Interstitial Lung Diseases:
Screening, diagnosis and initial management

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Disclosures

Under Accreditation Council for Continuing Medical Education guidelines disclosures must be made regarding financial relationships with commercial interests within the last 12 months.

Jad Kebbe, M.D.

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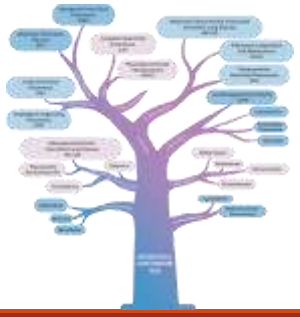
Objectives

01 Recognize the importance of timely screening and diagnosis of ILD

02 Adopt a personalized approach to ILD evaluation

03 Implement early treatment strategies

04 Partner with specialized ILD centers in referral and care



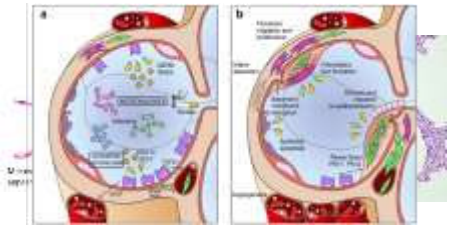
Interstitial Lung Diseases (ILD)

Broad category with many possible causes

- Idiopathic
- Autoimmune
- Smoking-related
- Work-related (pneumoconisosis)
- Environmental exposures (mold, Mycobacterium *avium*, hay, water damage, bird antigens)
- Drug-induced (chemotherapy; checkpoint inhibitors; antibiotics)
- Post-infectious (post-viral bronchiolitis or organizing pneumonia)
- Etc…

Mechanism of Disease

- A lung injury causes inflammation of the space between the alveoli and the capillaries
- The abnormal healing process involves expansion of the interstitium by inflammatory cells, and sometimes deposition of abnormal collagen and fibrosis (scarring and thickening)
- Lungs become stiff with limited capacity to expand, and decreased O2/CO2 exchange; early hypoxia; late hypercapnia



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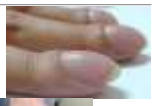
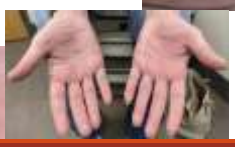
Early Screening and Suspicion of ILD

- History is very important:
  - Age
  - Gender
  - Exposures
  - Hobbies
  - Smoking/drugs
  - Family history
- Hints on history:
  - Chronic cough, mostly dry, lasting more than 12 weeks
  - Progressive dyspnea on exertion with no signs of heart disease

Physical Exam Signs

- Dry bibasilar inspiratory rales
- Clubbing of fingernails
- Thick skin of palms
- Ulcers or cracking of fingertips
- Rash on face/cheeks, neck, or knuckles
- Raynaud





Why is Early Diagnosis Important?

- Depending on type of ILD, prognosis can be very grim
- Lung function and quality of life lost may not be regained
- Risk of disease exacerbation is high without treatment, and can be lethal
- 50% of patients are initially given another diagnosis
- 55% of patients are evaluated on average by 3 physicians before correct diagnosis
- In 58% of cases, the diagnostic delay is often > 1 year
- Mean time from initial symptom onset to diagnosis is 1.5 years

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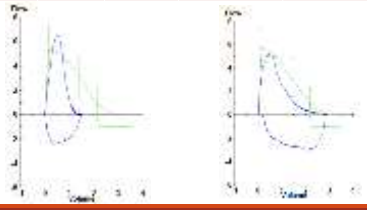
WWW.PULMONARYFIBROSIS.ORG

Which Tests to Order if ILD is Suspected

- Antinuclear antibody (ANA) by immunofluorescence
- Rheumatoid Factor (RF)
- Cyclic Citrullinated Peptide antibody (CCP)
- Other serology antibodies based on clinical suspicion
- High resolution chest CT scan without contrast
  - A chest X-ray can be normal in 10% of ILD patients
- Pulmonary Function Test
- If sarcoidosis is suspected: EKG; Vitamin D; 1,25-dihydroxy vitamin D

PULMONARY FUNCTION TESTING

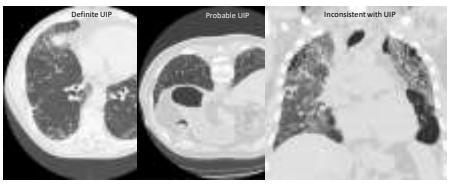
	FVC	FEV1	FEV1/FVC	RV, TLC, DLCO
Restriction	↓	↓	>70%; usually ≥80%	↓
Obstruction	N or ↓	↓↓↓	< 70%	Normal or↑; DLCO eventually ↓



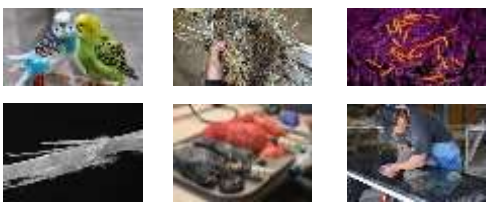
High resolution chest CT (HRCT)

- Necessary in all patients
- Supine & prone images (rules out atelectasis & fluid accumulation)
- Inspiratory & expiratory series may be needed
- Greater accuracy than chest X-ray
- Pattern and distribution correlate with various diseases
- Can even be sufficient to diagnose certain patterns, without a need for biopsy
- Helps in following disease progression

HRCT Pattern Examples



Inhalational & Occupational Lung Diseases



Asbestos-related Diseases

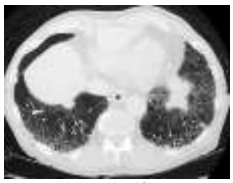
- Asbestos is present in material for fire protection and insulation
- Insulation lagging in buildings, on pipework, boilers and ducts
- Asbestos cement products: walls, roofs, tiles

Asbestosis (ILD)
- Parenchymal fibrosis
- Moderate/Heavy exposure
- Exposure >10 years
- Latency: 20-30 years

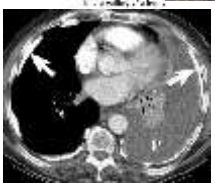
Asbestos exposure
- No ILD
- Little exposure is sufficient
- Latency 20-40 years
- Pleural plaques
- Increased Risk of Malignancy
  - Bronchogenic cancer
  - Mesothelioma

Crocidolite

Chrysotile



Asbestos-related fibrosis



Calcified asbestos pleural plaques

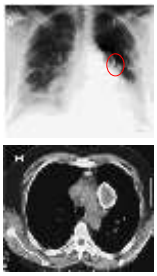
Brims FJH, Keng K, Harris EJA, Sodhi-Berry N, Reid A, Murray DP, Franklin PJ, Mack JB, de Klerk NH. Pleural Plaques and the Risk of Lung Cancer in Asbestos-exposed Subjects. Am J Respir Crit Care Med. 2020 Jan 1;201(1):57-62. doi: 10.1164/rccm.201905-0898OC. PMID: 31525932.

Silicosis

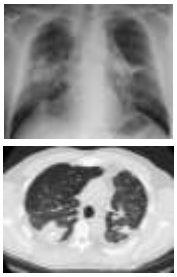
- Inhalation of crystalline silica
- Hard rock mining, construction, road work, tunneling, sandblasting, granite, stone work, glass manufacturing

Chest Imaging
- Upper lobe predominant nodules (< 5 mm)
- Hilar adenopathy
- 10% have "eggshell" hilar
- calcification
- Nodules may coalesce to form masses: progressive massive fibrosis

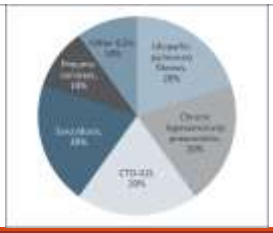
Simple Silicosis with eggshell calcifications



Silicosis with progressive massive fibrosis



Systemic Autoimmune Rheumatic Diseases (SARD)

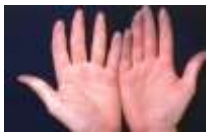


From New England Journal of Medicine
Estimated Relative Distribution of Specific Interstitial Lung Diseases (ILDs) in the United States.

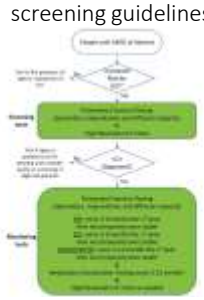
Prevalence of ILD in SARD

Diseases	Frequency of ILD (%)	Comment
Rheumatoid arthritis	30-30	Increased risk with cigarette smoking
Polymyositis-dermatomyositis	30-50	More common with antisynthetase antibodies
Systemic sclerosis	70 40 (clinically significant	More common in diffuse disease; topoisomerase-1 antibodies
Systemic lupus erythematosus	3-6	Usually in patients with multisystem disease
Mixed connective tissue disease	30-40	
Sjögren syndrome	Up to 25	

Interstitial lung disease is common in connective tissue disease and is the leading cause of mortality



American College of Rheumatology 2023 ILD screening guidelines



Idiopathic Pulmonary Fibrosis (IPF) Epidemiology

Systematic Review of published worldwide data:
- 241,851 cases identified in epidemiology articles between 1984-2008
- Incidence: 0.22-8.8/100,000
- Prevalence: 0.5-27.9/100,000

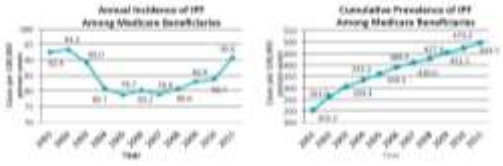
In the USA, based on IPF registries:
- Incidence: 7-16/100,000

Random sample of Medicare beneficiaries ≥65
- Incidence: 94/100,000
- Prevalence: 494/100,000

Higher predominance in men compared to women (1.5-1.7:1)

Why is IPF Epidemiologically Important?

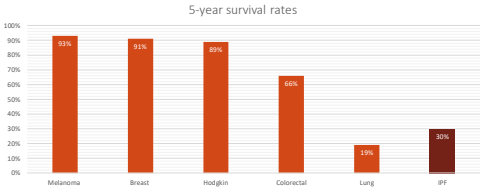
Both incidence and prevalence are increasing, especially with age



RAGHU G ET AL. LANCET RESPIR MED. 2014;2:566-572.

25

Survival Compared to Common Cancers



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FLAHERTY KR ET AL. CLINICAL SIGNIFICANCE OF HISTOLOGICAL CLASSIFICATION OF IDIOPATHIC INTERSTITIAL PNEUMONIA. EUR RESPIR J 2002;19:275–283.

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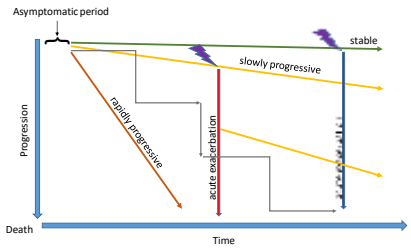
Clinical course of IPF



Adapted from Raghu et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183:788-824.

IPF prognosis

Prognosis is grim without treatment:

- Median survival 2.5-3.5 years from time of diagnosis
- 4.5 years with transplant
- Natural history is variable
- 5-year survival rate 20-40% (with transplant: 50-56%)
- Hospital mortality: 87%-96% in patients with respiratory failure who require mechanical ventilation

GUTIER ED ET AL. LUNG TRANSPLANTATION IN IDIOPATHIC PULMONARY FIBROSIS: A SYSTEMATIC REVIEW OF THE LITERATURE. BMC PULM MED. 2014;14(1):138.
KOMA JB ET AL. PROGNOSIS OF PATIENTS WITH ADVANCED IDIOPATHIC PULMONARY FIBROSIS REQUIRING MECHANICAL VENTILATION. FOR ACLS. RESPIRATORY FAILURE. CHEST. 2007;132:1213–1219.
MALLICK S. OUTCOME OF PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF) VENTILATED IN A TERTIARY CARE UNIT. RESPIR MED. 2006;100:1055–1059.

Nintedanib and Pirfenidone Since Approval

- Both medications are well tolerated though GI side effects can be limiting
- Nintedanib
  - remains efficacious in reducing the decline of FVC beyond 3 years (up to 63 months)
  - is efficacious irrespective of stage of disease (i.e. %FVC)
  - reduces risk of acute exacerbations
  - 19% permanently discontinue nintedanib (vs 25.2% in INPULSIS-1 & 23.7% in INPULSIS-2)
- Pirfenidone
  - improves life expectancy by 2.47 years compared with best supportive care
  - is tolerated and safe as an add-on therapy to nintedanib (phase 2 trial)
  - reduces the relative risk of mortality compared with placebo, over 120 weeks
  - up to 29% permanently discontinue pirfenidone

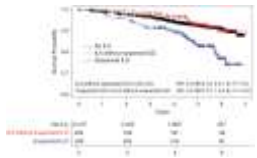
1) HUGHES G, MARKUS D, BD. JOURNAL OF CLINICAL MEDICINE. 2016;5(3):78. 2) JOSE ANTONIO RODRÍGUEZ-PORTAL. ONLIBS IN E D. 2017 DEC 5.
3) FISHER M. CARE SPEC PHARM. 2017 SEP;9(3):S1-9. SUPPL:S17-S26. 4) VANCHERI C, ET AL. INCLUSIVES™ TRIAL INVESTIGATORS. AM J RESPIR CRIT CARE MED. 2017 SEP 26. 5) RICHAN SD. LANCET RESPIR MED. 2017 JAN;5(1):33-41.

Signs that things are getting worse

- FVC decrease
- More shortness of breath, sustained >48h
- Increase in cough
- Drop in walking distance on a 6-minute walk test
- Needing more oxygen
- Lower appetite
- Losing weight
- Palpitations; faster heart beat
- Leg swelling (pulmonary hypertension)

Interstitial Lung Abnormalities (ILA)

- ILA increasingly described on chest CT scans performed for other reasons
- Non-dependent abnormalities affecting more than 5% of any lung zone. ILA include groundglass or reticular abnormalities, traction bronchiectasis, honeycombing, and non-emphysematous cysts.
- More common in advancing age, in smokers
- Almost 50% progress in subsequent 5 years to fibrosis
- Associated with higher mortality



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How to Improve Care and Outcomes

- High index of suspicion for ILD with lingering cough and dyspnea without clear asthma, COPD, heart failure or other more common diseases
- Attention to exam clues
- Workup for SARD when suspected
- Review of potential causative medications
- Attention to exposures and family history
- Screening for ILD in SARD with PFT and HRCT at least once
- Echocardiogram to screen for pulmonary hypertension (look for RVSP>35; dilated right hear; tricuspid regurgitation)
- If ILD is found, initiating nintedanib can be helpful, since it works for all types of fibrosis
- Early referral to ILD center for more advanced diagnosis, treatment, and consideration for trials

Treatment of Comorbidities

- Clinic walking test to assess for hypoxia and need for oxygen
- Treatment of GERD in all ILD patients
- Pulmonary rehabilitation
- Weight loss in cases of obesity
- Avoid the overuse of glucocorticoids
- Workup and treatment of sleep apnea
- Smoking cessation
- Follow OSHA guidelines in the workplace
- Vaccination counseling

Available Resources
Multidisciplinary ILD Team

HTTPS://APPSOKMED.OUHSC.EDU/CONFERENCEROOM/OUMEDICINE/OUMEDICINEWEBCLIENT/MOBILEINDEX.HTML#/0

Available Resources
Pulmonary Fibrosis Support Group

HTTPS://WWW.PULMONARYFIBROSIS.ORG/PATIENTS-CAREGIVERS/MEDICAL-AND-SUPPORT-RESOURCES/FIND-MEDICAL-CARE/CARE-CENTER-NEW/OKLAHOMA-CITY-IPF-SUPPORT-GROUP

Available Resources
Clinical Trials

- Since 2016, 5 clinical trials have been completed, and 1 ILD registry
- Active trials
  - 2 phase II IPF trials
  - 2 phase III IPF trials
  - 2 phase II scleroderma ILD trials
  - 1 phase III progressive pulmonary fibrosis trial
  - 1 IPF registry
  - 1 open label extension
- Upcoming trials
  - 1 phase II trial for cough in IPF
  - 2 phase II trials for new IPF therapies
  - 1 proof of concept AI-EKG model for early detection of pulmonary hypertension
  - 2 grant submissions to evaluate novel diagnostic and treatment strategies in ILD and IPF

OU Health is a
Pulmonary Fibrosis Foundation Care Center

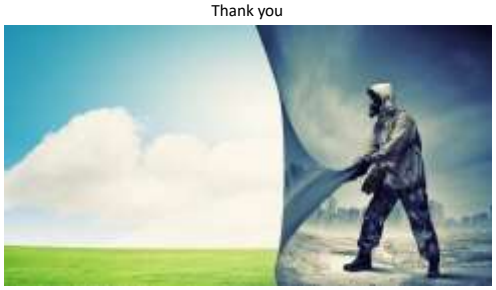
Pulmonary Fibrosis Foundation

OU Health
The Future of Health is Here

Final thoughts

- Integrate pulmonary disorder screening into routine medical care
- Pulmonary hygiene: tobacco, exposures, occupation
- Early referral for interstitial lung abnormalities/interstitial lung diseases
- Disease prevention: vaccination, infectious precautions

Thank you



OU Interstitial Lung Disease Program
We want to help the world breathe