

Conceptual Approach to Diffuse Lung Disease – July 22nd, 2020

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“The Greatest Obstacle to Discovery is not Ignorance, but the Illusion of Knowledge.”

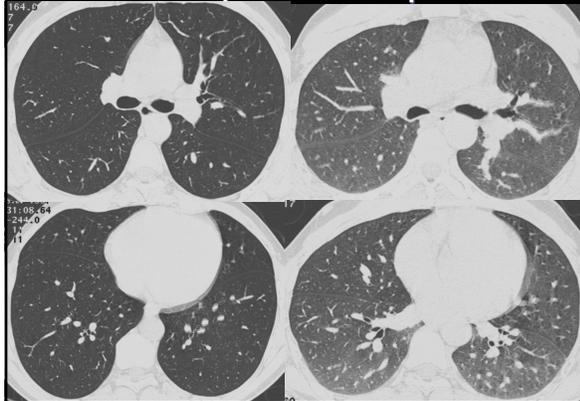
- Daniel J. Boorstin

Diffuse Lung Disease Objectives

- Case-based format with a conceptual approach *based on the report Impressions*
- Review Importance of **morphological abnormalities** and **Disease distribution**
- Emphasize difference between **Pathology Differential** and **Etiology Differential**
- *Polling questions – have some fun!*

This session will expose an old propagated Myth as definitely false: 'Chest imaging is just long differentials'

Normal Inspiration and Expiration



Conceptual Imaging Approach

2 Important Imaging Clues:

1. **Morphology of disease:** 'Airspace', 'Interstitial' and 'Reticulonodular' often *not* helpful. **Avoid** the term 'Infiltrate'
2. **Distribution of disease:** location, location, location!

Duration of Symptoms is also very helpful
Rule of Thumb: < 1 week is considered Acute

Morphological Patterns

- **Increased Opacity:** Consolidation & Ground glass
- **Decreased Opacity:** Emphysema, Cysts
Mosaic lung attenuation
- **Reticular Opacity:** Septal thickening and fibrosis
- **Nodular Opacity:** Solitary, Multiple and/or Cavitory
- **Airway Disease:** Tracheal, bronchiectasis and small airway patterns/Mosaic lung attenuation

Distribution of Disease

- Upper lobe: “SET PARC”
- Bronchovascular (Radiates from hilum)
- Peripheral
- Random/Perilymphatic/Centrilobular
- Diffuse distribution (Often Systemic cause)
- Focal or multifocal
- Dependent distribution ('Gravity' related)

Organization of Lung diseases is based on *Morphology, Distribution and duration of symptoms*

THORACIC DIFFERENTIAL DIAGNOSIS 1 (Marc Gosselin)

<p>GROUND GLASS OPACITIES</p> <p>ACUTE: Blood, Pus, Water PNA: PCP, CMV, resolving Bacterial Edema: hydrostatic & capillary leak Hemorrhage: Pulmonary Hemorrhage <i>Weg, Edema/ARDS</i> <i>Utz, PCP, CMV, HSP, hemorrhage</i></p> <p>CHRONIC (>4 weeks) No/Minimal Fibrosis Hypersensitivity Pneumonitis [HSP] EAA vs Drug-Induced [non-smokers] DIP/IR/ILD, Pulm LCH/EK [smokers] Cellular NSIP, Pulm Alveolar Proteinosis, Follicular Bronchiolitis LP (CVD, HIV), Pulmonary venoocclusive dz</p> <p>Moderate/Severe Fibrosis (+) Honeycombing: UIP (CVD, Drug-tox, IPF, Asbestosis?) (-) Honeycombing: Fibrotic NSIP (CVD, Drug-Induced) Chronic HSP (a/w air-trapping, spares costophrenic angles)</p> <p>CRAZY PAVING: GGO + septal thickening Acute: hemorrhage, edema (both), AIP, ARDS, PCP, chronic eosinophilic PNA, drug toxicity Chronic: Alv Prot, lipid PNA, COP, BAC</p> <p>UNILATERAL EDEMA Dependent (R>L), reexpansion, asymmetric emphysema, venous/lymphatic obstruction, mitral regurgitation (-RUL)</p>	<p>CONSOLIDATION</p> <p>ACUTE: Blood, Pus, Water PNA: Bacterial, Aspiration Edema: Hydrostatic & capillary leak Hemorrhage: Pulmonary Hemorrhage</p> <p>CHRONIC "ANGIO" Alveolar Proteinosis Neoplasm (Lymphoma, BAC) Granulomatous (TB/Fungal, Alv Sarcoid) Inflammatory (Eosinophilic PNA, COP) Qd (Chronic Aspiration, Lipoid Pneumonia) <i>Adenopathy favors Lymphoma or Granulomatous Dz</i></p> <p>INTERSTITIAL LUNG DISEASE</p> <p>Diffuse Reticular Opacities <i>(Kerley A, B lines)</i> Pulmonary Edema (Hydrostatic-cap leak) Lymphangitic tumor (AdenoCa/Lymphoma) Viral or Mycoplasma PNA</p> <p>Peripheral Reticular Opacities <i>(lace-like network, "Honeycombing")</i> UIP (Complications: PPHN, Lung Ca, AIP)</p> <p>Cystic Pattern (Curved Reticular) Severe Honeycomb Lung (Fibrosis), Severe Emphysema, Diffuse Central Bronchiectasis, EG/PLCH, PCP, LAM/FS, LIP, DIP, Cystic Mets (sarcomas: leiomyo, synovial, stromal cell, epithelioid, osteogenic)</p>	<p>MULTIPLE NODULES</p> <p>Random: Mets, granuloma dz, varicella, AVM Miliary: (1-2 mm, random but LL predom) Same size: TB/Fungal, sarcoid, alv mic; Var size: mets (thyroid, melanoma, breast, adeno)</p> <p>Upper lobe: HSP, EG/PLCH, Si & CW pneumo</p> <p>Erythematous: Lymphangitic tumor, Sarcoid Subacute/chronic (ill-defined nodules) Inhalational/Lymphatic Dz: HSP, EG/PLCH, Silicosis & Coal workers pneumoconiosis</p> <p>Centrilobular/Tree-in-Bud: Aspiration, Viral PNA (RSV, adeno, flu), BronchoPNA, Mycoplasma, MAI, Endobronchial TB Spread, Asthma, ABPA, CF, COP, Diff Pnbrochiolitis</p> <p>Centrilobular/Ill-Defined Ground Glass HSP (EAA), NSIP (Cellular), RB-ILD (smoker), Follicular Bronchiolitis (CVD, AIDS)</p> <p>CAVITARY NODULES</p> <p>Infection: Fungal: Cocc, Asperg, Crypto gattii Bact: septic emb, abscess, TB, Nocard, Legionella Neoplasm: Sq/CA (nodular wall), Sarcoma Cavitic: Wegener's, Angiocentric Lymphoma, RA (Necrotic Nodule)</p> <p>Trauma: Hematoma, pneumatocele/cyst</p> <p>SOLITARY PULM NODULE AdenoCa, SqCC, LrgCC, SmCC, Carcinoid, Lymphoma, Met, Hamartoma, Granuloma, Infection, RA, Trauma, Congenital cyst, AVM</p>
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THORACIC DIFFERENTIAL DIAGNOSIS 2 (Marc Gosselin)

<p>DISTRIBUTION OF DZ</p> <p>UPPER LOBE: "SET PARC" (1/1/0, Lymphatic clearance) Sarcoid, Silicosis, PCP EG/PLCH (Smoker), Aplysiozing Spondylitis EAA (Nonsmoker), Radiation therapy TB/Fungal, Cystic Fibrosis</p> <p>LOWER LOBE/DEPENDENT: (1/1/0, gravity) Hydrostatic edema, aspiration, ATX, CVD, UIP</p> <p>Bronchovascular <i>(airways, lymphatics)</i> Sarcoid, Lymphoma/lympho prolif dz, COP, Kaposi's Sarcoma, aspiration PNA (acute sx's)</p> <p>PERIPHERAL Chronic Eos PNA, pleural dz, infarct, COP, fungal infection, UIP, Wegener's</p> <p>RANDOM: <i>(follows blood flow, incl pleura)</i> Hematogenous spread of tumor or infection</p> <p>DIFFUSE: <i>(usually systemic dz)</i> Nonschistosomal edema, CF, Pulm-renal dz</p> <p>FOCAL: <i>(usually local dz)</i> Bacterial PNA, contusion, MAC, aspiration</p> <p>UNILAT PLEURAL EFFUSION</p> <p>Exudate: Hemots (Trauma, Iatrogenic), Tumor, Infectious/Inflam (Empyema), Chylots</p> <p>Transudate: Hepatohydrothorax</p>	<p>MEDIASTINAL DIAGNOSIS</p> <p>Anterior: Adenopathy, Lymphoma/Leukemia, Germ Cell Tumors, Thyroid (Goiter/Ca), Thymic Tumors, Vascular</p> <p>Middle: LAD, EBV, Castleman's, Neoplastic (SmCC, Lymphoma/Leuk), Granulomatous, Congenital Cyst, Vascular/Arch Anomalies</p> <p>Posterior: Adenopathy, Neurogenic tumor, Spine (Abscess, Tumor), Vascular (Aneurysm, Hematoma), Developmental (Lateral thoracic meningocele, Bochdalek hernia)</p> <p>HILAR ENLARGEMENT</p> <p>PULMONARY HEN Hypertrophy: LUSHR Hypodynamic: (L-R shunt), ASD, VSD, PDA, Endocardial cushion defect</p> <p>Obstructive: Chronic PE, Emphysema, PPHN, Drug Vasculitis, Schistosomiasis</p> <p>Hypoid: Chronic Bronchitis, CF, BO, Sleep Apnea, Fibrosis, Chronic High Altitude</p> <p>Pulmonary Venous HTN: Mitral Stenosis, CHF, Pulmonary Venocclusive Disease</p> <p>HILAR ADENOPATHY Neoplastic: Primary lung, Mets, Lymphoma, Leukemia (CLL) Granulomatous: Sarcoid, TB/Fungal Infectious: TB, AIDS Castleman's Disease</p>	<p>MOSAIC LUNG ATTENUATION</p> <p>Lucent Regions Normal: Vessels same size in all areas -> GGO dxs</p> <p>Lucent Regions Abnormal: Vessels are smaller in lucent areas: Air trapping (+): BO, Asthma, CF Air trapping (-): Pulm HTN dxs</p> <p>CHANGES IN LUNG VOLUME <i>Look for: deviated fissures, vascular crowding, hilar retraction, mediastinal shift, flattened diaphragm, sternum-diaphragm angle >90°</i></p> <p>Volume Loss: ATX, surgery, post infectious/inflammatory scarring, fibrosis, decreased compliance (ARDS, lymphangitic tumor)</p> <p>Hyperexpansion: Emphysema, CF, BO, Chronic Bronchitis, Asthma, TBM</p> <p>ACQUIRED HEART DISEASE <i>PC (pericardium), MC (myocardium), VD (valve dz)</i></p> <p>SMALL HEART (Restrictive, Pressure Overload) PC: Constrictive Pericarditis MC: Acute MI, Restrictive/Hypertrophic CM VD: Stenosis (-> cephalization or big SVC)</p> <p>LARGE HEART (MC failure, Volume Overload) PC: Pericardial Effusion MC: Dilated/Ishemic CM, RVF VD: Regurgitation (asym chamber enlargement) <i>PC & MC dz -> Global enlargement</i></p>
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Approach: What We Try To Diagnose

A Pathology or Pathological Differential

- **Pathology:** We look at Imaging Patterns of Injury: Morphology and Distribution
- A *pathological process* is suggested
- Importance to the Clinician: Prognosis and Therapeutic Options

What We Can Help With: Etiology

- **Etiology:** It is NOT the same as Pathology
- The Same etiology can have a **Variety of Pathological effects** in Patients - "PEOPLE ARE LIKE SNOWFLAKES"
- What are the common causes for the pathological injury likely present?
- For example: Fibrotic NSIP is a *Pathological Injury*. Drug Toxicity is an *Etiology*.

Report Impression:

Examples *Will Evolve* With Radiologist's Experience

- 5 *generalized options* for the radiologist:
- **Imaging is Normal!**
- **Imaging findings questionable or of uncertain significance:** Consider a follow up exam, Expiratory images or laboratory investigation? (i.e. Hypoxic? DLCO)
- **Imaging is characteristic** for a diagnosis

Report Impressions

- A **short differential diagnosis** that clinical history and laboratory tests can help sort out: Smoking history? Connective tissue disease? Fever? Medications? Pulmonary consultation is helpful.
- **Diagnosis not known/Indeterminate:** Is tissue or bronchial secretion sampling required?
* If so, How? Sputum, Bronchoscopy, CT guided lung biopsy, Open lung biopsy or EUS.

**Avoid terms like 'Infiltrate' 'Nonspecific' or 'Clinical correlation'

Images → Report Conclusions

Depends on Your Referring Clinician



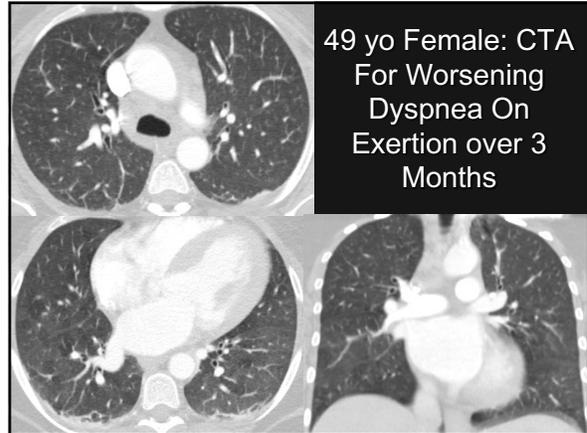
• “Moderately advanced pulmonary fibrosis, most likely Fibrotic NSIP *pathology*. UIP is possible, but less likely. Consider an Autoimmune disease or Drug Toxicity as *possible etiologies*. If tissue sampling is considered, suggest a VATS procedure.”

Southern Puget Sound, WA: October

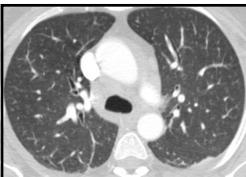


Imaging of Questionable Significance Common Examples

- Ground Glass versus expiration image?
(Progressive Increase dependent density?)
- Centrilobular Ground Glass Nodules
- Small airway disease/Mosaic Perfusion
- Airway Thickening
- Bronchiectasis
- Dependent atelectasis versus early fibrosis – Does it extend laterally?

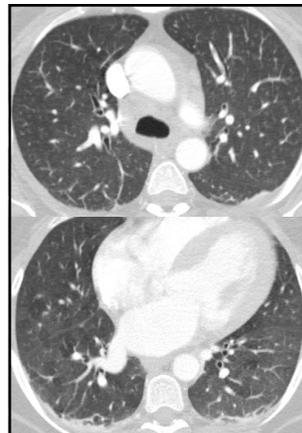


49 yo Female: CTA
For Worsening
Dyspnea On
Exertion over 3
Months



#1: Which report Impression would you use?

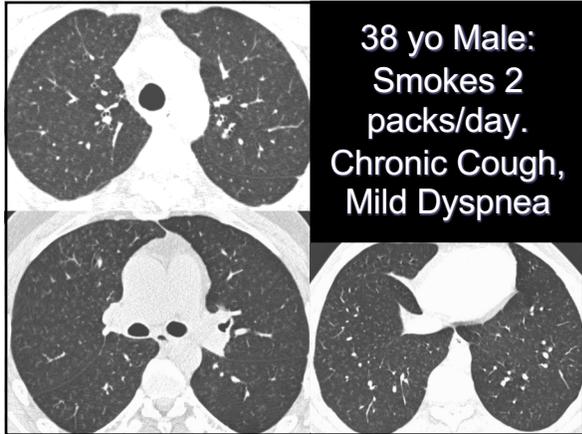
1. Nonspecific imaging, Clinically correlate
2. Suggest Pulmonary Consult and Dlco measurement or repeat CT full inspiration
3. Negative examination
4. Diffuse ground glass lung disease, suspected Cellular NSIP pathology/HSP



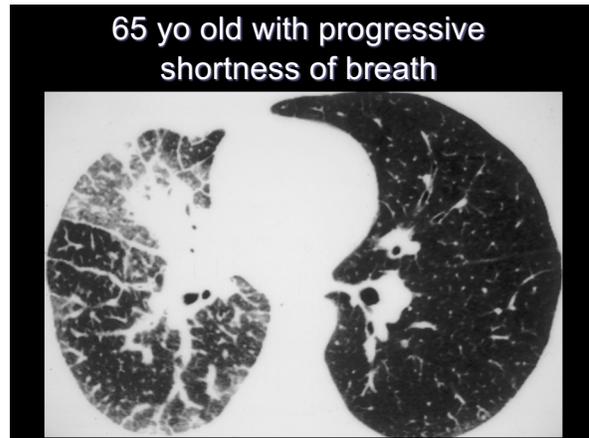
**Answers: 2 or 4
are both helpful**

Follow up: Dlco was 76%
of predicted and patient's
pulse O2 decreased into
the mid 80's with exertion

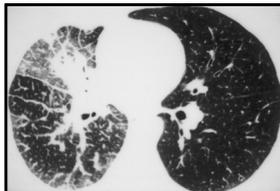
Bx: NSIP from HSP
Likely secondary to
Medication



38 yo Male:
Smokes 2
packs/day.
Chronic Cough,
Mild Dyspnea



65 yo old with progressive
shortness of breath



#2: Which report
impression
would you use?

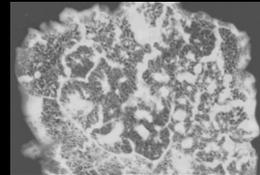
- Findings consistent with asymmetric
Congestive heart failure
- Findings suspect for Influenza/viral infection,
clinical correlation suggested
- Suspected Aspiration involving right lung
- Findings characteristic for Lymphangitic spread
of tumor

Answer: #4 - Lymphangitic Spread of Tumor.

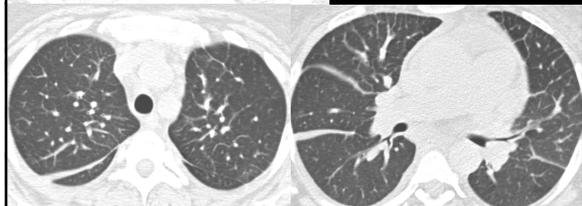
Findings are Characteristic – Usually it is
Adenocarcinoma or Lymphoma

Interlobular Septal Thickening:

Hydrostatic Pulmonary Edema
Lymphangitic Spread of Tumor
Acute Eosinophilic Pneumonia



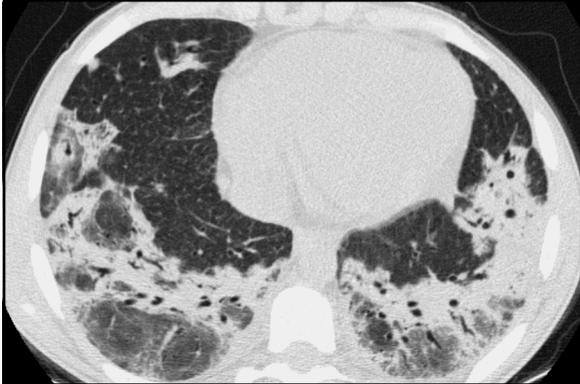
Hydrostatic
Edema



‘If you can’t explain it
simply...
You don’t understand it
well enough.’

Albert Einstein

28 Year Old Female with Chronic Cough

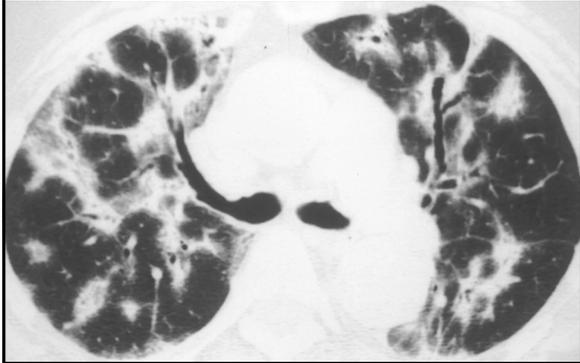


Chronic Consolidation:

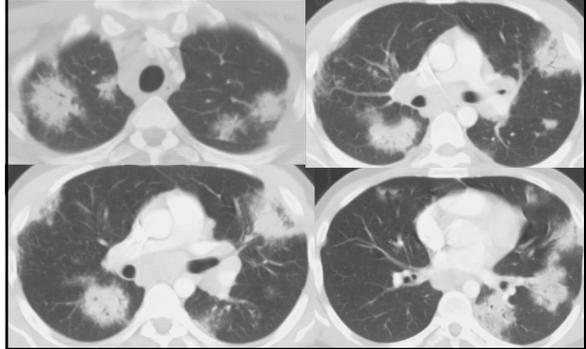
COP *and* Eosinophilic Pneumonia
Mucinous AdenoCA *and* Lymphoma
TB/Fungal *and* Alveolar Sarcoidosis
Chronic Aspiration *and* Lipoid
Pneumonia
Alveolar Proteinosis

Cryptogenic Organizing Pneumonia

The lung reacts as if there is a pulmonary infection



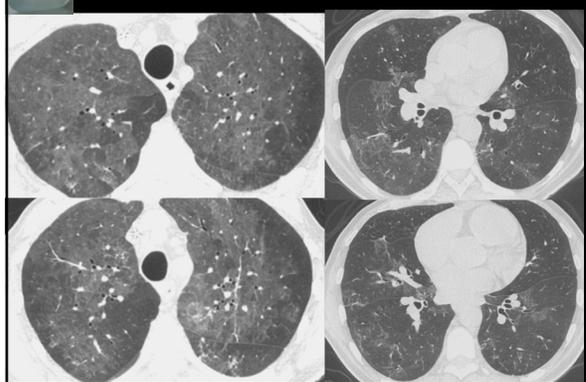
45 Year Old Male: Cough for 3 Months,
No Fever...Enlarged Lymph Nodes



Sunriver/Bend, Oregon

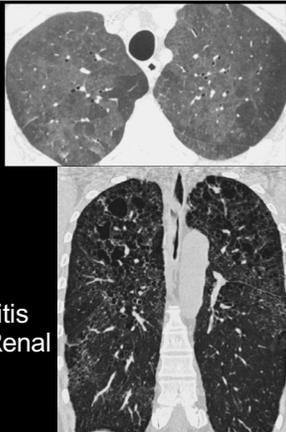


Ground glass: Upper Lobe Distribution



**Upper Lobe
Distribution:
"SET PARC"**

- S - Sarcoidosis/Silicosis
- E - EG/EAA
- T - TB/Fungal
- P - PJP
- A - Ankylosing Spondylitis
- R - Radiation Therapy/Renal
- C - Cystic Fibrosis



Ground Glass: Acute Symptoms

- Blood, pus or water
- Presence or absence of **pleural fluid** often helpful.
- **"Wet" Disease:** Hydrostatic and Non-cardiogenic edema/ARDS
- **"Dry" Disease:** PJP, CMV infections, acute hypersensitivity pneumonitis or Pulmonary hemorrhage syndromes

2 Patients with Acute Ground Glass Opacities

No Pleural Fluid ↑

Bilateral Pleural Effusions →

#3: 40 yo with Dyspnea over 2 days. What would you report as the most likely pathologic process?

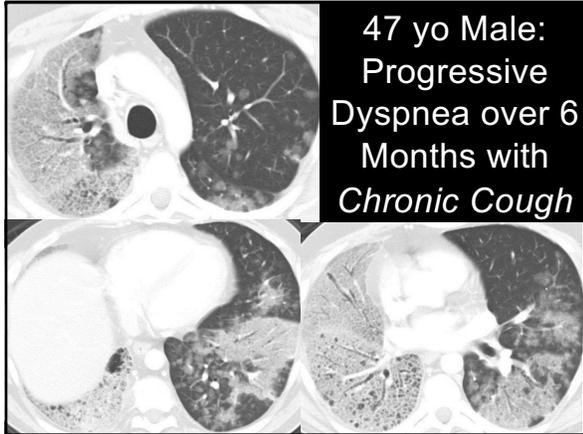
1. Hydrostatic Edema
2. Pulmonary Hemorrhage Syndrome
3. Non cardiogenic edema
4. Alveolar Proteinosis

Answer: #2 Pulmonary Hemorrhage Syndrome

****#3 is certainly possible and should also be mentioned**

- Symptoms are only 2 days (Acute)
- Extensive Ground glass *without septal lines nor pleural effusion*

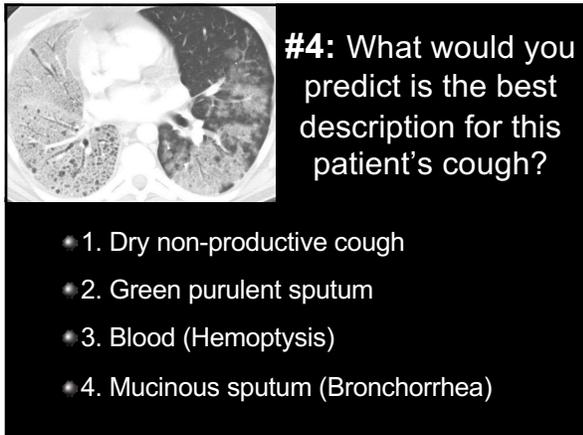




47 yo Male:
Progressive
Dyspnea over 6
Months with
Chronic Cough

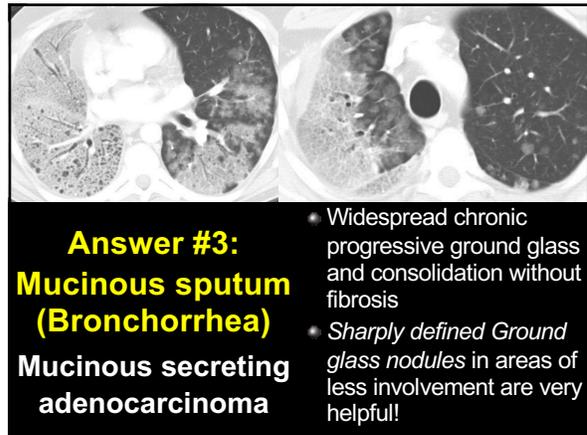


Look in the Regions with *Less Involvement*
for Clues: *Interesting there is no fibrosis, eh?*



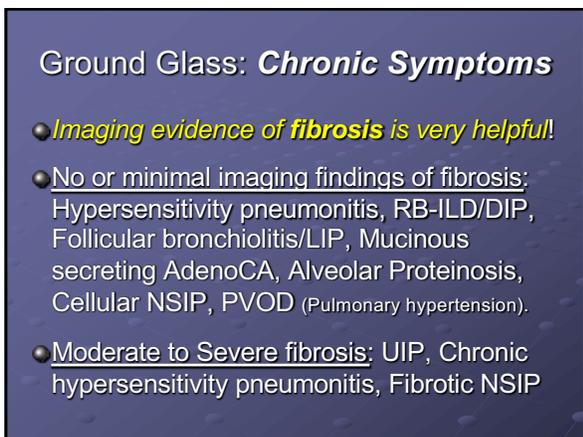
#4: What would you
predict is the best
description for this
patient's cough?

- 1. Dry non-productive cough
- 2. Green purulent sputum
- 3. Blood (Hemoptysis)
- 4. Mucinous sputum (Bronchorrhea)



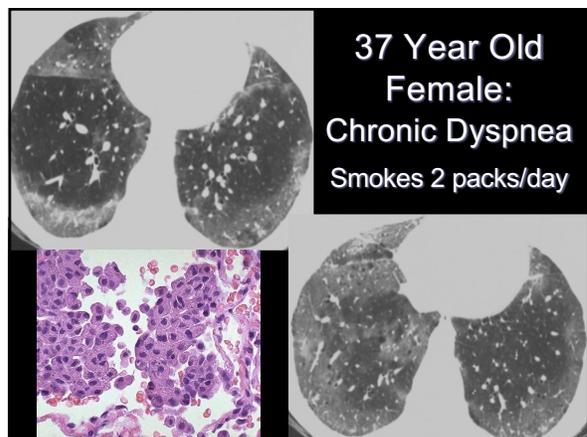
Answer #3:
**Mucinous sputum
(Bronchorrhea)**
**Mucinous secreting
adenocarcinoma**

- Widespread chronic progressive ground glass and consolidation without fibrosis
- *Sharply defined Ground glass nodules* in areas of less involvement are very helpful!

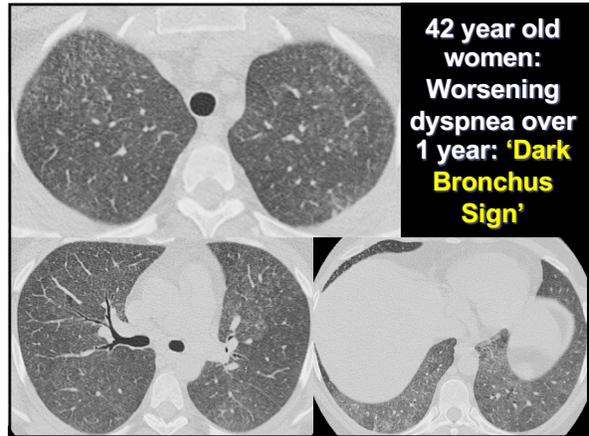
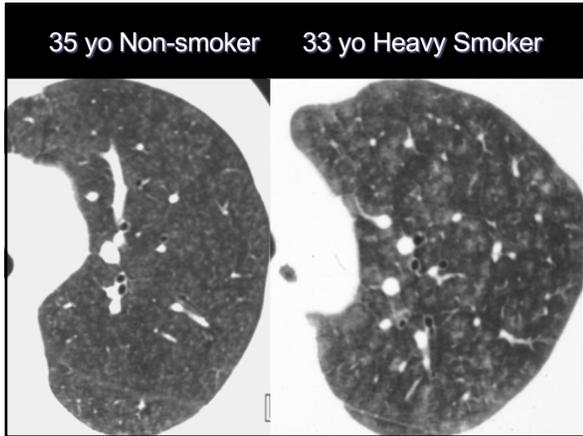


Ground Glass: **Chronic Symptoms**

- *Imaging evidence of fibrosis is very helpful!*
- No or minimal imaging findings of fibrosis: Hypersensitivity pneumonitis, RB-ILD/DIP, Follicular bronchiolitis/LIP, Mucinous secreting AdenoCA, Alveolar Proteinosis, Cellular NSIP, PVOD (*Pulmonary hypertension*).
- Moderate to Severe fibrosis: UIP, Chronic hypersensitivity pneumonitis, Fibrotic NSIP

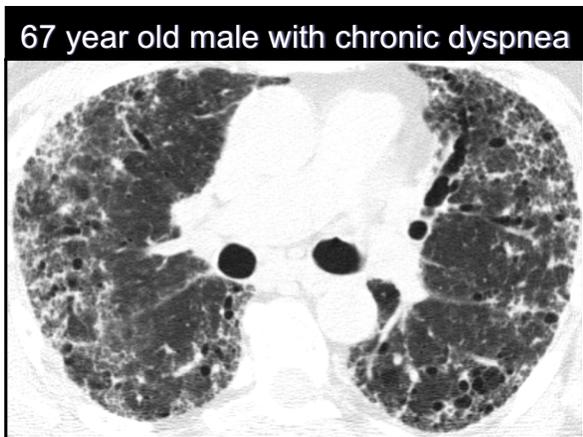
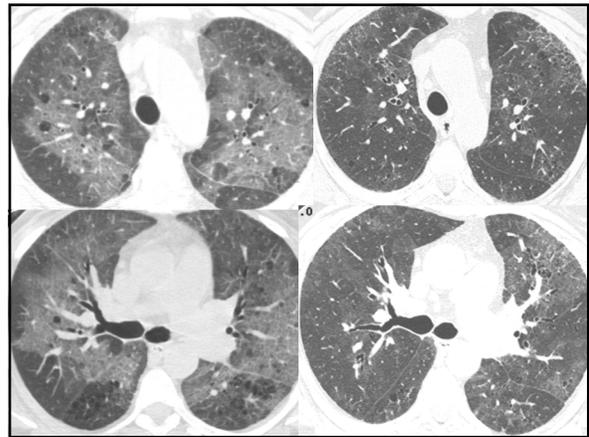


37 Year Old
Female:
Chronic Dyspnea
Smokes 2 packs/day

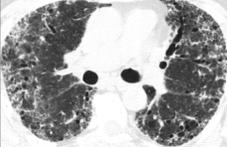


NSIP: Cellular to Fibrotic Spectrum

- **NSIP IS NOT A DISEASE!** It's an inflammatory/fibrotic pattern of **pathology**, often from collagen-vascular diseases or hypersensitivity pneumonitis. *Reflects the underlying etiology.*
- CT findings include GGO/consolidation and/or reticular opacities. *Reflects the underlying etiology.*
 - Honeycombing **much less common** than in UIP
 - GGO/consolidation predominates in cellular form
 - Reticular opacities predominate in Fibrotic form
- Prognosis: Cellular NSIP > Fibrotic NSIP > UIP
 - 10 year survival 100%, 35%, 15%, respectively



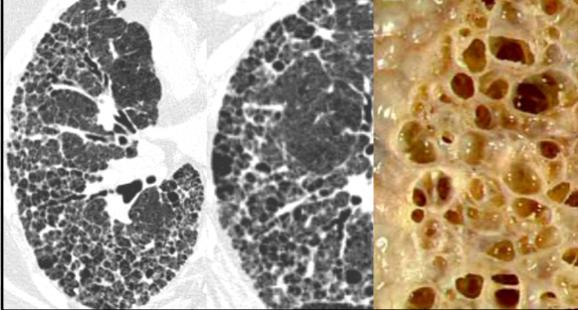
#5: What would be your report impression?



- 1. Indeterminate Pulmonary fibrosis, Consult pulmonology
- 2. Fibrosis likely represents Drug toxicity or connective tissue disease pathology.
- 3. Imaging typical for UIP.
- 4. Finding probable for UIP fibrosis versus possibly NSIP pathology.

Four Imaging Findings of Fibrosis:

- 1. Irregular Visceral Pleura
- 2. Short Reticular Opacities
- 3. Traction Bronchiectasis
- 4. Honeycombing



Subtle subpleural sparing and Bronchovascular distribution

Features associated with a Fibrotic NSIP pathology



Usual Interstitial Pneumonitis

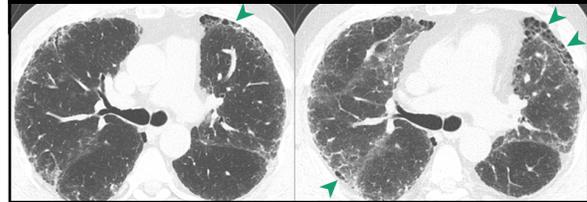
- Often *peripheral and basilar* distribution
- Imaging evidence of fibrosis: Reticular opacities, traction bronchiectasis, irregular visceral pleura +/- **Honeycombing**
- **Hypoxia/Low Dico** more severe than NSIP
- New medical therapies
- **Active search**: Pulmonary hypertension, any new nodules or ground glass opacities

Honeycombing:

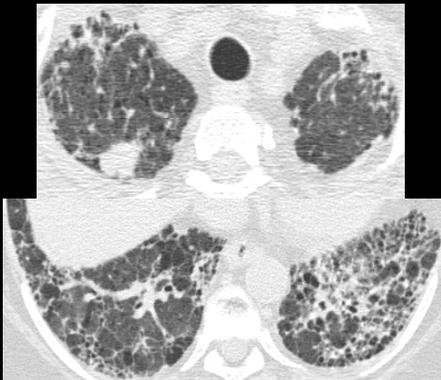
3-10 mm shared thickened wall cystic spaces that **contact the pleura**

Progression over time is often

Peripheral to Central



UIP: Increased Incidence of Lung Cancer

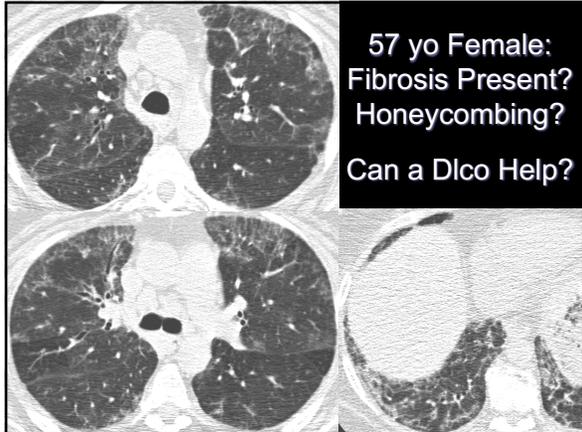


Inspiratory and Expiratory imaging:

Mosaic lung attenuation accentuated on the expiratory

Most consistent with Hypersensitivity pneumonitis/ EAA



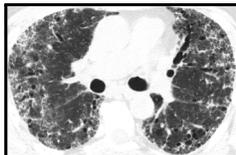


57 yo Female:
Fibrosis Present?
Honeycombing?
Can a Dico Help?

Importance of **Imaging** on Fibrosis Diagnosis (*Pathology not the Gold Standard*)

- **Typical UIP Pattern:** Subpleural basal distribution, Reticular opacities, **Honeycombing** +/- traction bronchiectasis and absence of features inconsistent with UIP
- **Probable UIP Pattern:** Same as Typical, except *no* identifiable honeycombing
- **Indeterminate UIP Pattern** or **consistent with another pathological diagnosis**

Lynch et al. Fleischner Society White paper. Lancet Respir Med. 2017;S2213-2600(17) 30433-2



Repeat #5: What would be your report impression?

- 1. Indeterminate Pulmonary fibrosis, Consult pulmonology
- 2. Fibrosis likely represents Drug toxicity or connective tissue disease pathology.
- 3. Imaging typical for UIP.
- 4. Finding probable for UIP fibrosis versus possibly NSIP pathology.



Answer #3:
Findings Typical for UIP

*Answer #4 is also acceptable

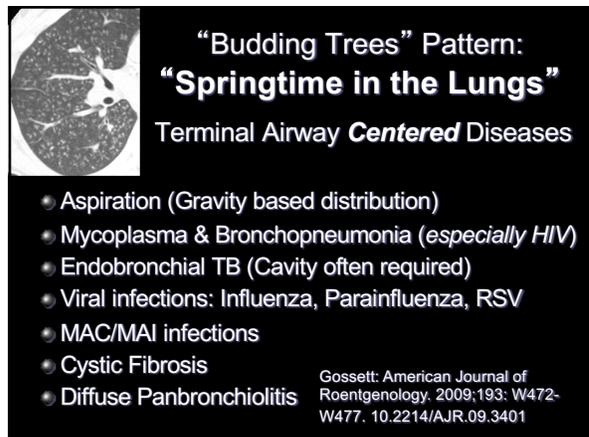
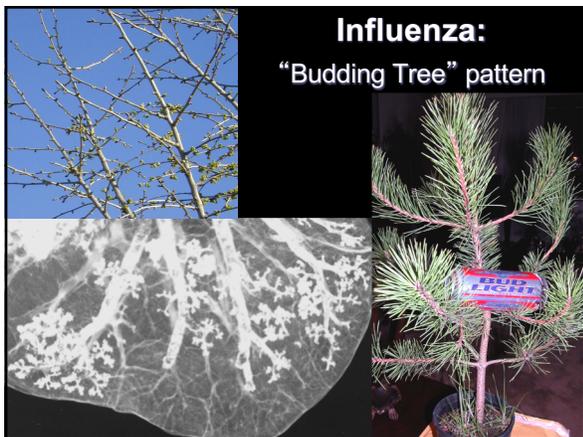
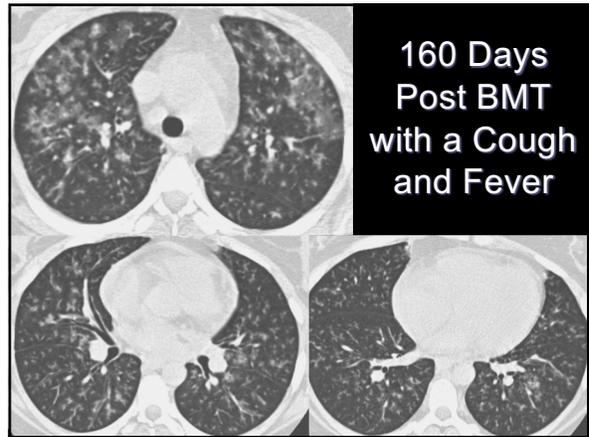
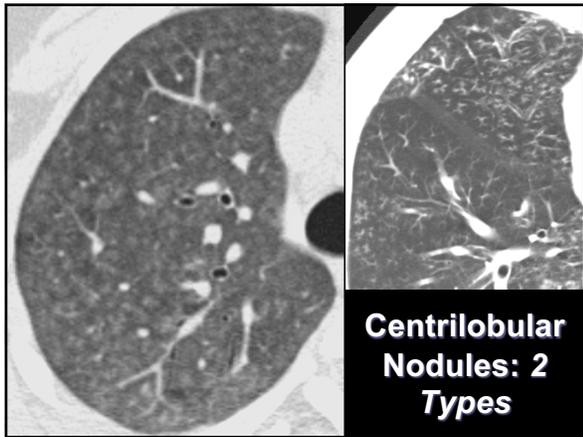
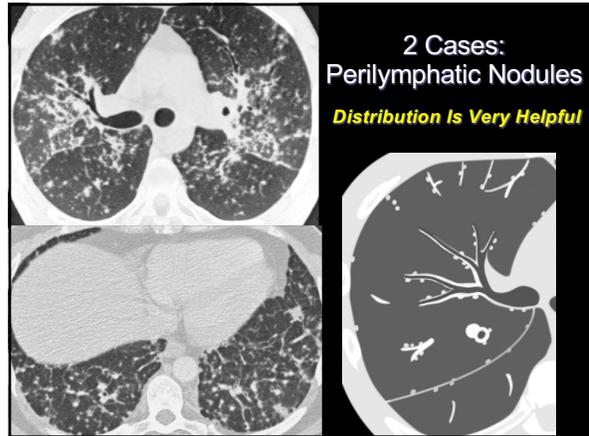
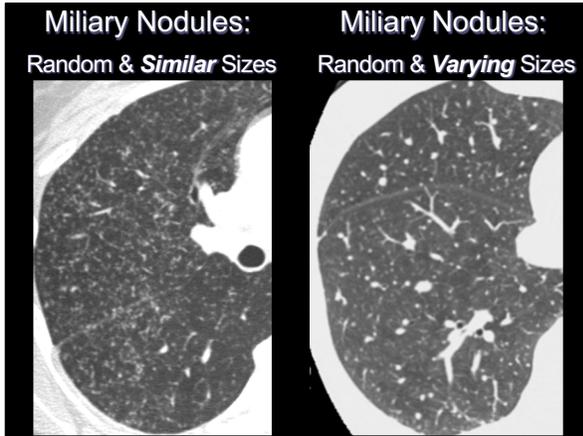
- **Typical UIP Pattern:** Subpleural basal distribution, Reticular opacities, **Honeycombing** +/- traction bronchiectasis and absence of features inconsistent with UIP
- **Probable UIP Pattern:** Same as Typical, except *no* identifiable honeycombing
- **Indeterminate UIP Pattern** or **consistent with another pathological diagnosis**

Saranac Lake, NY: Adirondack Park



Nodules

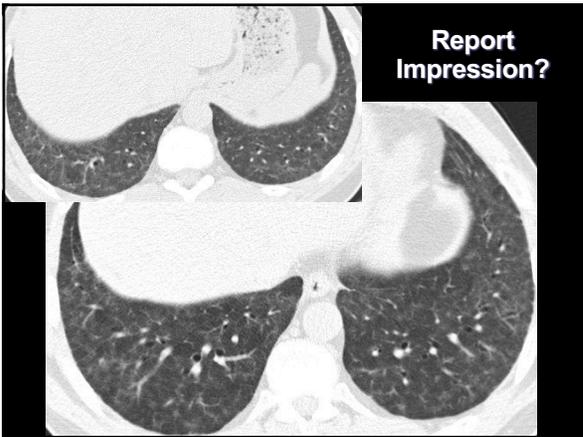
- **Perilymphatic distribution**
- **Random distribution**
- **Centrilobular distribution:** No nodules along fissures or sub-pleural regions
 1. Terminal bronchial filling ('Budding-Tree')
 2. Ill-defined respiratory bronchial inflammation





Diagnosis Is Not Know: Imaging Not Characteristic or Has a Longer Differential

- Common Imaging result
- Unusual presentations of more common diseases
- Uncommon to rare diseases that may not be considered during day to day work
- Follow up imaging, Laboratory tests, sputum and/or tissue sampling?

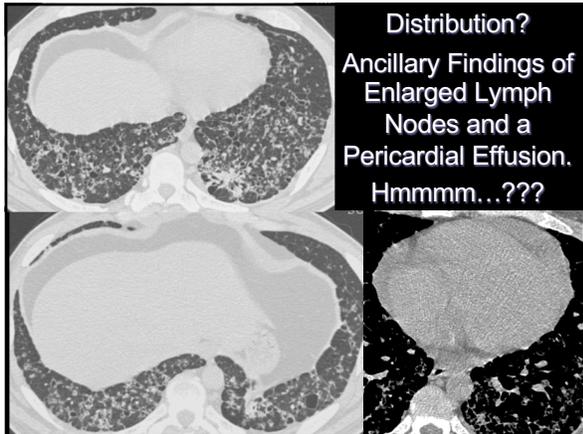


‘Medicine is the Science of Uncertainty and the Art of Probability’

Sir William Osler

JCA - GIE





#6: Which would best reflect your report Impression?

- 1. Findings characteristic for Langerhans Cell Histiocytosis.
- 2. Imaging highly suspect for widespread adenocarcinoma. Suggest tissue sampling
- 3. Nonspecific reticulonodular opacities. Clinical correlation suggested.
- 4. Probable Langerhans cell Histiocytosis, but with some features that are uncommon. Suggest tissue sampling.

Answer is #2 – Widespread adenocarcinoma was found on open lung biopsy and in the pericardial fluid.

Answer number #4 is more than acceptable as well

Remember: If something is not entirely consistent with a diagnosis, do not force it by saying it is 'characteristic'. It may very well be correct, but better to approach unusual imaging findings as a **red flag** that *something else may be present*.

Diffuse Lung Disease Summary

- 5 Major concepts of report impressions
- Separate between *Pathology Differential* and *Etiology Differential*
- Combine imaging of *Morphological abnormalities* and Disease *Distribution*
- Duration of symptoms, looking in areas of less involvement and Hypoxia/Dlco are helpful
- Pathology is **NOT** the Gold standard for diffuse lung disease...Earn your paycheck

Thank you!
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gosselin@ohsu.edu

Oregon Coast, 15 Miles South of Cannon Beach

Next talk

- Cystic Disease
- Mosaic lung attenuation vs Global
- Budding Tree

