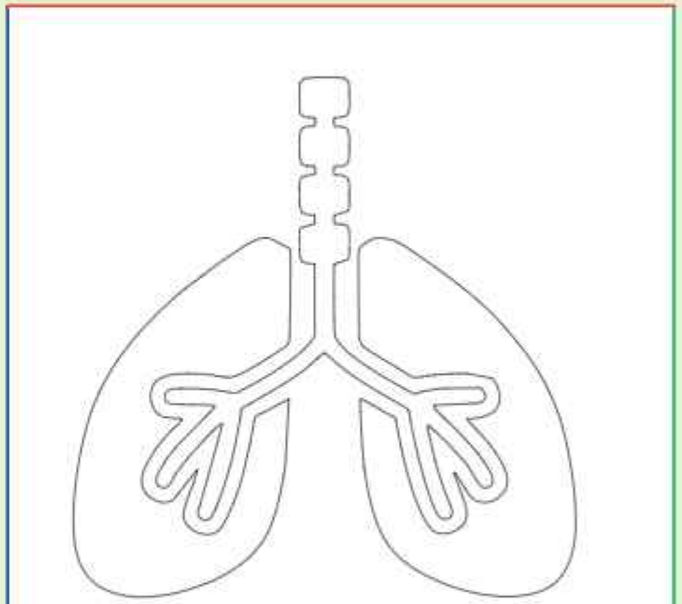
STANDARD TREATMENT GUIDELINES

RESPIRATORY MEDICINE



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GOVERNMENT OF KERALA

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for
RESPIRATORY MEDICINE

Foreword

At the outset, I appreciate the work done by the respective thematic teams and coordination done by the DME. The Standard Treatment Guidelines (STG) were prepared and published in 2021 in the thick of the Covid pandemic. On the last page of these volumes the road map was mentioned. The few points are mentioned here for the recall.

"The Department of Health has been taking a systematic approach of creating and enabling multiple initiatives with a focus on prevention along with improving health care services. Health care service delivery is one of the most important services and is always seen as a barometer to assess the Governance. While it is important to develop infrastructure, an essential prerequisite is to develop systems and processes to bring in standardization in management of patient care. .....The foundation is laid and we take up the challenge to work on the unfinished agenda."

It was mentioned in the road map to have institutional mechanism to ensure updation of Standard Treatment Guidelines. The next step that was suggested was to do analysis of Karunya Arogya Suraksha Padhati (KASP) and standard treatment guidelines to work on developing a Balance Score Card to give information regarding compliance from the Hospitals and to build a "feedback loop" to improve. These initiatives remained at concept level on the last page! But following detailed discussions with Dr Vishwanathan, Director Medical Education, some of the foundational things were prioritized and given an impetus to take it to finality. In this journey, many committed doctors from various Medical Colleges of respective specialties participated. The previous coordination team members and experts were also consulted and they also participated in discussions and these Standard Treatment Guidelines are prepared.

The standard treatment guidelines will be made available in the Kerala Health portal (health.kerala.gov.in). This will enable the resource book availability not only to people within the state but to all in the country and outside our borders as well. I am confident that it will be used by students and practicing doctors. We request inputs based on the research from the Specialists and Experts. The teams shall continue to update and make any required changes in the STG by doing periodic updates.

The most important thing we all need to internalize is to have a shared vision and

work as a team to reach to a state of 'excellence'. If we take a look at the preparation of the Directorate Medical Education Management Information System, documents of each Medical Colleges, it provides information regarding 'what we are, what we do and what we aspire to do', pandemic preparedness, AMR accreditation and many more such initiatives taken on scale, which are all outcomes of collective TEAM work. This has laid a foundation for involving all the stakeholders including undergraduate and postgraduate students. This should encourage the teams in Medical Colleges to believe in themselves and build future initiatives on such a sound platform.

I express my sincere thanks to Dr Vishwanathan for his patience and bearing with relentless follow ups! I also take this opportunity to thank each and every team and their members and everyone from Directorate Medical Education and Medical Colleges who supported these initiatives.

I would like to express my sincere gratitude to all those who have contributed to publish these Standard Treatment Guidelines.

I wish all the success to DME team to make Kerala MCH as a premier knowledge hub in Medical Science.

Dr Rajan Khobragade IAS

Additional Chief Secretary
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Message

Patient care today demands evidence-based, standardized, and contextually relevant clinical practice. In this regard, the publication of the **Second Edition of the Standard Treatment Guidelines** marks an important step forward in strengthening the quality, consistency, and accountability of healthcare delivery in Kerala.

The first edition laid a strong foundation for uniform clinical practice across specialties and super specialties. Since then, advances in medical knowledge, evolving treatment modalities, and the growing need for periodic updating have made it essential to revisit and refine these guidelines. The present edition reflects this commitment to continuous improvement and clinical excellence.

I am pleased to note that subject experts from various disciplines of Government Medical Colleges, private institutions and professional bodies have contributed as resource persons in the preparation of these guidelines. Their academic expertise, practical insight, and dedicated involvement have greatly enriched this edition. I deeply appreciate the sincere efforts of all the conveners, contributors, and coordinators whose collective commitment and teamwork made this publication possible.

These guidelines will serve as a valuable reference for clinicians, teachers, trainees, and healthcare institutions, helping to promote evidence-based decision-making and improve patient outcomes. I am confident that this edition will further support standardization of care and contribute to the advancement of medical education and clinical practice in the State.

I congratulate everyone involved in this commendable effort and commend this publication to all healthcare professionals.

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Contents

COMMUNITY ACQUIRED PNEUMONIA

1.Introduction

These guidelines refer to the management of adults with pneumonia in Indian settings.

There is a need for a guideline in Indian setting because our social and economic factors are different from western setting, population affected by pneumonia is different, microbial pathogens differ and resistance pattern of organisms to drugs vary considerably.

Definition

Pneumonia is defined as inflammation of lung parenchyma due to an infectious agent. It is broadly classified as.

1) Community acquired (CAP).
2) Hospital acquired pneumonia (HAP).
3) Pneumonia in immune-compromised Host
4) Aspiration pneumonia

Community acquired pneumonia is the pneumonia that develops in a community setting or is diagnosed within 48 h of admission to a hospital. Hospital acquired pneumonia is defined as pneumonia that occurs 48 hours or more after hospital admission, provided that the patient was not incubating the infection at the time of admission. Pneumonia in immune-compromised hosts is considered separately as these hosts are infected with rarer and unusual organisms apart from infection with common organisms. Aspiration pneumonia is the pneumonia that develop after a definite aspiration.

2. Diagnosis of pneumonia

Patients with pneumonia usually presents with fever, rigor and chills, cough, sputum production, pleuritic chest pain and dyspnoea. Extra pulmonary symptoms include headache, diarrhoea, myalgia, arthralgia and other gastro intestinal symptoms. On examination tachypnoea, findings of consolidation, crackles, pleural friction rub may be observed. Chest radiographic patterns are nonspecific but a lobar consolidation is usually associated with acute bacterial pneumonia. The presence of radiological infiltrate in a patient presenting with typical clinical features is diagnostic of pneumonia.

Table 1.1: Common pathogens causing pneumonia and their clinical and epidemiological features are summarized below.

Pathogen	Clinical features of pneumonia	Epidemiological features
Streptococcus pneumonia	Rigors, toxaemia, pleuritic chest pain, lobar pneumonia with air-bronchogram	Most common cause, more common in older patients and with co-morbidity
Mycoplasma pneumonia	Insidious onset, multi lobar, headache, malaise, myalgia, pharyngitis, otalgia, peri-bronchitis	More common in younger age group
Legionella sp.	Gradual onset, constitutional symptoms, dry cough, diarrhoea, neurological symptoms, multi-system involvement	Exposure to aerosols such as those from hot water systems and cooling systems, more common in younger patients
Staphylococcus aureus	Aggressive and cavitating multi lobar pneumonia with pleural complications, Pneumatoceles in radiograph	Intravenous drug abuse, recent influenza
Gram-negative organisms such as Klebsiella pneumoniae	Aggressive pneumonia, bulging fissure on chest radiograph	Alcoholics, elderly and chronically ill
Haemophilus influenzae	Symptoms preceded by coryza with sudden onset of pleuritic chest pain	Children and the elderly, COPD, especially in nursing homes
Chlamydia psittaci	Predominant headache and pleuritic pain, dry cough	Contact with infected birds and other animals
Anaerobes	History of vomiting and impaired consciousness, foul smelling sputum	Aspiration, Alcoholics, Poor oral hygiene
Respiratory viruses	Wide variety of symptoms	Often seasonal

3. Investigations

- Routine Chest X-ray and microbiological investigations are not required for Out Patients. But may be required if they fail to respond to therapy.
- All hospitalized patients should have a chest X-ray taken, since a diagnosis of pneumonia cannot be reliably established in the absence of infiltrates.
- Laboratory tests like complete blood count including ESR, Blood urea Nitrogen, creatinine, Blood glucose, Serum electrolytes, Liver Function Tests, O2 Saturation and ABG are also done depending on the condition of the patient.
- For patients with mild CAP being treated as OP, microbiologic testing is not needed. Testing for SARS CoV2, influenza, adeno virus, RSV and mycoplasma pneumonia can be considered when community incidence is high
- For patients with moderate CAP admitted to the ward, blood culture, sputum gram stain and culture, urinary antigen testing for streptococcus pneumoniae, PCR or urinary antigen testing for legionella are done. Testing for respiratory viruses are done when community incidence is high. Rapid nasal PCR or culture for MRSA is done in suspected cases.
- For patients with severe CAP including those admitted to ICU and those who fail to respond to initial antibiotic therapy, a bronchoscopic specimens for microbiologic testing can be obtained
- For patients with cavitatory pneumonia testing for tuberculosis, fungal, meloidosis, actinomycosis, nocardia etc may be done
- Other tests like pleural fluid gram stain, CBNAAT, routine, mycobacterial and fungal culture may be done in indicated cases
- Endotracheal aspirate culture may be done in intubated patients
- Multiplex molecular assays- By this method multiple etiological agents can be detected from a single specimen. Can be used in severe pneumonia and in cases of poor treatment response.
- If patients are unable to bring adequate sputum then induction of sputum should be done with hypertonic saline.
- CT thorax may be done to exclude other conditions and to reach a diagnosis if clinical suspicion is high and chest x ray is not suggestive of pneumonia

Risk Stratification

- Patients with CAP should be risk stratified.
- Initial assessment should be done with CRB-65.
- Accordingly, patients can be managed as either out-patient or in-patient (ward or ICU).

Table 1.2: CRB 65 Scoring system for risk stratification of pneumonia

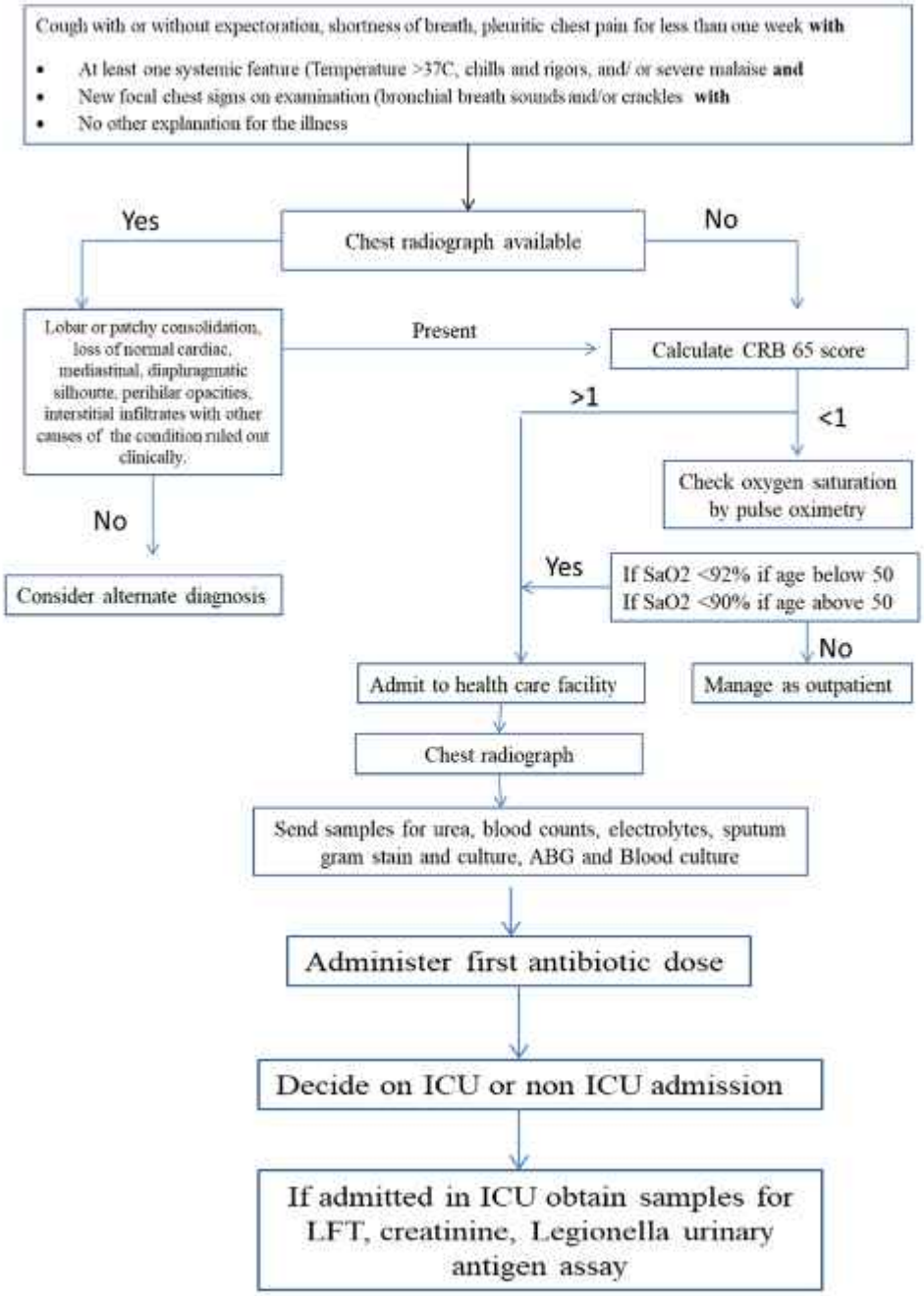
CRB-65	
Criteria	Score*
Confusion	1
Respiratory rate ≥30/min	1
Low blood pressure(Diastolic blood pressure ≤60 mmHg or Systolic blood pressure ≤90 mmHg)	1
Age ≥65 years	1

*If the score is >1, patients should be considered for admission.

- Clinical judgement should be applied as a decision modifier in all cases. The following features may indicate severity necessitating hospitalization.
- Leukopenia (WBC count<4000 cells/mm3)
- Thrombocytopenia (platelet count<100,000 cells/mm3)
- Hypothermia (core temperature< 36ºC)
- Hypoxemia (SaO2 < 90% and PaO2 < 60 mm Hg)
- Presence of multilobar infiltrates.
- Presence of shock or confusion

Other scoring systems like pneumonia severity index and CURB 65 can also be used

Figure 1.1: Algorithmic approach for the diagnosis and management of CAP.



Criteria for admission to ICU

- Patients selected for admission can be triaged to the ward (non-ICU / ICU) based upon the major / minor criteria. (IDSA ATS severity criteria)
- If any major criterion or ≥3 minor criteria are fulfilled, patients should generally be admitted to the ICU.

Table 1.3. Criteria for admission

Major criteria
Invasive mechanical ventilation
Septic shock with the need for vasopressors
Minor criteria
Respiratory rate > or = 30 breaths/min
PaO2/FiO2 ratio < or = 250
Multi-lobar infiltrates
Confusion/disorientation
Uremia (BUN level > or = 20 mg/dL)
Leukopenia (WBC count < 4000 cells/mm 3)
Thrombocytopenia (platelet count <100,000 cells/mm3
Hypothermia (core temperature <36 0 C)
Hypotension requiring aggressive fluid resuscitation

Antibiotics

- Antibiotics should be administered as early as possible; Delay in administration of antibiotics will lead to increased mortality and morbidity
- Timing is more important in severe CAP.
- For those patients referred to hospital with suspected CAP and where the illness is considered to be life threatening, general practitioners should administer antibiotics in the community.

- Choice of antibiotic depends on severity of illness and other factors like usage of antibiotics within last 3 months, immunosuppression etc

Antibiotic Therapy in the Out-patient Setting

- Therapy should be targeted towards coverage of the most common organisms, namely *Streptococcus pneumoniae*
- Out-patients should be stratified as those with or without comorbidities.

Recommended antibiotics

A) for out-patients without comorbidities

- oral β-lactams e.g. Amoxicillin 500-1000 mg thrice daily or
- oral macrolides (preferably Azithromycin) or
- oral doxycycline

for 5 days

B) For out-patients with comorbidities

- Oral combination therapy is recommended:- β-lactams and β-lactamase Inhibitors, third generation cephalosporin plus macrolides or doxycycline
- Duration of antibiotic treatment in out-patients is for five days.
- Respiratory Fluoroquinolones should be kept as reserve drug and not be used for empirical treatment in view of the high prevalence of tuberculosis in this country.

Antibiotic in the Hospitalised non-ICU Setting

- The recommended regimen is combination of a β-lactam and β-lactamase inhibitor, third generation cephalosporin plus a macrolide or doxycycline
- treatment duration for in-patients is for five to seven days
- In case of hypersensitivity to β-lactams, respiratory fluoroquinolones (e.g. Levofloxacin 750mg daily) may be used if tuberculosis (TB) is not a diagnostic consideration.
- Generally we favour administration of IV antibiotics for patients hospitalized for CAP. upon clinical improvement IV antibiotics can be switched to oral therapy.

Antibiotic Therapy in ICU Setting

1. For patients without risk factors for *Pseudomonas aeruginosa*,

   The recommended regimen is β-lactam and β-lactamase inhibitor, third generation cephalosporin plus a macrolide or doxycycline.

If *P. aeruginosa* is an aetiological consideration.

- an anti-pneumococcal / anti pseudomonal antibiotic should be given

  (e.g. cefepime, ceftazidime, piperacillin - tazobactam, Cefoperazone - sulbactam, imipenem or meropenem).

- Combination therapy may be considered with the addition of aminoglycosides / antipseudomonal fluoroquinolones (e.g. ciprofloxacin).

2. For community-acquired methicillin-resistant *Staphylococcus aureus* infection add vancomycin or linezolid.

   - The use of linezolid in India should be reserved because of its potential use in extensively drug-resistant TB.

3. For suspected influenza

   - Early treatment (within 48 h of the onset of symptoms) with oseltamivir or zanamivir is recommended.
   - Antimicrobial therapy should be changed according to specific pathogen isolated.
   - Timing of antibiotics – antibiotics should be started within four hours of presentation for patients being admitted to general ward. In patients with septic shock, antibiotics should be started within one hour.
   - For those with high severity microbiologically-undefined pneumonia, 7–10 days treatment is proposed.
   - This may need to be extended according to clinical judgement and development of complications.
   - Diagnostic/therapeutic interventions should be done for complications, e.g. thoracentesis, chest tube drainage, etc., as and when required

Switch from intravenous to oral therapy (De-escalation)

- Patients should be switched from intravenous to oral therapy when they are hemodynamically stable and improving clinically, are able to ingest medications, and have a normally functioning gastrointestinal tract.
- Patients should be discharged as soon as they are clinically stable.

Table 1.4. Dosages of antibiotics

Amoxicillin 0.5-1 g thrice daily (PO or IV)
Co-amoxiclav 625 mg thrice a day to 1 g twice daily (PO) / 1.2 g thrice daily (IV)
Azithromycin 500 mg daily (PO or IV)
Ceftriaxone 1-2 g Once Daily (IV)
Cefotaxime 1 g thrice daily (IV)
Cefepime 1-2 g two to three times a day (IV)
Ceftazidime 2 g thrice daily (IV)
Piperacillin-tazobactam 4.5 g four times a day (IV)
Imipenem 0.5-1 g three to four times a day (IV)
Meropenem 1 g thrice daily (IV)

Duration of Antibiotics

- CAP should be treated be treated for a minimum of 5 days. This may need to be extended according to clinical judgement ,etiological agent and development of complications.

Adjunctive Therapies

- Correction of dehydration with IV fluids, correction of hypoxemia with oxygen administration important supportive therapies to be considered in appropriate settings.
- Steroids should be used for septic shock or acute respiratory distress syndrome (ARDS) secondary to CAP according to the current guidelines.
- CAP-ARDS and CAP leading to sepsis and septic shock should be managed according to the standard management protocols for these conditions.
- Non-invasive ventilation and high flow nasal canula (HFNC) Oxygen therapy may be used in patients with CAP and acute respiratory failure.

Role of Immunisation and Smoking Cessation for Prevention of CAP

- Pneumococcal vaccine and Influenza vaccine may be considered for the prevention of CAP in special populations according to prevailing guidelines.

- Smoking cessation should be advised for all current smokers.

Failure to respond

Non responding pneumonia is a situation in which an inadequate clinical response is present despite adequate antibiotic treatment. There will be persistence of symptoms and <50% radiological clearance after 2 weeks with radiological infiltrates persisting after 30 days.

Failure to respond may be due to agent factors, host factors or due to extent of disease. At this stage a review of diagnosis should be done. Other causes which should be evaluated include:

- Resistant microorganism
- Nosocomial superinfection
- Spread of pneumonia
- Drug fever
- Non-infectious etiologies
- Post obstructive pneumonia.

In addition to microbiologic diagnostic procedures Chest CT, thoracocentesis and bronchoscopy should be considered at this stage.

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ALLERGIC RHINITIS

1.Introduction

Rhinitis is defined as inflammation of the nasal mucosa and is characterized by sneezing, nasal congestion, nasal itching, and rhinorrhea. The eyes, ears, sinuses, and throat can also be involved. It is an extremely common condition, affecting approximately 20% of the population. Allergic rhinitis, even though not a life threatening condition can significantly impair quality of life. Systemic effects, including fatigue, sleepiness, and malaise, can occur from the inflammatory response. Allergic rhinitis can frequently lead to significant impairment of quality of life. Symptoms such as fatigue, drowsiness, and malaise can lead to impaired work and school performance, missed school or work days, and traffic accidents.

Allergic rhinitis involves inflammation of the mucous membranes of the nose, eyes, eustachian tubes, middle ear, sinuses, and pharynx. The nose invariably is involved, and involvement of other organs may vary according to severity. Inflammation of the mucous membranes is triggered by immunoglobulin E (IgE) in response to an extrinsic allergen.

Classification of allergic rhinitis

Duration

1- Intermittent – symptoms are present less than 4 days a week or for less than 4 weeks.

2- Persistent – symptoms are present at least 4 days a week and for at least 4 weeks.

Severity

1- Mild – none of the following is present.

2- Moderate-severe – at least one of the following is present.

a) Sleep disturbance

b) Impairment of daily activities, leisure and/or sport

c) Impairment of school or work

d) Troublesome symptoms

Evaluation

Obtaining a detailed history is important in the evaluation of allergic rhinitis. Important elements include an evaluation of duration, and time course of symptoms; possible triggers, response to medications, comorbid conditions, family history of allergic diseases, environmental and occupational exposures. A thorough history may help identify specific triggers, suggesting an allergic etiology for the rhinitis.

Symptoms that can be associated with allergic rhinitis include sneezing, itching of nose, eyes, ears and palate, rhinorrhea, postnasal drip, congestion and headache. Significant

complaints of congestion, particularly if unilateral, might suggest the possibility of structural obstruction, such as a polyp, foreign body, or deviated septum.

Trigger factors

This might include exposure to pollen outdoors, mold spores while doing yard work, specific animals, or dust while cleaning the house. Irritant triggers such as smoke, pollution, and strong smells can aggravate symptoms in a patient with allergic rhinitis.

Response to treatment

Response to treatment with antihistamines supports the diagnosis of allergic rhinitis, although sneezing, itching, and rhinorrhea associated with nonallergic rhinitis can also improve with antihistamines. Response to intranasal corticosteroids supports the diagnosis of allergic rhinitis, although some cases of nonallergic rhinitis (particularly the nonallergic rhinitis with eosinophils syndrome [NARES]) also improve with nasal steroids.

Physical Signs

The mucosa of the nasal turbinates may be swollen and have a pale, bluish-graycolor. Some patients may have predominant erythema of the mucosa, which can also be observed with rhinitis medicamentosa, infection, or vasomotor rhinitis. While pale, boggy, blue-gray mucosa is typical for allergic rhinitis, mucosal examination findings cannot definitively distinguish between allergic and nonallergic causes of rhinitis.Thin and watery secretions are frequently associated with allergic rhinitis, while thick and purulent secretions are usually associated with sinusitis.Nasal examination may reveal deviation of septum or polyps.

Laboratory Studies

Allergy testing provides knowledge of the degree of sensitivity to a particular allergen. The most commonly used methods of determining allergy to a particular substance are allergy skin testing and in vitro diagnostic tests. Skin test is considered to be the most sensitive and specific test for detecting the culprit allergens. Testing for reaction to specific allergens can be helpful to confirm specific allergic triggers. If specific allergic triggers are known, then appropriate avoidance measures can be recommended. It is essential to know which allergens a patient is sensitive to in order to perform allergen immunotherapy (desensitization treatment).

In vitro allergy tests, ie, RAST, allow measurement of the amount of specific IgE to individual allergens in a sample of blood. The amount of specific IgE produced to a particular allergen approximately correlates with the allergic sensitivity to that substance. When selecting allergens, identify allergens that are present locally and are known to cause clinically significant allergic disease.

Total serum IgE

This is a measurement of the total level of IgE in the blood. While patients with allergic rhinitis are more likely to have an elevated total IgE level than the normal population, this test is neither sensitive nor specific for allergic rhinitis. As many as 50% of patients with allergic rhinitis have normal levels of total IgE, while 20% of nonaffected individuals can have elevated total IgE levels. Total blood eosinophil count. As with the total serum IgE, an elevated eosinophil count supports the diagnosis of allergic rhinitis, but it is neither sensitive nor specific for the diagnosis.

Imaging Studies

- Radiography

  While radiographic studies are not needed to establish the diagnosis of allergic rhinitis, they can be helpful for evaluating possible structural abnormalities or to help detect complications or comorbid conditions, such as sinusitis or adenoid hypertrophy.

- CT scanning

  Coronal CT scan images of the sinuses can be very helpful for evaluating acute or chronic sinusitis. CT scanning may also help delineate polyps, turbinate swelling, septal abnormalities (eg, deviation), and bony abnormalities (eg, concha bullosa).

- MRI

  For evaluating sinusitis, MRI images are generally less helpful than CT scan images, largely because the bony structures are not seen as clearly on MRI images. However, soft tissues are visualized quite well, making MRI images helpful for diagnosing malignancies of the upper airway.

Other Tests

- Nasal cytology
- Rhinoscopy:
- Nasal provocation testing

2. Treatment

The management of allergic rhinitis consists of 3 steps

(1) Environmental control measures and allergen avoidance,

(2) Pharmacological management, and

(3) Immunotherapy.

Environmental Control

Environmental control measures and allergen avoidance involve both the avoidance of known allergens and avoidance of nonspecific, or irritant, triggers.

Pharmacotherapy

Pharmacologic options for the treatment of allergic rhinitis include intranasal corticosteroids, oral and topical antihistamines, decongestants, intranasal cromolyn (Nasalcrom), intranasal anticholinergics, and leukotriene receptor antagonists. Intranasal corticosteroids are the mainstay of treatment of allergic rhinitis. The adverse effects most commonly experienced with the use of intranasal corticosteroids are headache, throat irritation, epistaxis, stinging, burning, and nasal dryness.

The second-generation oral antihistamines such as desloratadine, levocetirizine, fexofenadine, and loratadine are effective in controlling symptoms and have better side effect profile. Compared with oral antihistamines, intranasal antihistamines offer the advantage of delivering a higher concentration of medication to a specific targeted area, resulting in fewer adverse effects. Oral and topical decongestants improve the nasal congestion associated with allergic rhinitis. however, there is a chance that patients may develop rhinitis medicamentosa or have rebound or recurring congestion. So decongestants should not be used for more than 7 days at a time. ntranasal corticosteroids are effective in controlling symptom as well as nasal inflammation, especially in cases which are not controlled with antihistamines alone. Nasal sprays with anitihistamines and steroids in combination are also commercially available. The combination of intranasal H1-antihistamines with INCSs was found to be more effective than INCSs alone. Oral leukotriene receptor antagonist montelukast is also useful, especially in combination with antihistamines in controlling allergic rhinitis with refractory symptoms.

Immunotherapy (desensitization)

Immunotherapy is a long-term process. Therapy should be continued for 3-5 years. Success rates have been demonstrated to be as high as 80-90% for certain allergens. Sublingual immunotherapy (SLIT) is currently increasing in use, particularly in Europe. SLIT can produce significant clinical improvement in elderly patients with allergic rhinitis caused by house dust mites (HDMs). [13]. SLIT has also been shown to prevent the progression of allergic rhinitis to asthma.

Surgical Care

Surgical care is not indicated for allergic rhinitis but may be indicated for co morbid or complicating conditions, such as chronic sinusitis, severe septal deviation (causing severe obstruction), nasal polyps, or other anatomical abnormalities. The value of turbinectomy is not established.

Allergic conjunctivitis

- Allergic Conjunctivitis occurs in approximately 50%–70% of patients with Allergic rhinitis. May be treated with topical antihistaminics like olepatidine , or topical corticosteroids like loteprednol etabonate.

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COPD

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) - is a a heterogenous lung condition characterized by chronic respiratory symptoms (dyspnoea, cough, sputum production and/or exacerbations due to abnormalities of airways (bronchitis, bronchiolitis) and/or alveoli(emphysema) that cause persistent, often progressive ,airflow obstruction.

When to suspect COPD?

A diagnosis of COPD should be considered in persons having chronic symptoms of cough, sputum production, shortness of breath, and/or wheezing, chest tightness, fatigue, activity limitation especially among those with prolonged exposure to risk factors for the disease. COPD in Indian females are increasing due to exposure to biomass fuels. Females are more susceptible to effects of tobacco smoke than males. They may experience acute events characterized by increased respiratory symptoms called exacerbations that influence their health status and prognosis, and require specific preventive and therapeutic measures.

Risk factors for COPD

In the recent past, COPD has been classified based on etiotypes into various groups based on the aetiology responsible for COPD.

The details are given in table 1.

Table 1. Etiotypes for COPD

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

2. Diagnosis of COPD

A diagnosis of COPD should be considered in any patient who has dyspnoea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. A Post-bronchodilator FEV1/FVC < 0.7 should be used as the criteria for diagnosis of COPD. A diagnosis of COPD should not be excluded just because physical signs are absent.

Spirometry should not be used as a screening tool in asymptomatic individuals to detect airflow obstruction

Pre-bronchodilator spirometry can be used as an initial test to investigate whether symptomatic patients have airflow obstruction. If the pre-bronchodilator values show obstruction the diagnosis of COPD should be confirmed using post bronchodilator measurements. If pre-bronchodilator spirometry does not show obstruction performing post-bronchodilator spirometry is not necessary unless there is a very high clinical suspicion of COPD.

Some individuals can have respiratory symptoms without airflow obstruction(FEV1.>/0.7 PBD).These subjects are labelled "Pre-COPD'.The term 'PRISm'(preserved ratio impaired spirometry) has been proposed to identify those with normal ratio but abnormal spirometry.Subjects with Pre-COPD or PRISm are at risk of developing airflow obstruction over time ,but not all of them do.They need close follow up.

PEF should not be routinely used for screening, diagnosis, or monitoring of COPD

Classification of severity of COPD

Classification of severity of the disease should be done for all COPD patients based on the FEV1 and exacerbation frequency

Level of patient's disability due to symptoms should be assessed using modified Medical Research Council (mMRC) dyspnoea questionnaire or the COPD assessment test (CAT)

Classification of Severity of Airflow Limitation in COPD

In patients with post bronchodilator FEV 1/FVC < 0.70

GOLD 1: Mild - FEV1 >/= 80% predicted

GOLD 2: Moderate - 50%=/< FEV 1 < 80% predicted

GOLD 3: Severe - 30%=/< FEV 1< 50% predicted

GOLD 4: Very Severe - FEV1< 30% predicted

*Based on Post-Bronchodilator FEV 1

Combined COPD assessment

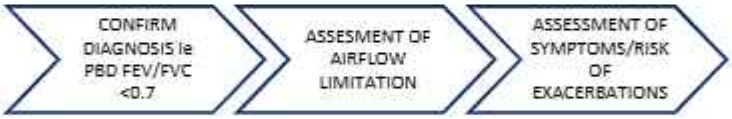
COPD assessment must focus on determining the following five fundamental aspects:

- severity of airflow obstruction
- nature and magnitude of current symptoms
- previous history of moderate and severe exacerbations
- blood eosinophil count
- presence and type of other diseases

In the GOLD -2023revised assessment scheme (see Figure), the impact of COPD on an individual patient is assessed by combining the symptomatic assessment using mMRC or COPD Assessment Tool (CAT), with the patient'srisk of exacerbations.

The number provides information regarding severity of airflow limitation (spirometric grade 1 to 4) while the letter (groups A to E) provides information regarding symptom burden and risk of exacerbation which can be used to guide therapy .the severity of airflow obstruction was subsequently removed from this combined assessment scheme considering its lower precision at individual level to predict outcomes and drive treatment decisions.

Figure 3.1. Diagnosis of COPD



GRADE	FEV1 (% predicted)
GOLD 1	>/=80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	<30

EXACERBRATION HISTORY	GROUPS	
Atleast one exacerbation requiring hospitalisation or 2 or more exacerbration a year	E	
0 or 1 moderate exacerbations which does not require hospitalization	A	B
SYMPTOMS ⟹	mMRC 0-1 Cat score less than 10	mMRC OF 2 OR MORE Cat score of 10 or more

Additional investigations in COPD

1. All new COPD suspects with cough of more than 2 weeks' duration should undergo sputum AFB examination as per RNTCP.
2. Pulse Oximetry & ABG – To screen for hypoxemia especially when there is clinical suspicion and FEV1 < 50%. ABG recommended if SPO2 < 92%.
3. Chest X-ray

   Diagnosis of COPD should not be made on the basis of a chest radiograph.

   Chest radiograph may be done during the initial evaluation of COPD to look for comorbidities, complications, and alternative diagnosis.
4. Special investigations like HRCT scan, lung volumes, DLCO, and exercise testing should be done in situations of diagnostic difficulty or whenever clinically indicated.
5. 6MWT may be used for monitoring of exercise capacity in COPD.
6. Testing for alpha-1 antitrypsin deficiency is not routinely recommended. It may be done in young patients with lower lobe emphysema. □ COPD patients should be routinely evaluated and appropriately treated for comorbid conditions such as Cardiovascular diseases, Osteoporosis, Skeletal muscle dysfunction, Cachexia, Respiratory infections, Anxiety and Depression, Diabetes, Lung cancer and Bronchiectasis

These comorbid conditions may influence the mortality and hospitalizations and should be looked for routinely, and treated appropriately

3.Treatment options

Management of stable COPD

Includes Pharmacological and Non-Pharmacological therapies

Pharmacotherapy –

- Inhaled therapy is now established as the mainstay of treatment for patients with stable COPD.
- The choice of inhaler device will depend on availability, cost, the prescribing physician, and the skills and ability of the patient.
- It is essential to ensure that inhaler technique is correct and to recheck this at each visit.

A .Bronchodilators –

Inhaled bronchodialators in COPD are central to symptom management.

a) Antimuscarinic agents

LAMAs have a greater effect on exacerbation reduction compared with LABAs and decrease hospitalizations.

- Short-acting antimuscarinic agent (SAMA) like iptratropium can be used as rescue medication to relieve patient symptoms.
- Long term SAMA monotherapy on regular basis is not recommended.
- Long-acting antimuscarinic agents (LAMA) are useful in stable COPD (FEV1 < 80%) to control symptoms and decrease the risk of exacerbations. Eg tiotropium, aclidinium, glycopyrronium bromide and umeclidinium
- LAMA should be preferred over SAMA
- LAMAs improve the effectiveness of pulmonary rehabilitation.

Inhaled anticholinergic drugs are well tolerated.

- The main side effect is dryness of mouth.
- Occasional urinary symptoms have been reported

b) Beta2 -Agonists

- Short-acting beta-agonist (SABA) can be used to relieve symptoms of dyspnea as and when needed. The effect of SABAs usually wears off within 4-6hrs

- Long term SABA monotherapy on regular basis is not recommended
- Long-acting beta-agonist (LABA) Improve lung function,dyspnoea,health status,and reduce exacerbation rates.

Long acting Beta 2 agonists, salmeterol and formetrol need to be given twice daily

Ultra long acting Indacaterol is given once daily.Oladaterol and vilanterol are additional once daily LABAs .

B. Inhaled corticosteroids

COPD-associated inflammation has limited responsiveness to corticosteroids. Regular treatment with ICS does not modify the long-term decline of FEV1 nor mortality in patients with COPD.So use of ICS in COPD have a beneficial effect in subgroup of COPD patients with

- one moderate exacerbation per year & AEC <300eosinophils/μL
- ≥2 moderate exacerbations per year atleast one severe exacerbation requiring hospitalization in the prior year & eosinophil counts ≥300cells/μL history of, or concomitant asthma

Prolonged use of ICS has shown to increases risk of pneumonia in COPD esp in those with severe disease

- Long-term monotherapy with oral or inhaled corticosteroids is not recommended in COPD.

Dosage of inhaled corticosteroids has already been described in Section 1. Please see table 1.1.

In patients of severe COPD (FEV1 < 50%), triple therapy (ICS + LABA + LAMA) may be used in those who are symptomatic despite single or dual bronchodilator therapy and has shown to have better symptom control and reduction of exacerbations.

LABA +ICS combination is not encouraged in COPD.IF there is an indication for an ICS, the combination LABA+LAMA+ICS is the preferred choice.

If patients with COPD have features of asthma,treatment should always contain an ICS

Blood eosinophil count & Inhaled Corticosteroid use

- Recent studies have shown that blood eosinophil counts predict the magnitude of the effect of ICS in preventing future exacerbations
- GOLD 2025 guidelines suggest that that an absolute eosinophil count (AEC) > 300 cells/μL identifies the patients with the greatest likelihood of treatment benefit with ICS

- ICS containing regimens have little or no effect at a blood eosinophil count < 100 cells/μL

Methylxanthines

- There is only evidence for a modest bronchodilator effect compared with placebo in stable COPD.
- Clearance of the drug declines with age.
- Addition of theophylline to salmeterol produces a greater improvement in FEV1 and breathlessness than salmeterol alone.
- Adverse effects. Toxicity is dose-related, which is a particular problem with xanthine derivatives because their therapeutic ratio is small and most of the benefit occurs only when near-toxic doses are given
- Methylxanthines are not recommended as first line

They can be used

- As alternative in patients noncompliant with inhalers for any reason.
- As add-on therapy in patients continuing to have symptoms despite optimum inhaled therapy. Sustained release preparations are preferred.

Roflumilast (PDE 4 Inhibitor)may be used in patients when FEV1 <50% and chronic bronchitis.,it improves lung function and reduces moderate and severe exacerbations.

PDE 4 Inhibitors should always be used in combination with a bronchodilator

Ensifentrine (PDE 3 & 4 inhibitor) significantly improves lung function ,dyspnoea,and health status

Combination of ICS/Bronchodilator Therapy

- ICS + LABA -more effective than individual components in improving lung function,health status, decreasing exacerbations in moderate exacerbations.

If there is no relevant exacerbation history,then consider changing to LABA+LAMA

If there is an indication for ICS use then LABA+LAMA+ICS has been shown to be superior to LABA+ICS.

Blood eosinophil count can be used to guide treatment with ICS.

Combination of bronchodilators :

Available combinations:

SABA + SAMA – Salbutamol + ipratropium

LABA + LAMA - Formeterol + Tiotropium

Ultra LABA + Ultra LAMA - Inadacaterol + Glycopyronium

Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation with a lower risk of side-effects compared to increasing the dose of a single bronchodilator. Combinations of a LABA and LAMA in a single inhaler improve lung function greater than long acting bronchodilator monotherapy effects. Such a combination is found to decrease exacerbations to a greater extent than an ICS/LABA combination.

Combination treatment with a LABA and a LAMA increases FEV1 and reduces symptoms compared to monotherapy.

Combination treatment with a LABA +LAMA reduces exacerbations compared to monotherapy.

Combination of ICS/Bronchodilator Therapy

More effective than individual components in improving lung functions, health status, decreasing exacerbations in moderate to severe COPD with frequent exacerbations.

An ICS/LABA combination OD does not show relevant differences in efficacycompared to BD dosing

Other pharmacological treatments

a. Vaccines – Patients with COPD should receive all recommended vaccinations,

- yearly influenzal vaccination. Influenza vaccination can reduce serious illness and death in COPD patients. The strains are adjusted each year for appropriate effectiveness and should be given once each year.
- SARS-CoV-2 vaccination
- Either one dose of 21-valent pneumococcal conjugate vaccine(PCV21) or one dose of PCV20.Pneumococcal vaccination has been shown to reduce the incidence of community acquired pneumonia and exacerbations for people with COPD.
- Respiratory syncytial virus vaccination,Tdap vaccination against pertussis,zoster vaccine is also recommended in select patients

b. Alpha 1 Antitrypsin Augmentation Therapy

- Young patients with severe hereditary alpha 1 antitrypsin deficiency and established emphysema may be candidate for alpha 1 augmentation therapy . Very expensive and is not recommended for patients with COPD that is unrelated to alpha 1 antitrypsin deficiency
- It should be prescribed only after discussion with an expert committee.

c. Antibiotics – may be prescribed for treating all exacerbations of COPD especially when patients present with purulent expectoration.

Recent studies have shown that regular use of some antibiotics may reduce exacerbation rate.

Azithromycin (250 mg/day or 500 mg three times per week) or erythromycin (500 mg two times per day) for one year in patients prone to exacerbations reduced the risk of exacerbations. Butpatients on long term azithromycin should be cautioned about increased incidence of bacterial resistance, prolongation of QTc interval, and impaired hearing tests

d. Mucolytics:

In COPD patients not receiving inhaled corticosteroids, regular treatment with mucolytics such as erdosteine, carbocysteine and N-acetylcysteine may reduce exacerbations and modestly improve health status

e. Antitussives - Regular use not recommended

f. Vasodilators - Nitric oxide contraindicated in stable COPD

Others drugs - Nedocromil, leukotriene modifiers like montelukast not adequately tested in COPD

Symptom control and palliative care

Even when receiving optimal medical therapy many patients with COPD continue to experience distressing breathlessness, impaired exercise capacity, fatigue, and suffer panic, anxiety and depression. Such patients should be referred to palliative care. Treatment with opioids (low dose morphine) has been found to be beneficial.

Non pharmacological therapies

1. Smoking Cessation most important intervention for COPD patients who smoke regardless of disease severity . Greatest capacity to influence natural history of COPD

2. Physical activity

   Daily physical activity recommended for all COPD patients.

3. Pulmonary Rehabilitation

   Improves exercise tolerance and decreases dyspnoea and fatigue

   Components of Pulmonary Rehabilitation Programme

   - Exercise training.
   - Smoking Cessation

- Patient Education
- Assessment and Follow-up
- Nutritional support

4. Identify and reduce the exposure to risk factors like environmental, occupational and indoor and outdoor air pollution.

Other treatments

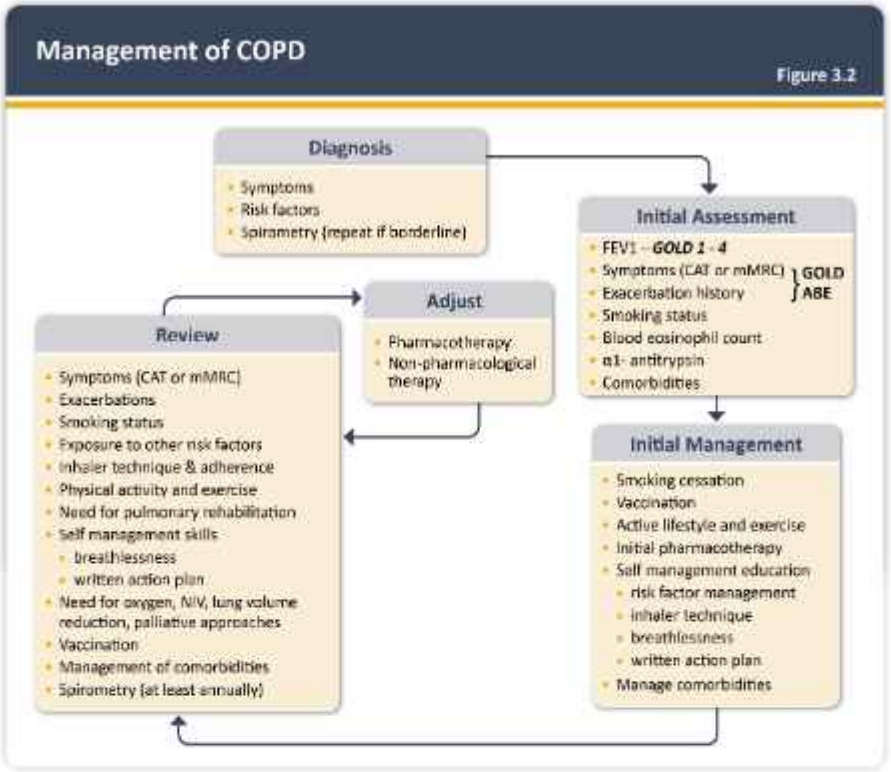
- Oxygen therapy
- Ventilatory Support
- Surgical treatments

Table 3.2. INITIAL Pharmacological treatment of stable COPD

≥2 moderate exacerbations or ≥1 leading to hospitalization	GP ELABA+LAMA (consider LABA+LAMA+ICS if blood eos>300	
0 or 1 moderate exacerbations (not leading to hospitalisation)	Gp A A bronchodilator	Gp B LABA + LAMA (LAMA or LABA)
	mMRC 0 – 1; CAT<10	*mMRC ≥ 2; CAT ≥ 10*

* For highly symptomatic patients

** If Eosinophils > 300



Follow-up pharmacological management

Patient on maintenance treatment should be periodically followed up and treatment options altered, on the basis of improvement or worsening of dyspnea/exercise limitation and frequency of exacerbations.

If a change in treatment is considered necessary then select the corresponding algorithm for dyspnea or exacerbations

Follow up pharmacological management should be guided by the principles of first *review* and *assess*, then *adjust* if needed:

- Review- • Review symptoms (dyspnea) and exacerbation risk.
- ➢ Assess - • Assess inhaler technique and adherence, and the role of non-pharmacological approaches
- ➢ Adjust • Adjust pharmacological treatment, including escalation or de-escalation.

Any change in treatment requires a subsequent *review* of the clinical response, including side effects.

Dyspnea

Table 3.2. Adjusting the medications for COPD based on symptoms

Current treatment	Action advised
Symptomatic on LABA or LAMA	LABA + LAMA
Not better with LABA + LAMA	Switching inhaler device or molecules can also be considered Dyspnea due to other causes should be investigated Implement or escalate non-pharmacological treatment Consider addind ensifentrine
On LABA + ICS	Consider triple combination LABA + LAMA + ICS

Stopping ICS:

This can be considered if there are adverse effects (such as pneumonia) or a reported lack of efficacy

Exacerbations

Table 3.4 Management of COPD exacerbations

Current treatment		Action advised
Persistent exacerbations on LABA / LAMA alone	History or findings suggestive of asthma /ACO	Escalation to either LABA/LAMA or LABA/ICS
	≥ 300 eosinophils/µL	LABA+LAMA+ICS
	If blood eos<300	LABA+LAMA
Persistent exacerbations on LABA + LAMA	AEC > 100 cells/µL	LABA+ ICS + LAMA(if persistent exacerbation and blood eos>300, and chronic bronchitis,add Dupilumab)
	AEC < 100 cells/µL with an FEV1 < 50% predicted and chronic bronchitis	Add roflumilast
	AEC < 100 cells/µL And former smokers	Long term macrolides

INTERSTITIAL LUNG DISEASE

1.Introduction

Interstitial Lung Disease (ILD) is a term that encompasses a large group of disorders characterized by progressive scarring (fibrosis) of lung tissue. This fibrosis affects the interstitium, the tissue and space around the air sacs of the lungs. The scarring eventually impacts the ability to breathe and get enough oxygen into the bloodstream. ILD includes more than 200 lung disorders, most of which cause progressive scarring of lung tissue. This review article provides a comprehensive overview of ILD, including its classification, pathogenesis, clinical presentation, diagnostic methods, and treatment options.

Classification of interstitial lung diseases

The ATS / ERS / JRS / ALAT Update of 2022 revised the 2013 Classification of ILD. They now classified ILDs other than IPF indicating their tendency to progressively develop fibrosis. This classification includes 5 main groups as follows:

1. IIPs
2. Autoimmune ILDs
3. Exposure related
4. ILDs with cysts or airspace filling
5. Sarcoidosis

For ILDs in each category, the diagram indicated the likelihood of developing progressive pulmonary fibrosis - from conditions where fibrosis is very common (e.g., Acute fibrinous and organising pneumonia, Systemic Sclerosis and Rheumatoid Arthritis), to those less likely to fibrose (e.g., Cryptogenic Organising Pneumonia) and those that do not or are extremely unlikely to fibrose (e.g., Lymphangioleiomyomatosis LAM).

Further classification of each sub-type has been included, with changes in nomenclature. Hypersensitivity Pneumonitis (HP) earlier was sub-typed as Acute, sub-acute and chronic. The ATS / ERS / JRS / ALAT 2020 guideline on Diagnosis of Hypersensitivity in Adults now subtypes HP as follows:

1. Fibrotic HP
2. Non-fibrotic (or cellular) HP

ILDs can also be further subtyped by their etiology and time course.

- Idiopathic Interstitial Pneumonias (IIPs)– those of yet unknown cause, further sub-classified by time course:
    - Idiopathic pulmonary fibrosis which is chronic and has a high risk of developing a progressive-fibrosing phenotype.

- Chronic IIPs: e.g., desquamative interstitial pneumonia, pleuroparenchymal fibroelastosis, idiopathic nonspecific interstitial pneumonia.

- Acute IIPs: e.g., acute interstitial pneumonia.
- Subacute IIPs: e.g., cryptogenic organizing pneumonia.
- Unclassifiable interstitial lung disease: IIPs that cannot be accurately categorized due to their individual characteristics that do not permit neat classification into one or another group. Often these are in a stage of evolution and may evolve into one of the other ILDs over time.

Over time, one may also expect that with research especially in the areas of genetics and molecular diagnostics, and hence better recognition of etiologies, the number of conditions classified as idiopathic may reduce.

An alternative suggestion for classification involves etiologies:

This identifies four categories of diseases, all of which affect the lung interstitium

(1) Conditions where only the lung is involved: IIPs, and developmental disorders.

(2) Conditions where the lung is involved as part of a systemic disease: CTD, vasculitides like GPA, EGPA and LAM

(3) Exposure-related disorders e.g., HP, drug induced ILD, pneumoconioses, radiation pneumonitis

(4) Conditions where the lung is involved as part of a vascular disorder e.g., Diffuse alveolar haemorrhage, Pulmonary capillary haemangiomatosis, Pulmonary veno-occlusive disease.

Pathophysiology of ILD

As it is difficult to discuss about all ILDs, we have discussed only pathophysiology of IPF.

Pathology of IPF:

IPF is characterized histologically by the usual interstitial pneumonia pattern, with heterogeneous areas of lung parenchymal fibrosis and tissue preservation, dispersed fibroblastic foci (FF), areas of interstitial inflammation and honeycombing (Oliveira, 2018). The FF are crescent shaped, patchy bulge of immature fibroblasts and ground substance, located beneath reactive cuboidal alveolar lining epithelium and have been presumed to be the active zone of injury in UIP. Honeycombing corresponds to bronchiolar cysts, measuring between 3 and 10 mm but up to 2.5 cm in size that develop after collapse of fibrotic alveolar septa and dilatation of terminal airways. Microscopically, honeycomb cysts are lined by columnar ciliated epithelium and filled

with mucus and variable inflammatory infiltrate. The lung parenchymal remodelling is radiologically seen as architectural distortion with reticular opacities, honeycombing, ground-glass opacities, traction bronchiectasis with sub-pleural preservation. The remodeling process appears to be a continuum from traction bronchiectasis to honeycombing and the conceptual separation of the two processes is thought to be misleading by some (Piciucchi, 2016). BAL fluid examination reveals increased neutrophils and/or absence of lymphocytosis (Raghu, 2022). The latest IPF clinical Practice Guideline, (Raghu, 2022) has updated the radiological and histopathological criteria for IPF with regard to transbronchial lung cryobiopsy as an acceptable alternative to surgical lung biopsy in centers with appropppriate expertise. However, no recommendation was made for or against genomic classifier testing in these guidelines.

Physiology of IPF:

Patients with IPF have increased physiological dead space ventilation (increased ratio of dead space volume to tidal volume (VD/VT)) at rest and at exercise (Agusti, 1991). This feature results from both increased anatomical dead space due to the increased volume of conducting airways (Plantier, 2016) and from regional increases in V/Q ratios, i.e. alveolar dead space. The relationship between individual histologic features has been correlated with disease progression in idiopathic pulmonary fibrosis (Nicholson, 2002; Harada, 2013). They observed strong correlations between increasing interstitial mononuclear cell infiltrate or FF scores and greater declines in forced vital capacity (FVC) or DLCO at 6 months. Increasing FF scores were independently associated with greater declines in FVC and DLCO at both 6 and 12 months. Importantly, although no correlation was observed between standard physiological studies (VC, TLC, DLCO) and pathological severity, static lung compliance was strongly correlated with the degree of fibrosis assessed by scoring of lung biopsies (Plantier, 2018). V/Q lung scans demonstrate that fibrotic lesions, and honeycomb lesions in particular, are very poorly perfused although they still receive some ventilation (Strickland, 1993).

2. Clinical Presentation and diagnosis of ILDs

Accurate diagnosis of interstitial lung disease is essential as the prognosis and treatments vary widely depending on the cause. Whenever ILD is suspected, a detailed evaluation using an algorithmic approach is the key to diagnosis of the causative disease, if there is one. Unfortunately, a specific ILD diagnosis remains elusive in up to 20% of cases; and is often delayed. This chapter aims to discuss precisely on the various diagnostic tools for the diagnosis of ILD in clinical practice. A comprehensive evaluation should include detailed history including symptom assessment with stress on organic and inorganic exposures, physical examination, pulmonary function tests (PFT), and chest imaging (plain chest radiography/high-resolution computed tomography [HRCT] chest) and histopathology as

indicated with multidisciplinary discussion (MDD) between pulmonologists, radiologists, rheumatologists and pathologists which is considered the current "gold standard" method for ILD diagnosis.

Physical findings related to ILD are nonspecific. The characteristic finding is dry bibasilar crackles, although inspiratory high-pitched rhonchi ("squeaks") can be heard with bronchiolitis. Clubbing (most common in idiopathic pulmonary fibrosis) and signs of right heart failure can also be seen in patients with advanced disease. The physical examination is particularly helpful when it uncovers signs of an underlying connective tissue disorder. The presence of a rash (malar, heliotropic, vasculitis, or due to erythema nodosum), Raynaud phenomenon, joint deformity, synovial swelling, or muscle weakness should prompt a more complete evaluation for an underlying rheumatologic disorder.

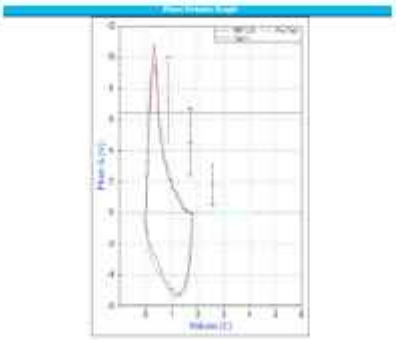
A history of exposures in the home and workplace should be obtained, including to mold, asbestos, and other relevant occupational dusts, which may point toward an underlying inciting agent. Similarly, physical signs detected during the examination might support presence of an ILD (nail clubbing, fine inspiratory crackles) or suggest an underlying connective tissue disease diagnosis (sclerodactyly, inflammatory arthritis, typical skin rash).

Pulmonary function tests in ILD:

Spirometry

Spirometry measures the maximum volume of air that an individual can inspire and expire with maximal effort. The classical pattern on spirometry in ILD is a restrictive ventilatory abnormality with decreased FVC and normal or increased FEV1/FVC ratio with preserved FEV1. Reduced vital capacity (VC) alone is not sufficient evidence of restriction because air trapping due to severe obstruction can also decrease it. Therefore, the restrictive abnormality cannot be diagnosed with spirometry alone, and should be confirmed by lung volumes. Total lung capacity (TLC) is the crucial lung volume to confirm restriction, defined as a TLC value less than the fifth percentile of predicted value together with a normal or increased FEV1/FVC ratio.

Figure 4.1: Flow volume loop in restrictive lung diseases



Spirometry plays a significant role in the early diagnosis of CTD-ILD. In the lungs in CTDs, there can be involvement of airways, vasculature, and respiratory muscles apart from the parenchyma. Hence, spirometry findings should be corelated with DLCO to differentiate between parenchymal and extra parenchymal causes for restrictive pattern. In systemic sclerosis (SSc), spirometry is vital in the diagnostic workup for ILD but is not sensitive for detecting early ILD as lung volumes are preserved in the early stages.

TLCO:

TLCO, also called the transfer factor, measures the capacity to transfer gas from alveolar spaces into alveolar-capillary blood. CO is commonly used because of its extreme avidity for haemoglobin (200–250 times as oxygen), which exerts negligible backpressure. The factors affecting the amount of CO transferred from the alveoli to the blood capillaries are surface area, the thickness of the alveolar-capillary membrane available for gas exchange, and blood volume in the pulmonary capillary. Therefore, decreased surface area, increased thickness of alveolar capillary membrane, and decreased pulmonary flow reduce TLCO. TLCO is reduced in ILDs due to decreased surface area and increased thickness of the alveolar-capillary membrane by inflammation and fibrosis, thereby limiting gas exchange. DLCO helps in detecting mild (early or preclinical) ILD as lung volumes get affected only late in the disease. Pulmonary hypertension should be suspected in ILD if TLCO is very low and there is severe exercise-related desaturation.

6MWT:

Six-minute Walk test is a simple, standardized measure of the distance walked during a defined period of 6 minutes to assess the submaximal level of functional capacity. It is the most widely used exercise test, which is inherently safe test that can be performed in the advanced stages of the disease and has ease of administration and is reproducible. During a 6MWT, healthy participants can typically walk 400 – 700 m. 6MWT provides prognostic information complementary to pulmonary function tests.

Imaging:

Chest radiographs and HRCT chest are the essential tools in the diagnosis of ILD. The chest radiograph is used in the initial diagnostic assessment, which helps rule out left heart failure, infection, or malignancy encountered in ILD. Diffuse reticulonodular opacities are a common finding. Chest radiographs may be normal in ILD and is inferior to HRCT for the diagnosis and prognostication. HRCT chest is more sensitive in detecting early disease than lung function tests and chest radiographs. The pattern of the radiographic abnormalities on HRCT helps in identifying specific ILDs. Reticulation, traction bronchiectasis, and honeycombing reflect fibrosis. The extent of fibrosis at

baseline predicts mortality in ILD. HRCT chest may also be used to guide lung biopsy site and treatment decisions. The pattern and distribution of radiographic abnormalities can predict the histopathology.

CTD-ILDs are often associated with NSIP than UIP patterns as compared to idiopathic pulmonary fibrosis. In the context of usual interstitial pneumonia, the presence of the anterior upper lobe sign, along with the exuberant honeycombing sign, the four-corner sign and the straight-edge sign, has a fairly high specificity but moderate sensitivity for being the result of connective tissue disease-associated interstitial lung disease (CTD-ILD) rather than idiopathic pulmonary fibrosis (IPF).NSIP pattern is more frequently seen in systemic sclerosis, dermatomyositis, and mixed connective tissue diseases, while rheumatoid arthritis is frequently associated with UIP. In scleroderma, HRCT is the primary tool to diagnose ILD. Abnormalities in other thoracic structures (e.g., oesophageal diameter or pulmonary artery dilatation) should raise the suspicion for the presence of CTD in isolated NSIP patterns.

Serology:

Serology plays a significant role in the evaluation of CTD-related ILD. An antinuclear antibody is a preliminary screening test in the diagnosis of CTD with high sensitivity and poor specificity. Based on ANA patterns with nuclear staining (homogenous, speckled, nucleolar) or cytoplasmic staining combined with the clinical context, targeted antibody testing to diagnose specific CTD can be planned. Autoantibodies play a role in the prediction of progression of ILD in CTD, such as anti-topoisomerase (Scl 70), Th/To antibodies in scleroderma, anti-CCP antibodies in rheumatoid arthritis, and non-Jo 1 antibodies in antisynthetase syndrome. List of autoantibodies in CTD-ILD are given in Table 1

Table 4.1: List of autoantibodies in CTD-ILD

Autoantibody	**Associated CTD(s)**
Antinuclear antibody (ANA; ≥1:320)	SSc, SLE, Sjögren's, PM/DM
Systemic sclerosis associated	
Anti-topoisomerase (ATA/anti-Scl70)	SSc (diffuse)
Anti-centromere	SSc (limited)
Anti-RNA polymerase (RNA-pol)	SSc
Anti-Th/To	SSc
Anti-PM/Scl-75/100	SSc-myositis overlap, SLE, Sjögren's

Anti-U3 ribonucleoprotein (anti-U3 RNP)	SSc
Anti-U1 ribonucleoprotein (anti-RNP or anti-U1 RNP)	SSc-overlap, MCTD
Anti-U11/U12 ribonucleoprotein (anti-U11/U12 RNP)	SSc
Rheumatoid arthritis associated	
Rheumatoid factor (≥60 IU/mL)	RA, Sjögren's, SLE
Anti-cyclic citrullinated peptide (anti CCP)	RA
Myositis associated	
Anti-synthetase (Jo-1, PL-7, PL-12, EJ, OJ, KS)	PM/DM (anti-synthetase syndrome)
Anti-Mi2	PM/DM
Anti-CADM140 (anti-MDA5)	Clinically amyopathic DM
Overlap syndromes	
Anti-Ku	SSc, SSc-PM overlap, SLE, myositis
Anti-SS-A/Ro, anti SS-B/La	Sjögren's, SLE. Sjögren's/SLE overlap, SSc, RA, DM
Systemic lupus erythematosus associated	
Anti ds-DNA	SLE
Anti-Smith	SLE
Note: SSc, Systemic sclerosis; SLE, systemic lupus erythematosus; PM/DM, polymyositis/dermatomyocitis; MCTD, mixed connective tissue disease; RA, rheumatoid arthritis.	

Bronchoalveolar Lavage (BAL):

According to ATS guideline (2012), following the initial clinical and radiographic evaluation of patients in suspected ILD, BAL cellular analysis may be a helpful adjunct in the diagnostic evaluation, though it does not have a role in the prognostication and assessment of treatment response.

BAL remains a routinely performed diagnostic test in patients with newly detected ILD who do not have a definite UIP pattern on HRCT. Cellular analysis of BAL fluid can reveal lymphocytosis in hypersensitivity pneumonitis or sarcoidosis; a high BAL eosinophil counts suggests a diagnosis of eosinophilic pneumonia. BAL cultures help to exclude infection as an alternate cause of lung infiltrates prior to institution of specific immunosuppressive or antifibrotic therapies.

Lung Biopsy:

When clinical and radiologic data are insufficient to make a firm diagnosis, lung biopsy plays a role. Lung biopsies are done either by surgical or transbronchial approach. Surgical lung biopsy is the gold standard but is limited by morbidity and mortality. Transbronchial cryobiopsy of the lung is minimally invasive and tissue sampling is similar to surgical lung biopsy and is hence gaining interest. Overlap patterns are seen with noninflammatory ILDs, drug pneumonitis, and infections. Biopsy findings are to be collaborated with proper clinical and radiologic context with MDD to arrive at a diagnosis. Histopathologic patterns commonly seen are summarized in Table. 2

Table 4. 2: Histopathologic patterns in ILD

Radiological Pattern	Histopathology
UIP	Patchy subpleural fibrosis and fibroblastic foci at the interface between fibrosis and uninvolved lung parenchyma, architectural distortion, spatial and temporal heterogeneity with minimal inflammation
NSIP	**Cellular NSIP**- lymphoid aggregated with germinal centres and minimal fibrosis **Fibrotic NSIP**- dense paucicellular interstitial fibrosis, spatially and temporally homogenous that maintains the underlying lung architecture.
Organising pneumonia	Patchy distribution, intraluminal organising fibrosis in distal airspaces (bronchioles, alveolar ducts and alveoli)

	with preservation of lung architecture and mild interstitial chronic inflammation.
Acute interstitial pneumonia	**Diffuse Alveolar Damage (DAD)**- Diffuse distribution with alveolar septal thickening due to organising fibrosis along with airspace organisation (patchy or diffuse) and hyaline membranes (focal or diffuse

Emerging ILD diagnostic tests under investigation

Genetic testing:

- The advent of biobanks and evolution of methods for molecular analysis, including targeted next-generation sequencing and whole genome sequencing revolutionized the concept of genetic testing in ILD. In genes encoding for proteins expressed by airway epithelial cells such as MUC5B, Single nucleotide polymorphisms (SNPs), have been identified to have both diagnostic and prognostic significance in IPF and other fibrotic ILDs such as rheumatoid arthritis-associated ILD and chronic hypersensitivity pneumonitis.
- Genetic testing should also be considered where a "short telomere syndrome" is suspected and there is mounting evidence that screening of unaffected family members may be reasonable to facilitate earlier diagnosis and treatment institution. FIP is usually defined as a case of ILD in which the patient also has a family history of two or more relatives with ILD.

Table 4.3. Diagnosis of IPF

IPF suspected	**Histopathological patterns**				
HRCT pattern		UIP	Probable UIP	Indeterminate for UIP	Alternate diagnosis
	UIP	IPF	IPF	IPF	Non IPF
	Probable UIP	IPF	IPF	IPF likely	Non IPF

	Indeterminate for UIP	IPF	IPF likely	Indeterminate	Non IPF
	Alternate diagnosis	IPF likely	Non IPF	Non IPF	Non IPF

Progressive Pulmonary Fibrosis (PPF)

The ATS/ERS 2022 Update of IPF has recently defined PPF (Raghu, 2022) as occurrence of at least two of the following three criteria occurring within the past year with no alternative explanation, in a patient with ILD of known or unknown etiology:

1.Worsening respiratory symptoms

2. Physiological evidence of disease progression (either of the following):

   a. Absolute decline in FVC ⩾5% predicted within 1 yr of follow-up

   b. Absolute decline in DLCO (corrected for Hb) ⩾10% predicted within 1 yr of follow-up

3.Radiological evidence of disease progression (one or more of the following):

   a. Increased extent or severity of traction bronchiectasis and bronchiolectasis

   b. New ground-glass opacity with traction bronchiectasis

   c. New fine reticulation

   d. Increased extent or increased coarseness of reticular abnormality

   e. New or increased honeycombing

   f. Increased lobar volume loss

The expert group consensus statement (Rajan, 2023) provides guidance on the diagnosis, treatment and monitoring of F-ILDs with specific focus on the recognition of PPF and the management of pulmonary fibrosis progressing despite initial management.

Importance of a Multidisciplinary Approach in Diagnosis of ILD

MDM is accepted as a *gold standard* for ILD diagnosis worldwide. It involves the clinician caring for the individual patient along with other specialists such as Pulmonologists, Radiologists, Pathologists ± Rheumatologists. Each specialty contributes unique insights and skills to the diagnosis, treatment, and ongoing management of ILD patients. The aim of ILD MDM is to generate a consensus and working ILD diagnosis for the patient. As per the published data, MDM diagnosis of IPF

more closely associated with mortality than clinician or radiologist diagnosis of IPF alone

A multidisciplinary team (MDT) approach ensures comprehensive assessment, personalized treatment planning, and coordinated care delivery, ultimately improving patient outcomes and quality of life.

Key Components of a Multidisciplinary Team

1. Pulmonologist: Plays a central role in diagnosing and managing ILD, overseeing treatment decisions, and coordinating care with other team members.
2. Radiologist: Interprets imaging studies (e.g., chest CT scans) to aid in the diagnosis and monitoring of ILD progression.
3. Pathologist: Provides expertise in interpreting lung biopsy samples to confirm the specific type of ILD and guide treatment decisions.
4. Rheumatologist: Collaborates in cases of connective tissue disease-associated ILD, addressing underlying autoimmune conditions and optimizing treatment.
5. Respiratory Therapist: Assists in pulmonary function testing, oxygen therapy management, and patient education on pulmonary rehabilitation.
6. Nurse Specialist: Coordinates patient care, provides education on medications and self-management strategies, and serves as a point of contact for support.
7. Pharmacist: Ensures appropriate medication selection, dosing, and monitoring for ILD patients, minimizing drug interactions and adverse effects.
8. Social Worker: Addresses psychosocial factors, financial concerns, and caregiver support to enhance the holistic care of ILD patients.

Who Should Attend?

At least two respiratory physicians

At least one CT radiologist (experienced in ILD radiology)

At least one tissue pathologist (experienced in lung pathology)

External physicians, either in-person or via videoconferencing (if online)

At least one participant should have more than 5 years' experience in an ILD practice

Where it should be conducted?

Quiet setting - to enable uninterrupted discussion and encourage participation

When should MDM occur?

MDM should be conducted on Regularly scheduled meeting date and time

What technology is needed?

Visual projection system allowing real time viewing of HRCT images is must.

How Should the Meeting be Organized? A meeting coordinator to ensure all relevant information is available prior to each MDM and moderate the meeting.

Strategies should exist to prioritize urgent cases for discussion

Regular review of ILD MDM policies and protocols is also very important.

What Information is Required for each case?

1. Thorough clinical history (one slide), good quality HRCT scan and autoimmune serology (Figure: 1)
2. Serial PFTs (including DLCO)
3. Histopathology images for patients who have undergone lung tissue sampling
4. Pre-meeting review of radiology and pathology (where indicated by MDD experts)
5. Preparation Prior to the MDM

Core Data Required

Following information should be collected for the cases to be discussed in advance and should be put in pre-specified unified format for each case prior to the MDM. (Figure: 2)

- Comprehensive clinical history and physical examination findings
- History of smoking, Occupational, environmental, drug or other exposures known to be associated with HP or occupational lung disease
- Family history of pulmonary fibrosis or autoimmune disease
- Symptoms and signs suggestive of underlying CTD

Core Outputs of MDD

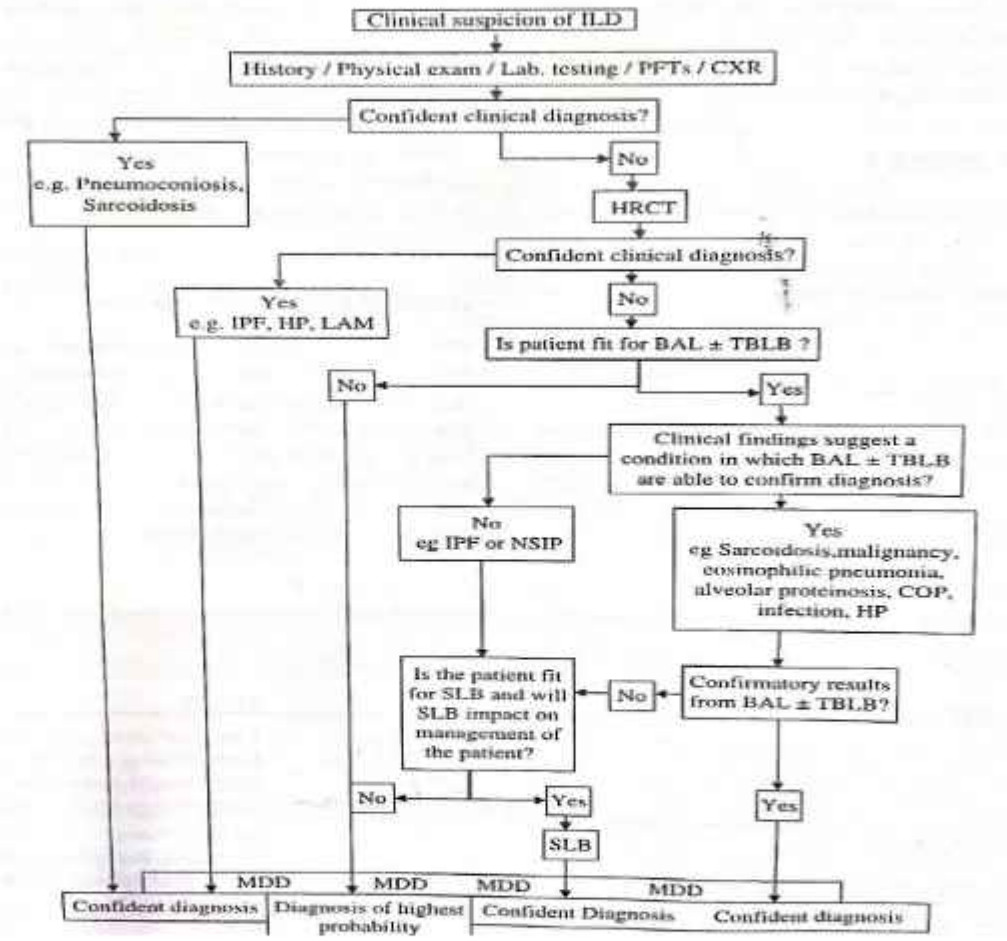
After each MDM the following outcomes to be documented.

1. Consensus (Working) ILD diagnosis
2. Degree of diagnostic confidence
3. Differential diagnoses (if any)
4. Expected disease behavior
5. Suggested management plan: including need for additional investigations - BAL, TBLC, or surgical lung biopsy

Consensus diagnosis is very essential for any ILD MDM. The moderator needs to make every effort to achieve it. The 'loudest' voice shouldn't 'win'! If there isn't consensus

and there are strong opposing views among the experts, these need to be *documented* and conveyed to and discussed with the patient

Figure 4. 2. Algorithm for diagnosis of ILD



3. Treatment of Interstitial Lung Disease (ILD)

Interstitial Lung Disease (ILD) represents a diverse group of disorders characterized by inflammation and fibrosis of the lung interstitium. These diseases can lead to progressive lung damage, compromised respiratory function, and decreased quality of life. Treatment strategies for ILD are tailored to the specific subtype of the disease, its underlying cause, and individual patient factors. This comprehensive review covers the treatment options for various ILD subtypes, including Idiopathic Pulmonary Fibrosis (IPF), Nonspecific Interstitial Pneumonia (NSIP), Hypersensitivity Pneumonitis (HP), Sarcoidosis, and Connective Tissue

Disease-Associated ILD (CTD-ILD). The review also discusses emerging therapies and future directions in ILD treatment.

Idiopathic Pulmonary Fibrosis (IPF)

Overview

Idiopathic pulmonary fibrosis (IPF) is a chronic, fibrosing interstitial pneumonia of unknown etiology that is associated with radiological and histologic features of usual interstitial pneumonia (UIP). It occurs primarily in older adults and is characterized by progressive worsening of dyspnea and lung function. Generally, it is associated with poor prognosis and treatment options revolves around prevention of progression of fibrosis and control of symptoms. Treatment options include pharmacological and non-pharmacological modalities aimed at primary disease process and associated comorbidities.

Pharmacological Treatments

Antifibrotic Agents

Currently two antifibrotics are approved for the treatment of IPF: Pirfenidone and Nintedanib.

Pirfenidone

Pirfenidone is an oral medication with antifibrotic, anti-inflammatory, and antioxidant properties. It inhibits fibroblast proliferation and collagen synthesis, primarily through regulation of TGFβ. Clinical trials with pirfenidone showed a benefit on the primary endpoint FVC decline over 1 year in IPF patients. A relative benefit of pirfenidone on the composite endpoint of death or disease progression (driven primarily by FVC), but not on dyspnea or mortality, was also observed. It is generally administered at a dose of 1800-2400 mg/day in divided doses.

Most common adverse effects associated with pirfenidone include gastrointestinal symptoms (primarily nausea) and skin-related events (rash and photosensitivity) and are two- to sixfold more common in patients treated with pirfenidone compared with placebo. Reduction of drug dosage, dietary modifications, and skin protection are widely used strategies to manage adverse effects.

Nintedanib

Nintedanib is an oral antifibrotic agent that inhibits multiple tyrosine kinases involved in fibrosis, such as platelet-derived growth factor receptor (PDGFR), fibroblast growth factor receptor (FGFR), and vascular endothelial growth factor receptor (VEGFR). Clinical trials with nintedanib showed approximately 50% less decline in FVC compared with placebo. In addition, reduction in acute exacerbation and improvement

in patients' quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ), was also observed. The drug is administered at a dose of 150 mg twice daily.

Diarrhea is the major adverse effect of nintedanib and affects about two-thirds of patients. Diarrhoea is observed due to dysfunction in water absorption and secretion in the intestinal lumen and is partially mediated by increased activity of the chloride channel in the luminal membrane of enterocytes. Nintedanib-associated diarrheas can be effectively controlled with loperamide, an opioid-receptor agonist. Reported side effects also include nausea, vomiting, and weight loss. In addition, elevated liver enzymes were observed in approximately 5% of nintedanib-treated patients compared with <1% of placebo-treated patients. Dose reduction to 100 mg twice daily, dietary modification, temporary discontinuation, and rechallenging with a lower dose are widely used strategies to successfully manage adverse effects.

Combination of Antifibrotics in IPF

Two clinical trials tried to address the clinical issues with the combination of antifibrotics in IPF. The studies suggested a potential role for this combination but were not powered to assess for efficacy. Since definite clincal data on efficacy is lacking as of now, the combination therapy with dual antifibrotics is advised only as a part of clinical trial.

Antacid medications:

Antacid medications should not be used for treating patients with IPF for the purpose of improving respiratory outcomes. Studies reveal conflicting data on the efficacy of antiacid treatment in patients with IPF with some reporting lesser mortality whereas others have not found significant improvement.

Corticosteroids

Historically, corticosteroids like prednisone have been used to manage IPF. **Currently there is no evidence to support the routine use of corticosteroids alone in the management of idiopathic pulmonary fibrosis.** However, corticosteroids may be used in specific situations, such as acute exacerbations of IPF.

Non-Pharmacological Treatments

Oxygen Therapy

Supplemental oxygen is used to manage hypoxemia, a common complication of advanced IPF. Oxygen therapy can improve exercise tolerance, reduce dyspnea, and enhance quality of life. However, studies evaluating supplemental oxygen in ILD patients experiencing exertional hypoxemia are lacking.

Pulmonary Rehabilitation & Nutritional support

Pulmonary rehabilitation programs include exercise training, breathing techniques, and education on disease management. These programs aim to improve physical function, reduce symptoms, and enhance overall quality of life. Though pulmonary rehabilitation resulted in improvements in individuals with ILD, the quality of evidence was deemed low-to-moderate due to concerns regarding study methodology.

Nutritional Support & Vaccination

Proper nutrition is crucial for IPF patients, particularly those experiencing weight loss or muscle wasting. Nutritional counseling can help maintain weight, support physical function, and improve overall health. Influenza and pneumococcal vaccination are recommended for individuals with IPF.

Lung Transplantation & Palliative care

Lung transplantation is considered for IPF patients with progressive disease despite optimal medical management. Criteria include advanced disease, a decline in FVC, desaturation on exertion and absence of contraindications such as significant comorbidities.

Studies have demonstrated that palliative care can improve management of symptoms, improve health-related quality of life, and end-of-life care for individuals with IPF, leading to reduced incidence of critical events, hospitalization, and overall healthcare expenditures. It is essential to address goals of care early in the process due to poor outcomes associated with mechanical ventilation.

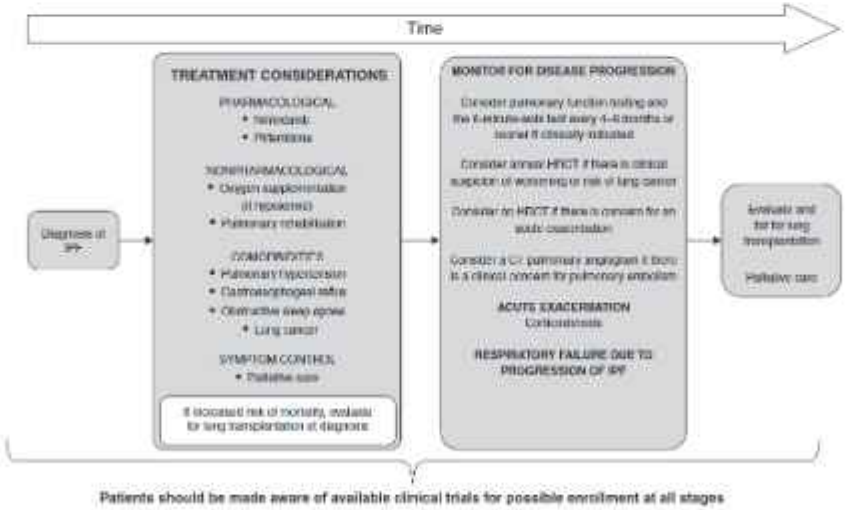


Figure 3: Raghu G, Remy-Jardin M, Richeldi L, Thomson CC, et al. Idiopathic Pulmonary Fibrosis (an Update) and ProgressivePulmonary Fibrosis in Adults. Am J Respir Crit Care Med. 2022 May 1;205(9):e18-e47.

Acute exacerbation of IPF

Acute exacerbations can occur in IPF, leading to a rapid decline in lung function. When suspected, it is pivotal to rule out other close differential diagnoses like heart failure, pneumothorax, pneumonia, and pulmonary embolism. Imaging during acute exacerbations may reveal ground-glass opacities and consolidations. IPF primarily affects the lungs, with no observed involvement of other organs. The disease progression varies among patients, with some remaining stable for years after diagnosis, others experiencing rapid decline, and some having periodic exacerbations that contribute to declining lung function and increased mortality. So further studies are needed to identify the different clusters or phenotypes among IPF patients.

Baseline lung function at diagnosis, the presence of comorbidities (especially coexisting emphysema and pulmonary hypertension), smoking history, low BMI (Body mass index), and older age are associated with a worse prognosis. Monitoring the disease progression typically involves regular evaluations, usually every 3 to 6 months or more frequently as needed, to assess for worsening symptoms such as dyspnea and oxygenation. This monitoring process includes assessing symptoms such as dyspnea and oxygenation, as well as conducting a 6-minute walk test and PFTs to provide more objective data on the disease's progression.

Palliative care with a focus on progressive end-stage fibrotic ILD is highly advised. Studies have demonstrated that palliative care improves symptom management, health-related quality of life, and end-of-life care for individuals with IPF, leading to reduced incidence of critical events, hospitalization, and overall healthcare expenditures. Given the association of mechanical ventilation with poor outcomes, it is essential to address goals of care early in the process.

Complexities of IPF management and its comorbidities:

Navigating the complexities of IPF, a disease with potentially life-limiting symptoms, requires early diagnosis and a multidisciplinary approach.

- Interdisciplinary management often involves collaboration among various specialists, including pulmonologists, chest radiologists, thoracic surgeons, rheumatologists, and pathologists.
- Patients with IPF benefit from referral to an ILD specialty clinic for discussions regarding antifibrotic drug therapies and timely consideration for lung transplant.

- Given the increased risk of CAD and acute coronary syndrome in these patients, cardiac calcification scores or other risk stratification measures should be considered as part of their comprehensive care.
- All patients should undergo screening for obstructive sleep apnea, GERD, and hypothyroidism, with appropriate treatment initiated as necessary.
- Given the progressive nature of lung disease, it is imperative to address advanced care plans and end-of-life issues proactively.

Hypersensitivity Pneumonitis (HP)

Overview

Hypersensitivity Pneumonitis (HP) is an immune-mediated lung disease caused by exposure to inhaled organic antigens. The disease can be acute, subacute, or chronic, and treatment primarily involves identifying and avoiding the offending antigen.

Pharmacological Treatments

Corticosteroids

Corticosteroids are used to manage acute exacerbations and inflammation in HP. They help to reduce the inflammatory response and improve symptoms. Oral corticosteroids for 4–12 weeks are considered as appropriate treatment option for patients with acute/subacute hypersensitive pneumonitis. Generally, prednisolone is initiated at 1 mg/kg body weight and it is tapered to 0.25 mg/kg body weight over weeks to months. There is a lack of evidence pertaining to duration and dose of corticosteroids for long-term therapy in HP. Long-term use is avoided unless the patient has persistent symptoms despite antigen avoidance.

Immunosuppressive Agents

In cases of chronic HP that do not respond to corticosteroids or where there is a progressive course, immunosuppressive agents such as azathioprine or mycophenolate mofetil (MMF) may be used. These agents help to control inflammation and prevent further lung damage.

Azathioprine is given at a dose of 50 mg twice a day and may be associated with cytopenias, nausea and vomiting. Dose of MMF is 1.5 to 3 gm/day and dose limiting side effect include diarrhoea and leukopenia.

Antifibrotics:

Though antifibrotics are not considered the primary pharmacological treatment for hypersensitive pneumonitis, they may be considered when the disease meets the criteria for progressive pulmonary fibrosis. Data from INBUILD trial which involved 663 patients with fibrosing ILDs other than IPF who met criteria for ILD progression

within the previous 2 years despite management, administration of nintedanib slowed the rate of decline in FVC (mL·year−1) over 52 weeks by 57% compared with placebo. The risk of an acute exacerbation of ILD or death was also reduced in the nintedanib group. In this study, patients with fibrotic HP comprised 173 (26%) of the enrolled patients. Subgroup analyses suggested that the rate of FVC decline, the effect of nintedanib on reducing the rate of FVC decline, and the adverse events associated with nintedanib were consistent across subgroups based on ILD diagnosis.

Though the study was prematurely terminated due to low recruitment, an analysis of data from the 127 patients enrolled, of whom 57 had HP, demonstrated a smaller decline in FVC % predicted over 48 weeks in patients who received pirfenidone compared with placebo in the RELIEF study indicating a potential role of this drug in treatment.

Non-Pharmacological Treatments

Antigen Avoidance

The most critical aspect of managing HP is the identification and avoidance of the offending antigen. This may involve changes in occupational or environmental exposures. Inability to identify the inciting antigen is associated with worse survival.

Pulmonary Rehabilitation and Nutritional Support

Pulmonary rehabilitation and nutritional support can help manage symptoms and improve overall quality of life in HP patients, particularly those with chronic disease.

Lung Transplantation

Lung transplant improved survival in select patients with progressive fibrotic ILDs. Among 31 patients with HP who underwent lung transplantation at a single US centre between 2000 and 2013, 1-, 3- and 5-year survival rates were 96%, 89% and 89%, respectively.

Sarcoidosis

Sarcoidosis is a granulomatous disease that can affect various organs, including the lungs. The lung involvement can range from asymptomatic to severe respiratory impairment. The course of the disease is variable, with some patients experiencing spontaneous resolution while others may develop chronic lung disease. The decision to treat pulmonary sarcoidosis is influenced by symptom severity, quality of life impairment, risk of progression, organ dysfunction and propensity for spontaneous remission.

Pharmacological Treatments

Corticosteroids

Corticosteroids are the primary treatment for symptomatic sarcoidosis, particularly when there is significant lung involvement. Prednisone is commonly used and can help to reduce inflammation and improve symptoms. Long-term treatment is generally reserved for patients with persistent or progressive disease. The optimal dosage and duration of glucocorticoid therapy is unknown and are guided by expert opinion and consensus guidelines. Though prior recommendations suggest initial treatment with prednisone or its equivalent at a dose of 20–40 mg/day for 4–6 weeks, latest ERS guidelines favors the initial dose of 20 mg/day. General recommendation is to taper glucocorticoids to the lowest effective maintenance dose or consideration for steroid sparing or replacement therapy in efforts to minimize toxicity associated with steroids. Duration of treatment varies widely in clinical practice and may range from 2 to 24 months.

Disease-Modifying Antirheumatic Drugs (DMARDs)

Agents: For patients with refractory sarcoidosis or those who cannot tolerate corticosteroids, DMARDs such as methotrexate or hydroxychloroquine may be used. In addition, other immunomodulators like azathioprine, mycophenolate mofetil, lefluonamide have also been tried. TNF – alpha inhibitors like infliximab, adalimumab and golimumab are reserved as third-line agents for use in patients whose disease is refractory to second-line agents. These agents help to reduce inflammation and modulate the immune response.

Antifibrotics:

In the INBUILD study, only 12 patients in the study cohort of 663 patients had pulmonary sarcoidosis. Though there may be a role for anti-fibrotic therapy in stage IV sarcoidosis, the small cohort size in the INBUILD study obscures the definitive role of anti-fibrotic therapy specifically in stage IV sarcoidosis.

Non-Pharmacological Treatments

Observation

In many cases, particularly with asymptomatic or mild sarcoidosis, observation may be appropriate as the disease can resolve spontaneously. Regular monitoring is essential to detect any progression.

Pulmonary Rehabilitation and Nutritional Support

Pulmonary rehabilitation and nutritional support can improve quality of life and physical function in patients with significant respiratory symptoms or complications.

Palliative Care, Oxygen Therapy and lung transplantation may be considered for end stage refractory sarcoidosis patients.

Nonspecific Interstitial Pneumonia (NSIP)

Overview

Nonspecific Interstitial Pneumonia (NSIP) is a form of interstitial lung disease characterized by inflammation and fibrosis of the lung interstitium. Unlike IPF, NSIP may be associated with autoimmune diseases or occur idiopathically. The disease can be divided into inflammatory and fibrotic phases, and treatment strategies often depend on the dominant phase.

Pharmacological Treatments

Corticosteroids

Corticosteroids are often the first-line treatment for NSIP, particularly during the inflammatory phase. They can help reduce inflammation and improve symptoms. The response to corticosteroids can also guide further management. Common corticosteroids used include prednisone, which is typically tapered based on clinical response and tolerability. Pneumocystis jirovecii pneumonia (PJP) prophylaxis should be considered in those patients on greater than 20 mg prednisone daily for more than 1 month, or those on multiple immunosuppressive agents, as this infection may significantly worsen lung function.

Immunosuppressive Agents

For NSIP that does not respond adequately to corticosteroids, or for those with a fibrotic component, immunosuppressive agents like azathioprine or mycophenolate mofetil may be used. These agents help to modulate the immune response and reduce inflammation and fibrosis. Their use is guided by individual patient factors and response to therapy.

Antifibrotic Agents

While not the primary treatment for NSIP, antifibrotic agents like pirfenidone and nintedanib may be considered if fibrosis progresses despite corticosteroid therapy.

Non-Pharmacological Treatments

Oxygen Therapy and Pulmonary Rehabilitation

Indications: Similar to IPF, supplemental oxygen and pulmonary rehabilitation are beneficial for managing symptoms and improving quality of life in NSIP patients.

Nutritional Support

Maintaining adequate nutrition is crucial for patients with NSIP, especially if there is significant weight loss or muscle wasting.

Emerging Therapies and Future Directions

New Pharmacological Agents

- **JAK Inhibitors:** Research into Janus kinase (JAK) inhibitors, such as tofacitinib, is ongoing. These agents may offer new treatment options by targeting specific inflammatory pathways involved in ILD.
- **New Antifibrotic Agents:** Development of new antifibrotic drugs and combination therapies aims to enhance treatment efficacy and minimize side effects.

Personalized Medicine

- **Genomics and Biomarkers:** Advances in genomics and biomarker discovery are paving the way for more personalized treatment strategies. Identifying specific disease mechanisms and patient profiles may lead to targeted therapies that improve outcomes.

Clinical Trials

- **Innovative Therapies:** Participation in clinical trials offers access to cutting-edge therapies and contributes to the advancement of ILD management. Ongoing research explores novel drug classes, combination therapies, and novel approaches to disease modification.

CTD ILD

Connective tissue diseases (CTD) are a group of immune mediated systemic inflammatory disorders with circulating auto-antibodies and heterogeneous manifestations leading to multi-organ dysfunction. These include Systemic sclerosis (SSc), Sjogren's disease, (SjD), Systemic Lupus Erythematosus (SLE), Rheumatoid arthritis (RA), Mixed Connective tissue disease (MCTD) and Idiopathic inflammatory myopathies (IIM). In addition to these, a brief description of ILD associated with ANCA vasculitis and IPAF will also be included here. While pulmonary involvement is a target in all CTDs and can be multi compartmental, the involvement of the interstitium in the form of ILD is common.

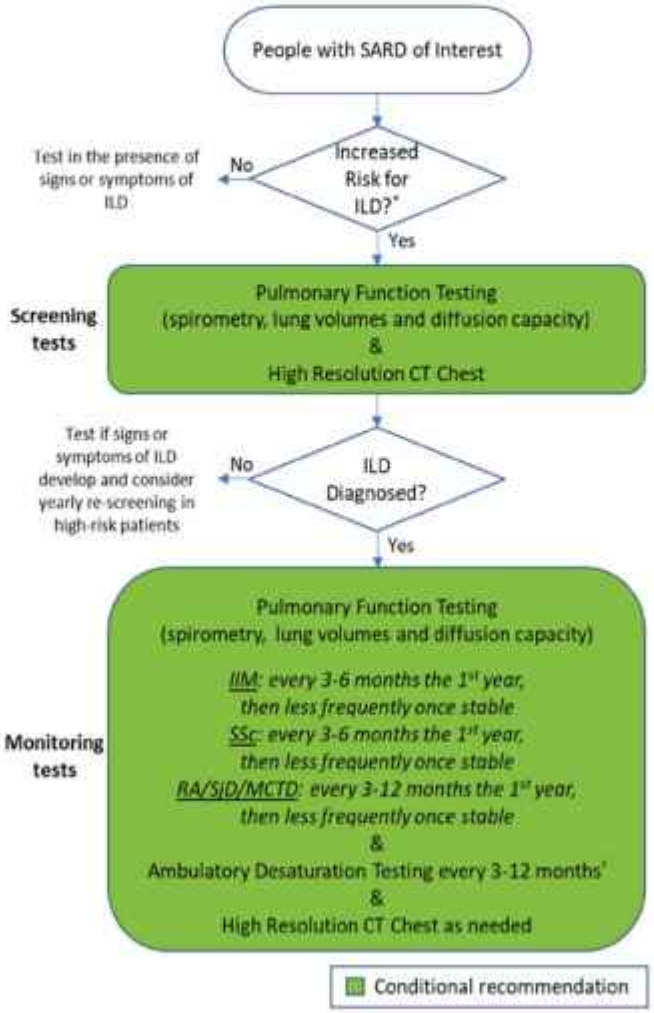
Screening guidelines

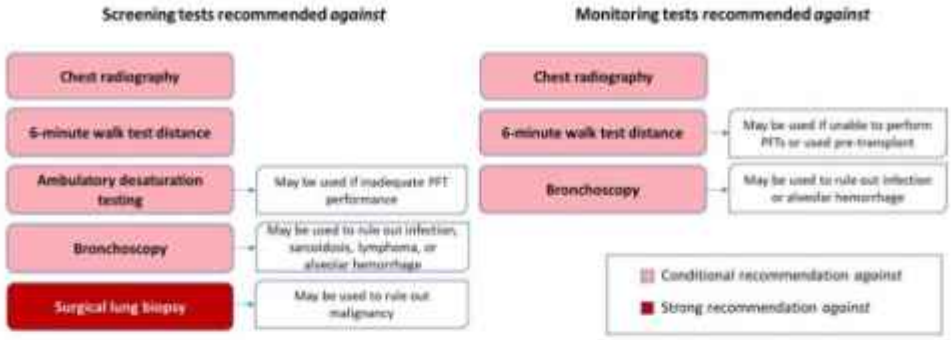
The American College of Rheumatology (ACR) in 2023 released screening and monitoring guidelines for ILD in patients with Systemic auto immune rheumatic

disease (SARD). The nomenclature SARD-ILD has been used in these guidelines instead of CTD-ILD.

Screening recommendations include PFTs and HRCTs over HRCT alone and the use of PFTs, HRCT thorax and ambulatory desaturation testing for assessing progression of ILD

Figure: 4.3 ILD screening and monitoring tests recommended against (Reproduced with permission the American College of Rheumatology





Treatment

Treatment of ILD in patients with CTD is generally initiated if there is significant disease at presentation or if there is evidence of disease progression manifesting as any combination of symptomatic worsening, radiologic or physiologic deterioration over time.

Other than symptomatic disease, treatment is initiated if there is

i)>/=10 % relative dip in FVC or

ii)>/=5% to < 10 % relative dip in FVC and >/=15% decline in DLCO or

iii) Absolute FVC < 70 % or

iv) > 20 % of the lung is involved on HRCT

The pattern of ILD may also predict the patient's response to treatment with the more inflammatory patterns responding better to immunosuppression than the more fibrotic patterns.

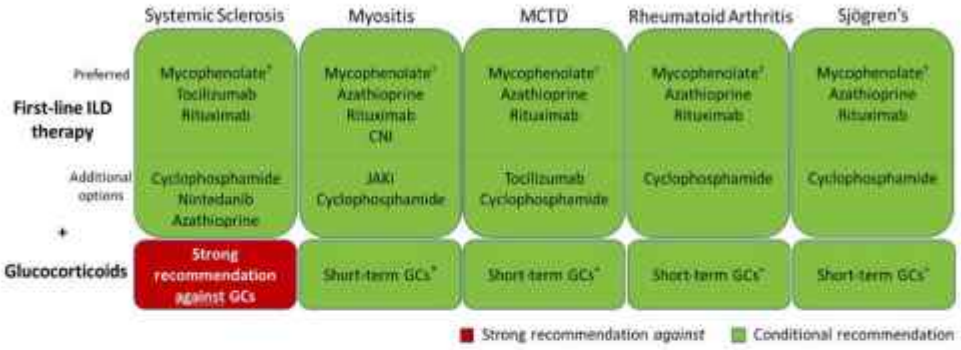
Corticosteroids: The usage and dosage of corticosteroids depends on the underlying CTD. In RA-ILD and MCTD-ILD, steroids are used in low to moderate doses with 0.5mg/kg / day, the usual dose at initiation. Higher doses of 1mg / kg / day can be considered in IIM-ILD. In IPAF, the pattern of ILD (NSIP and LIP respond better to corticosteroids than UIP) and presence of other autoimmune features determine corticosteroid use. In SSc - ILD, pulse steroids and prolonged corticosteroid use > 10 mg / day are avoided on account of the risk of precipitating a scleroderma renal crisis.

ACR treatment guidelines

ACR has also released evidence-based treatment guidelines for the management of adult patients with SARD - ILD (SSc, IIM, MCTD, SjD and RA).

Summarised in the following figures are the first line treatment options in CTD - ILD and the treatment for progressive ILD and RP-ILD.

Figure: 4.4 showing Recommendations for the management of SARD – ILD (First line ILD treatment) (reproduced with the permission of the American College of Rheumatology



CTD - ILD is challengingly heterogeneous and is associated with significant morbidity and mortality. A careful balance has to be struck between adequate immunosuppression and the risk of infection. A collaborative multidisciplinary effort between different specialities helps in early diagnosis and individualized treatment and the future lies in personalised precision medicine.

Pulmonary hypertension in ILD:

Pulmonary Hypertension (PH) encountered in patients with chronic lung disease is categorized as Group III PH. It is the second most frequent cause of PH, following PH due to Left heart Disease. It is not an uncommon association in patients with Fibrotic-Interstitial Lung Diseases (ILD), the commonest being IPF. The majority of PH-ILD is included in Group III and is related to the worsening parenchymal involvement and subsequent hypoxia. However, given the diversity of potential pathological mechanisms leading to PH, pulmonary hypertension, associated with sarcoidosis and pulmonary Langerhans cell histiocytosis is currently classified in group V, i.e., with unclear and/or multifactorial mechanisms. The prevalence of PH in ILD varies between 3.5–15% at an early stage, 30–50% at the time of advanced disease, and 60–90% in patients listed for lung transplantation. Classically WHO group III PH due to ILD is associated with the greatest morbidity and mortality and hence early detection is paramount to improving outcomes in this subgroup.

The PH in patients with ILD is generally mild/moderate, with only a small minority developing severe PH (mPAP ≥35 mmHg/PVR > 5 WU). Hence when encountering severe PH, alternative causes of PH such as Left Heart failure, thromboembolic disease, Sleep disordered breathing, obesity hypoventilation or underlying COPD contributing to PH need to be considered.

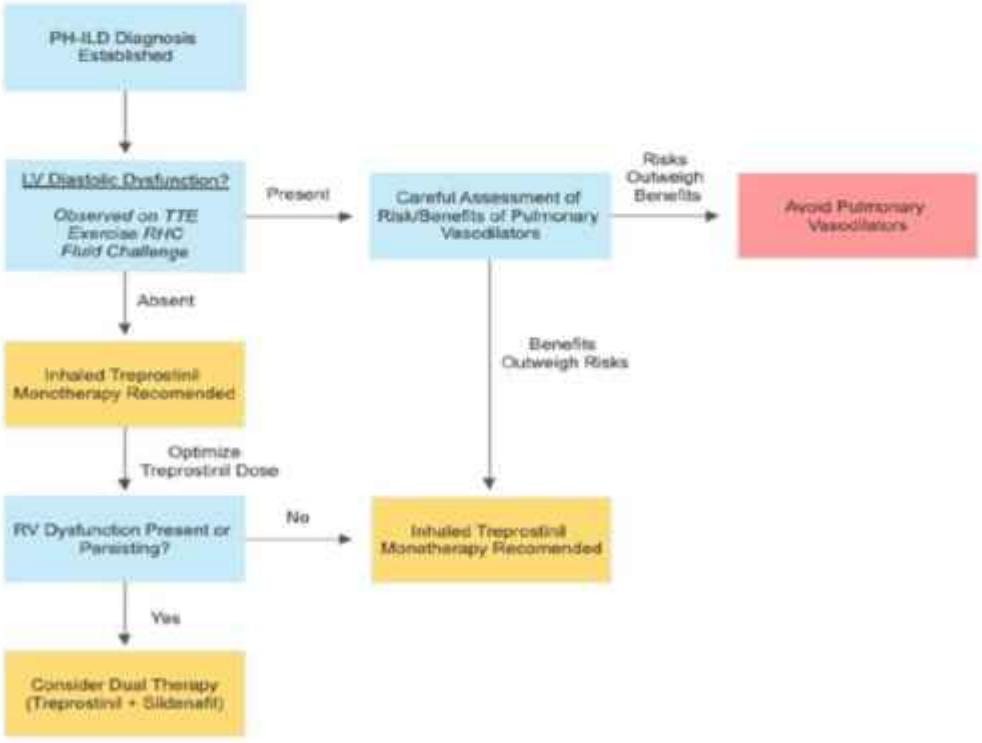
Screening & Diagnosis

Generally, a transthoracic echocardiography (TTE) is the screening tool of choice and should be asked for in each patient of ILD who is deemed to be at risk of developing PH on basis of history, clinical examination, findings on exercise testing, PFT and Imaging. Also, in patients with an established diagnosis, TTE should be repeated annually at least. Serial screening is the norm given the progressive nature of ILDs.

Confirmation Of Diagnosis

Although TTE is a good screening tool, the accuracy of echocardiographic assessment is insufficient to confirm diagnosis of PH in patients with ILD. The poor echo window in patients with chronic respiratory diseases also contributes to the difficulties in precise TRV measurement. In a study on lung transplant candidates with ILD, only modest correlation was found between pulmonary artery systolic pressure (PASP) calculated from TRV on Echocardiography and measured directly during Right heart catheterization (RHC) ($r = 0.609$; $p < 0.01$). Echocardiography overestimated or underestimated PASP in 35% and 11.6% of patients, respectively.

Figure 4.5 Flowchart showing diagnosis and management of PH- ILD



Clearly in the last decade, with improved understanding of the intricacies of disease process, huge strides have been made in the management of patients with PH-ILD, and the prognosis of this dreaded condition which was once miserably poor, is now steadily improving.

ILD presenting with acute respiratory failure

The two most common scenarios in which ILD presents with acute respiratory failure are

1. Rapid deterioration in a patient with previously diagnosed ILD. Eg: acute exacerbation of IPF
2. Initial presentation with rapidly progressive disease.

Eg: acute interstitial pneumonia, fulminant COP

Decision on admission to ICU

On a case-by-case basis.

Compare previous CXRs and HRCT; Evidence of extensive fibrotic change or a pattern of disease typical of IPF usually indicates that invasive ventilation is highly unlikely to have a successful outcome.

Pre-emptive counselling of patients that palliation or non-invasive supportive therapy rather than invasive ventilation is appropriate is an important component of management.

In management of pre-existing ILD, **non ILD processes such as pulmonary oedema, malignancy, drug induced lung disease and infection** has to be excluded.

Pharmacological management

- Intravenous corticosteroid therapy is the initial treatment of choice.
  - Methyl prednisolone 750mg or 1g given on three consecutive days and maintanence therapy of 0.5-1mg/kg depending on clinical response.
  - Assess response after 5-7 days.
- Intravenous cyclophosphamide- second line.
  - Dose: 600-650mg/m2
- In suspected vasculitis – IV cyclophosphamide first choice.

Summary of General principles of management:

- To maintain a healthy weight and engage in regular physical exercise. Pulmonary rehabilitation can be utilized for formal exercise training.
- To ensure vaccinations for influenza, pneumococcus, and COVID-19, as individuals with IPF have reduced lung reserve to tolerate respiratory infections.

- All patients with ILD should have access to **a multidisciplinary** team based in a regional centre with expertise in ILD.
- Patients with ILD who are current smokers should receive opportunistic **smoking cessation** advice from healthcare professionals and this advice should be recorded in the clinical notes.
- Patients with ILD should have access to a local **pulmonary rehabilitation programme.**
- Patients with clinically significant resting hypoxemia (resting SpO2<88%) should receive **long term oxygen therapy.**

Follow up

Follow up of ILD patients is recommended every 3 -6 months with clinical assessment, spirometry, DLCO and 6MWT.Timing of follow up HRCT to be decided by the treating physician.

Rare ILDs

Cystic interstitial lung diseases

Cystic lung disease (CLD) is a group of lung disorders characterized by the presence of multiple cysts, defined as air-filled lucencies or low-attenuating areas, bordered by a thin wall (usually < 2 mm). The Cystic lung diseases are lymphangioleiomyomatosis, pulmonary Langerhans cell histiocytosis, Birt-Hogg-Dube syndrome, lymphocytic interstitial pneumonia/follicular bronchiolitis, and amyloidosis.

Lymphangioleiomyomatosis

This multisystemic, progressive disorder primarily affects the lungs of females of childbearing age. LAM can develop both sporadically (S-LAM) and genetically in patients with tuberous sclerosis complex (TSC-LAM). On HRCT, LAM cysts are typically round and small (usually 2 to 5 mm but as large as 30 mm), without zonal predominance. Pathologically, abnormal smooth muscle-like LAM cells proliferate and result in cystic changes in the lungs and axial lymphatics and angiomyolipomas in the kidney or liver. The management of LAM includes treatment of the pulmonary lesion and control of the concomitant problems. Airflow obstruction is relieved using bronchodilators. Recurrent pneumothorax can often be controlled with pleurodesis. Renal angiomyolipomas > 4 cm have an increased risk of bleeding and should be treated with embolization, nephron-sparing surgery, or an mTOR inhibitor. Sirolimus, an mTOR antagonist, has been associated with improvements in patients with a forced expiratory volume in 1 second (FEV_1) < 70%.

Pulmonary Langerhans cell histiocytosis

This is another rare disease that is predominantly identified in young adults (typically < 40 years of age) but also in cigarette smokers, without a sexual predilection. The clinical presentation of PLCH varies, from asymptomatic to shortness of breath, coughing, weight loss, fever, pneumothorax (15%), skin rash, and diabetes insipidus. The most common CT findings in PLCH are cysts and nodules, predominantly in the upper and middle lobes, with almost complete sparing of the costophrenic angles. The cysts are often bizarre, in contrast to the round-shaped cysts in LAM or BHD. As the disease progresses, nodules gradually lead to cavitation. Due to the rareness of PLCH, treatment is not standardized, although smoking cessation can be a primary intervention.

Birt-Hogg-Dube syndrome

This rare disease has an autosomal dominant inheritance pattern and involves multiple areas of the body, including hair follicle tumors, renal neoplasm, and pulmonary cysts. BHD syndrome is seen in patients in their fourth and fifth decades of life, without a difference in males versus females. Pneumothorax is (typically) recurrent in 75% of BHD syndrome patients. On HRCT, the cysts in BHD syndrome are multiple, thin-walled, round or lentiform, and well defined. Along with lung manifestations, potential skin and renal involvement should be meticulously examined.

Lymphocytic interstitial pneumonia (LIP)/follicular bronchiolitis (FB)

LIP is an extremely rare disorder with diffuse involvement of the lung parenchyma by reactive lymphoid tissues, whereas FB is characterized by a lymphoid follicular hyperplasia centered on the airway, vessels, and interlobular septa and presenting as a lymphatic distribution but lacking extensive alveolar septal infiltration. The lymphatic distribution in the lung parenchyma may be idiopathic or a secondary to Sjogren's disease or Human Immunodeficiency Virus (HIV) infection. On HRCT, the cysts in LIP or FB are randomly distributed, have an internal structure, measure < 30 mm in diameter, and are typically fewer than in LAM. They frequently accompany GGOs, centrilobular nodules, or septal thickening. The natural history of LIP or FB remains unclear, and the efficacy of immunosuppression, including glucocorticoid as treatment, has yet to be confirmed.

Amyloidosis

Amyloidosis is an extremely rare and heterogeneous group of disorders characterized by the deposition of a specific protein (amyloid) in extracellular spaces in an abnormal fibrillary fashion. CT findings include multiple nodules that may be cavitated (4 to 45 mm in diameter) or calcified (> 1 cm). The cysts are usually multiple, round, and have thin walls (< 2 mm), with a small to moderate size, up to 1 to 2 cm. The typical apple-

green birefringence on Congo red staining originates from the fibrillary deposits in the lung. There is currently no established curative therapy.

Smoking related Interstitial Lung Diseases

Smoking-related interstitial lung diseases (SR-ILDs) are a heterogeneous group of diseases with major clinical significance. Smoking-related interstitial lung disease embraces the following entities:

- Pulmonary Langerhans cell histiocytosis (PLCH)
- Respiratory-bronchiolitis—associated interstitial lung disease (RB-ILD)
- Desquamative interstitial pneumonia (DIP)

Respiratory bronchiolitis-associated interstitial lung disease

Respiratory bronchiolitis is an expression of the chronic inflammatory response to inhalation of tobacco smoke and can be demonstrated in all smokers. If the changes are sufficiently pronounced to be discernible on diagnostic imaging, then the respiratory bronchiolitis is accompanied by interstitial lung disease, which may become symptomatic. HRCT in RB-ILD shows bronchiolocentric interstitial ground-glass opacifications, accentuated in the upper part of the lung. Beyond giving up smoking, no specific treatment is required, because the prognosis is very good.

Desquamative interstitial pneumonia

Desquamative interstitial pneumonia is related to smoking in over 90% of cases. HRCT IN DIP shows increased interstitial ground-glass and partly reticular patterns with geographical distribution. Untreated, around two thirds of patients with DIP show disease progression; however, spontaneous improvement has also been described. The mortality of DIP ranges from around 6 to 28%. The patient should be strongly advised to stop smoking. Administration of systemic corticosteroids usually achieves stabilization, rarely improvement.

Prognosis and Future Directions

The prognosis of ILD varies widely depending on the specific type and severity of the disease. IPF has a particularly poor prognosis, with a median survival of 3-5 years from the time of diagnosis. Early and accurate diagnosis, along with appropriate management, can significantly impact the course of the disease. Research is ongoing to better understand the pathogenesis of ILD and to develop more effective therapies. Advances in genetics, molecular biology, and imaging techniques hold promise for earlier diagnosis and personalized treatment approaches.

Conclusion

Interstitial Lung Disease encompasses a broad spectrum of lung disorders that can lead to significant morbidity and mortality. A thorough understanding of the classification, pathogenesis, clinical presentation, diagnostic methods, and treatment options is essential for effective management. Continued research and advances in medical science are critical to improving outcomes for patients with ILD.

LUNG CANCER

Lung cancer

Lung cancer is usually managed by the oncologist in most institutions. Advanced centres use the services of tumour board for decision making in which a pulmonologist is a member. These guidelines are intended to provide information to the Pulmonologist on early diagnosis, management of complications and proper referral to the concerned specialist as well as assisting in management.

1. Introduction

Lung cancer is the most common cause of cancer death in the world. Tobacco smoking is most important among the modifiable risk factors for lung cancer. About 90% of lung cancers are caused by smoking. Now that fewer men smoke, lung cancer deaths in men have decreased by more than a quarter. However, the number of women who smoke has risen and deaths from lung cancer in women have increased. Lung cancers in never smokers even though account for a minority of lung cancer burden, the absolute numbers are substantial especially in women.

Only about 5.5% of lung cancers are currently cured. Although the cure rate is rising slowly, the rate of improvement has been slower than for other common cancers. There is evidence that outcomes vary in different countries, which among other factors may be explained by variations in the standard of care.

Lung cancer may be broadly divided into small cell lung cancer and non small cell lung cancer based on histo pathological examination.

Recommendations are included on communication, diagnosis and staging, selection of patients with non-small-cell lung cancer (NSCLC) for treatment with curative intent, treatment for small- cell lung cancer (SCLC) with curative intent, managing endobronchial obstruction, managing brain metastases, smoking cessation, and follow-up and patient perspectives.

Patient-centred care

People with lung cancer should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should interact with his close relatives.

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and

care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care. Families and carers should also be given the information and support they need.

2. Diagnosis and staging

- The development of newer tools to diagnose lung cancer at an early stage have got dramatic impact on lung cancer related outcomes.
- Choose investigations that give the most information about diagnosis and staging with least risk to the patient. Think carefully before performing a test that gives only diagnostic pathology when information on staging is also needed to guide treatment.
- Low dose computed tomography trials have shown reduced lung cancer mortality in high risk groups. It involves appropriate patient selection, considering potential harms and benefits and management of detected findings.
- Sputum cytology is rarely indicated and should be reserved for the investigation of patients who have centrally placed nodules or masses and are unable to tolerate, or unwilling to undergo, bronchoscopy or other invasive tests.
- An X-ray should be performed in the first instance for all patients presenting with symptoms and signs suggestive of a primary or metastatic tumour.
- Patients with known or suspected lung cancer should be offered a contrast-enhanced chest CT scan to further the diagnosis and stage the disease. The scan should also include the liver and adrenals and lower neck. Contrast to be used with caution in renal impairement.
- In the assessment of mediastinal and chest wall invasion CT alone may not be reliable. Surgical assessment may be necessary if there are no contraindications to resection.
- All people with lung cancer with potential for treatment with curative intent shall be offered PET-CT before treatment. Ideally a system for rapid access to PET-CT should be made available to eligible people.
- Magnetic resonance imaging (MRI) should not routinely be performed to assess the stage of the primary tumour (T-stage) in NSCLC. MRI should be performed, where necessary to assess the extent of disease, for patients with superior sulcus tumours3.
- EBUS-guided TBNA for biopsy of paratracheal and peri-bronchial intra-parenchymal lung lesions is a relatively safe choice. Ensure adequate samples are taken without

unacceptable risk to the patient to permit pathological diagnosis including tumour

sub-typing and measurement of predictive markers.

- CT- or ultrasound-guided transthoracic needle biopsy is done in patients with peripheral lung lesions when treatment can be planned on the basis of this test. Biopsy any enlarged mediastinal nodes (≥ 10 mm maximum short axis on CT) or other lesions in preference to the primary lesion if determination of stage affects treatment.
- Fibreoptic bronchoscopy is to be considered in patients with central lesions on CT where nodal staging does not influence treatment. Enlarged lymph nodes (≥ 10 mm maximum short axis on CT) may be simultaneously sampled with TBNA (non-ultrasound-guided) if required for diagnosis.
- PET-CT is the preferred first test after CT showing a low probability of mediastinal malignancy (lymph nodes 10 mm maximum short axis on CT) for patients who are potentially suitable for treatment with curative intent.
- Consider neck ultrasound with sampling of visible lymph nodes or non-ultrasound-guided TBNA to patients with a high probability of mediastinal malignancy (lymph nodes > 20 mm maximum short axis on CT). If neck ultrasound is negative, follow with non-ultrasound- guided TBNA, EBUS-guided TBNA or EUS-guided FNA. If non-ultrasound-guided TBNA is negative follow with EBUS-guided TBNA or EUS-guided FNA.
- Evaluate PET-CT-positive mediastinal nodes by mediastinal sampling (except when there is definite distant metastatic disease or a high probability that N2/N3 disease is metastatic [for example, if there is a chain of lymph nodes with high 18F-deoxyglucose uptake]).
- Confirm negative results obtained by EBUS-guided TBNA and/or EUS-guided FNA using surgical staging if clinical suspicion of mediastinal malignancy is high. [1B SSF]
- Confirm the presence of isolated distant metastases/synchronous tumours by biopsy or further imaging (for example, MRI or PET-CT) in patients being considered for treatment with curative intent. Consider MRI or CT of the head in patients selected for treatment with curative intent, especially in stage III disease. CE- CT may be done in NSCLC stage II under treatment with curative intent and if CT shows suspicion of brain metastasis. Contrast enhanced brain MRI may be suggested
- Dedicated brain MRI should not be suggested in NSCLC stage I without neurological symptoms and are being treated with curative intent.
- Cone Beam Computed Tomography (CBCT) has emerged as a valuable tool for the evaluation of pulmonary nodules. CBCT provides detailed visualization of small lung nodules.

- Pulmonologist should thrive to get maximum sample size , so that there will be enough material for molecular testing. Upfront molecular testing is recommended in all non squamous NSCLC, all non smoking NSCLC even if histology turns out to be squamous, mixed histology and in case of small primary biopsy specimen

Multidisciplinary teams

The care of all patients with a working diagnosis of lung cancer should be discussed at a lung cancer MDT meeting (Tumour board). Rapid access clinics should be provided where possible for the investigation of patients with suspected lung cancer, because they are associated with faster diagnosis and less patient anxiety.

3.Treatment

Smoking cessation

Inform patients that smoking increases the risk of pulmonary complications after lung cancer surgery. Advise patients to stop smoking as soon as the diagnosis of lung cancer is suspected and tell them why this is important. Offer nicotine replacement therapy and other therapies including Varenicline and behavioural therapy to help patients to stop smoking.

Assessment before radiotherapy

A clinical oncologist's in thoracic oncology should determine suitability for radiotherapy with curative intent, taking into account performance status and comorbidities.

Surgery for non-small-cell lung cancer

In patients with NSCLC who are medically fit and suitable for treatment with curative intent, lobectomy (open or thoracoscopic) is the treatment of first choice. For patients with borderline fitness and smaller tumours (T1a–b, N0, M0), consider lung parenchymal-sparing operations (segmentectomy or wedge resection) if a complete resection can be achieved. More extensive surgery (bronchoangioplastic surgery, bilobectomy, pneumonectomy) are considered only when needed to obtain clear margins. Perform hilar and mediastinal lymph node sampling or en bloc resection for all patients undergoing surgery with curative intent.

For patients with T3 NSCLC with chest wall involvement who are undergoing surgery, complete resection of the tumour should be the aim by either extrapleural or en bloc chest wall resection.

Radiotherapy for non-small-cell lung cancer

Radical radiotherapy is indicated for patients with stage I, II or III NSCLC who have good performance status (WHO 0,1) and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage.

Also radical radiotherapy with stereotactic ablativer adiotherapy (SABR) or sublobar resection, can be suggested for patients with Stage I to IIA who decline lobectomy or where it is contraindicated. I people in whom SABR is contraindicated, either conventional of hyperfractionated radical RT can be considered.

All patients should undergo pulmonary function tests (including lung volumes and transfer factor) before having radical radiotherapy for NSCLC. Patients who have poor lung function but are otherwise suitable for radical radiotherapy should still be offered radiotherapy, provided the volume of irradiated lung is small.

Chemotherapy for non-small-cell lung cancer

Chemotherapy should be offered to patients with stage III or IV NSCLC and good performance status (WHO 0,1 or a Karnofsky score of 80–100), to improve survival, disease control and quality of life.

Chemotherapy for advanced NSCLC should be a combination of a single third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine) plus a platinum drug. Either carboplatin or cisplatin may be administered, taking account of their toxicities, efficacy and convenience. Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy with a third-generation drug.

Docetaxel monotherapy should be considered if second-line treatment is appropriate for patients with locally advanced or metastatic NSCLC in whom relapse has occurred after previous chemotherapy.

Biological agents such as gefitinib or erlotinib may be considered for non-small-cell lung cancer having EGRF mutation detected in the histopathological specimen.

Combination treatment for non-small-cell lung cancer

Patients with stage I–III NSCLC who are not suitable for surgery need to be assessment by a clinical oncologist specialising in thoracic oncology for radiotherapy with curative intent. Consider chemoradiotherapy for patients with stage II or III NSCLC who are not suitable for surgery. Consider potential benefit in survival with the risk of additional toxicities before this treatment. 144

Consider postoperative chemotherapy in patients with good performance status (WHO 0 or 1) and T2–3 N0 M0 NSCLC with tumours greater than 4 cm in diameter. Offer a cisplatin-based combination chemotherapy regimen for adjuvant chemotherapy.

Ensure eligible patients have the benefit of detailed discussion of the risks and benefits of adjuvant chemotherapy.

Treat Pancoast tumours in the same way as other types of NSCLC. Offer multimodality therapy according to resectability, stage of the tumour and performance status of the patient.

To conclude

Non metastatic Non small cell carcinoma (NSCLC) is treated by (a) surgery followed by chemo, neoadjuvant chemo followed by surgery or sugery followed by concurrent chemo radio therapy (CCRT) or CCRT alone on a case to case basis.

In metastatic NSCLC without any driver mutation chemo+ immunotherapy is the preferred option

In metastatic NSCLC with driver mutation first line therapy is targeted therapy (eg Tyrosine kinase inhibitors in EGFR mutation) . If there is progression on targeted therapy, next preferred option is chemotherapy + immunotherapy.

Assessing patients with small-cell lung cancer

All patients with small-cell lung cancer (SCLC) should be assessed by a thoracic oncologist within 1 week of deciding to recommend treatment.

First-line treatment for limited-stage disease small-cell lung cancer

The small cell lung cancer patients may be categorized into limited stage disease and extensive stage disease. When the disease burden can be covered within a single radiation field, it is called a limited stage. Only one third of the cases at presentation will have limited stage. Disease which cant be covered within a single radiation field is called extensive stage.

Patients with limited-stage disease who are stage 1 (T1–2, N0, M0) is usually treated with surgery followed by adjuvant chemotherapy and other limited stages with concurrent chemoradiotherapy (CCRT). Extensive stage disease is treated by systemic therapy (chemo and immunotherapy) .

Surgical treatment for patients with small-cell lung cancer

Consider surgery in patients with limited -stage SCLC (T1–2, N0, M0), if medically fit.

First-line treatment for extensive-stage disease of small-cell lung cancer

Standard of care is chemotherapy and immunotherapy. Platinum-based combination chemotherapy is preferred in patients with extensive-stage disease SCLC (T1–4, N0–3, M1a/b – including cerebral metastases) if they are clinically fit. Assess the patient's

condition before each cycle of chemotherapy for extensive-stage disease SCLC and offer up to a maximum of six cycles, depending on response and toxicity.

For patients with extensive-stage disease SCLC, thoracic radiotherapy should be considered after chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax.

Immunotherapy options include Durvalumab/Atezolizumab, Pembrolizumab. Immunotherapy is continued as maintenance till the patient can tolerate or disease progression

Prophylactic cranial irradiation in small-cell lung cancer

Prophylactic cranial irradiation is offered at a dose of 25 Gy in 10 fractions to patients with limited-stage disease SCLC and WHO performance status 2 or less, if their disease has not progressed on first-line treatment. Prophylactic cranial irradiation is given to patients with extensive-stage disease SCLC and WHO performance status 2 or less, if their disease has not progressed on first-line treatment.

Second-line treatment for patients with small-cell lung cancer that has relapsed after first-line treatment

SCLC that has relapsed after first-line treatment is assessment by a thoracic oncologist. Inform patients whose disease has not responded to first-line treatment that there is very limited evidence that second-line chemotherapy will be of benefit. Treatment with an anthracycline- containing regimen or further treatment with a platinum-based regimen to a maximum of six cycles is the choice in such situations. Offer radiotherapy for palliation of local symptoms to these patients.

Supportive and palliative care

Supportive and palliative care of the patient should be provided by general and specialist palliative care providers. Patients who may benefit from specialist palliative care services should be identified and referred without delay.

Palliative radiotherapy

Patients who cannot be offered curative treatment, and are candidates for palliative radiotherapy, may either be observed until symptoms arise and then treated, or be treated with palliative radiotherapy immediately.

Managing endobronchial obstruction

When patients have large airway involvement, monitor (clinically and radiologically) for endobronchial obstruction to ensure that treatment is given early. Offer external beam radiotherapy and or endobronchial debulking or stenting to patients with impending endobronchial obstruction.

Other palliative treatments

Pleural aspiration or drainage should be performed in an attempt to relieve the symptoms of a pleural effusion. Patients who benefit symptomatically from aspiration or drainage of fluid should be offered talc pleurodesis or Indwelling Pleural Catheter (IPC) on a case to case basis for longer-term benefit.

Non-drug interventions based on psychosocial support, breathing control and coping strategies should be considered for patients with breathlessness.

Non-drug interventions for breathlessness should be delivered by a multidisciplinary group, coordinated by a professional with an interest in breathlessness and expertise in the techniques (for example, a nurse, physiotherapist or occupational therapist). Although this support may be provided in a breathlessness clinic, patients should have access to it in all care settings.

Opioids, such as codeine or morphine, should be considered to reduce cough.

Patients with troublesome hoarseness due to recurrent laryngeal nerve palsy should be referred to an ear, nose and throat specialist for advice.

Patients who present with superior vena cava obstruction should be offered chemotherapy and radiotherapy according to the stage of disease and performance status.

Stent insertion should be considered for the immediate relief of severe symptoms of superior vena caval obstruction or following failure of earlier treatment.

Managing brain metastases

Offer dexamethasone to patients with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. Consider palliative whole- brain radiotherapy for patients with symptomatic brain metastases with good performance status (WHO 0 or 1).

Hypercalcaemia, bone pain and pathological fractures

For patients with bone metastasis requiring palliation and for whom standard analgesic treatments are inadequate, single-fraction radiotherapy should be administered. Managing other symptoms: weight loss, loss of appetite, difficulty swallowing, fatigue and depression.

Other symptoms, including weight loss, loss of appetite, depression and difficulty swallowing, should be managed by multidisciplinary groups that include supportive and palliative care professionals.

Follow-up and patient perspectives

Offer all patients an initial specialist follow-up appointment within 6 weeks of completing treatment to discuss ongoing care. Offer regular appointments thereafter, rather than relying on patients requesting appointments when they experience symptoms.

Offer protocol-driven follow-up led by a lung cancer clinical nurse specialist as an option for patients with a life expectancy of more than 3 months.

Ensure that patients know how to contact the lung cancer clinical nurse specialist involved in their care between their scheduled hospital visits.

The opinions and experiences of lung cancer patients and carers should be collected and used to improve the delivery of lung cancer services. Patients should receive feedback on any action taken as a result of such surveys.

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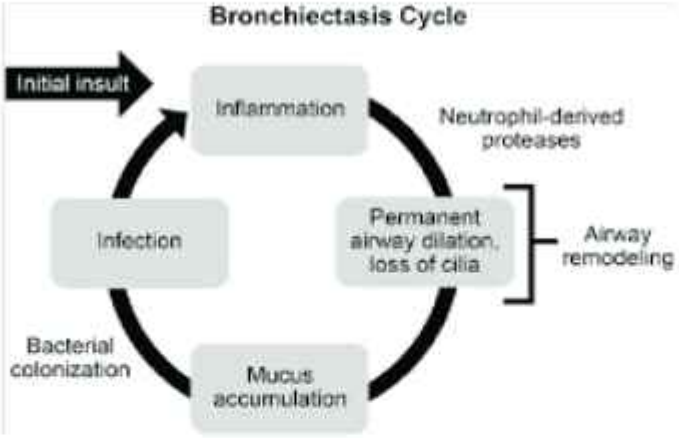
BRONCHIECTASIS

1. Introduction

Bronchiectasis refers to abnormal, irreversibly dilated and thickened airways. It represents the end stage of a variety of pathologic processes that cause destruction of bronchial wall and its surrounding supporting tissue.



Clinical features

- Chronic cough with sputum production (occur in more than 90%), Dyspnea (72%), hemoptysis(45-51%), fever, chest pain
- **Exacerbation of bronchiectasis** : either a change in one or more of the common symptoms of bronchiectasis (increasing sputum volume or purulence, worsening dyspnea, increased cough, declining lung function, increased fatigue/malaise) or the appearance of new symptoms (fever, pleurisy, hemoptysis, requirement for antibiotictreatment)
- The number of infective exacerbations per annum should be noted including frequency and nature of antibiotic usage
- Psychosocial symptoms : patients have increased anxiety and depression scoresincreased fatigue , lower quality of life.

2. Investigations

Investigations are done to confirm the diagnosis of bronchiectasis and also to identify theunderlyingcause of it. In approximately 40-50% patients even after extensive evaluation nospecific cause is found **(Idiopathic)**. Investigations into underlying cause can changemanagement, while sometimes have important treatment and /or prognostic implications(eg: cystic fibrosis, immune deficiency, ciliary dyskinesia).

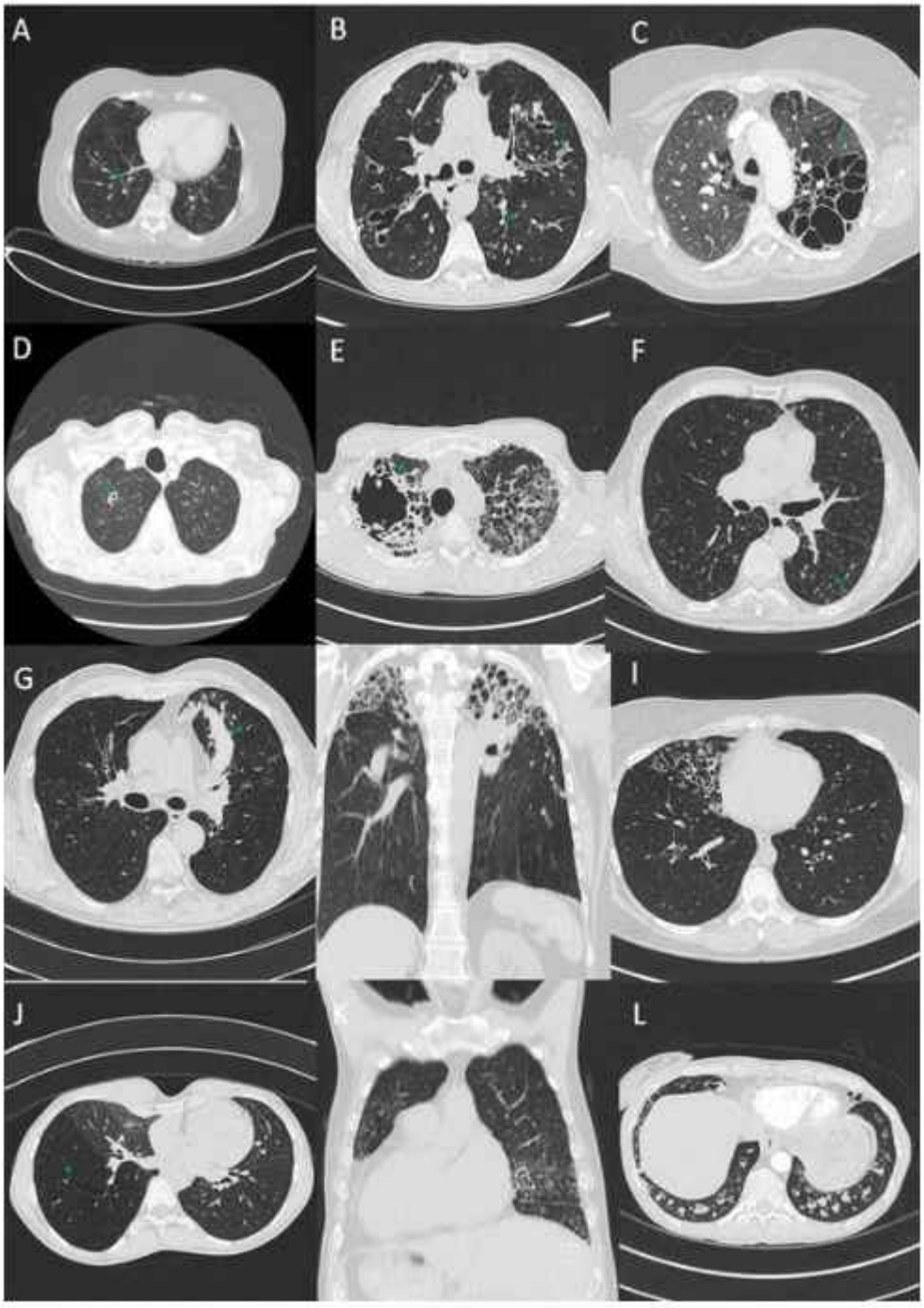
- **Complete blood count with differential count, ESR, CRP**
- **Respiratory tract specimen for microbiology:** Send **sputum** for bacterial, mycobacterial and fungal culture & sensitivity, Gram staining accordingly based onclinical suspicion, before starting antibiotics.
- **Blood Culture**
- When atypical mycobacterial infection is suspected, bronchoscopy with **bronchial washings** may be done if sputum culture negative.

Chest x-ray

- A baseline chest x-ray should be done in all patients.

HRCT Chest

- HRCT CHEST is the gold standard investigation for diagnosis of bronchiectasis
- Routine repeat chest x-ray or HRCT is not necessary; repeat imaging should beconsidered when there is clinical need.
- In cases of humoral immune deficiency, repeat HRCT at intervals may be necessary todetect asymptomatic progression.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Radiological phenotypes. (A) Cylindrical bronchiectasis with signet ring sign. (B) Varicose bronchiectasis. (C) Cystic bronchiectasis. (D) Cavity in the right upper lobe. (E) Chronic pulmonary aspergillosis with right upper lobe cavitation with intracavitary material. (F) Tree-in-bud appearance. (G) Bronchocele in the left upper lobe in allergic bronchopulmonary aspergillosis. (H) Bilateral upper lobe bronchiectasis. (I) Isolated right middle lobe bronchiectasis. (J) Bronchiectasis in an area of hyperlucent lung with reduced vascularity (Swyer–James syndrome). (K) Situs inversus and bronchiectasis. (L) Mucus impaction of bronchiectatic airways.

Investigations to determine the underlying cause of bronchiectasis

- Raised Serum IgE , skin prick testing , peripheral blood eosinophilia positive specific IgE and IgG to aspergillus and aspergillus precipitins to rule out **ABPA .**
- To rule out underlying **connective tissue disorder**: RA, ANA and ANCA (if clinically relevant).
- To rule out **primary Immunodeficiency**:
  - Screening measurement of serum IgG, IgA, IgM levels with electrophoresis in allpatients.
- **Second line immunological investigations** are performed in appropriate clinicalcircumstances.

Cystic fibrosis should be evaluated:

a) Unless a confident alternative cause can be identified, all children withbronchiectasis will need investigation to exclude Cystic fibrosis

b) In adults, investigations should also be considered in those with:–

- age at presentation <40 years and no other identified cause
- persistent isolation of S aureus in the sputum
- features of malabsorption
- male primary infertility
- upper lobe bronchiectasis
- a history of childhood steatorrhoea.

c) the**screening investigations** should include two sweat chloride measurement andCFTR genetic mutation analysis.

Ciliary dyskinesia should be evaluated:

a) Ciliary investigations should be considered in adults only if there is a history ofchronic upper respiratory tract problems or otitis media.

Factors favouring investigation include:

- symptoms since childhood
- childhood chronic otitis media
- predominantly middle lobe bronchiectasis
- infertility or situs anomalies.

a) **Screening tests is nasal nitric oxide test.** Nasal niricoxidelevels< 100 parts per billion indicates need to test further ciliary function test

b) **Confirmatory test to assess the structure and function of cilia**(ciliary beatfrequency / pattern tests and electron microscopy studies)

Gastro intestinal investigations :

If gastric aspiration is suspected as a cause

- Investigations chosen normally include one or more of 24 h oesophageal pHmonitoring, barium studies,or the identification of foam-laden macrophages onbronchoscopic samples.

Bronchoscopy

- Bronchoscopy can identify and be used to **remove foreign bodies** in the endobronchialtree and can show anatomical abnormalities of the bronchi.
- In adults with **localized disease**, bronchoscopy may be indicated to exclude proximalobstruction
- When **atypical mycobacterial** infection is suspected, bronchoscopy with bronchialwashings significantly increases the yield of mycobacterial cultures above that ofsputum culture alone.

Lung function tests

- Pre and post bronchodilator spirometry . All adults with bronchiectasis should havemeasures of FEV1, FVC and PEF.
- Repeat lung function may be done annually.

3. Management

- **General approach and treatment of the specific underlying cause**
- **Education for patients and parents of children with bronchiectasis**
- **Airway clearance**
  - Physiotherapy and exercise

- Mucolytic and hyperosmolar therapies

- **Pulmonary rehabilitation**
- **Immunisation**
- **Airway drug therapy**
  - Bronchodilators
  - Anti-inflammatory therapy
- **Antibiotic therapy**
- **Surgical management**

Management of complications

General approach and treatment of the specific underlying cause

- Identify and treat underlying cause(immunodeficiency, foreign body, aspiration)
- To maintain or improve pulmonary function and reduce exacerbations and improvequality of life
- Patients with primary or secondary immune deficiency should be under joint care with aclinical immunologist.
- Patients with CF should be referred to a CF specialist centre.

Patient education

- Explain treatment approaches including airway clearance techniques, airway therapiesand management of infections.
- Explain how to recognise an exacerbation
- Explain the usefulness of sending a sputum sample for culture and sensitivity to aidappropriate management with antibiotics.

Patients who should have regular follow-up in secondary care Include:

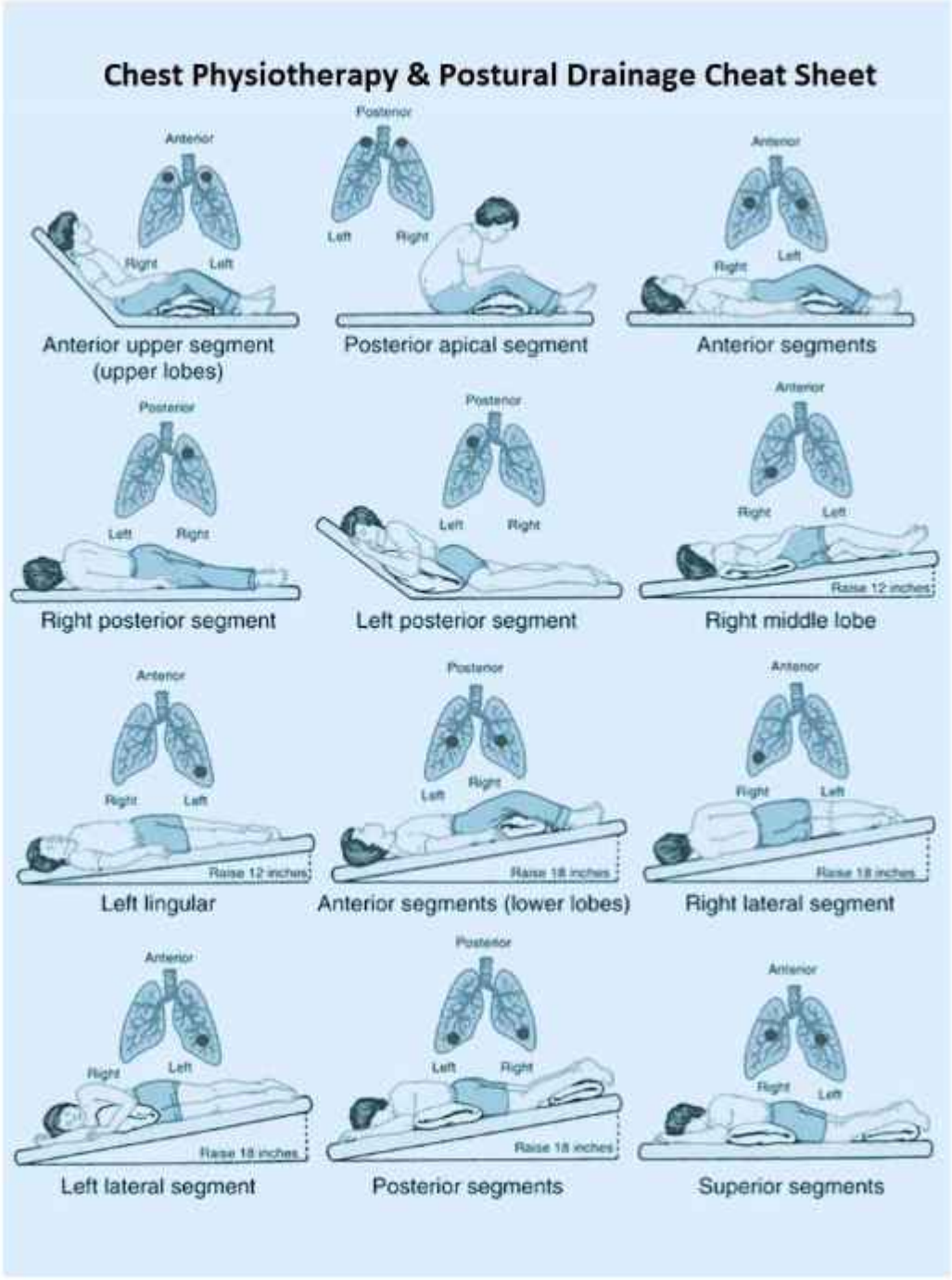
- All children with bronchiectasis
- Patients with chronic P aeruginosa, opportunist mycobacteria or methicillin-resistant Saureus colonisation
- Deteriorating bronchiectasis with declining lung function
- Recurrent exacerbations (>3 per year)
- Patients receiving prophylactic antibiotic therapy (oral or nebulised)

- Patients with bronchiectasis and associated rheumatoid arthritis, immune deficiency,inflammatory bowel disease and PCD
- Patients with ABPA
- Patients with advanced disease and those considering transplantation

Chest physiotherapy and postural drainage

(Airway clearance techniques & exercise)

- All patients with bronchiectasis should be taught chest physiotherapy and posturaldrainage of secretions accordingly based on anatomical segments affected.
- The active cycle of breathing techniques and oscillating positive expiratory devices (pluspostural drainage and the forced expiration technique) may be considered
- Airway clearance therapy should be for 20-30 min once or twice daily. This may alterwith periods of infective exacerbation.
- Effectiveness and acceptability to the patient of the airway clearance technique shouldbe reviewed within approximately3 months of the initial visit.


Chest Physiotherapy & Postural Drainage Cheat Sheet
Anterior
Right
Left
Anterior upper segment (upper lobes)
Posterior
Left
Right
Posterior apical segment
Anterior
Right
Left
Anterior segments
Posterior
Left
Right
Right posterior segment
Posterior
Left
Right
Left posterior segment
Anterior
Right
Left
Raise 12 inches
Right middle lobe
Anterior
Right
Left
Raise 12 inches
Left lingular
Posterior
Left
Right
Raise 18 inches
Anterior segments (lower lobes)
Anterior
Right
Left
Raise 18 inches
Right lateral segment
Anterior
Right
Left
Raise 18 inches
Left lateral segment
Posterior
Left
Right
Raise 18 inches
Posterior segments
Anterior
Right
Left
Superior segments

Adjuncts to airway clearance

- Sterile water inhalation, nebulized hypertonic saline may be used before airway clearance to facilitate clearance. When nebulised hypertonic saline is first administered, watch for bronchoconstriction in susceptible patients
- Nebulization with beta 2 agonists enhance sputum clearance.
- NIV/intermittent positive pressure breathing may be used to augment tidal volume and reduce the work of breathing in those patients who are becoming fatigued and finding their standard airway clearance difficult.

Pulmonary rehabilitation

- Pulmonary rehabilitation should be offered to individuals who have breathlessness affecting their activities of daily living. Inspiratory muscle training can be used inconjunction with conventional pulmonary rehabilitation to enhance the maintenance of the training effect

Vaccination

- Pneumococcal vaccination and yearly influenza vaccination are advised

Airway pharmacotherapy

Bronchodilators and anti inflammatory drugs

1. Beta 2 agonist: if PFT shows airway obstruction which is reversible with betaagonist may beused. May also be used in management of coexistent asthmaand bronchiectasis
2. Anticholinergics : no evidence of benefits of its use in children, some adults maygain a useful response
3. Methylxanthines : have no routine role in bronchiectasis
4. Inhaled steroids : should not be used in children with bronchiectasis(outside ofuse for those patients with additional asthma). In adults,may be used in aselected subset of patients
5. Oral steroids and Leukotriene receptor antagonist: no evidence of role of oralsteroids in bronchiectasis without other indications like ABPA, chronic asthma, COPD andinflammatory bowel disease.

Antibiotic therapy

- Antibiotics should be given **for exacerbations** that present with an acute deterioration with worsening symptoms (cough, increased sputum volume or change in viscosity,increased sputum purulence with or without increasing wheeze, breathlessness,hemoptysis) and/or systemic upset

- Patients with an infective exacerbation of bronchiectasis should be assessed for theneed for inpatient or outpatient treatment.

Inpatient treatment recommendations

a) Unable to cope at home

b) Development of cyanosis or confusion

c) Breathlessness with respiratory rate ≥25/min

d) Circulatory failure

e) Respiratory failure

f) Temperature ≥ 38˚C

g) Unable to take oral therapy

h) IV therapy required in patients with clinical failure with oral therapy

Recommendations for antibiotic usage

- Before starting antibiotics, a sputum sample should be sent off for culture.
- Empirical antibiotics should be started whilst awaiting sputum microbiology.
- If there is no previous bacteriology, first-line treatment is amoxicillin 500 mg three timesa day or clarithromycin500 mg twice daily (in patients that are penicillin-allergic) for 14days
- High-dose oral regimens (eg, amoxicillin 1 g three times a day or amoxicillin 3 g twicedaily) may be needed in patients with severe bronchiectasis chronically colonised with Hinfluenzae.
- Antibiotics can be modified subsequently once the pathogen is isolated only if there isno clinical improvement and the treatment should then be guided by antibioticsensitivity results.
- Failure to respond to an antibiotic course should prompt a repeat sputum culture.
- Intravenous antibiotics should be considered when patients are particularly unwell,have resistant organisms or have failed to respond to oral therapy (this is most likely toapply to patients with P aeruginosa).
- There is no evidence to support the routine use of antiviral drugs in exacerbations
- In patients who culture Psuedomonas aeruginosa that is sensitive to ciprofloxacin,monotherapy with oral respiratory flouroquinolone can be used as first-line treatment if tuberculosis has been ruled out

- In patients who have not responded to oral ciprofloxacin, monotherapy with anantipseudomonal intravenous antibiotic should be considered
- Combination antibiotics should be used for infections due to strains ofPsuedomonas aeruginosa that are resistant to one or more antipseudomonal antibiotics(including ciprofloxacin) or if the clinician suspects the patient will require many subsequent antibiotic courses to reduce the development of drug resistance.

Third generation cephalosporin (ceftazidime) and aminoglycoside (gentamycin) for 14 days

Long term antibiotics

- Patients having ≥ 3 exacerbations per year requiring antibiotic therapy or patients withfewer exacerbations that are causing significant morbidity should be considered for long term antibiotics.

P aeruginosa colonised patients: Use inhaled colistin for patients with chronic P aeruginosa infection. Inhaled gentamycin may be considered as a second line alternative.

Azithromycin or Erythromycin may be considered as alternative if the patient does not tolerate inhaled antibiotics.

Macrolides may also be considered as an additive treatment to inhled antibiotics for patients with high exacerbation frequency.

Non P. aeruginosa colonised patients. Use Azithromycin or Erythromycin as first choice. Consider inhale gentamycin as an alternative.

Consider doxycycline as an alternative in patients intolerant of macrolides or in whom they are ineffective.

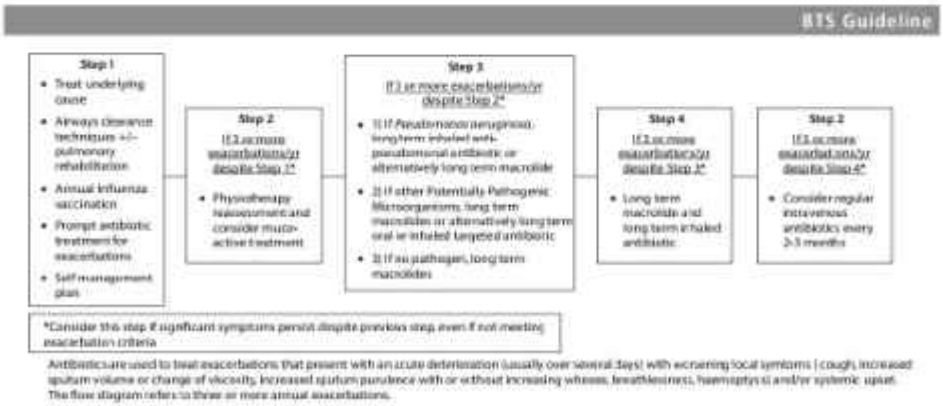


Figure 2 Stepwise management.

Eradication algorithm for psuedomonas aeruginosa in adults

For patients with new or first isolation of P. aeruginosa, eradication treatment may be considered. First line treatment is ciprofloxacin 500-750 mg bd for 2 weeks. Alternative choice is intravenous antipseudomonal beta lactum ± an intravenous aminoglycoside for 2 weeks. This should be followed by a 3 month course of nebulised colistin, gentamycin or tobramycin. Risk and benefits of an eradication treatment should be discussed, like likelihood of achieving sustained eradication, risk of developing chronic infection and the risk of adverse events to eradication treatment.

Role of surgery

- Lung resection surgery may be considered in patients with localised disease in whomsymptoms are not controlled by medical treatment.
- Surgical option decided by expert committee in a tertiary care centre

Lung transplantation for bronchiectasis

- Consider transplant referral in bronchiectasis patients below 65 years, if the FEV1 is < 30% with significant clinical instability or if there is rapid clinical deterioration despite optimal medical management.
- Earlier referral for transplant may be considered in patients with poor lung function and the following additional factors- massive hemoptysis, severe secondary pulmonary hypertension, ICU admissions or respiratory failure requiring NIV.

Massive hemoptysis

- Haemoptysis is a potentially life-threatening complication of bronchiectasis.
- Bronchial artery embolisation and/or surgery may be required in the management ofmassive haemoptysis.

Treatment of Respiratory Failure

Consider long term oxygen therapy for patients with respiratory failure, using the same eligibility criteria as for COPD.

Consider domiciliary NIV with humidificationfor patients with associated hypercapnia, especially where it is associated with recurrent hospitalisation.

BTS Guideline

Figure 1 Management of the deteriorating patient.

TUBERCULOSIS

1. Introduction

Pulmonary tuberculosis (TB) is a disease affecting the lung parenchyma caused by mycobacterium tuberculosis (*Mtb*). This chapter deals with Pulmonary tuberculosis.

Traditionally TB has been classified as Pulmonary and extra-pulmonary TB. The term Pulmonary TB is limited to TB affecting the lung parenchyma. Even TB of the pleura and mediastinal nodes, which are in close proximity with the lung, are classified as extra-pulmonary TB (TB affecting all other organs in the body, other than lung parenchyma).

WHO defines Pulmonary TB as "Pulmonary tuberculosis (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Miliary TB is classified as PTB because there are lesions in the lungs. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of PTB." (1)

Pulmonary TB has always been accorded the highest importance in TB control / elimination programs all over the world because spread of TB happens from Pulmonary TB. When a person with pulmonary TB coughs, speaks or sneezes, aerosols are generated with droplets containing the TB bacteria, which infects other persons when they inhale the droplets.

Lungs are the portal of entry of the TB bacteria in most infected people, even though, in rare cases, the entry of organism can be through other routes, like gastrointestinal system (eg. Bovine TB), ascending infection through the vagina in female children living in un-hygienic places or direct implantation of the organisms into the skin through cuts and abrasions (This is seen in some forms of extra-pulmonary TB causes by non-tuberculous mycobacteria (NTM) – through skin pricks or through contact – eg. fish handler's disease– caused by *M. marinum)*. This form of TB can also be a health hazard in health care workers and laboratory staff who handle materials infected with *Mtb*. These lesions were termed "Prosector's warts". Unfortunately, Laennec, the inventor of the stethoscope, acquired TB in this fashion which eventually led to his death.

Pulmonary TB is also accorded importance in TB control programs as they form the greatest proportion of TB patients, are easier to diagnose at peripheral health institutions and cause the highest proportion of mortality. Also, the greatest numbers of TB bacteria exist in the cavities in the lungs of patients. Since the selection of naturally occurring resistant mutants, which is the prime mechanism of resistance occurring in TB, is most likely to occur when bacterial populations are high, drug resistance in TB generally develops in patients with pulmonary TB.

2. Diagnosis

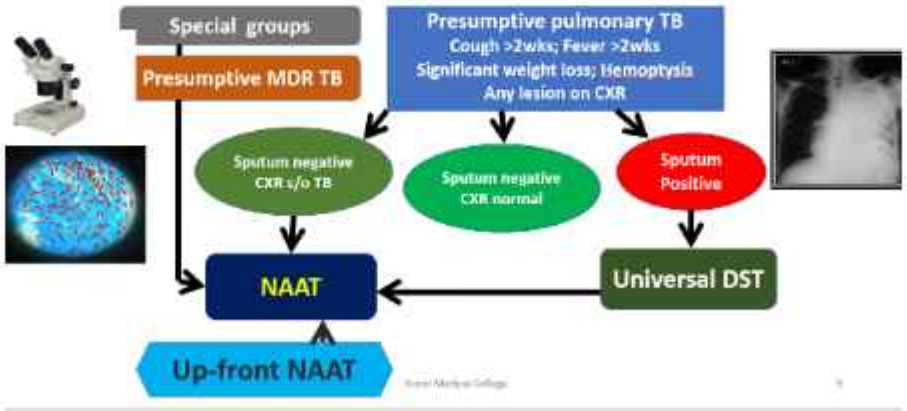
Presumptive pulmonary tuberculosis

1. Cough > 2 weeks
2. Fever > 2 weeks
3. Night sweats
4. Weight loss
5. Haemoptysis
6. Shortness of breath
7. Chest pain
8. Loss of appetite
9. Tiredness
10. Symptoms of signs of extrapulmonary TB

All patients with symptoms of pulmonary TB must be subjected to evaluation as per the diagnostic algorithm in figure 1.

Many districts of Kerala are striving towards moving to up-front NAAT (Nucleic acid amplification test; CBNAAT (GeneXpert) and Truenat), wherein all patients are offered NAAT as the first test for TB. Wherever upfront NAAT is not available, such patients should be subjected to Chest X-ray and Sputum examination together, and based on the results of these tests, a NAAT may be done.

Figure 7.1. Diagnostic algorithm for Pulmonary TB



* The old 4 symptom screening is now replaced by 10 symptom screening

* NAAT includes CBNAAT and Truenat

Patients who are diagnosed as TB also need to undergo further evaluation to determine if the patient has any form of drug resistant TB. This is called universal DST (drug susceptibility testing). Every diagnosed TB patient should be offered testing to determine at least Rifampicin resistance. If Rifampicin resistance is present, then further testing is offered at least for fluoroquinolones. The U-DST algorithm is as given in figure 2. Further testing in Rifampicin resistant patients would also depend on availability in state of testing for new drugs like Bedaquiline, Pretomanid and Delamanid.

Figure 7.2.

3. Treatment of TB

The vast majority of TB would be drug sensitive TB. These patients are provided a regime containing four drugs (Isoniazid, Rifampicin, Pyrazinamide and Ethmabutol) for eight weeks followed by three drugs (Isoniazid, Rifampicin and Ethmabutol) for 16 weeks. The drugs are provided as FDCs (Fixed dose combinations) as per the weight band of the patient. The regime and dosage is as follows

Table 7.1

Treatment regime – 8 weeks H R Z E followed by 16 weeks HRE					
	Doses range as per recommended dose in mg/kg				
Wt Band	**R**	**H**	**Z**	**E**	**No. of Tablets**
25-34	300	150	800	550	**2**

35-49	450	225	1200	825	**3**
50-64	600	300	1600	1100	**4**
65-75	750	375	2000	1375	**5**
>75	900	450	2400	1650	**6**

Drug resistant TB is treated based on the resistance pattern. There are one treatment regimes for INH resistant TB (H mono-poly resistant TB) and three treatment regimes for Rifampicin resistant TB. The treatment regimes are as follows. The indications and contraindications of each regime is given in detail in the NTEP guidelines document for Drug resistant TB.

- H mono/poly resistant TB

  (6 or 9) Lfx R E Z

- MDR TB
- BPALM regime

  26 wks Bdq Pretomanid Lzd Moxi

- Short MDR regime

  (4-6) Bdq $_{(6\,m)}$, Lzd$_{(2\,m)}$, Lfx, Cfz, Z, E, H^{h}/ (5) Lfx, Cfz, Z, E

- Longer MDR regime / modified longer MDR regime

  (18-20) Lfx Bdq(6m) Lzd# Cfz Cs (may be modified by nodal centres)

The treatment is initiated for drug resistant TB either at nodal centres at district level or those for the state (located at medical colleges at Thiruvananthapuram, Thrissur and Kozhikode). Treatment is to be initiated after appropriate pretreatment evaluation

All TB patients have to undergo proper follow-up, follow-up evaluations, including sputum smear / culture, have to be done and at the end of treatment, the appropriate treatment outcome has to be assigned.

Please note: Since the state of Kerala manages TB as per NTEP guidelines, this chapter has been kept short and covers only the broad summary of the guidelines.

Detailed guidelines for diagnosis and treatment of TB, including pulmonary and extra-pulmonary TB and TB preventive therapy are available on the NTEP website @ https://tbcindia.mohfw.gov.in/guidelines/