PULMONARY WORKSHOP

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Objectives

- Learn proficiency in spirometry and other lung function tests in the evaluation of obstructive lung diseases
- Demonstrate understanding of underwriting an incidental finding of solitary pulmonary nodule
- Acquire basic understanding of evaluation of interstitial lung diseases, including relevant pulmonary function studies, **with particular emphasis on sarcoidosis**
- Review of the essential findings and significance on Obstructive Sleep Apnea Reports

Question #1

- 47-year-old female executive asking for $1 million WL
- Denies smoking cigarettes or use of any illicit drugs
- BMI is 35; taking 2 anti-hypertensive medications with good control of her BP
- Her only hospitalization was 6 years ago with a viral URI and wheezing
- Since then, she's had 2-3 exacerbations a year requiring 5-day course of oral steroids
- Otherwise "stable", taking inhaled corticosteroid combined with a long-acting beta-agonist twice daily
- Normal chest x-ray 6 years ago and again prior to application for insurance

Question #1 - continued

- Spirometry also done pre-application with the following findings
  - FVC 81%p post-bronchodilator
  - FEV1 53%p post-bronchodilator (17% improvement over pre-bronchodilator)
  - FEV1/FVC 65%
  - FEV_{25-75} 47%p post-bronchodilator

1. What is the spirometry diagnosis?
2. What conclusion can be drawn by the lack of complete reversibility following inhalation of a bronchodilator?
3. How would the severity of her lung disease be classified?
4. What are the considerations regarding her mortality assessment?

1. Airway obstruction with significant but incomplete reversibility
2. The patient has COPD, not asthma. She likely had asthma initially, but underwent asthma remodeling (change from eosinophilic inflammatory cascade to neutrophilic cascade)
3. By the GOLD criteria, with the diagnosis of ”COPD” being confirmed with an FEV1/FVC ratio < 70% AND “moderate” being determined by the FEV1 58% predicted
4. She is female with adult-onset of her asthma, obese and therefore has increased mortality with COPD. Careful review of potential comorbidities, particular cardiovascular diseases, is advised

Spirometry

Obstruction

- FEV1 is reduced
- FVC is also reduced, but reduced to a lesser degree than FEV1
- **FEV1/FVC therefore reduced**
- (Diagnosis is valid but addition of lung volume and lung diffusion may help define Emphysema)

Restriction

- FEV1 is reduced
- FVC is also reduced, but reduced in proportion to reduction in FEV1
- **FEV1/FVC therefore is normal or increased**
- (Confirmation of diagnosis of restriction requires measurement of lung volume)

Question #1 - continued

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Question #2

- 56-year-old male applicant for $1 million WL
- Listed on his application that he had been seen by his PCP 6 months previously for a dry, non-productive cough and worsening shortness-of-breath that has persisted
- A chest x-ray revealed mild bibasilar infiltrates
- Spirometry post-bronchodilator ordered by his PCP revealed:
- FVC 56%p
- FEV1 54%p
- FEV1/FVC 96%
- FEF_{25-75} 49%p

Question #2 - continued

- Again, spirometry revealed:
  - FVC 56% of predicted
  - FEV1 54% of predicted
  - FEV1/FVC 96%
  - FEF_{25-75} 49% of predicted

1. What is the spirometry diagnosis?
2. Is further lung function testing indicated?

1. RESTRICTION
2. YES – restriction on spirometry may be due to suboptimal or poor patient effort, and further testing of lung volumes and lung diffusion is ALWAYS indicated
3. The lower FEF25-75 would further suggest suboptimal effort

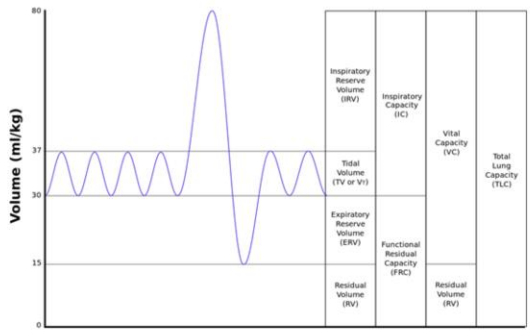
Question #2 - continued

- Because of abnormal spirometry, the patient was referred to a university hospital for complete Pulmonary Function Studies (PFTs). Spirometry results were essentially similar
  - TLC 76% predicted
  - FRC by plethysmography 81% predicted
  - DLCO 42% predicted

3. What diagnosis would these findings suggest?
4. What radiographic imaging would be indicated?
5. Would your diagnosis change if the TLC remained at 75% but the FRC was *normal* (95% predicted)?

3. Interstitial Lung Disease
4. HRCT (high-resolution CT) Lung
5. The TLC is the addition of the *measured* FRC and then the addition of the IC (Inspiratory Capacity); the latter may be low because of sub-optimal or poor effort

LUNG VOLUMES



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Diffusing Capacity (DLCO)

- DLCO decreased in obstruction
  Increased FRC } Emphysema

- DLCO decreased in restriction
  Decreased FRC } Interstitial Lung Disease

- DLCO decreased without obstruction
  or restriction } Pulmonary Vascular Disease

- Pulmonary Vascular Diseases: Occult Pulmonary Embolus
  Pulmonary Hypertension
  Pulmonary Veno-occlusive disease
  Sickle Cell Disease (SS Hemoglobin)

- DLCO Increased } Left to Right Shunt
  } Pulmonary Hemorrhage

Question #3

- 61-year-old female applicant for $1 million WL
- 30 pack-year history of smoking, quit smoking 15 years ago
- She revealed that she had recently undergone screening CT Lung
- This study revealed a 7mm nodule in her right upper lung

1. What findings might allow underwriting to proceed with a potentially favorable rating decision?
2. Would a normal PET(Positron Emission Tomography)-CT be helpful?

1. Smooth nodule border, nodule calcification (except for eccentric calcification), history of know positive skin or serum testing (+) for pulmonary tuberculosis
2. The lower limit of resolution of current PET imaging is 8 mm nodules, so failure to "see" the lesion for uptake of isotope would be expected

Question #3 -- continued

- 7 mm nodule in her right upper lobe

3. What if fiberoptic bronchoscopy with transbronchial lung biopsy + brushings + washings were negative – would that help with a more favorable rating?
4. And what if, following negative fiberoptic bronchoscopy, the patient had undergone a VATS (video-assisted thoracoscopy) or open lung sub-segmental wedge resection, with all findings negative for any diagnosis other than "normal lung". Would that help with a more favorable rating?

3. These studies are valuable *only* if they reveal malignancy or some other diagnosis (such as granulomatous disease) to explain the presence of the nodule
4. Again, the only significant finding would be malignancy or some other diagnosis. A nodule this small cannot usually be felt by a surgeon if an open wedge-resection is done. At bronchoscopy, injection of dye around a peripheral lesion is often done to help the surgeon decide where to remove lung

Question #3 - continued

7 mm nodule in her right upper lobe

- 5. Assuming the case is postponed, when might a decision be made (assuming correct surveillance follow of the nodule is done)?
- 6. Would any features of the nodule call for a significantly longer observation period than "usual"?

5. Usually, two years of no change in nodule size or appearance by CT allows for the assumption that the nodule is not cancerous (consult Fleischner Society Pulmonary Nodule recommendations !)
6. If the nodule was associated with ground-glass change on CT imaging, suggesting a diagnosis of bronchioalveolar carcinoma (now called AIS – Adenocarcinoma In Situ)

OSA – Apnea-Hypopnea Index (AHI) Severity

AHI Frequency	Severity of OSA
0 to 4.9 events/hr	Normal (No OSA)
5 to 14.9 events/hr	Mild
15 to 29.9 events/hr	Moderate
30 or more events/hr	Severe

Punjabi in PLoS Med 2009

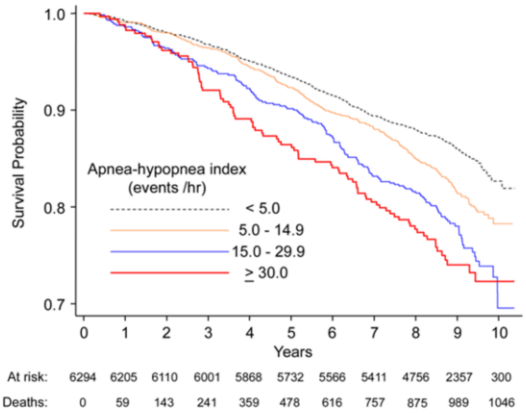
- Does AHI predict mortality?
- 6441 men + women, 40+ years
- 8.2-year follow-up (average)
- 1,047 deaths – All cause (especially CAD)

OSA Severity	Hazard Ratio
Mild	0.93
Moderate	1.17
Severe	1.46

WORSE = MEN < 70 YEARS OLD WITH DECREASED OXYGEN SATURATIONS (HR=2.0)

Does AHI predict mortality?

Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. (2009) Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study. PLoS Med 6(8): e1000132. https://doi.org/10.1371/journal.pmed.1000132

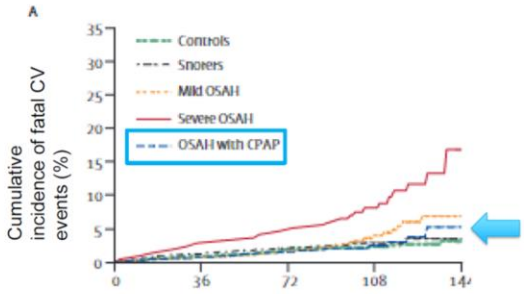


Marin in Lancet 2005

- Does CPAP save lives?
- 1651 men – Observational Study
- Untreated -- Severe
- Increased risk fatal + nonfatal CV events
- CPAP helped reduce these risks

Does CPAP save lives?

Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005 Mar 19-25;365(9464):1046-53. doi: 10.1016/S0140-6736(05)71141-7. PMID: 15781100.

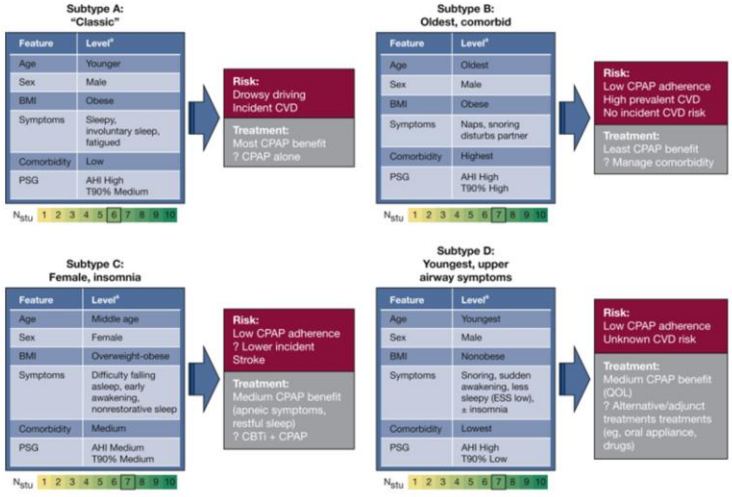


M^{C}EVORY NEJM 2016

- 2717 adults (45-75 years old)
- All cause mortality
- 3.7 years of follow up
- Adherence 3.3 hours per night (average)
- CPAP did NOT change mortality or CVD events
- CPAP did improve BP control, Quality of Life, especially decreased snoring and decreased daytime somnolence

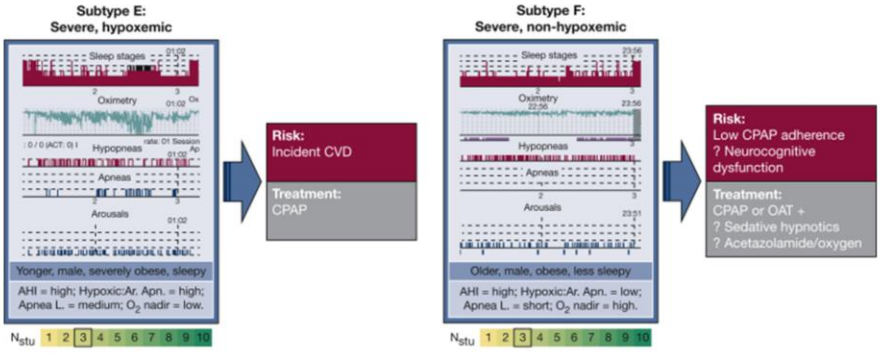
OSA Phenotypes 1/2

From Zinchuk and Yaggi in Chest. 2020 Feb; 157(2): 403–420



OSA Phenotypes 2/2

From Zinchuk and Yaggi in Chest. 2020 Feb; 157(2): 403–420.



OSA - Case #4

- 66 yo male smoker applies for $1,500,000 whole life
- BMI=33.4, BP=118/78
- Medical hx:
  - HTN (controlled on medication)
  - Hyperlipidemia (TC/HDL=10 on medication)
  - Chronic back and shoulder pain (on narcotics and muscle relaxants)
  - ECG shows LVH (no echocardiogram available)
- Home sleep study 2 years ago showed AHI=44, oxygen saturation nadir at 79%, (59 minutes at or below 89% saturation)
- Automatic titrating PAP initiated; given trazadone for "insomnia"

OSA - Case #4 continued

- One year ago, complained of concentration and memory problems. His PCP questioned if the patient had "mild cognitive impairment" and prescribed donepezil (Aricept)
- There has been no follow-up with the sleep specialist
- The patient states he uses his PAP "almost every night for a few hours each night"
- Questions (see appendix):
  - A) How severe is his OSA?
  - B) What is his phenotypic subtype?
  - C) What impairments are influencing his mortality?
  - D) What do you want to know to complete the mortality risk assessment?

A) An AHI of 44 indicates severe OSA

B) Subtype B (Oldest, comorbid), or Subtype E (Severe, hypoxemic)

C) Severe OSA; cardiovascular risk from HTN, possible LVH, hyperlipidemia; polypharmacy with narcotics, muscle relaxers, trazadone; possible cognitive impairment from OSA or meds or vascular disease or some combination of these? The strongest mortality driver is his cardiovascular risk, and his polypharmacy and cognitive decline contribute to this mortality risk. His OSA is a secondary concern.

D) What is his cardiovascular risk? (Needs a cardiac evaluation.) Is his PAP treatment effective? (Needs to see the sleep specialist and have a laboratory-based sleep study.) Does he have MCI? (May need a neurological evaluation, medication adjustments, better pain management.) What does his MVR show?

OSA - Case #5

- 34 yo male nonsmoker applies for $1,000,000 whole life
- BMI=36.2, BP=129/86, neck size=17.5 inches
- No diagnosis of HTN, no other medical problems, on no mediations
- One year previously, he saw his PCP and complained of morning headaches and daytime somnolence
- Wife complained he “snores and stops breathing, then chokes” at night; she noticed that he “has difficulty remembering things”
- Home sleep study showed AHI=88, with nadir oxygen saturation=91%
- He was placed on an automatic titrating PAP device

OSA - Case #5 continued

- He returns to his physician 6 months later and reports that he feels a little better when he uses his PAP device, but he only uses it "a couple of nights a week" because it is "uncomfortable"
- His weight is unchanged
- A laboratory-based sleep study performed while using his PAP device shows AHI=17, nadir oxygen saturation=94%, frequent PVCs and frequent periodic limb movements in sleep (PLMS) with arousals
- He expresses a desire to lose weight so he can sleep better and have less daytime fatigue

OSA - Case #5 continued

- Summary: 34 yo M nonsmoker with obesity, HTN, snoring, witnessed apneas, morning headaches, daytime somnolence, and worsened memory
  - AHI=88 without hypoxemia on home sleep study
  - Inconsistent compliance with PAP; no weight loss
  - AHI=17 without hypoxemia while using PAP on laboratory sleep study
- Questions (see appendix):
  - A) How severe is his OSA?
  - B) What is his phenotypic subtype?
  - C) What impairments are influencing his mortality?
  - D) What do you want to know to complete the mortality risk assessment?

A) An AHI of 88 indicates severe OSA, even if there is no hypoxemia and even if his PAP study shows improvement.
B) Subtype A (Classic) or Subtype F (Severe, non-hypoxemic)
C) Severe OSA, obesity, HTN, daytime sleepiness (risk of accidents), PVCs while sleeping. The strongest mortality driver is his severe OSA without hypoxemia.
D) How will he improve compliance with PAP? Has he been fitted with a new mask with new pressure settings? Will he exercise and lose weight? What does his MVR show?

OSA - Case #6

- 55 yo female nonsmoker applies for $5,000,000 whole life
- BMI=30, BP=118/84
- No medical diagnoses and not on any medications
- Three years ago, told her gynecologist of worsening insomnia with difficulty falling asleep and staying asleep. The physician attributed her symptoms to life stressors and perimenopausal state, then prescribed hormonal therapy which was unhelpful.

OSA - Case #6 continued

- One year ago, the patient self-referred to a sleep specialist, who found the patient occasionally snores. The home sleep study showed an AHI=13 with nadir oxygen saturation=90%.
- Automatic titrating PAP therapy was initiated, and at a 3-month follow-up visit, the patient's symptoms were mildly improved.
- At a 6-month follow-up, the patient stated that her adherence to PAP usage had diminished, as the benefits of treatment were not worth the "inconvenience".
- A laboratory-based sleep study indicated the presence of insomnia and the need for a better-fitting PAP mask and pressure titration.
- The patient was also advised to seek cognitive behavioral therapy for sleep initiation insomnia (CBTi).

OSA - Case #6 continued

- One month before she applied for insurance, the patient saw her gynecologist and reported substantial improvement of her symptoms, using the new PAP device at the new settings, and employing techniques learned from CBTi.
- Questions (see appendix):
  - A) How severe is her OSA?
  - B) What is her phenotypic subtype?
  - C) What impairments are influencing her mortality?
  - D) What do you want to know to complete the mortality risk assessment?

A) An AHI of 13 indicates mild OSA
B) Subtype C (Female, insomnia)
C) Mild OSA, life stressors, insomnia, overweight. She has multiple common mild drives of mortality.
D) What does her MVR show? Routine age/amount requirements.

OSA Take-aways

- AHI does predict mortality
- No high-quality evidence to document CPAP decreases mortality
- OSA is associated with increased atrial fibrillation, hypertension, CVA, CAD, HF
- CPAP helps reduce resistant HTN, QoL, snoring, daytime somnolence
- **Think beyond AHI !!!**
  - **Hypoxemia**
  - **Obesity**
  - **CAD**
  - **DM**

OSA Appendix
Cognitive Behavioral Therapy for Sleep Initiation Insomnia

- Cognitive interventions: Cognitive restructuring attempts to change inaccurate or unhelpful thoughts about sleep.
- Behavioral interventions: Relaxation training, stimulus control, and sleep restriction promote relaxation and help to establish healthy sleep habits.
- Psychoeducational interventions: Providing information about the connection between thoughts, feelings, behaviors, and sleep is central to CBT-I.

From Sleep Foundation. https://www.sleepfoundation.org/insomnia/treatment/cognitive-behavioral-therapy-insomnia

Definitions

- **PFTs = Pulmonary Function Tests**
- **FVC = Forced Vital Capacity** (total volume of air exhaled in a forced exhalation from total inspiration to total exhalation -- ideally with the best of three efforts recorded)
- **FEV1 = Forced Expiratory Volume in one second** (total volume of air exhaled in the first second of a FVC maneuver -- ideally should be 6 seconds or more of exhalation effort with the best of three efforts recorded)
- **FEV1/FVC = Percentage expired in one second**
- **FEF25-75 = Forced Expiratory Flow in the 25th to 75th portion of flow-volume curve** (also sometimes listed as MMEF 25-75: Maximal Mid-expiratory Flow Rate)
- **TLC = Total Lung Capacity**
- **FRC = Functional Residual Capacity** (amount of air in the lung at end-of-normal tidal volume exhalation)
- **DLCO = Diffusing Capacity for Carbon Monoxide**

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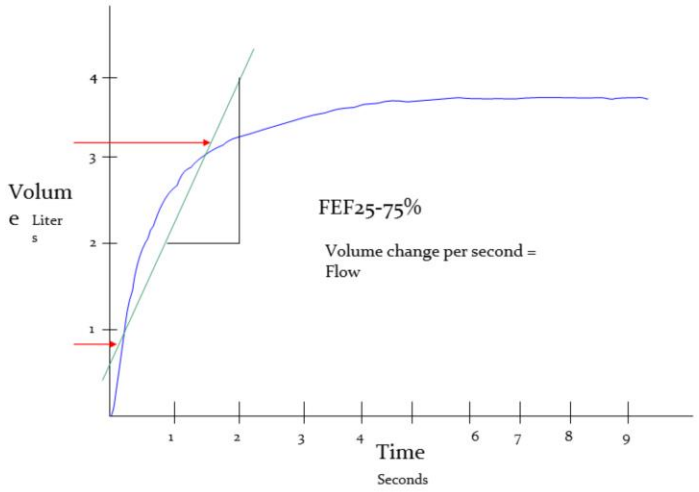
SPIROMETRY



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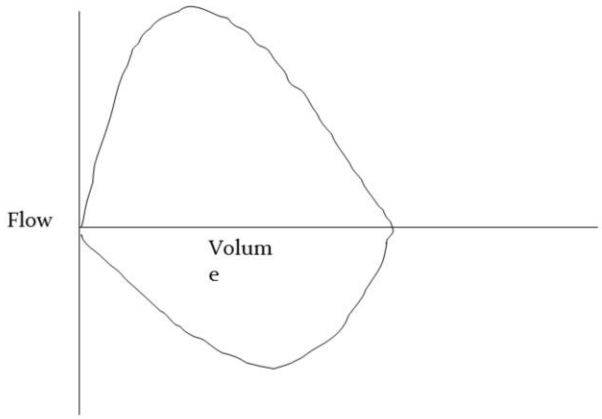
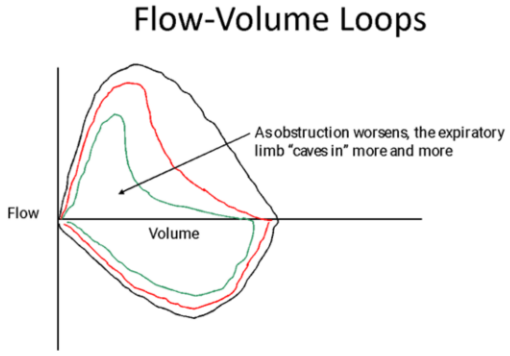
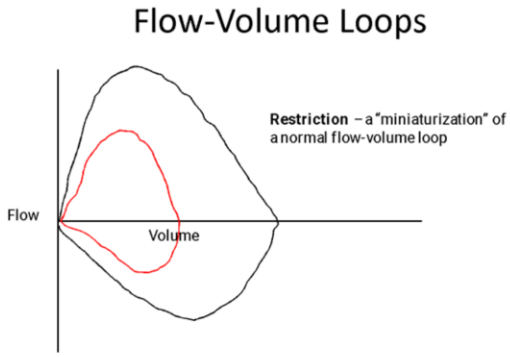
Flow-Volume Loops



Visual interpretation of severity of airway obstruction



Visual representation of restriction on FV loops



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- FEV1/FVC therefore is normal or increased
- (Confirmation of diagnosis of restriction requires measurement of lung volume)

Obstruction

Asthma – reversible obstruction

Chronic Obstructive Pulmonary Disease (COPD) /Emphysema – irreversible obstruction

GOLD Criteria for COPD

- FEV1/FVC ratio < 70 %
  - Defines person as having “COPD”
- FEV1 % predicted (FEV1%p)
  - Defines severity of COPD
    - Mild Stage I FEV1%p ≥ 80%
    - Moderate Stage II FEV1%p 50 – 79%
    - Severe Stage III FEV1%p 30 – 49%
    - Very Severe Stage IV FEV1%p < 30%

Slide courtesy of R. Richie

Restriction

Causes include

- Interstitial Lung Disease / Pulmonary Fibrosis
- Autoimmune Disorders with Lung Disease
- Drug-Induced / Therapy-Induced
- Mechanical / Chest Wall Disease
- Obesity

Diffusing Capacity (DLCO)

- Measures the ability of the lung to exchange oxygen for carbon dioxide (gas-exchange units)
- Surrogate for estimating quantity of functioning alveolar-capillary units in a lung