompanied by hemodynamic instability/abnormality in gas exchange.[6] However, there is no consensus on the exact amount of bleeding to define massive hemoptysis.[7] Evaluation of hemoptysis is a major indication for bronchoscopy in both emergency and elective setting.[8,9] Nearly 11% of the bronchoscopy at our center are performed in subjects with hemoptysis.[9] A survey of chest physicians attending the respiratory emergency symposium showed that the majority (64%) favored an early bronchoscopy within 24h for the evaluation of massive hemoptysis.[10] Bronchiectasis, lung cancer, cavity, fungal ball, healed or active pulmonary tuberculosis are common reasons for massive hemoptysis, and the blood supply is usually from bronchial arteries. Generally, a multimodality approach for treatment is followed. Though surgery may be a definitive treatment in some cases, stabilizing the patient, securing the airway and avoiding flooding of the normal lung by blood are the most important aspects of management. Bronchoscopy aids in localizing the bleed, clearing the airway, and allows temporary measures to control bleed.

Diagnostic role

FB is highly useful in localizing the site of bleed (up to 93% cases), and the nature of lesion responsible for the massive bleed.[11, 12] Even in cases where exact localization is not possible, the side or the lobe from which the bleeding occurs can be identified. The culprit lesion, responsible for massive hemoptysis can be endobronchial infiltration (due to malignancy or infections), a cavity with or without aspergilloma, or telangiectasia. The information obtained from FB isessential in guiding further management, including bronchial artery embolization or surgery.[13] In a subset of patients with massive hemoptysis, the etiology or even localization of bleed may not be possible even after evaluation with imaging and bronchoscopy (Cryptogenic hemoptysis). Unusual causes such as Dieulafoy's disease of the bronchus may be identified subsequently in few of them.[14]

Therapeutic role

Hemoptysis often can be controlled with simple modalities such as wedging the bleeding segment with the bronchoscope, suctioning or topical medications. Further, rigid bronchoscopy enables suctioning with a larger suction catheter, and the tamponade effect provided by the rigid bronchoscope may itself help in controlling the bleed.

Topical agents

Bronchoscopic administration of ice-cold saline, vasoconstrictive or procoagulant agents have been used to achieve temporary hemostasis before more definitive measures can be performed. *Cold saline lavage* is believed to cause local vasoconstriction, reduce blood flow and achieve hemostasis.

Irrigation with 50 mL aliquots of ice-cold saline (4˚C) has been found to be useful, though no controlled trials are available.[15]

***Topical instillation of adrenaline (1:10000 or 1:20000 concentration) or vasopressin*is** another effective way to stop bleeding.(16) These may be tried as temporary measures to control bleed, especially after bronchoscopic procedures such as biopsy, brushing or bronchoalveolar lavage (BAL). Negligible but definite risk of systemic absorption of epinephrine exists and this can potentially precipitate a cardiac arrhythmia or hypertension.[17,18]

Small case series have demonstrated the utility of ***bronchoscopic instillation of gelatin-thrombin slurry, fibrinogen-thrombin combination in*** cases where topical adrenaline failed to control the bleed.[19-21]

Topical hemostatic therapy with oxidised regenerated cellulose (ORC) was shown to have a high success rate in controlling the bleed, when other techniques failed. The ORC is a knitted sterile fabric which absorbs the blood and becomes swollen, promoting clot formation. Valipour et al., used ORC mesh in patients with massive hemoptysis under rigid bronchoscopy; 98% success was achieved and there was no recurrence of hemoptysis till 48 h of therapy.[22]

Bronchial blockage

Once the site of bleeding is localizedandtopical agents could not control the bleed, occluding the bleeding bronchus with bronchial blockers, spigots, and balloon tamponade using the ***Fogarty arterial embolectomy*** balloon can be tried. The *Fogarty balloon* (Figure 3) comes in various sizes,and they may be chosen as per the size of the bronchus or the segment to be occluded (usually a 4F or 5F catheter is sufficient). The balloon may be deflated once the bleeding is controlled.

However, it is cumbersome to leave the Fogarty balloon in-situwhile removing the bronchoscope. In these situations, alternatives such as modified balloon tamponade and *spigots* have been tried.[23-25] A small case series demonstrated 78% success rate with silicon *spigots* (Figure 4). The spigots were removed bronchoscopically once definitive management such as surgery or bronchial artery embolization was performed.[26]

Bronchial blockers are used by anesthetists as an alternative to double lumen tubes for single lung ventilation. Several commercially available catheter-based bronchial blockers (Arndt blocker, Cohen blocker, EZ-blockers) used for this purpose can be introduced through endotracheal tube in the management of massive hemoptysis as well.[27]

Thermal ablation

Thermal ablative measures to control hemoptysis are useful when an endobronchial lesion such as a tumour or vascular malformation has been identified as the source of bleed.[11] Nd:YAG and Nd:YAP LASER can debulk airway tumors, as well as control bleeding. Electrocautery and Argon plasma coagulation (APC) are alternatives to laser therapy. APC is a non-contact thermal ablative method and is ideal for superficial lesions. APC can offer definitive management for vascular causes of bleeding such as endobronchial Dieulafoy's disease (Figure 5).

Central airway obstruction

Airway obstruction can be upper airway obstruction (from oral/nasal cavity till the glottis), central airway obstruction (trachea and the main bronchi) or lower airway obstruction (asthma, chronic obstructive pulmonary disease, bronchiectasis,etc.). A variety of causes are known to produce central airway obstruction which includesboth malignant and benign disorders. Primary lung cancers, other primary tumors of the airway (adenoid cystic carcinoma, carcinoids andmucoepidermoid carcinoma), and metastatic tumors to the airway are the major malignant causes of central airway obstruction. Extrinsic compression from malignant mediastinal masses may also present as central airway obstruction. Whereas, foreign body aspiration, tracheal stenosis (following intubation or tracheostomy), tracheomalacia are the most common non-malignant causes of central airway obstruction. In our country, it is not uncommon to find tracheal or bronchial stenosis as a sequela of healed endobronchial tuberculosis.[28]

The clinical features of central airway obstruction are non-specific dyspnoea with or without noisy breathing, and cough. It can be easily mistaken for more common airway diseases such as asthma and COPD. The duration of illness varies from weeks to months (sub-acute) or more acutely depending on the nature of etiology

and rapidity of progression. The modality of evaluation also depends on the patient's stability. History and physical examination are vital. Nevertheless, a definite diagnosis would require imaging such as computed tomography with or without three-dimensionalreconstructions (also known as "virtual bronchoscopy") and bronchoscopy. Though chest radiograph and flow-volume loops obtained from spirometry can provide some clues to the existence of central airway obstruction, they are insufficient and lack sensitivity to guide further management.[29,30] Imaging of the airways and direct inspection of airway using a bronchoscope are the most important modalities of evaluation in suspected central airway obstruction. The diagnosis and management depend on the criticality of the subjects. If the airway obstruction is critical and life-threatening; the focus is on establishing a patent airway,andbronchoscopic procedures are the management of choice. On the other hand, in a stable patient, confirming a diagnosis and therapy directed against the basic disease are the management goals.

Diagnostic role

Direct visualization of the airway using bronchoscopy answers several important questions such as: (a) level of obstruction and the length of the narrowed segment, (b) nature of obstruction (infiltration, extrinsic compression by a mass, scarring/stenosis), (c) diagnostic samples (endobronchial biopsy, bronchoalveolar lavage) can be obtained in stable subjects. Further, bronchoscopy enables clearing of secretions beyond the obstruction, thereby improving gas exchange and providing time for definitive management.

Therapeutic role of bronchoscopy

- In patients who are unstable and an airway cannot be secured by conventional means, ***flexible bronchoscopy-guided intubation*** may be performed.[28]
- ***Rigid bronchoscopy*** is the procedure of choice in subjects with unstable airway due to central airway obstruction.[31] The choice of further intervention depends on whether the obstruction is extra luminal (mass compressing the trachea) or intraluminal (endobronchial tumors with infiltration). Though some subjects may have both intraluminal and extraluminal components, therapy is chiefly guided by the predominant pathology.
- ***Malignant central airway obstruction***: If the disease is extraluminal, dilatation with rigid bronchoscopy and deploying stents would be the treatment option (Figure 6).[32] When the intraluminal component is significant, coring the tumor with the rigid bronchoscope ensures a patent airway.

Often, coring is followed by debulking of cancerby one of the following methods;

- *Heat therapy* (Laser, electrocautery or APC),
- *Cold therapy* (cryotherapy) or
- *Mechanical debulking* (using forceps or micro-debrider).[31]
- *Brachytherapy and photodynamic therapy*. If the patient is not critically-ill, treatments which have a delayed effect can also be used. In photodynamic therapy, photosensitizing agents (such as dihematoporphyrinether) which localize to the tumorsare used.[32,33] These agents when exposed to the light of particular wavelength promote cell death. *Brachytherapy* involves placement of encapsulated radioactive sources into or in the vicinity of the tumor, usually under rigid bronchoscopy guidance.

d. *Non-malignant central airway obstruction*: Post-intubation or post-tracheostomy tracheal stenosis are the primary non-malignant etiologies of central airway obstruction. The life expectancy of malignant central airway obstruction is generally short, owing to the advanced nature of the underlying malignancy. Hence restoring the airway patency by rigid bronchoscopy and maintaining the patency by insertion of metallic stents (usually nitinol stents covered with silicon sheath) are the best palliative options.[33] Whereas post-intubation tracheal stenosis has a better long-term prognosis and more definitive options such as surgery are to be offered.[34]

The primary role of bronchoscopy is to diagnose tracheal stenosis, assess its severity and extent, plan definitive procedures. However, many subjects with post-intubation tracheal stenosis (PITS) are picked up late in the course of illness and may present with respiratory failure. In such cases, therapeutic bronchoscopy can help to establish an airway and to stabilise the patient.[35,36] Rigid bronchoscopy is the procedure of choice, and serial dilatation with a rigid bronchoscope or balloon dilatation can be performed. If the stenosis is operable and facilities for the same are available, surgery offers a cure. In a retrospective study of 42 patients with post-intubation stenosis, bronchoscopic therapies alone offered a 43% cure rate whereas surgery/multimodality therapy offered a 95% cure rate.[37] When PITS is inoperable, dilatation using rigid bronchoscopy, ballooning and silicone stent deployment can be tried.[38, 39] The success rate is variable, with some series reporting successful stent removal in 40% of subjects after 12 months.(40)Hence, whenever possible surgical resection of the stenotic segment (3-4 cm of the trachea can be easily resected, by mobilizing the trachea in the mediastinum) and end to end anastomosis should be offered. The role of bronchoscopy is thus vital to diagnose, assess the extent of stenosis, and in stabilizing the subject with PITS.

Apart from PITS which may develop after weeks or months after extubation, another entity known as obstructive fibrinous tracheal pseudomembrane (OFTP) may present in the immediate post-extubation with stridor.[41,42] A high index of suspicion is required to suspect this uncommon condition, which usually develops after a median time of 36 hours following extubation.[41] Flexible bronchoscopy can diagnose this condition; while therapeutic removal of the pseudomembrane can be done with rigid or flexible bronchoscopy depending on the patient's stability.

Lung Collapse or Atelectasis

Endobronchial obstruction of any etiologyincluding malignancy, foreign body, mucous plug or clot can lead to the complete collapse of a lung or a lobe of the lung.[43] The presentation varies widely, and some of these entities can have an acute presentation. The management of lung collapse due to malignancies is similar to that described in the previous section on malignant central airway obstruction. Rigid bronchoscopy and coring can help in establishing patency of the main bronchus.

Mucous plugs and blood clots can be removed either in flexible bronchoscopy or rigid bronchoscopy.[43] Dislodgement of clotcould result in massive bleeding if the underlying source of bleed was controlled by the former. Therefore, performing the procedure under rigid bronchoscopy is preferred. The clot or mucous plug can be removed by bronchoscopic suction or by the use of cryoprobe. Cryoprobes can be introduced through the flexible or rigid bronchoscope, and the clot/mucous plug/foreign body can be removed en-masse after freezing it (by using a coolant gas -usually liquid nitrogen).[44]

Retained secretions are an important reason for impaired gas exchange and difficulty weaning in intensive care units (ICU). In a study from Germany, nearly 88% of the emergency bronchoscopic procedures were performed in ICU; the major indications being retained secretions and bronchopulmonary bleeding.(8) Muscle weakness, immobilization, weak cough contributes to the development of atelectasis in ICU. Flexible bronchoscopy is indicated for tracheal toileting to remove retained secretions, especially when there is difficulty in the clearing, or if the secretions are very thick (as in asthmatics, or COPD patients).

Foreign body aspiration

Foreign body aspiration is one of the most common respiratory emergencies in children. However it is less common in adults.[45] History of foreign body aspiration followed by choking and cough with or without breathlessness are the classical symptoms. Though

chest radiograph may provide clues, it is not sufficient to rule out, especially if the foreign body is not radiopaque. Metallic, followed by organic foreignbodies are the most common in adults (Figure 7). We can retrieve foreign bodies either under rigid or flexible bronchoscopy. Rigid bronchoscopy is regarded as the gold standard for retrieval of foreign bodies, owing to the wide working channel and better aurwaycintrol. However, in a stable patient who can tolerate the procedure under intravenous sedation, foreign body retrieval may be attempted using flexible bronchoscope (introduced through the mouth). In fact, a success rate of 89.6% was seen in the systematic review of published literature describing foreign body retrieval in adults.[45] While removing sharp objects one must excise utmost care, lest injury to the tracheobronchial tree or vocal cord may occur during attempted removal.Various instruments, such as basket, shark-tooth, alligator and magnetic forceps are available for foreign body retrieval (Figure 8). The instrument used for retrieval depends on the nature and shape of the foreign body. Depending on the duration for which the foreign body is present within the bronchus, it may present as non-resolving pneumonia or recurrent infections leading on to destruction/bronchiectasis of the lung distal to the obstruction.

Difficult airway and intubation

A difficult airway is one that requires multiple attempts or more than one operator/ device tovisualize the glottis properly during intubation. Approximately 3% of the emergency intubations are difficult,and the proportion varies on several factors such as the expertise available, patient factors as well as the criteria used to define difficult intubation.[46, 47]

When intubation with standard methods fail, the endotracheal tube may be loaded over the bronchoscope,and then the bronchoscope is introduced through the nose/mouth. Once the vocal cord is crossed and the flexible bronchoscope reaches the carina, the endotracheal tube is advanced over the bronchoscope. Bronchoscopic intubation is particularly useful when there is limited mouth opening, distorted anatomy due to trauma/disease, immobilization of the spine is required (as in cervical spine injury) when direct laryngoscopy is not possible or difficult.

Placement of a double-lumen endotracheal tube (DLT) is routinely performed using a flexible bronchoscope. DLT is commonly employed during surgeries when single lung ventilation is required. It may also be used to prevent bleeding or secretions from flooding the contralateral lung, as in the case of massive hemoptysis

Bronchoscopy in trauma patients

Trauma to the chest can be blunt or penetrating, and both of these can be associated with a variety of pulmonary problems. Physical examination and chest radiograph can reveal several findings including, pneumomediastinum, pneumothoraces, rib fracture, subcutaneous emphysema and flail chest.[48] Urgent flexible bronchoscopy might be required; (a) to rule out a *tracheobronchial tree injury/rent* or laceration, (b) to evaluate *acute lung collapse*, which could be due to blood clot occluding the trachea or bronchus. Though CT can provide information regarding the presence of tracheobronchial tear or rupture, a bronchoscopic examination is mandatory to gauge the extent and plan further treatment. Trauma patients may also develop a *bronchopleural fistula* (BPF). Bronchoscopy is useful in the diagnosis of BPF and several options for bronchoscopic management are available.[49] The latter includes stents, coils, amplatzer devices, occlusive devices (such as spigots and endobronchial valves).[50,51] Bronchoscopic management is typically used in individuals who are not candidates for surgery or the site of the leak is unhealthy or to stabilize the patients until surgery/definitive management. A detailed description of diagnosis and management of BPF is beyond the scope of this chapter.

Miscellaneous Indications

In general, diagnostic procedures are performed in an elective setting, howevera specific group of individuals may present acutely. As an instance, bronchoscopy is highly useful in obtaining samples such as BAL in *immunocompromised individuals with pneumonia* and *post-transplant patients.* Though surgical lung biopsy is preferred in unstable patients for evaluating diffuse parenchymal diseases, our center has previously described the usefulness of bronchoscopic lung biopsy using non-invasive ventilator support.[52] The risk-benefit ratio needs to be considered before undertaking bronchoscopy for diagnostic lung biopsies.Occasionally other diagnostic bronchoscopic procedures such as endosonography-guided transbronchial needle aspiration may be performed in critically-ill subjects. The latter may be particularly useful when a malignant mediastinal mass is suspected to be the reason for respiratory failure and therapy directed towards it may enable weaning of the patient.[53]

With increasing number of lung transplantations being performed in India, the complications following transplantation may present as acute emergencies,and a physician needs to be aware of them.[54] In post-lung transplant recipients, emergency

bronchoscopy would be required to evaluate for anastomotic site dehiscence, development of stricture at the anastomotic site, and in the evaluation of undiagnosed pulmonary infiltrates.[55-57]

Contraindications of Bronchoscopy

The lack of expertise, adequate facilities and informed consent are the absolute contraindications for bronchoscopic procedures. When patients are at high risk of complications either from the bronchoscopic procedure or the sedation used during the procedure, this may be a relative contraindication. However, if the bronchoscopy procedure is considered life-saving, the risk-benefit ratio needs to considered on a case to case basis. The following are the relative contraindications:

1) *High risk for cardiac or pulmonary complications*: recent myocardial infarction (less than four weeks), poorly controlled heart disease, acute exacerbation or poorly controlled COPD, cardiac arrhythmias. As previously mentioned, these contraindications are relative, and bronchoscopy has been performed safely in subjects with recent acute myocardial infarction.[58]

2) *High risk of bleeding*: Patients on warfarin, other anticoagulants, antiplatelet drugs or have a bleeding diathesis, chronic kidney disease. Several other factors are to be considered in such patients; the indication for the procedure, functional reserve to tolerate hypoxemia or a bleed, alternate modalities to establish a diagnosis. After taking into account all the factors if the procedure is deemed essential, it should be done under close observation. Transbronchial lung biopsy has a higher risk of bleed and is poorly amenable to measures that can control bleed. Presence of pulmonary hypertension or superior vena cava syndrome are in particular associated,with a higher chance of bleed and complications. Bronchoscopy for airway inspection or bronchoalveolar lavage can be performed safely above a platelet count of 30,000 per/microL. Several other factors including the expertise available, facilities to handle complications must also be taken into account while doing bronchoscopic procedures under high-risk. Management of antiplatelets and anticoagulants before bronchoscopy are described in the British Thoracic Society guidelines on bronchoscopy.[3]

Complications of Bronchoscopy

Bronchoscopy is generally a safe procedure,and severe complications are rare. Mortality following diagnostic bronchoscopy is uncommon.[59] However, a variety of minor complications are well-known. In a systematic review of published literature, minimal

bleeding (defined as less than five mL) was encountered in nearly 90% of the subjects undergoing diagnostic bronchoscopy; whereas moderate bleeding (20-100 mL) was seen in 2.1% subjects only.[60] Pneumothorax following transbronchial lung biopsies is seen in approximately 1-3% subjects.[59] Bronchospasm could be troublesome in individuals who have underlying asthma or COPD,and British Thoracic Society guidelines recommend nebulization with bronchodilators in these subjects before bronchoscopy.[3] Hypoxemia, hemodynamic instability, fever,and cough are few other complications which occur following bronchoscopy.[60] The complications are likely to be more in the emergency setting rather than during electively performed procedures. Optimising the patient's general condition before undertaking bronchoscopic procedures canminimize the rate of complications.

Conclusion

Bronchoscopy is an indispensable tool in the evaluation and management of major respiratory emergencies such as massive hemoptysis, central airway obstruction,and foreign body aspiration. Flexible bronchoscopy is primarily for diagnosis, whereas rigid bronchoscopy is for therapeutic indications. In unstable patients' rigid bronchoscopy is the procedure of choice. It can be life-saving and may act as a bridge in patients awaiting more definitive treatment such as surgery. In expert hands and with adequate precautions, bronchoscopy is a relatively safe procedure.

Table 1: Comparison of flexible and rigid bronchoscopy

	Flexible bronchoscopy	**Rigid bronchoscopy**
Instrument & procedure	A thin tube (generally up to 6 mm diameter) containing optical fibres or camera, light source and working channel. The instrument is flexible and can be passed through the nose. The distal end of the flexible scope can be angulated forwards and backwards	A rigid straight hollow metal tube available in various diameters is introducedinto the trachea through the mouth. The external diameter of the tube can be up to14 mm A rigid telescope which transmits light from the light source is introducedinto the rigid barrel. The processed images can be viewed directly or displayed on a monitor (Figure 1)
Site	Can be performed in the bronchoscopy suite, emergency room or the ICU	Performed in the operating room
Anaesthesia	Local anaesthesia using lignocaine spray, nebulization with or without conscious sedation using intravenous agents	General anaesthesia
Expertise & availability	Commonly available and easier to perform	Requires expertise

	Flexible bronchoscopy	Rigid bronchoscopy
Advantages	• Preparing the patient and performing the procedure is simple • Widely available • Can be performed in awake subjects • The flexible instrument can reach third order or distal bronchial tree beyond carina and main bronchi • Transportation is simple and can be performed bedside in critically-ill subjects in the ICU	• Larger lumen allows introduction of several instruments for various diagnostic/ therapeutic procedures (figure 2) • Suctioning can be performed more effectively • Therapeuticprocedures such as coring of tumours, control of bleeding by tamponade effect of the rigid barrel, deployment of stents and dilatation of the tracheal stenosis • Allows for better control of the airway. • Larger forceps can be introduced through the rigid barrel for foreign body removal
Disadvant-ages	• FB is not suited in subjects with unstable airway and massive hemoptysis (which may obscure the bronchoscopic vision) • Critical central airway obstruction cannot be managed with FB and airway stenting	• Requires general anaesthesia • May not be readily available • Predominantlysuited for visualising and undertaking procedures in the larger central airways (however, a flexible bronchoscope can be passed through the barrel of the rigid bronchoscope and procedures of the distal bronchial tree may be performed)

FB - flexible bronchoscopy; ICU – intensive care unit

Figures with legends

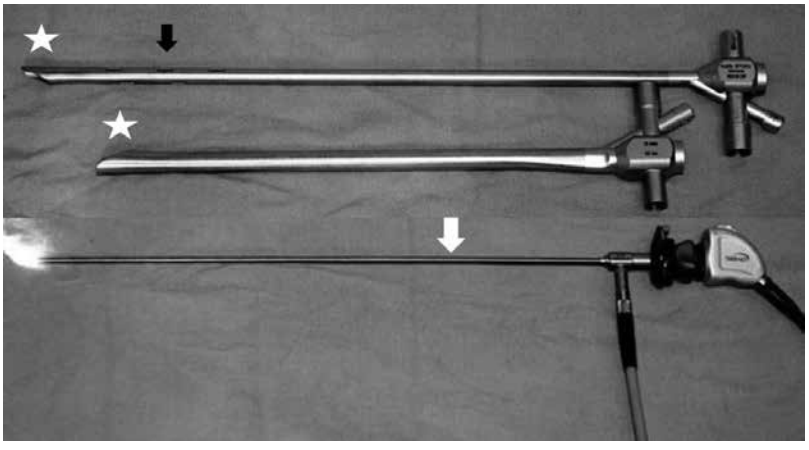

Figure 1: Rigid bronchoscopes of different sizes (marked by asterisk) with a bevel tip that can be used for coring tumours. The black arrow indicates the ports available for ventilating the patient during the procedure. The white arrow denotes the telescope and the light source attached to it.

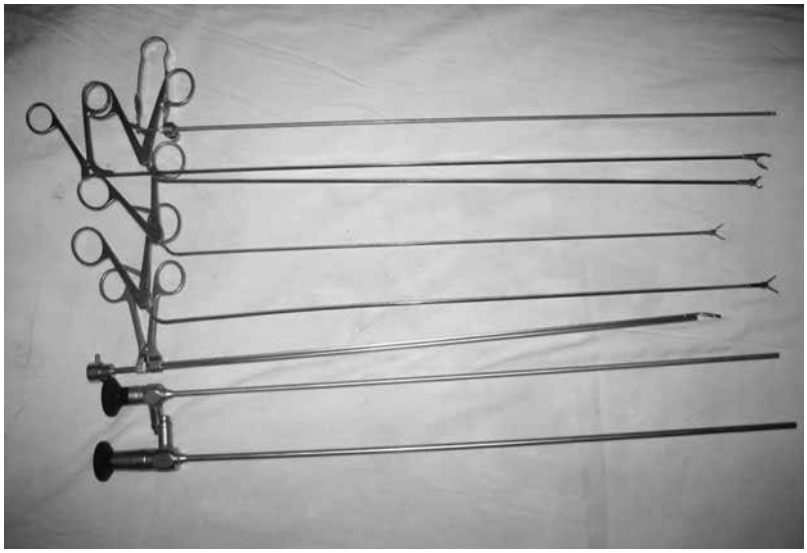

Figure 2: Various forceps and instruments available for use during rigid bronchoscopy. These instruments can be introduced through the working channel of the rigid bronchoscopy barrel.

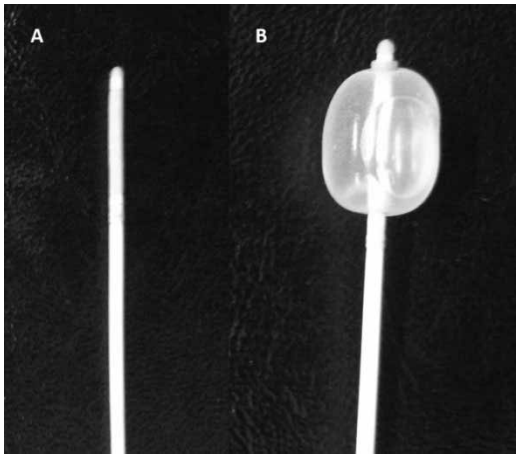

Figure 3: Fogarty balloon (6F) depicted here before (A) and after (B) inflating with saline.

Figure 4: Silicone spigot with studs over its surface. Spigots can be used for bronchial blockage in the management of hemoptysis and bronchopleural fistula.

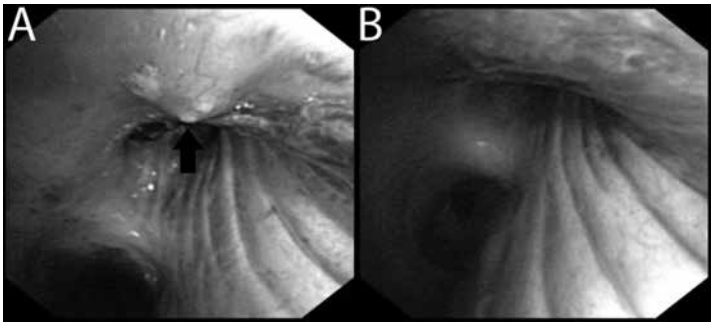

Figure 5: In a patient presenting to us with massive hemoptysis, flexible bronchoscopy showed endobronchialDieulafoy's lesion (black arrow) adjacent to the opening of the right upper lobe bronchus (A). Bronchoscopy performed three months after Argon-plasma coagulation (APC) of the Dieulafoy's lesion showed complete resolution (B).

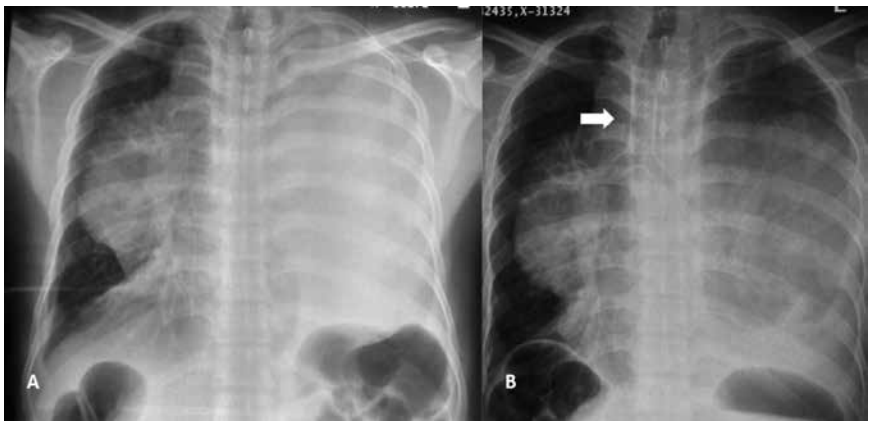

Figure 6: Chest radiograph of a 34-year old male with stridor due to extrinsic compression by bulky mediastinal and lung masses (A). The patient underwent emergency rigid bronchoscopy and palliative stenting (covered metallic Y stent denoted by arrow) (B). Biopsy of the bulky tumour revealed poorly differentiated sarcoma.

Figure 7: Various foreign bodies retrieved from adult patients (from our archives): (A) light emitting diode (LED) bulb. (B) A small metallic instrument used in dental procedure. (C) *Litchi* **seed. (D) whistle (toy)**

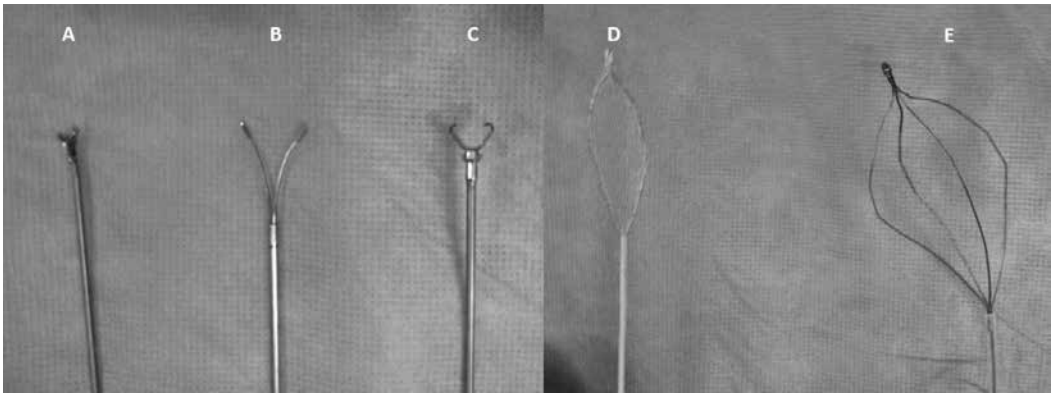

Figure 8: Some of the instruments and forceps available for retrieving foreign bodies: (A-C) Rat tooth forceps of different sizes, (D) Roth net, (E) foreign body retrieval basket.

Acknowledgement: We thank the technical staff of our bronchoscopy suite for their inputs in preparing the figures.

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Respiratory Emergencies in Pregnancy

Dr. M.Sabir

Pregnancy marks a major physiological shift in the life of a woman. Significant anatomical and physiological adaptations related to respiratory and cardiovascular systems occur during pregnancy. These changes are necessary to meet increased metabolic demands of mother and fetus. Various respiratory diseases may encounter during pregnancy affecting mother & fetus and may have impact on pregnancy outcome. It is important to understand how pregnancy will be affected by the disease and also how the presentation, diagnosis, treatment & prognosis of the disease itself will be altered during pregnancy.

During normal pregnancy, act of respiration including pulmonary functions, and gas exchange are affected through both biochemical and mechanical pathways.

Biochemical changes affecting respiratory function in pregnancy

Progesterone is the major hormone affecting respiratory physiology. During the course of pregnancy it gradually increases and acts as trigger to primary respiratory centre by increasing the sensitivity of the respiratory centre to carbon dioxide, as indicated by the steeper slope of the ventilation curve in response to alveolar carbon dioxide changes. Progesterone also alters the tone of smooth muscles of the airways resulting bronchodilation. Both these impact leads to increase in oxygen consumption& increase tidal volume leading to increase minute ventilation, causing increased arterial PO2, and decrease PCO2.Progesterone also mediates hyperemia and edema of mucosal surfaces, causing nasal congestion.[1]

Increased **oestrogen** levels during pregnancy parallel the progesterone levels and it increases the number and the sensitivity of progesterone receptors in the hypothalamus and medulla, the areas near by the central neuronal respiratory control is located.[1]

Prostaglandins F2α causes smooth muscle contraction leading to increase airway resistance, whereas bronchodilator effect can be caused by prostaglandins E1 and E2.[1]

Mechanical effects of pregnancy

Increasing abdominal distension caused by progressive uterine distension is responsible for changes in lungvolume and chest wall during pregnancy. These changes comprise

of elevation of the diaphragm and altered thoracic configuration. The enlarging uterus causes increases in intra-abdominal pressure, displacing the diaphragm upwards, which causes:

- The changes in chest wall and diaphragm to accommodate the enlarging uterus, causes increase in negative pleural pressure, leading to an earlier closure of the small airways with consequent reduction in Functional reserve capacity (FRC) and its componants eg Expiratory reserve volume (ERV) and Residual Volume (RV) with little or no change in Total Lung Capacity (TLC) but increase in minute ventilation leading to decrease in PaCO2 causing respiratory alkalosis.
- Shortening of the chest height, and increase in the other thoracic dimensions in order to maintain constant total lung capacity resulting in reduced PaCO2 and chronic respiratory alkalosis. There is no significant change in spirometry, DLCO, or oxygenation.[2]
- Increased plasma volume, leading to increased cardiac output, and reduction in vascular resistance are the major cardiovascular changes.
- Because of these cardiovascular & respiratory changes in pregnancy, physiological dyspnea occurs in many pregnant women, which has to be differentiated from breathlessness caused by coexisting diseases with pregnancy.[1, 2, 3]

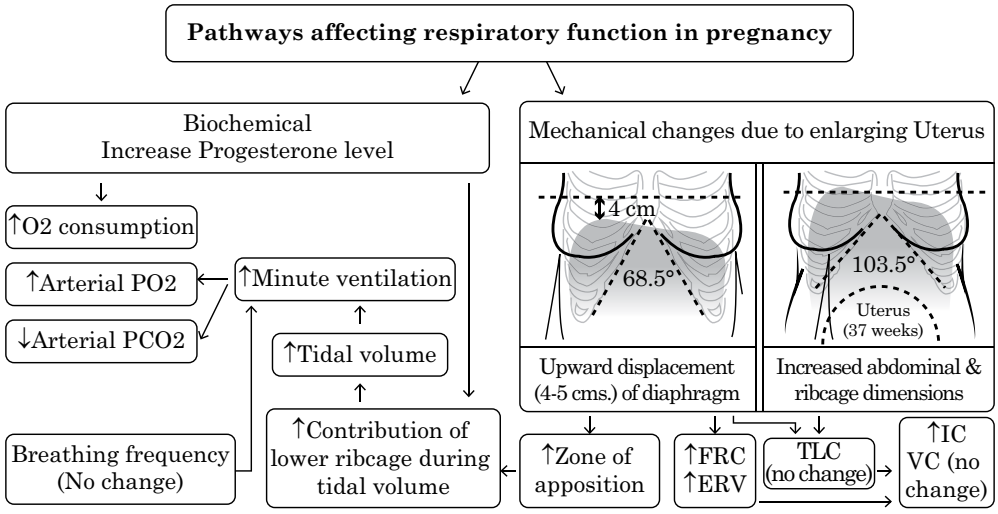

Figure-1: Changes affecting respiratory function in pregnancy[2]

Abbreviations: PO2-oxygen tension; PCO2- carbon dioxide tension; FRC- fractional residual capacity; ERV- expiratory reserve volume; TLC-total lung capacity; IC - inspiratory capacity; VC - vital capacity.

Clinical situations creating respiratory emergencies during pregnancy

Clinical situation creating respiratory emergencies during pregnancy are either acute exacerbation of already present diseases in a pregnant woman or are comorbidities of pregnancy:

- Breathlessness
- Pulmonary Thromboembolic Disease
- Amniotic Fluid Embolism
- Pneumothorax
- Severe Pneumonia
- Bronchial Asthma
- Covid-19 And Pregnancy
- Pulmonary Edema
- ARDS And Acute Respiratory Failure

Breathlessness

Breathlessness is a frequent complaint in the first trimester. It is due increased awareness of hyperventilation, caused by an increased ventilatory drive due to the increased concentration of progesterone. A degree of hyperventilation persists throughout pregnancy so that $PaCO_2$ is low and the pH may be towards little on the alkaline side. The PaO_2 is normal or may show a small rise.

Though the PaO_2 as mentioned above is generally normal or, slightly raised, at full term, particularly when the uterus is very large, there could be mild hypoxia with an increased alveolar-arterial O_2 gradient. When the patient is supine, this is related to premature closure of the small airways causing reduced functional reserve capacity (FRC). Oxygen consumption is increased during pregnancy, may be 25-30% above the normal at full term. The combination of increased oxygen consumption and reduced FRC diminishes oxygen reserve so that any emergency or catastrophe that causes apnea or alveolar hypoventilation can render both the mother and fetus dangerously hypoxic.

Due to various physiological changes as described above and the stress of pregnancy, some amount of dyspnea is expected and should be explained to the patient as occurring due to normal physiological changes.

Such breathlessness should be differentiated from pathological dyspnea occurring due to multiple possible disease entities may be associated with the pregnancy labor or postpartum period. Any dyspnea that is sudden in onset, rapidly progressive, associated with marked limitation of activity or incapacitation with or with ought other respiratory manifestations, should be thoroughly investigated and treated. Under such conditions,

any delay in diagnosis of such respiratory emergencies may result in adverse maternal and fetal outcome. A brief review of these emergencies along with specific treatment changes with respect to pregnancy are discussed below.

Pulmonary thromboembolic disease

Pregnancy is a hyper-coagulable state and associated compression of inferior vena cava by the uterus and hormone related venous stasis in lower limbs predispose to venous thromboembolism (VTE). VTE is considered as one of the most common respiratory emergency in the pregnancy and has been found to be more common in post-partum period.[4]

The clinical features and presentation of both deep venous thrombosis (DVT) and pulmonary embolism (PE) are same as in non-pregnant women but they may be missed due to confounding by pregnancy related pedal edema and breathlessness. Thus, at even the slightest suspicion the condition should be evaluated properly.

A Doppler ultrasound of lower limbs along with D-dimer test is useful, as negative tests points against possibility of DVT.[5] If pulmonary embolism is suspected with no immediate life threatening emergency and if facilities are available, a lung perfusion scan with less than 50 m rad exposure to the fetus is preferred modality.[4, 5] In an emergency and for definite evidence, a CT pulmonary angiography should be done while keeping fetal exposure as less as possible. Although there is danger of teratogenicity to the fetus and increased incidence of childhood leukemia has been reported with as low a radiation exposure as 2-5 rad, a definite diagnosis of pulmonary embolism is a must because of the hazard for the mother's life. [4]

If the condition occurs early in pregnancy, warfarin should be avoided and low molecular weight heparin is the treatment of choice. The use of novel oral anticoagulants in pregnancy is still under study and not recommended. IVC filters can be used if indicated but their placement is difficult due to venous dilation and increased blood flow. In post-partum period, warfarin can be used safely with less risk to infant. In case of life threatening pulmonary embolism, thrombolytic therapy should be used without hesitation but only after conforming the diagnosis and risk to mother's life. Pregnancy related VTE is considered as a provoked VTE and lifelong therapy is not needed if any associated diseases such as thrombophilia or lupus anti-coagulant are not found. [4]

Amniotic fluid emoblism

Amniotic fluid embolism is a rare disastrous obstetric emergency which is very often fatal with mortality rates reaching up-to 80% according to old estimates. The newer studies show that it may be lesser (13-26%), but still unacceptably high. [6]

Amniotic fluid embolism occurs classically during labor and delivery. Rarely, it occurs in the 2nd and 3rd trimester. Amniotic fluid contains cell debris, cells and humoral

factors. The cellular debris together with the amniotic fluid and its contents result in two major disturbances. The first is obstruction together with severe vasoconstriction of the pulmonary vasculature leading to sudden severe pulmonary hypertension. The other is an anaphylactic reaction caused by sensitivity to the amniotic fluid debris and to the humoral factors within the fluid.

This leads to hypotension (most common presenting sign) rapid desaturation, delirium, pulmonary hypertension and coagulopathy. Investigations necessary are complete blood count, coagulation profile, arterial blood gas (ABG), ECG, C3 and C4 levels (decreased), and where possible trans-esophageal echo and invasive hemodynamic monitoring. [6, 7]

Diagnosis is suggested based on clinical presentation and exclusion of other causes. Four criteria must be present to make the diagnosis of AFE:

- Acute hypotension or cardiac arrest.
- Acute hypoxia.
- Coagulopathy or severe hemorrhage in the absence of other explanations.
- All of these occurring during labor, cesarean delivery, dilation and evacuation, or within 30 min postpartum with no other explanation of findings.

Other tests that are useful include detection of serum sialylTn (STN) a fetal antigen, in mother; detection of fetal squamous cells in maternal pulmonary circulation. [6]

The treatment is difficult with poor outcome for mother. No definite therapy is present and only supportive care can be given to the patient. The management includes rapid correction of maternal hemodynamics, supplemental oxygen and ventilatory support, correction of coagulopathy with FFP transfusion and platelet transfusion as indicated. Drug therapy includes inotropic support, steroids, digoxin for severe heart failure. Other therapies which have shown successful results include sildenafil, inhaled and intravenous prostacyclin to reduce right heart afterload; oxytocin to manage associated uterine atony (if present). [6, 7, 8]

Pneumothorax

Pneumothorax occurring during pregnancy is a rare entity and its exact incidence is not known. But what complicates it, is the fact that there is 30-40% chance of recurrence and it frequently occurs during the labor putting both maternal and fetal life at risk. The presentation is similar to pneumothorax in general population but what makes it an emergency is the fact that pregnancy is a state of compromised functioning for mother and even a small insult can lead to decompensation. The management of pneumothorax in pregnant women is same as that in non-pregnant women. Care should be taken to avoid fetal exposure to X-rays and proper shielding should be done. Up to 75% of patients are treated with chest tube drainage as a first line of treatment. Small pneumothorax can be treated conservatively or aspirated. Patients who develop pneumothorax early in pregnancy must be advised to be watchful of the symptoms

occurring later in pregnancy and care should be taken during labor.[9, 10]

For patients who develop recurrent pneumothorax despite adequate treatment, surgery is a viable option. Surgery could be either via thoracotomy or VATS, which is commonly done through pleurectomy or mechanical scrubbing of the pleural surface. VATS is preferred over the more conventional approach (thoracotomy) whenever available. The optimal time for the surgical intervention is during the second trimester or after delivery.[9, 10]

Severe pneumonia

Pneumonia in pregnancy is a common occurrence with incidence no different than in non-pregnant women. Though it is not usually an emergency but delay associated with its diagnosis and restricted use of radiographs often means the disease gets complicated. The risks and outcome of pneumonia changes with advancing maternal age, multiple gestations, maternal smoking and use of illicitdrugs, advanced gestation, preeclampsia, pre-existing lung diseases like anemia, asthma, HIV infection; and pregnancy related immunological changes.[11] Patients receiving tocolytics and betamethasone (for fetal lung maturity) are found at increased risk.[12]

Though most cases of pneumonia are mild with no residual effects on mother and child, but severe pneumonia is the most common fatal non-obstetric infection in pregnant women. Additional challenges posed are restriction on drug use and safety during pregnancy, need for repeated radiographs, need for hospitalization and undue stress.

Microorganisms observed to be responsible for causing pneumonia in pregnancy may be (in order of decreasing frequency); streptococcus pneumoniae, H. Influenzae, leginella, mycoplasma pnemonae, clamydophila pnemonae, viral pneumonias caused by influenza A & varicella, staphylococcous aureus, psedomonas and fungus like coccidiodomycosis.

Since pneumonia presents with less dramatic symptoms compared to pneumothorax or pulmonary embolism and physicians often try to avoid radiographs during pregnancy, there are more chances of delayed diagnosis with advanced or complicated disease and mistreatment. This does not mean that radiography should be actively sought in pregnancy, a focused physical examination and history can be equally helpful.

The management of pneumonia in pregnancy is same but the threshold for admission should be kept low in such cases. Viral pneumonia is also very common in pregnancy and it should be included as a possibility while making differentials. Antibiotic choices should be made carefully and avoid drugs with potential fetal toxicities.[12]

Bronchial asthma

Asthma in pregnancy presents clinical challenge in fact that the disease itself is complicated by pregnancy and in turn it change pregnancy outcomes significantly.

Previously asthmatic females have a higher chance of asthma exacerbation during pregnancy and non-asthmatics are at risk of developing new onset asthma. Even without exacerbations asthma significantly affects outcome in pregnancy as has been verified in multiple longitudinal studies over the years. Pregnant females with asthma are more likely to have ante-partum and post-partum hemorrhage, placenta previa, placental abruption, gestational diabetes mellitus, premature rupture of membranes, cesarean delivery, low birth weight, gestational hypertension and preeclampsia and these risks only increase with poor disease control. [13]

Adequate control of asthma is important to avoid adverse pregnancy out comes. In life threatening situations; drugs such as high doses of parental corticosteroid, leucotriens & theophylins which are otherwise considered relatively unsafe in pregnancy; can be used with cautions.

The safest treatment strategy for asthma in pregnancy is inhaled steroids with long acting bronchodialators and short acting beta agonists on an as need basis. Additional drugs labeled safe in pregnancy includes leukotriene receptor antagonist montelukast and zafirlukast. Theophylline is considered safe but due to narrow therapeutic range and need to regularly monitor drug levels the use is not recommended unless absolutely necessary. The other drugs such as monoclonal antibodies should not be used in pregnancy. Any exacerbations should be managed as per regular protocol and early use of steroids is recommended. [13, 14]

Covid-19 and pregnancy

After its first identification in December 2019, Corona Virus disease 2019 has become pandemic and is responsible for large number of infected individuals, morbidity and deaths. Limited data are available about impact and course of corona virus disease 2019 during pregnancy; however, past experiences associated with other highly pathogenic corona viruses i.e. severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) might provide some insight into its impact on pregnancy. One can learn from the experience of H1N1 influenza virus (2009) and Zika virus infection that infections have been shown to have an impact on pregnant women and their fetuses with the increased risk of complications.

The study of data so far available has shown definite increase of risk of complication and death in pregnant women with Covid-19. Though it is not yet clear if the disease passes from mother to fetus via placenta, cases of infection occurring soon after birth have been documented. Despite of all possible precautions, newborn is at an increased risk of acquiring infection. Till the vaccine or treatment becomes available, our only precaution is appropriate strategies at infection prevention.

Covid-19 can lead to acute respiratory distress syndrome, disseminated intravascular coagulopathy, renal failure, secondary bacterial pneumonia and sepsis. Mechanical ventilation was three times more likely among pregnant compared with non-pregnant

women. There have also been reports of pre-term labor and spontaneous abortion associated with it.[15, 16]

In view of the rapidly spreading infection unique need of care of pregnant women should be considered:

- It is important that pregnant women should not be denied lifesaving interventions unless there is a compelling reason to exclude. Such interventions should be judiciously considered in light of benefit and potential threat to life of mother & fetus.
- Unnecessary hospital visits should be avoided but at the same time patients having Covid-19 should be admitted with a lower threshold compared to general population.
- Appropriate care should be taken during labor and delivery to avoid mother to child transmission.
- Drugs under trial which have not been tested for pregnancy safety and any other experimental treatment should be avoided.

Pulmonary edema

Pulmonary edema, though not an etiological entity, encompasses broad range of conditions during the pregnancy that also put an undue strain on the heart. The predominant cause is either a diseased heart which is unable to cope up with the increased demands of pregnancy (as in patients with valvular heart disease or cardiomyopathies) or excessive demand and stress related to pregnanacy (as in pre-eclampsia).[17] In both cases the final outcome and management is more or less the same, sudden onset of severe breathlessness, tachypnea, orthopnea, desaturation and air hunger. Pulmonary edema is more likely to develop immediately after delivery than before owing to massive volume shifts.

Rarely, a normal heart may decompensate suddenly due to iatrogenic causes with resulting pulmonary edema. Such reasons include overzealous blood transfusion or aggressive fluid resuscitation, use of tocolytics causing pulmonary edema, [18] or ovarian hyperstimulation syndrome.[19]Immediately after pregnancy, peripartum cardiomyopathy is an important cause for pulmonary edema. [20]

Treatment of all such cases is uniform and includes discontinuing offending agent (eg. tocolytics, intravenous fluids), diuretics, fluid restriction and oxygen supplementation when hypoxic. More serious cases with significant cardiac dysfunction may need inotropic support and mechanical ventilation. If all other measures fail and the patient fails to improve, urgent delivery of the fetus provides the best chances of survival to the mother. [21]

Ards and acute respiratory failure in pregnancy

All the respiratory emergencies discussed above usually present with acute respiratory failure and have potential to worsen into ARDS with fatal consequences. Associated changes such as including the increased circulating blood volume, reduced serum albumin level, a possible up- regulation of components of the acute inflammatory response and increased capillary leak may predispose to development of ARDS. [22] Apart from diseases discussed above, other possible causes of ARDS include aspiration of gastric contents with pH 2.5 or lower causing chemical pneumonitis with permeability edema and transfusion related acute lung injury.[22]

Respiratory failure in pregnancy poses several unique challenges. The reduced FRC and increased oxygen consumption in pregnancy means that patient has rapid oxygen desaturation during apnea or hypoventilation. Endotracheal intubation in the pregnant patient carries considerable risk. Failed intubation is 8 times more common in the obstetric population and the risk of aspiration is very high owing to gravid uterus. Over-enthusiastic ventilation may lead to respiratory alkalosis and consequential uterine vasoconstriction.[21, 22]

All pregnant patients with acute respiratory failure must be pre-assessed regarding need for potential intubation and anesthetists skilled in dealing with pregnant patients should be available. Patients with need for ventilation support who have potential for rapid reversal of underlying condition, good sensorium and hemodynamic stability should be assessed for fitness for non-invasive ventilation and a trial should be given if the patient qualifies. [22]

Though information available on invasive ventilation is limited, a few things are clear to us. Chest wall compliance is reduced by the enlarging uterus, and the usual pressure limits (e.g. plateau pressure of 35 cmH2O) may not be appropriate. Slightly higher airway pressures (without increased trans-pulmonary pressure) may be needed to achieve appropriate tidal volumes in pregnant women near term.

Hypoxia should be avoided at all costs as it can adversely affect fetus and maternal PaO2 target of >70mm Hg is suggested. Hypocapnia should be avoided as it can cause fetal harm by reducing placental flow but the effects of hypercapnia on fetus are not clear. Lung protective ventilation and permissive hypercapnia, has not been assessed in pregnancy on a large scale but few small studies comparing permissive hypercapnia to hypocapnia have shown that fetuses whose mother had hypercapnia had a statistically significantly higher Apgar score at delivery. Thus, if necessary, mild hypercapnia with PaCO2 maintainedat less than 60 mmHg, has been recommended for pregnancy. [21, 22]

Though it has been suggested that delivery of a pregnant patient with respiratory failure should improve her condition, a consistent evidence of the same is lacking. Term pregnancy with viable fetus and significant maternal hypoxia should be delivered as it reduces the risk to the fetus. The decision regarding delivery in mid-gestation is less straightforward and depends on fetal viability and proposed maternal risk.[22]

Conclusion

To manage & prevent respiratory emergencies during pregnancy, following tips may be helpful:

- Breathlessness in the absence of an underlying pathology is common in pregnancy especially during second & third trimester because of physiological adaptation, but such breathlessness should be differentiated from pathological dyspnea occurring due to multiple possible disease entities may be associated with the pregnancy labor or postpartum period.
- Radiological investigations e.g. X-ray chest etc, in routine should be avoided, but when underlying disease is suspected it should be done with due precautions after evaluating benefits over risk incurred.
- Most drugs can be used safely in pregnancy except few. It is important that pregnant women with chronic cardio respiratory diseases and other risk factors to develop respiratory emergencies, should receive multi-disciplinary consultations, pregnancy counseling and education regarding the risk of pregnancy and the importance of continuing therapy with specific precautions.
- Respiratory diseases complicated with comorbidities like pulmonary hypertension and corepulmonale have a poor prognosis in pregnancy.
- It should be kept in mind that inadequately managed respiratory emergencies can induce life threatening hypoxia to mother & fetus leading to adverse pregnancy outcome.

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Printed at .....

With the help of unconditional academic grant from M/S Cipla Ltd.