

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

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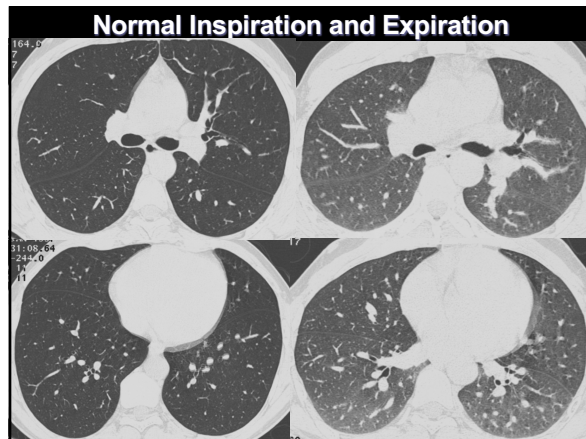
“The Greatest Obstacle to Discovery is not Ignorance, but the Illusion of Knowledge.”

- 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'



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 Cavitary
- **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)		
GROUND GLASS OPACITIES ACUTE: Blood, Pus, Water PNA: PCP, CMV, resolving Bacterial Edema: hydrostatic & capillary leak Hemorrhage: Pulmonary Hemorrhage <i>Wt: Edema/ARDS</i> <i>Uz: PCP, CMV, HSP, hemorrhage</i> CHRONIC (>4 weeks) No/Minimal Fibrosis Hypersensitivity Pneumonitis [HSP] [EAA vs Drug-Induced] [non-smokers]/ [DIPHR-ILD, Pulm LCH/EOS] [smokers] Cellular NSIP, Pulm Alveolar Proteinosis, Follicular Bronchiolitis LIP (CVD, HIV), Pulmonary venoocclusive dz 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) CRAZY PAVING GGO + septal thickening Acute: hemorrhage, edema (both), AIP, ARDS, PCP, chronic eosinophilic PNA, drug toxicity Chronic: Alv Prot, lipoid PNA, COP, BAC UNILATERAL EDEMA Dependent (R-L), reexpansion, asymmetric emphysema, venous/lymphatic obstruction, mitral regurgitation (→RUL)	CONSOLIDATION ACUTE: Blood, Pus, Water PNA: Bacterial: Aspiration Edema: Hydrostatic & capillary leak Hemorrhage: Pulmonary Hemorrhage CHRONIC "ANGIO" Alveolar Proteinosis Neoplasm (Lymphoma, BAC) Granulomatous (TB/Fungal, Alv Sarcoid) Inflammatory (Eosinophilic PNA, COP) Qid (Chronic Aspiration, Lipoid Pneumonia) <i>Adenopathy favors Lymphoma or Granulomatous Dz</i> INTERSTITIAL LUNG DISEASE Diffuse Reticular Opacities <i>(Rerley A, B lines)</i> Pulmonary Edema (Hydrostatic=cap leak) Lymphangitic tumor (AdenoCa/Lymphoma) Viral or Mycoplasma PNA Acute Eosinophilic PNA Peripheral Reticular Opacities <i>(Rerley A, B lines)</i> Severe Honeycomb Lung (Fibrosis), Severe Emphysema, Diffuse Central Bronchiectasis, EG/PLCH, PCP, LAM/ITS, LIP, DIP, Cystic Mets (sarcomas: leiomyo, synovial, stromal cell, epithelioid, osteogenic)	MULTIPLE NODULES 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) Upper lobe: HSP, EG/PLCH, SI & CW pneumo Perilymphatic: Lymphangitic tumor, Sarcoid Subacute/chronic (ill-defined nodules) Inhalational/Lymphatic Dz: HSP, EG/PLCH, Silicosis & Coal workers pneumoconiosis Centrilobular/Tree-in-Bud: Aspiration, Viral PNA (RSV, adenov, flu), BronchoPNA, Mycoplasma, MAI, Endobronchial TB Spread, Asthma, ABPA, CF, COP, Diff Pustulochilitis Centrilobular/ill-Defined Ground Glass HSP (EAA), NSIP (Cellular), RB-ILD (smoker), Follicular Bronchiolitis (CVD, AIDS) CAVITARY NODULES Infection: Fungal: Cocci, Asperg, Crypto gattii Bact: septic emb, abscess, TB, Nocard, Legionella Neoplasm: SqCCa (nodular wall), Sarcoma Caviticities: Wegener's, Angiocentric Lymphoma, RA (Necrotic Nodules) Trauma: Hematoma, pneumatocele/cyst SOLITARY PULM NODULE AdenoCa, SqCC, LrgCC, SmCC, Carcinoid, Lymphoma, Met, Hamartoma, Granuloma, Infection, RA, Trauma, Congenital cyst, AVM

THORACIC DIFFERENTIAL DIAGNOSIS 2 (Marc Gosselin)		
DISTRIBUTION OF DZ UPPER LOBE: "SET PARC" <i>(1/1/0, lymphatic clearance)</i> Sarcoid, Silicosis PCP EG-PLCH (Smoker) Aplysiozing Spondylitis EAA (Nonsmoker) Radiation therapy TB/Fungal Cystic Fibrosis LOWER LOBE/DEPENDENT: <i>(1/1/0, gravity)</i> Hydrostatic edema, aspiration, ATX, CVD, UIP BRONCHOVASCULAR <i>(airways, lymphatics)</i> Sarcoid, Lymphoma/lympho prolif dz, COP, Kaposi's Sarcoma; aspiration PNA (acute sx's) PERIPHERAL: Chronic Eos PNA, pleural dz, infarct, COP, fungal infection, UIP, Wegener's RANDOM: <i>(follows blood flow, incl pleura)</i> Hematogenous spread of tumor or infection DIFFUSE: <i>(usually systemic dz)</i> Noncardiogenic edema, CF, Pulm-renal dz FOCAL: <i>(usually local dz)</i> Bacterial PNA, contusion, MAC, aspiration UNILAT PLEURAL EFFUSION Exudative: Hemots (Trauma, Iatrogenic), Tumor, Infection/Infl'n (Emphysema), Chylots Transudative: Hepatohydrothorax	MEDIASTINAL MASSES Anterior: Adenopathy, Lymphoma/ Leukemia, Germ Cell Tumors, Thyroid (Gottex/Ca), Thymic Tumors, Vascular Middle: LAD, EBV, Castleman's, Neoplastic (SmCC, Lymphoma/Leuk), Granulomatous, Congenital Cyst, Vascular/Arch Anomalies Posterior: Adenopathy, Neurogenic tumor, Spine (Abscess, Tumor), Vascular (Aneurysm, Hematoma), Developmental (Lateral thoracic meningocele, Bochdalek hernia) HILAR ENLARGEMENT PULMONARY VEIN Hyperdynamic: (L→R shunt): ASD, VSD, PDA, Endocardial cushion defect Obstructive: Chronic PE, Emphysema, PPHITN, Drug Vasculitis, Schistosomiasis Hypoxic: Chronic Bronchitis, CF, BO, Sleep Apnea, Fibrosis, Chronic High Altitude Pulmonary Venous HTN: Mitral Stenosis, CHF, Pulmonary Venocclusive Disease HILAR ADENOPATHY Neoplastic: Primary lung, Mets, Lymphoma, Leukemia (CLL) Granulomatous: Sarcoid, TB/Fungal Infectious: EBV, AIDS Castleman's Disease	MOSAIC LUNG ATTENUATION Lucent Regions Normal: Vessels same size in all areas → GGO ddx Lucent Regions Abnormal: Vessels are smaller in lucent areas: Air trapping (+): BO, Asthma, CF Air trapping (-): Pulm HTN ddx CHANGES IN LUNG VOLUME <i>Look for: deviated fissures, vascular crowding, hilar retraction, mediastinal shift, flattened diaphragm, sternum-diaphragm angle >90°</i> Volume Loss: ATX, surgery, post infectious/ inflammatory scarring, fibrosis, decreased compliance (ARDS, lymphangitic tumor) Hyperexpansion: Emphysema, CF, BO, Chronic Bronchitis, Asthma, TBM ACQUIRED HEART DISEASE <i>PC (pericardium), MC (myocardium), VD (valve dz)</i> SMALL or SMALL HEART (Restrictive, Pressure Overload) PC: Constrictive Pericarditis MC: Acute MI, Restrictive/Hypertrophic CM VD: Stenosis (→ cephalization or big SVC) LARGE HEART (MC failure, Volume Overload) PC: Pericardial Effusion MC: Dilated/Isthemic CM, RVF VD: Regurgitation (assym chamber enlargement) <i>PC & MC dz → Global enlargement</i>

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



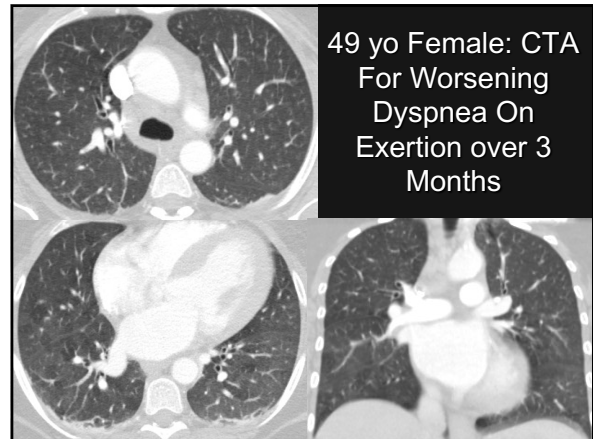
• “Moderately advanced pulmonary fibrosis, most likely Fibrotic NSIP *pathology*. UIP is possible, but less likely. Consider an Autoimmune disease or Drug Toxicity as *possible etiologies*. If tissue sampling is considered, suggest a VATS procedure.”

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?

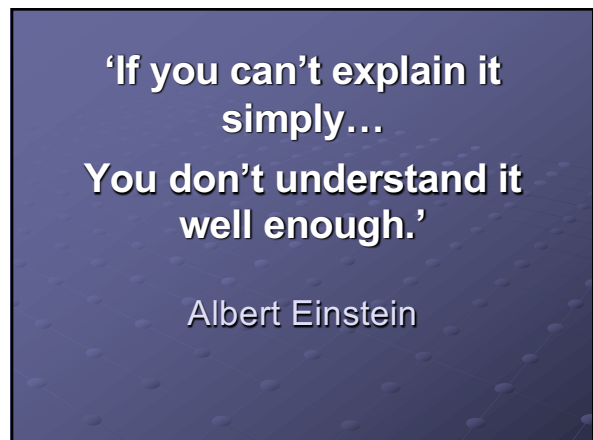
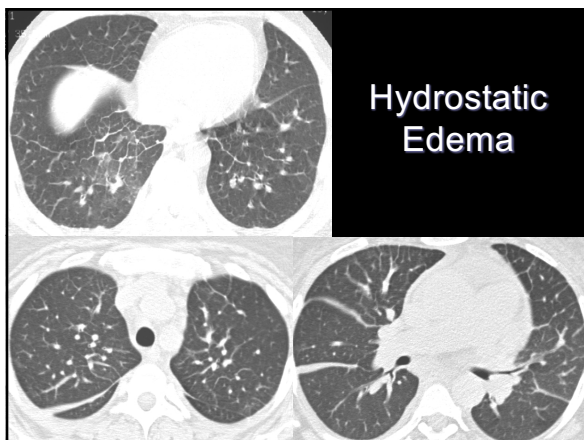
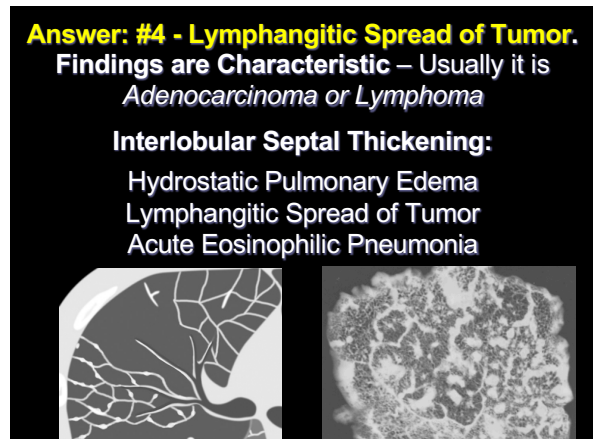
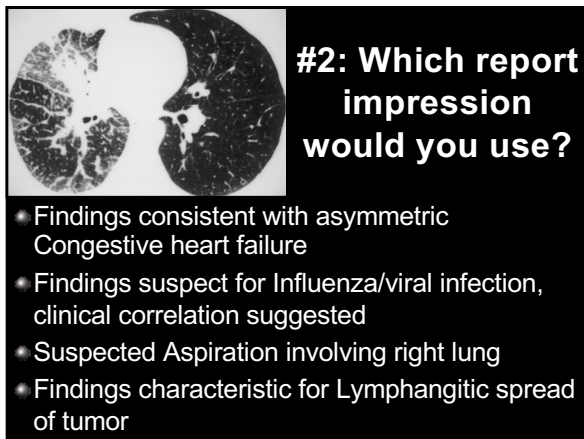
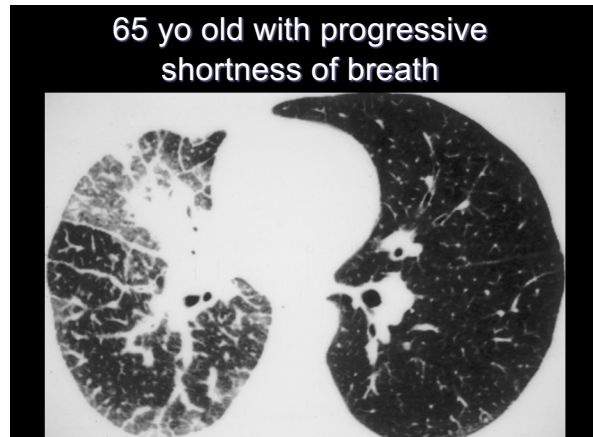
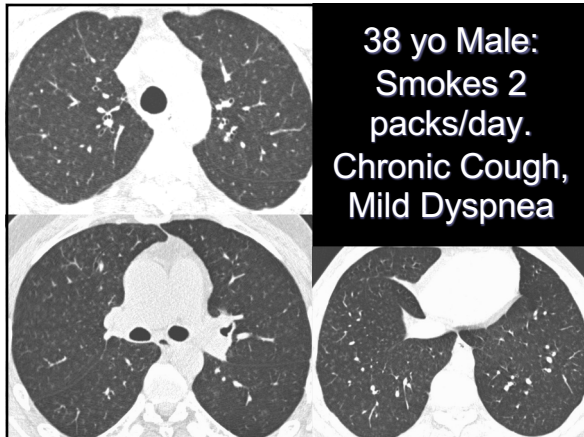
- 1. Nonspecific imaging, Clinically correlate
- 2. Suggest Pulmonary Consult and Dlco measurement or repeat CT full inspiration
- 3. Negative examination
- 4. Diffuse ground glass lung disease, suspected Cellular NSIP pathology/HSP



**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



28 Year Old Female with Chronic Cough

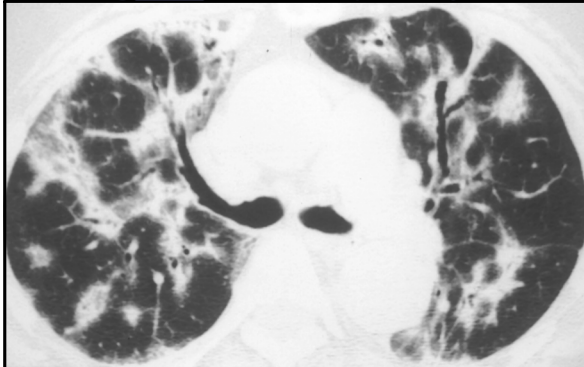


Chronic Consolidation:

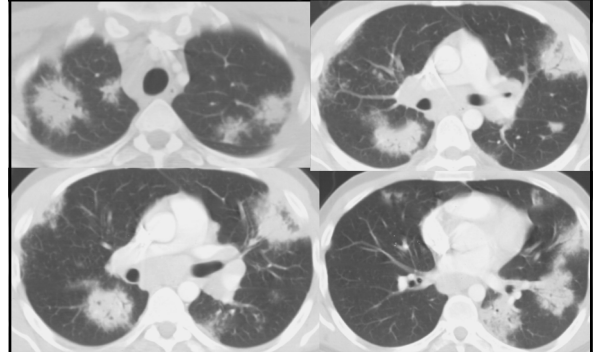
COP *and* Eosinophilic Pneumonia
Mucinous AdenoCA *and* Lymphoma
TB/Fungal *and* Alveolar Sarcoidosis
Chronic Aspiration *and* Lipoid
Pneumonia
Alveolar Proteinosis

Cryptogenic Organizing Pneumonia

The lung reacts as if there is a pulmonary infection



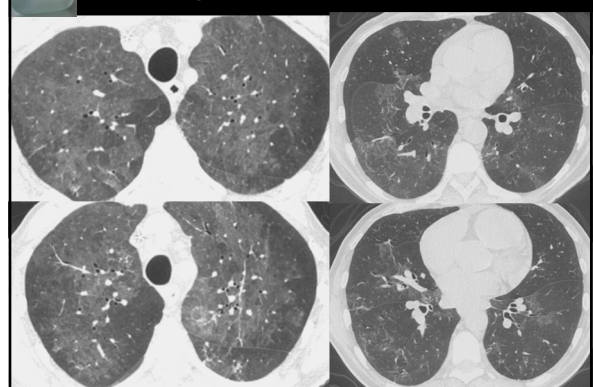
45 Year Old Male: Cough for 3 Months,
No Fever...Enlarged Lymph Nodes



Sunriver/Bend, Oregon

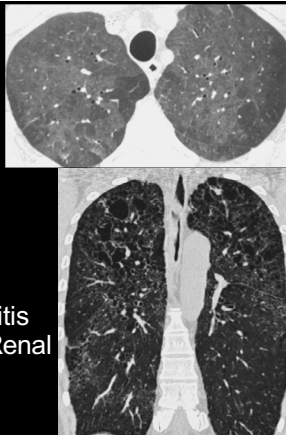


Ground glass: Upper Lobe Distribution



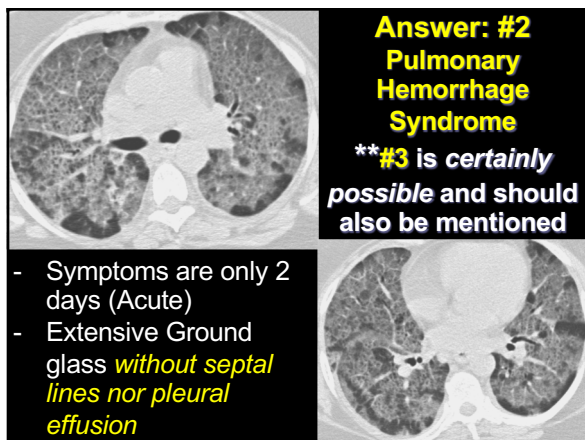
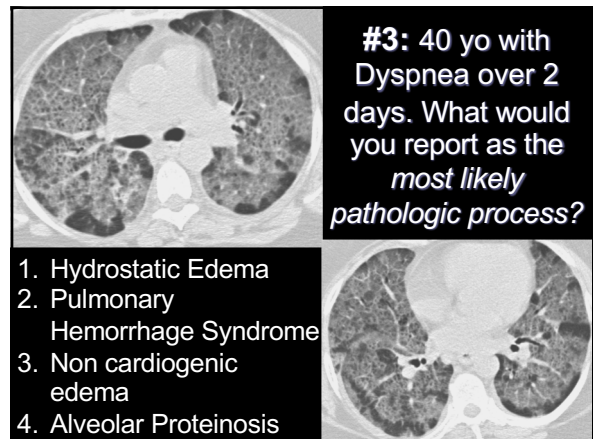
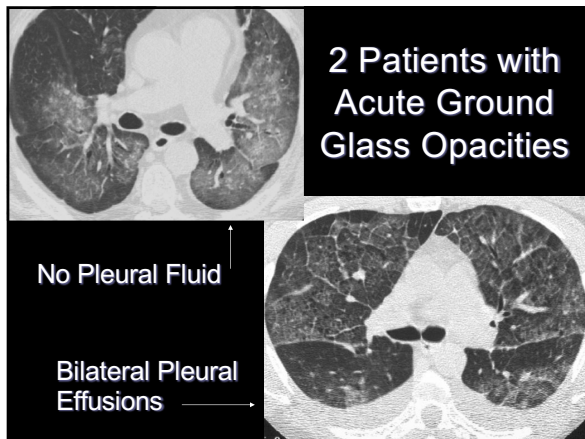
Upper Lobe Distribution: "SET PARC"

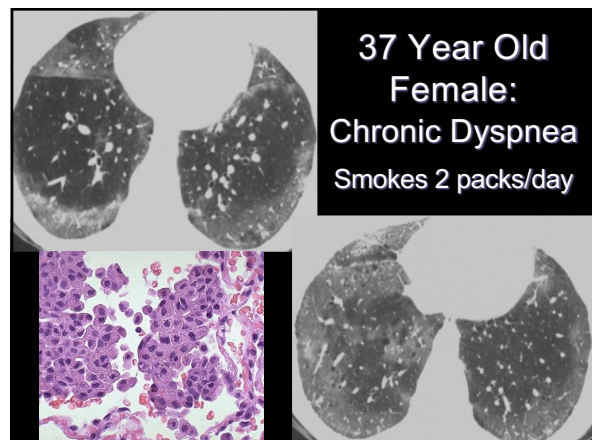
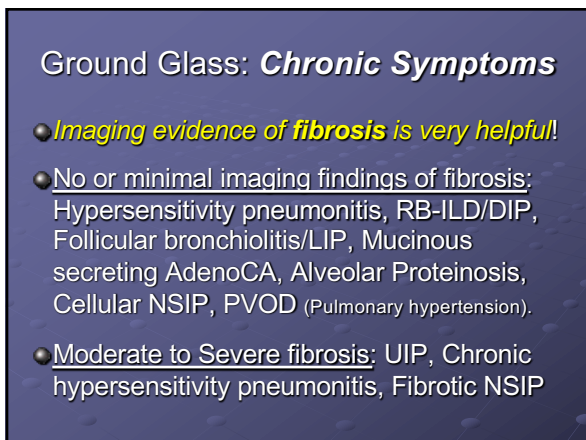
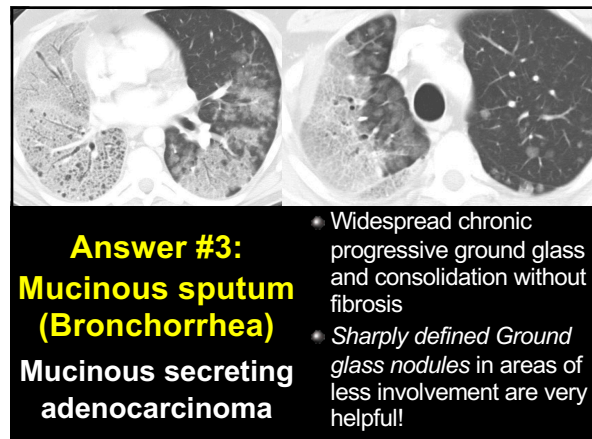
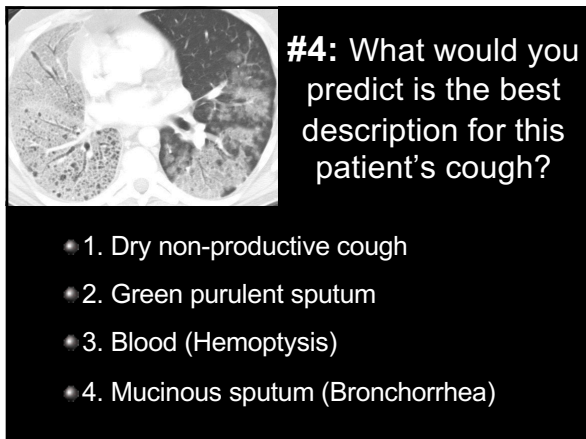
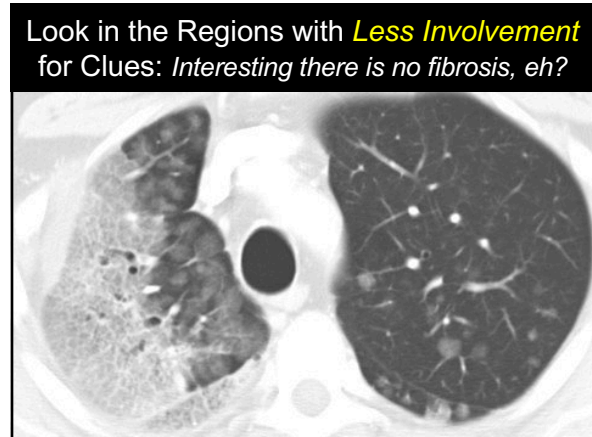
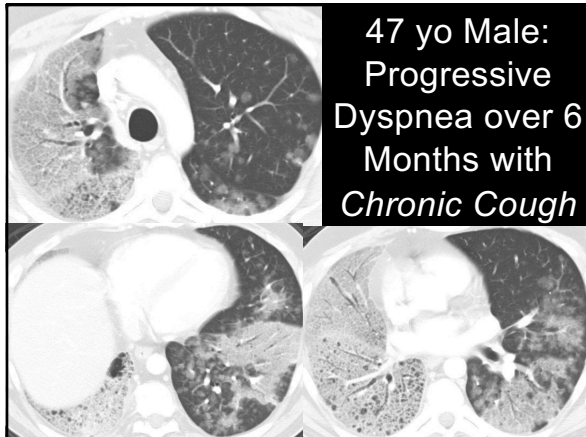
S - Sarcoidosis/Silicosis
E - EG/EAA
T - TB/Fungal
P - PJP
A - Ankylosing Spondylitis
R - Radiation Therapy/Renal
C - Cystic Fibrosis

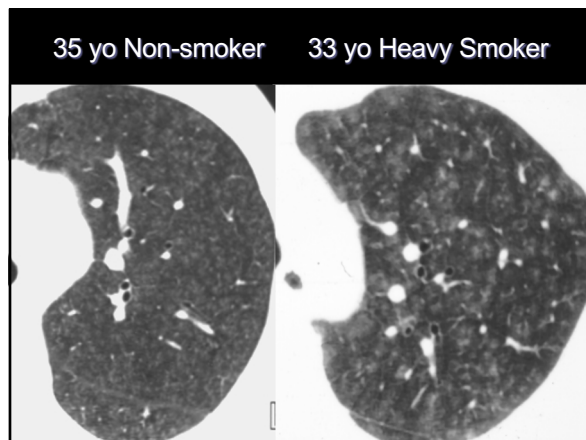


Ground Glass: Acute Symptoms

- 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

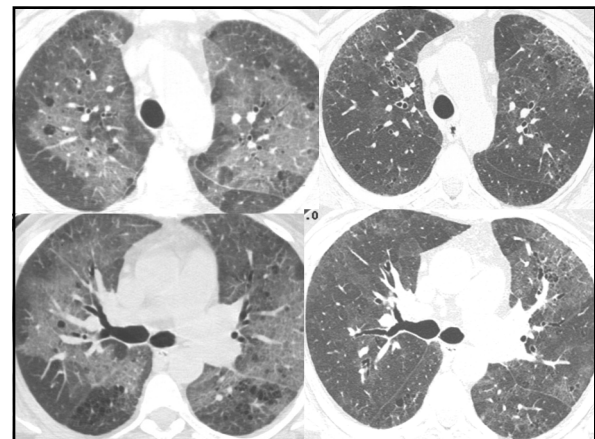




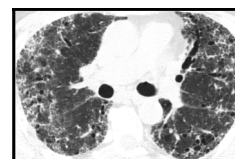


NSIP: Cellular to Fibrotic Spectrum

- **NSIP IS NOT A DISEASE!** It's an inflammatory/fibrotic pattern of **pathology**, often from collagen-vascular diseases or hypersensitivity pneumonitis.
- 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



67 year old male with chronic dyspnea

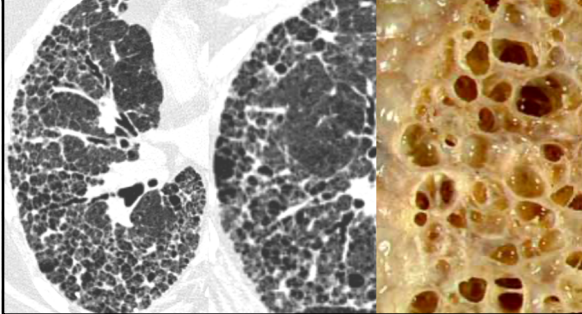


#5: What would be your report impression?

- 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.

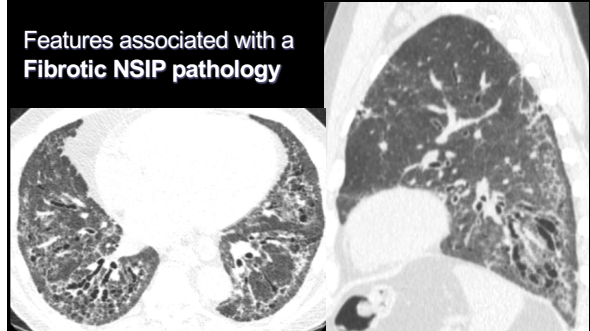
Four Imaging Findings of Fibrosis:

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

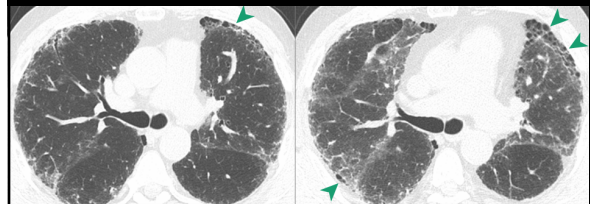
- Often *peripheral and basilar* distribution
- Imaging evidence of fibrosis: Reticular opacities, traction bronchiectasis, irregular visceral pleura +/- *Honeycombing*
- *Hypoxia/Low Dlco* more severe than NSIP
- New medical therapies
- **Active search**: Pulmonary hypertension, any new nodules or ground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

Honeycombing:

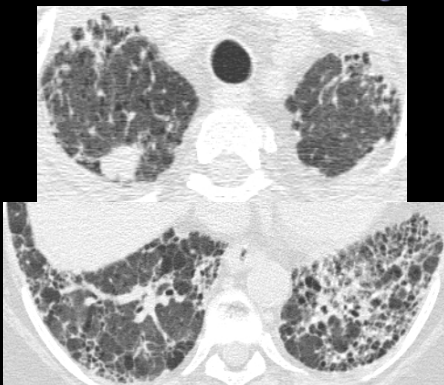
3-10 mm shared thickened wall cystic spaces that *contact the pleura*

Progression over time is often

Peripheral to Central



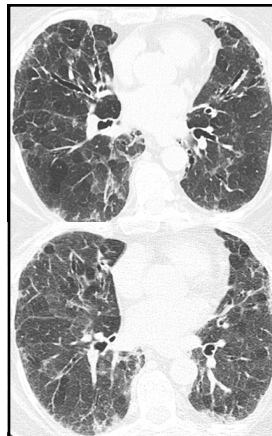
UIP: Increased Incidence of Lung Cancer

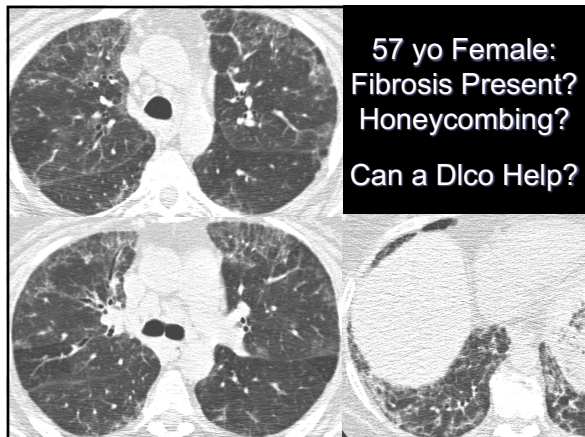


Inspiratory and Expiratory imaging:

Mosaic lung attenuation accentuated on the expiratory

Most consistent with Hypersensitivity pneumonitis/ EAA

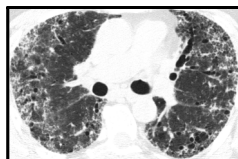




Importance of **Imaging** on Fibrosis Diagnosis (*Pathology not the Gold Standard*)

- **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

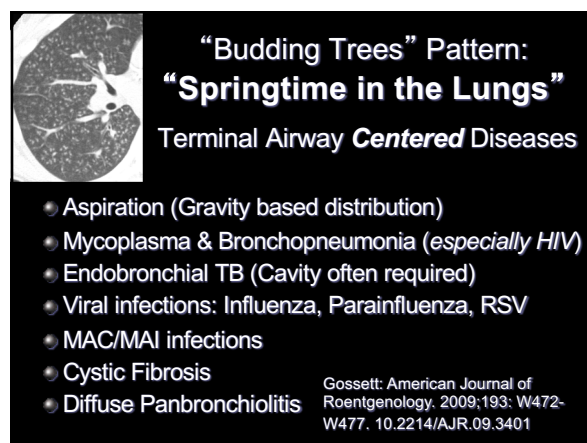
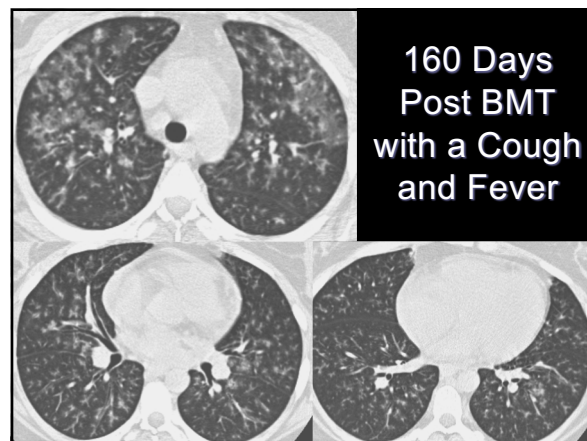
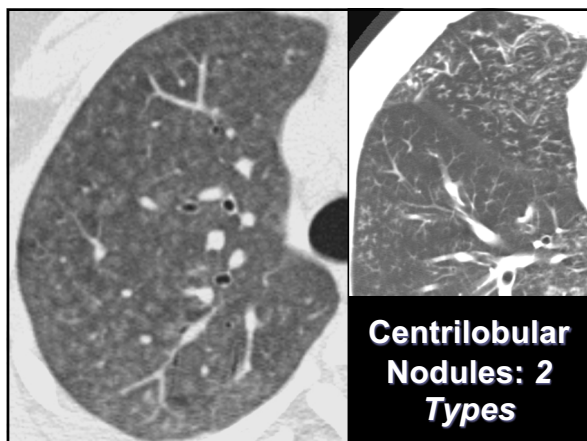
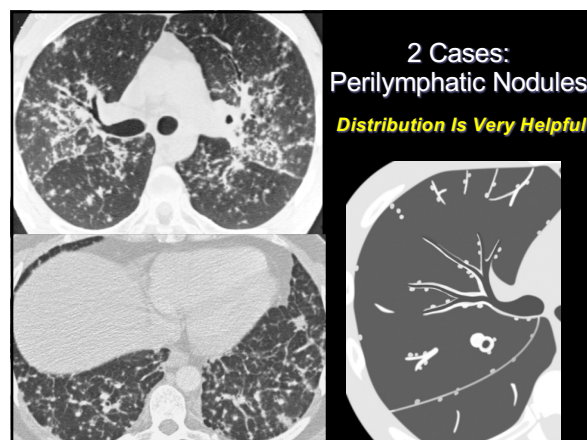
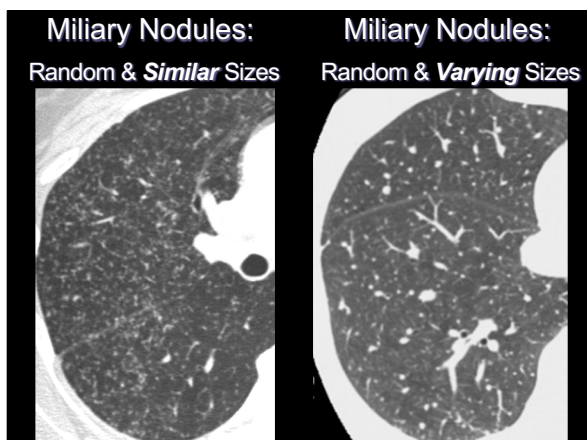
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Saranac Lake, NY: Adirondack Park



Nodules

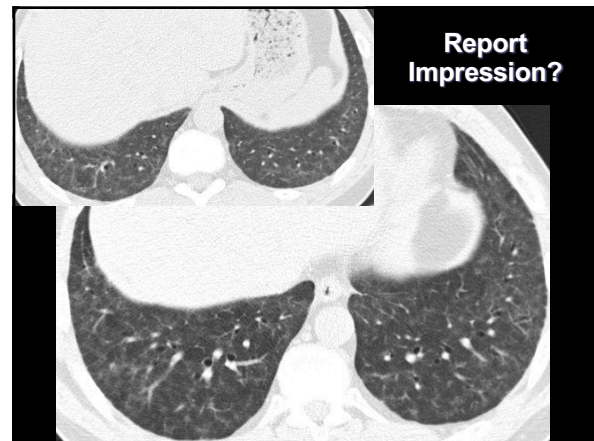
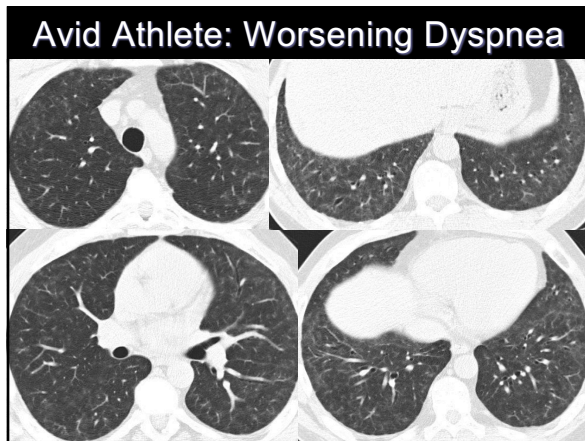
- **Perilymphatic distribution**
- **Random distribution**
- **Centrilobular distribution:** No nodules along fissures or sub-pleural regions
 1. Terminal bronchial filling ('Budding-Tree')
 2. Ill-defined respiratory bronchial inflammation





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?

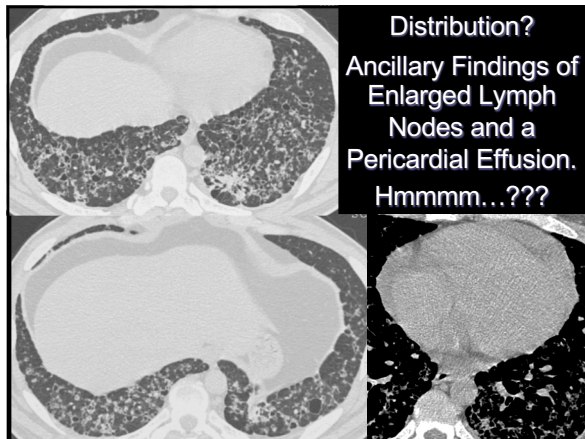


**‘Medicine is the Science
of Uncertainty and the
Art of Probability’**

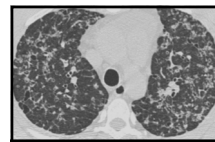
Sir William Osler

JCA - GIE



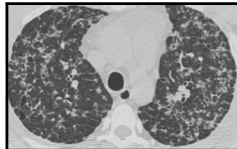


Distribution?
Ancillary Findings of
Enlarged Lymph
Nodes and a
Pericardial Effusion.
Hmmm...???



#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!

mgosselin@visionradiology.com or

gosselin@ohsu.edu

Oregon Coast, 15 Miles South of Cannon Beach



Next talk

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

