

ADVANCED CLINICAL TRAINING IN COPD

Registration, Exhibitor Breakfast
Saturday September 30, 2017 – 7:00 a.m. – 8:00 a.m.

Program Welcome
Saturday September 30, 2017 – 8:00 a.m. – 8:10 a.m.

COPD 2017 UPDATE: PATHOPHYSIOLOGY AND PHARMACOLOGY

Richard Casaburi, PhD, MD
Harbor UCLA

Saturday September 30, 2017 – 8:10 a.m. – 8:55 a.m.

Dr. Richard Casaburi, PhD, MD is Professor of Medicine at UCLA School of Medicine and Harbor-UCLA Medical Center in Torrance, California. He occupies the Grancell/Burns Chair in the Rehabilitative Sciences at the Los Angeles Biomedical Research Institute. He established the Rehabilitation Clinical Trials Center in 1999, a facility dedicated to COPD research. He has published more than 290 papers and 260 abstracts on exercise physiology, pulmonary rehabilitation and COPD therapeutics. Dr. Casaburi is president of the Pulmonary Education and Research Foundation and is on the Board of Directors of the COPD Foundation and the American Thoracic Society.

Note that copies of Dr. Casaburi's presentation will be available at the conference.

THE ROLE OF PHYSIOLOGIC TESTING IN COPD

William Stringer, MD

Harbor UCLA

Saturday September 30, 2017 – 8:55 a.m. – 9:40 a.m.

Dr. William Stringer received his undergraduate and medical degree from the University of California, San Diego. He is currently an attending at Harbor-UCLA Medical Center in Torrance, California and a Professor of Medicine in the David Geffen School of Medicine at UCLA. He is a board certified in Internal Medicine, Pulmonary, and Critical Care Medicine, and is active in patient care, teaching, administration, and research. His research interests are in Chronic Obstructive Lung Disease (COPD), exercise physiology, pulmonary function testing, and rehabilitation science. He is married and has four college age children. His hobbies include cycling, playing a banjo, and the humanities.

Physiologic Testing in COPD Patients

William Stringer, MD, FACP, FCCP

Los Angeles Biomedical Research Institute (LABIOMED)
at Harbor-UCLA Medical Center
Torrance, California, USA

CALIFORNIA THORACIC SOCIETY

Advanced Clinical Training in COPD
September 30th, 2017 (8:55 - 9:40 am)

The Role of Physiologic Testing in COPD Patients

- Standard Testing
 - PFTs – Review
 - Out with the Old (Lose the FEF 25-75...)
 - In with the new... (e.g. FEV3/FEV6, PRISM)
 - Tests of COPD Physiology
 - 6 minute walk (+/- oxygenation)
 - Shuttle Walk
 - Cardiopulmonary Exercise Testing
 - Assessing Exercise Induced Hyperinflation
 - Constant Work Rate Testing
 - Measuring improvement from rehabilitation
- Recent Articles of Interest

Disclosures

William W. Stringer, MD

William W. Stringer ,MD	Updated	September-17
Disclosure		
	<u>What is Received</u>	<u>Type of Financial Relationship</u>
<u>Company / Entity</u>		
NIH	Grant/Research Support	Research Grant in COPD
Department of Defense	Grant/Research Support	Research Grant in COPD
AstraZenica	Grant/Research Support	Research Grant in COPD
Boehringer-Ingelheim	Grant/Research Support	Research Grant in COPD
Astellas	Grant/Research Support	Research Grant in COPD
<u>Publishing</u>		
Walters Kluwer - Lippincott Williams & Wilkins - CPET Book	Royalties	Authorship
<u>Leadership Positions</u>		
California Thoracic Society	Past President	Volunteer
American College of Chest Physicians - ACCP Simulation Group (PFT and CPET)	Member	Volunteer

PFTs

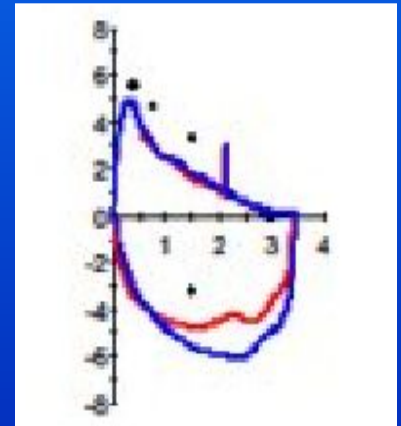
- Define the Degree of Airflow Obstruction
 - GOLD 0,1,2,3,4...
 - Assess response to BD
 - ACOS
 - Estimate or Measure MVV? $40 \times \text{FEV}_1$?
 - FEV3/FVC or FEV3/FEV6
 - Assess Gas Transfer / DLCO
 - Assess the degree of hyperinflation

Patient

78 year old Asian woman presents for evaluation of slowly progressive dyspnea for several years.



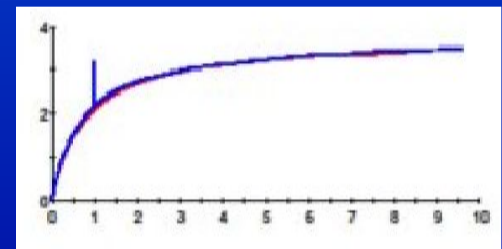
She has an intermittent cough, but denies wheezing, chest discomfort, other pulmonary or cardiac symptoms. She is a former smoker with a 20 pack year history.



Height is 64 in (162.6 cm), BMI 17.8. Physical exam and chest radiograph are normal.

Spirometry:

FVC	3.42 L (115% pred)
FEV ₁	2.11 L (94% pred)
FEV ₁ /FVC	62%



Indications for Spirometry

TABLE 1 Indications for spirometry

Diagnostic

- To evaluate symptoms, signs or abnormal laboratory tests
- To measure the effect of disease on pulmonary function
- To screen individuals at risk of having pulmonary disease
- To assess pre-operative risk
- To assess prognosis
- To assess health status before beginning strenuous physical activity programmes

Monitoring

- To assess therapeutic intervention
- To describe the course of diseases that affect lung function
- To monitor people exposed to injurious agents
- To monitor for adverse reactions to drugs with known pulmonary toxicity

Disability/impairment evaluations

- To assess patients as part of a rehabilitation programme
- To assess risks as part of an insurance evaluation
- To assess individuals for legal reasons

Public health

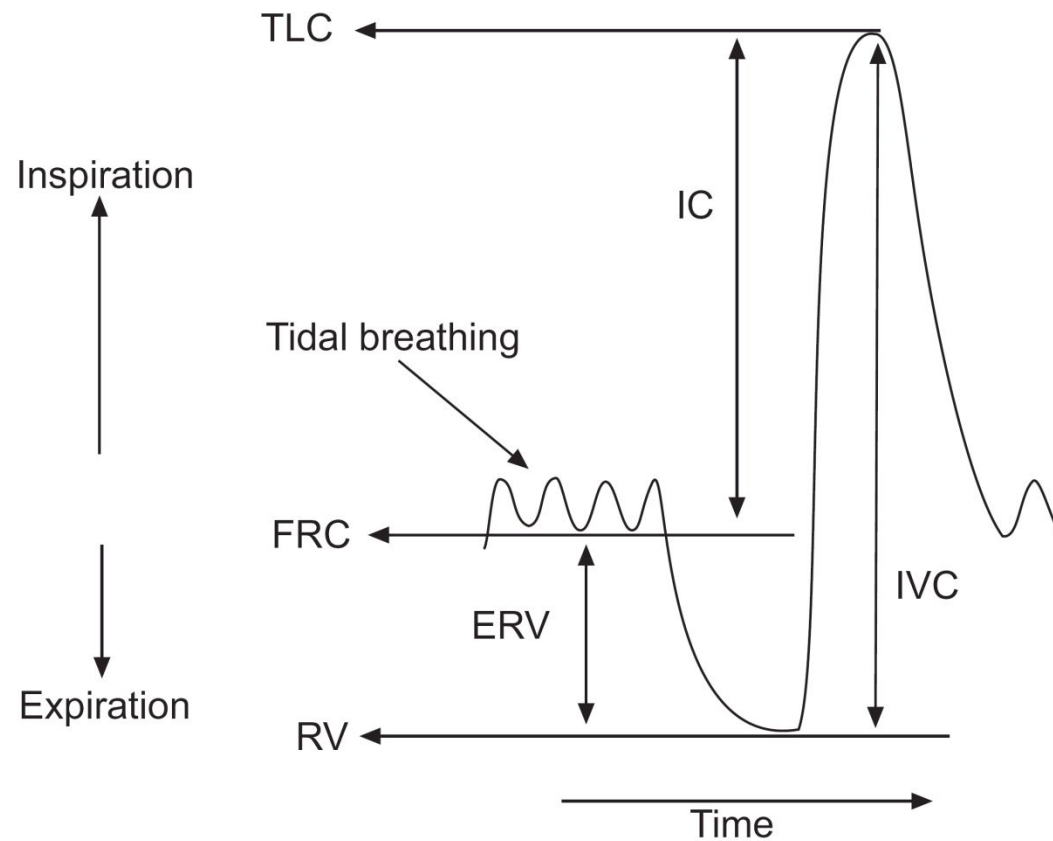
- Epidemiological surveys
- Derivation of reference equations
- Clinical research

SERIES "ATS/ERS TASK FORCE: STANDARDISATION OF LUNG FUNCTION TESTING"
Edited by V. Brusasco, R. Crapo and G. Viegi
Number 1 in this Series

General considerations for lung function testing

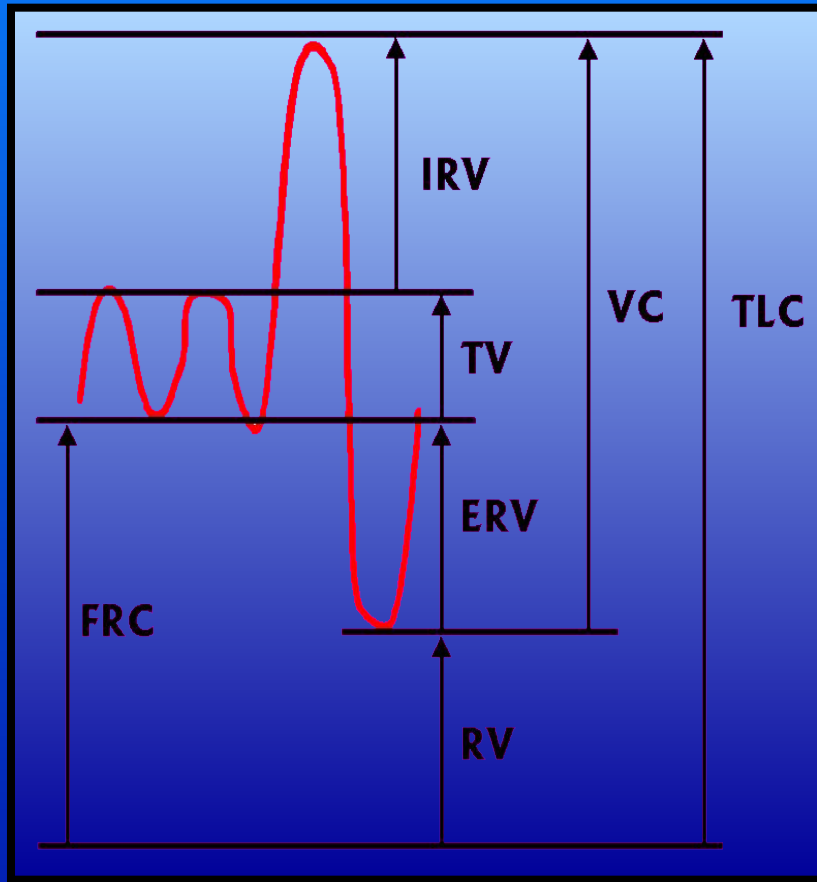
M.R. Miller, R. Crapo, J. Hankinson, V. Brusasco, F. Burgos, R. Casaburi, A. Coates, P. Enright, C.P.M. van der Grinten, P. Gustafsson, R. Jensen, D.C. Johnson, N. MacIntyre, R. McKay, D. Navajas, O.F. Pedersen, R. Pellegrino, G. Viegi and J. Wanger

Spirometry



Lung Volumes & Flows

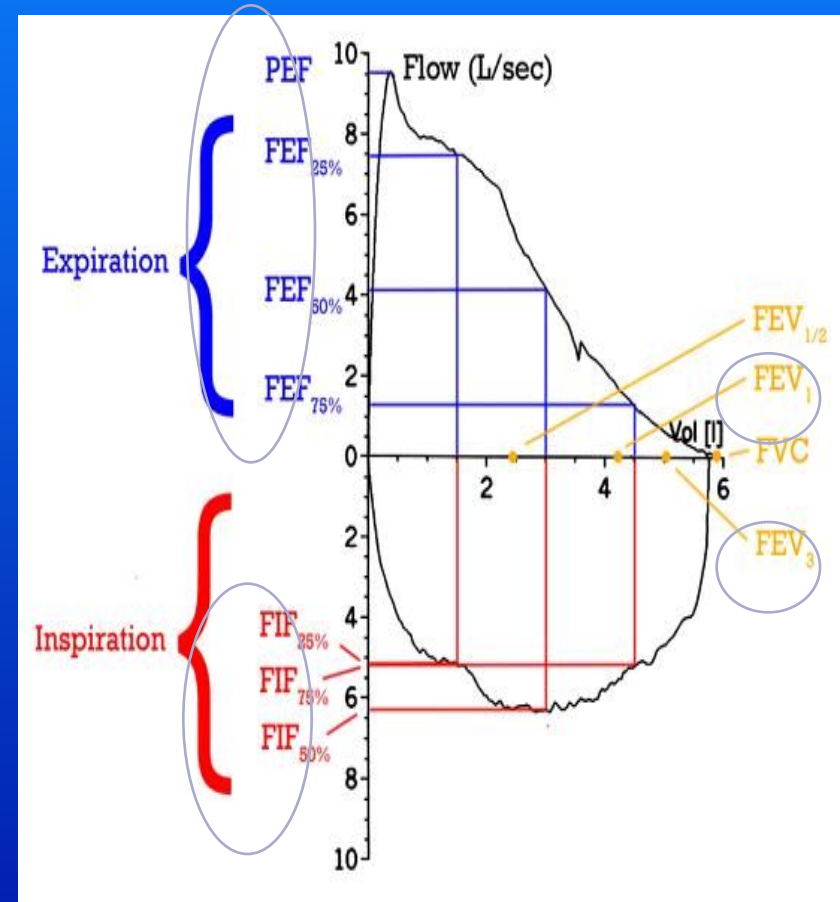
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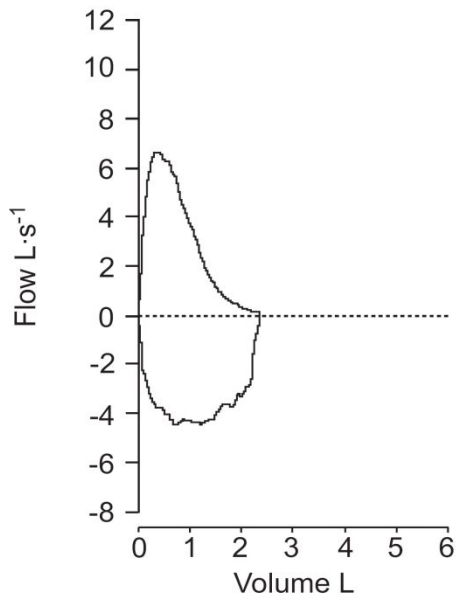
VOLUME

Obstruction – Decreased Flow Rates
vs.
Restriction – Reduced Lung Volumes

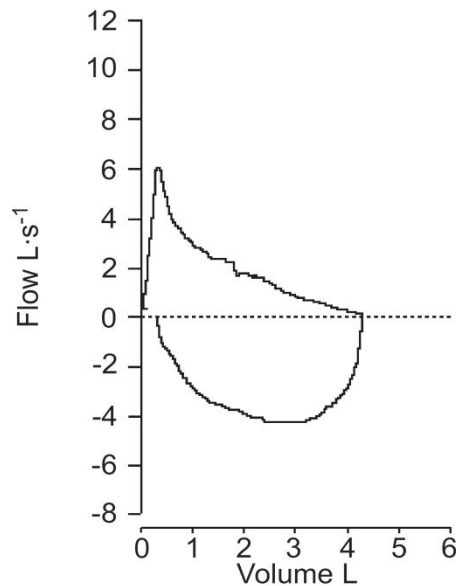
	FEV ₁	FVC	FEV ₁ / VC	TLC
Obstruction	↓	↔ Or ↓	↓	↔ Or ↑
Restriction	↓	↓	↔ Or ↑	↓

↓ = < 80% predicted, ↑ = > 120 % predicted, ↔ = normal

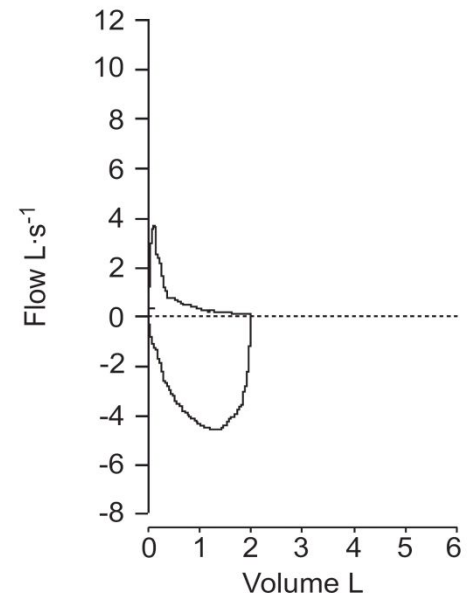
Airflow Obstruction: Flow Volume Loop



Normal



Moderate



Severe

Acceptability Criteria for Spirometry

TABLE 5 Summary of within- and between-manoeuvre acceptability criteria

Within-manoeuvre criteria

Individual spirograms are “acceptable” if

They are free from artefacts [3]

Cough during the first second of exhalation

Glottis closure that influences the measurement

Early termination or cut-off

Effort that is not maximal throughout

Leak

Obstructed mouthpiece

They have good starts

Extrapolated volume $< 5\%$ of FVC or 0.15 L, whichever is greater

They show satisfactory exhalation

Duration of ≥ 6 s (3 s for children) or a plateau in the volume–time curve or

If the subject cannot or should not continue to exhale

Between-manoeuvre criteria

After three acceptable spirograms have been obtained, apply the following tests

The two largest values of FVC must be within 0.150 L of each other

The two largest values of FEV₁ must be within 0.150 L of each other

If both of these criteria are met, the test session may be concluded

If both of these criteria are not met, continue testing until

Both of the criteria are met with analysis of additional acceptable spirograms

or

A total of eight tests have been performed (optional) or

The patient/subject cannot or should not continue

Save, as a minimum, the three satisfactory manoeuvres

Gas Transfer: DLCO = Diffusing Capacity of the Lung for CO (Carbon Monoxide)

Reduced DLCO	Elevated DLCO
“Loss” of Pulmonary Vascular Bed	“Gain” of Pulmonary Vascular Bed
Anemia	Polycythemia
Pulmonary Embolism	CHF
Emphysema	Asthma / Chronic Bronchitis
Pulmonary Fibrosis	Obesity
Sarcoidosis	Left to Right Shunt
PCP (PJP)	Alveolar Hemorrhage

COPD - PFTs

Location: Pulmonary

SpO2%: 95

Age: 68

Gender: Male

Race: Caucasian

Diagnosis: Pre-Op/Chemotherapy Lung Cancer

Weight: 210(Lb) 95.5(kg) Height: 69(In) 175 (cm)

BMI: 31.2



Spirometry

		Ref	Pre Meas	LLN	Pre %Ref	Post Meas	Post %Chg
FEV1	Liters	3.30	1.85	2.53	56	1.76	-5
FVC	Liters	4.42	4.88	3.52	110	4.74	-3
FEV3	Liters	3.94	2.69	3.04	73	2.76	-4
FEV6	Liters	4.19	3.63	3.31	87	3.48	-4
FEV1/FVC	%	75	38	65		37	
FEV3/FVC	%	89	59	84		59	
FEV1/FEV6	%	78	51	69		51	
PEF	L/sec	8.58	4.82	6.33	56	4.72	-2
PIF	L/sec	6.14	5.12		83	5.48	7
MVV	L/min	132	57	112	43		



Lung Volumes

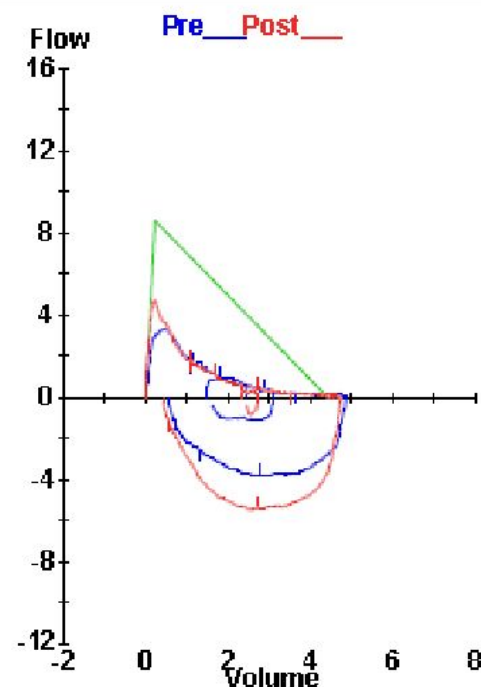
VC	Liters	4.42	4.88	3.52	110
IC	Liters	2.96	2.79		94
ERV	Liters	1.46	1.77		121
FRC N2	Liters	3.95	4.08		103
FRC PL	Liters	3.95	4.61		117
TLC	Liters	6.91	7.39	5.53	107
RV	Liters	2.49	2.51		101
RV/TLC	%	36	34		



Gas Transfer

Predicted DLCO Adjusted to Patient Hb of: 12.6 gmidL

		Ref	Meas	LLN	%Ref
DLCO	mL/mmHg/min	24.8	13.6	20.1	55
DLCO/VA	mL/mHg/min/L	3.59	2.49		69
VA	Liters	6.91	5.46		79
IVC	Liters		4.26		



Asthma - PFTs

Location: Medicine Physician: SpO2%: 99 Gender: Female
 Weight: 228(Lb) 103.6 (kg) Height: 59(In) 151 (cm) BMI: 45.4 Race: Black
 Diagnosis: Asthma



Spirometry

		Ref	Pre Meas	LLN	Pre %Ref	Post Meas	Post %Chg
FEV1	Liters	2.31	0.97	1.78	42	1.42	46
FVC	Liters	2.70	1.59	2.09	59	2.16	36
FEV3	Liters	2.79	1.30	2.14	49	1.83	30
FEV6	Liters	2.66	1.55	2.05	58	2.09	35
FEV1/FVC	%	85	61	74		66	
FEV3/FVC	%	98	86	93		86	
FEV1/FEV6%		86	63	76		68	
PEF	L/sec	6.10	2.71	4.37	44	3.31	22
PIF	L/sec	3.96	2.05		52	2.45	20
MVV	L/min	92	38	77	41		



Lung Volumes

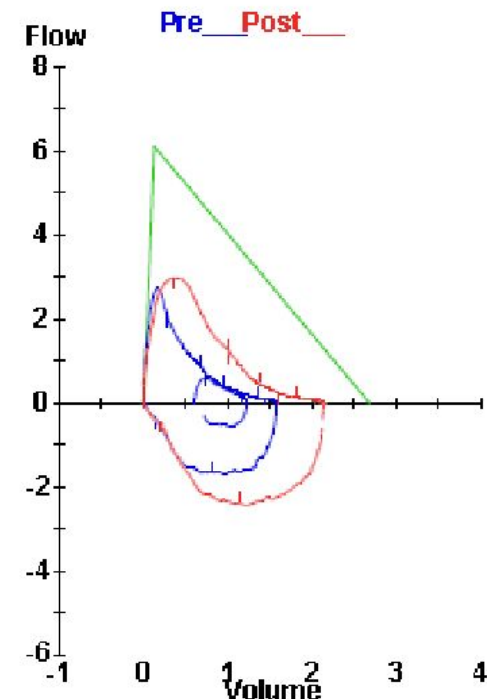
VC	Liters	2.70	1.58	2.09	59
IC	Liters	1.81	1.27		70
ERV	Liters	0.89	0.32		36
FRC N2	Liters	2.05	2.42		118
FRC PL	Liters	2.05			
TLC	Liters	3.86	3.69	3.09	96
RV	Liters	1.16	2.10		181
RV/TLC	%	30	57		



Gas Transfer

Predicted DLCO Adjusted to Patient Hb of: 15.0 g/mL

		Ref	Meas	LLN	%Ref
DLCO	mL/mmHg/min	22.0	20.3	16.5	92
DLCO/VA	mL/mHg/min/L	5.71	7.31		128
VA	Liters	3.86	2.78		72
IVC	Liters		1.46		



ATS/ERS PFT References

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Standardisation of spirometry

M.R. Miller, J. Hankinson, V. Brusasco, F. Burgos, R. Casaburi, A. Coates, R. Crapo, P. Enright, C.P.M. van der Grinten, P. Gustafsson, R. Jensen, D.C. Johnson, N. MacIntyre, R. McKay, D. Navajas, O.F. Pedersen, R. Pellegrino, G. Viegi and J. Wanger

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Standardisation of the measurement of lung volumes

J. Wanger, J.L. Clausen, A. Coates, O.F. Pedersen, V. Brusasco, F. Burgos, R. Casaburi, R. Crapo, P. Enright, C.P.M. van der Grinten, P. Gustafsson, J. Hankinson, R. Jensen, D. Johnson, N. MacIntyre, R. McKay, M.R. Miller, D. Navajas, R. Pellegrino and G. Viegi

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Standardisation of the single-breath determination of carbon monoxide uptake in the lung

N. MacIntyre, R.O. Crapo, G. Viegi, D.C. Johnson, C.P.M. van der Grinten, V. Brusasco, F. Burgos, R. Casaburi, A. Coates, P. Enright, P. Gustafsson, J. Hankinson, R. Jensen, R. McKay, M.R. Miller, D. Navajas, O.F. Pedersen, R. Pellegrino and J. Wanger

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Interpretative strategies for lung function tests

R. Pellegrino, G. Viegi, V. Brusasco, R.O. Crapo, F. Burgos, R. Casaburi, A. Coates, C.P.M. van der Grinten, P. Gustafsson, J. Hankinson, R. Jensen, D.C. Johnson, N. MacIntyre, R. McKay, M.R. Miller, D. Navajas, O.F. Pedersen and J. Wanger

Obesity Effects on Lung Volumes and Flow

Review

HIGHLIGHTED

Physiology of

Cheryl M

¹Woolcock

Royal North

Submitted 30

J Appl Physiol 108: 206–211, 2010.

doi:10.1152/jappphysiol.00694.2009.

Obesity

Respiratory Medicine,

Obesity

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Luciana Costa

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nática

Nascimento Calles¹

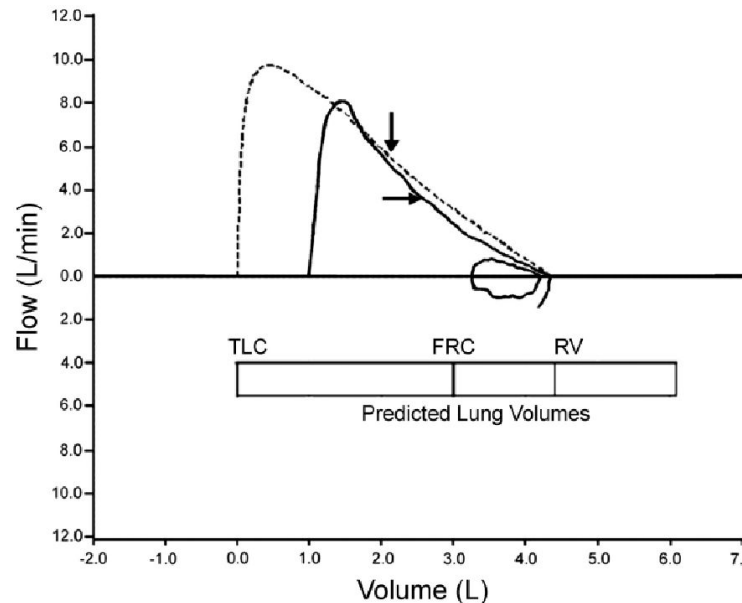
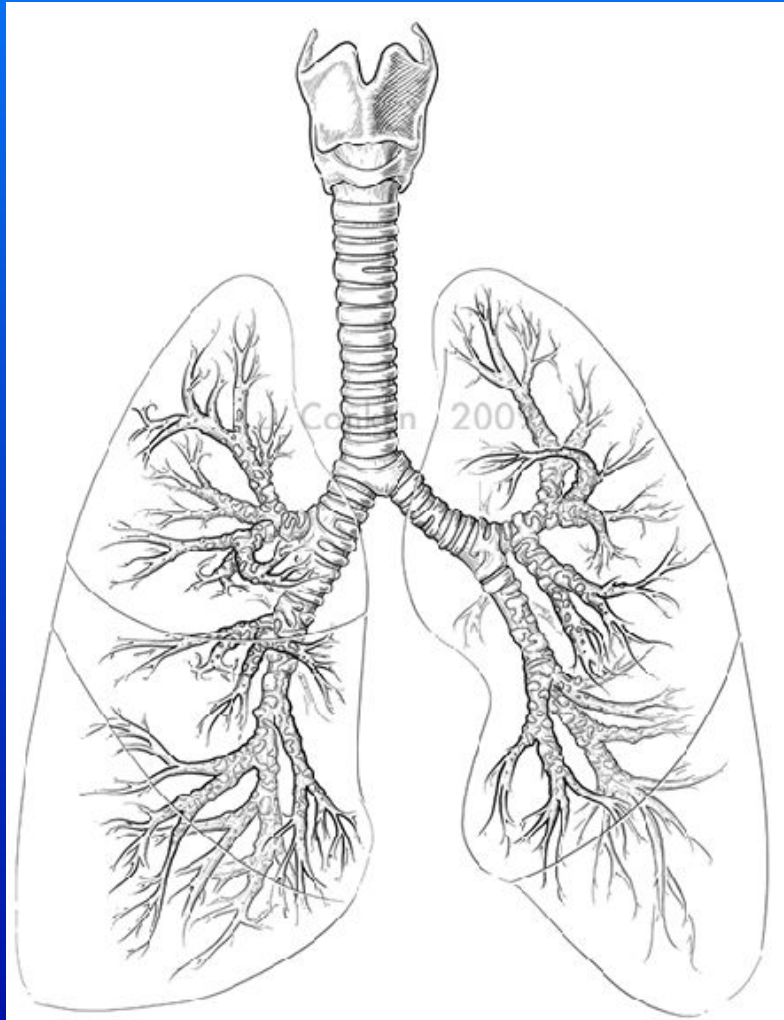


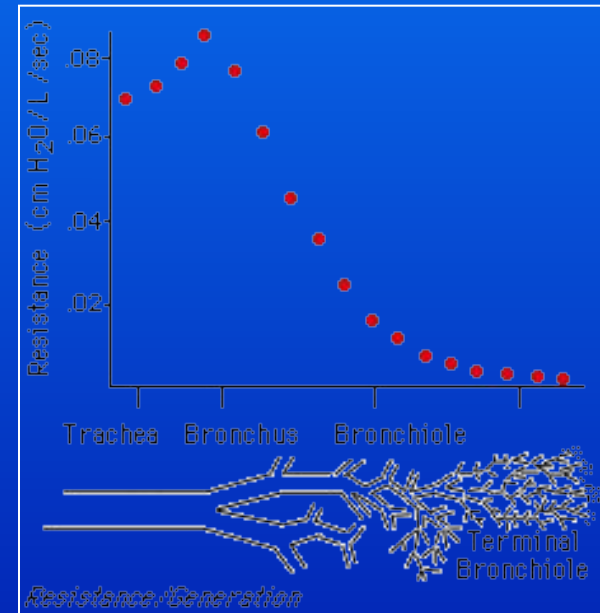
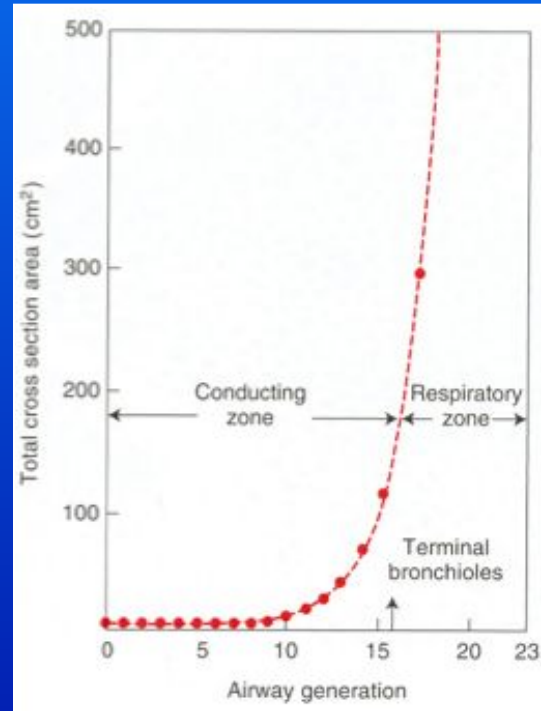
Fig. 1. Flow-volume loops from healthy obese female, aged 35 yr, BMI = 43 kg/m², with reduced total lung capacity (TLC), functional residual capacity (FRC), and vital capacity, but well-preserved expiratory flows. The dashed line shows the predicted flow-volume loop; the solid line is the actual loop. The predicted lung volumes are shown on the bar, vertical arrow shows predicted flow at 50% vital capacity, and horizontal arrow shows the actual value. RV, residual volume.

Tracheal Bronchial Tree and Alveoli



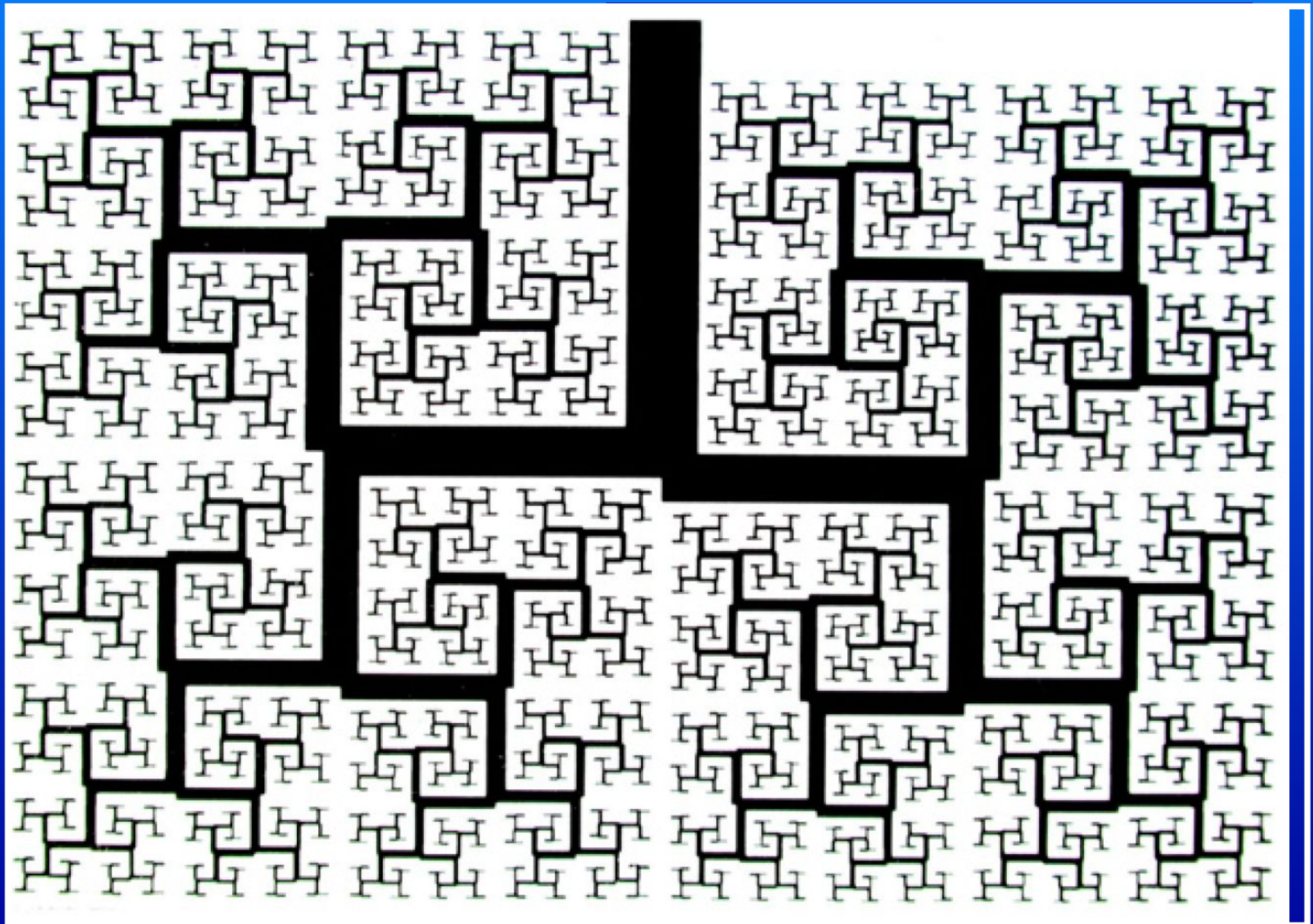
Bronchial and Alveolar Anatomy

Large airways (> 2 mm)	Conducting zone	Trachea	z
			0
		Bronchi	1
			2
			3
Small airways (< 2 mm)	Transitional and respiratory zones	Bronchioles	4
			5
		Terminal Bronchioles	16
		Respiratory bronchioles	17
			18
			19
		Alveolar ducts	20
			21
			22
		Alveolar sacs	23



1. Weibel ER. Principles and methods for the morphometric study of the lung and other organs. Lab Invest. 1963; 12: 131–55.

Bronchiole Generations (12)

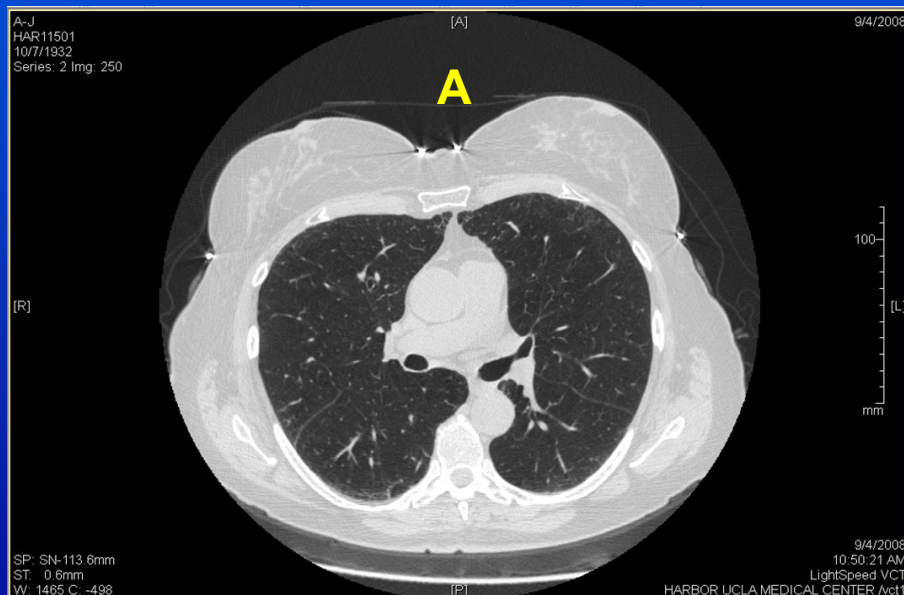


Emphysema Dominant COPD Phenotype

Quantitative CT analysis is used to assess presence of disease

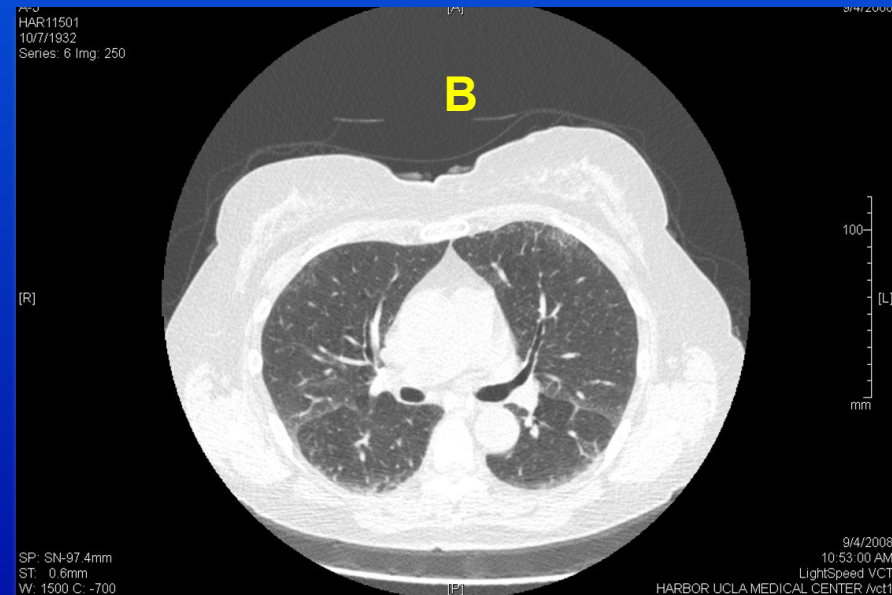
% Emphysema : percentage of lung voxels ≤ -950 Hounsfield Units (HU) on end-inspiratory scans

Emphysema% = 5.9%



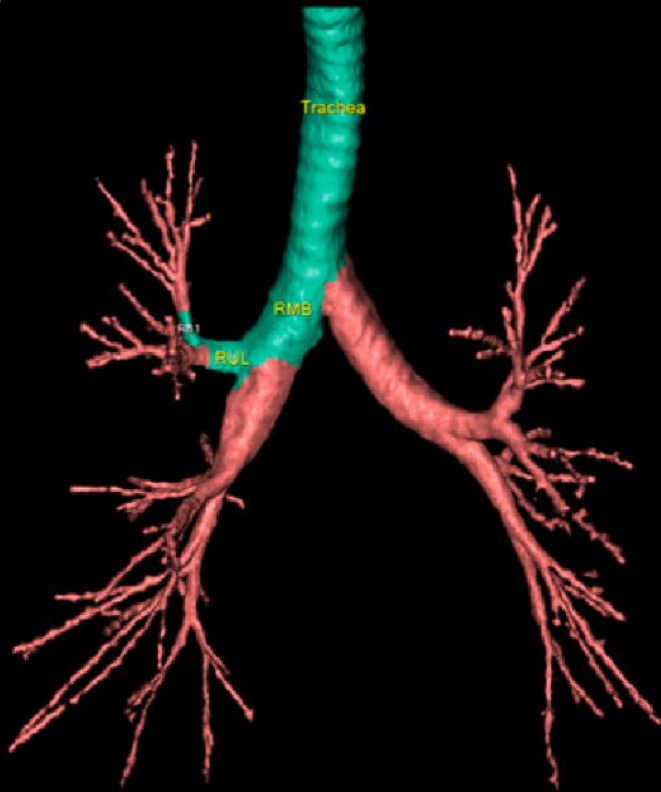
% Air trapping : percentage of lung voxels ≤ -856 HU on expiratory scans

Air trapping% = 24.7%

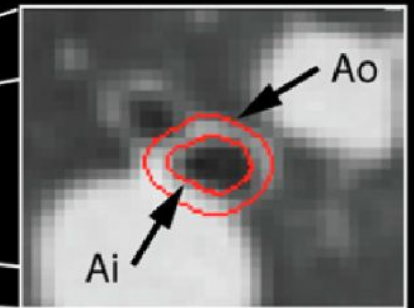


Airway Dominant COPD Phenotype

A



B



$$A_{aw} = A_o - A_i$$
$$WA\% = \frac{A_{aw}}{A_o} \times 100$$

“The Smoking Gun” - Basal Cells

PULMONARY PERSPECTIVE



Airway Basal Cells

The “Smoking Gun” of Chronic Obstructive Pulmonary Disease

Ronald G. Crystal

Department of Genetic Medicine, Weill Cornell Medical College, New York, New York

Am J Respir Crit Care Med Vol 190, Iss 12, pp 1355–1362, Dec 15, 2014
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Originally Published in Press as DOI: 10.1164/rccm.201408-1492PP on October 29, 2014
Internet address: www.atsjournals.org

“The Smoking Gun” - Basal Cells

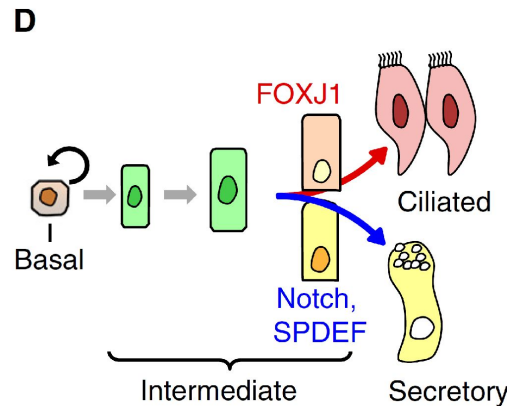
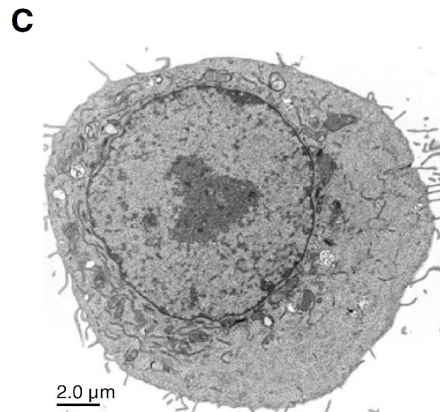
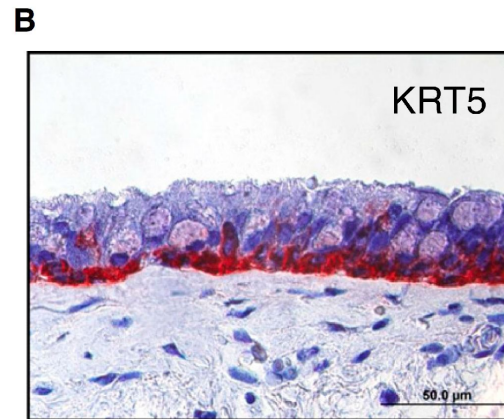
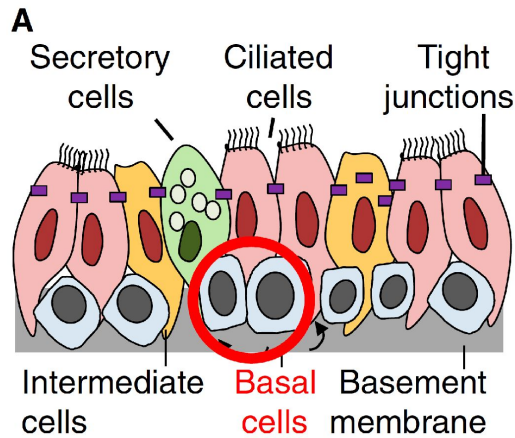


Figure 1. Basal cells and the airway epithelium in the normal human nonsmoker. (A) Schematic of the normal human airway epithelium. Basal cells represent 34% of the cell population in the trachea, decreasing generally to 10% in the small airways. Ciliated, secretory, and undifferentiated intermediate cells represent the other cell types. Tight junctions connecting the differentiated ciliated and secretory cells contribute to the integrity of the epithelial barrier. All of the epithelial cells are attached to the basement membrane. (B and C) Basal cells in the normal nonsmoker. (B) Human large airway epithelium. The basal cells are cuboidal, KRT5⁺ cells lining the basement membrane. Hematoxylin and eosin; bar = 50 μm. (C) Transmission electron microscopy of a basal cell purified from the normal human airway epithelium. Bar = 2 μm. (D) Normal differentiation of the airway epithelium. The basal cell population contains stem/progenitor cells, which can self-renew and generate differentiated airway epithelium. During normal turnover and repair, the basal cells proliferate and differentiate, generating undifferentiated intermediate cells, which further differentiate into ciliated cells under the control of FOXJ1 and other transcriptional regulators shown and to secretory cells under the control of the Notch pathway. Generation of mucus-producing cells is governed by transcription factors SPDEF and FOXA3.

Am J Respir Crit Care Med Vol 190, Iss 12, pp 1355–1362, Dec 15, 2014

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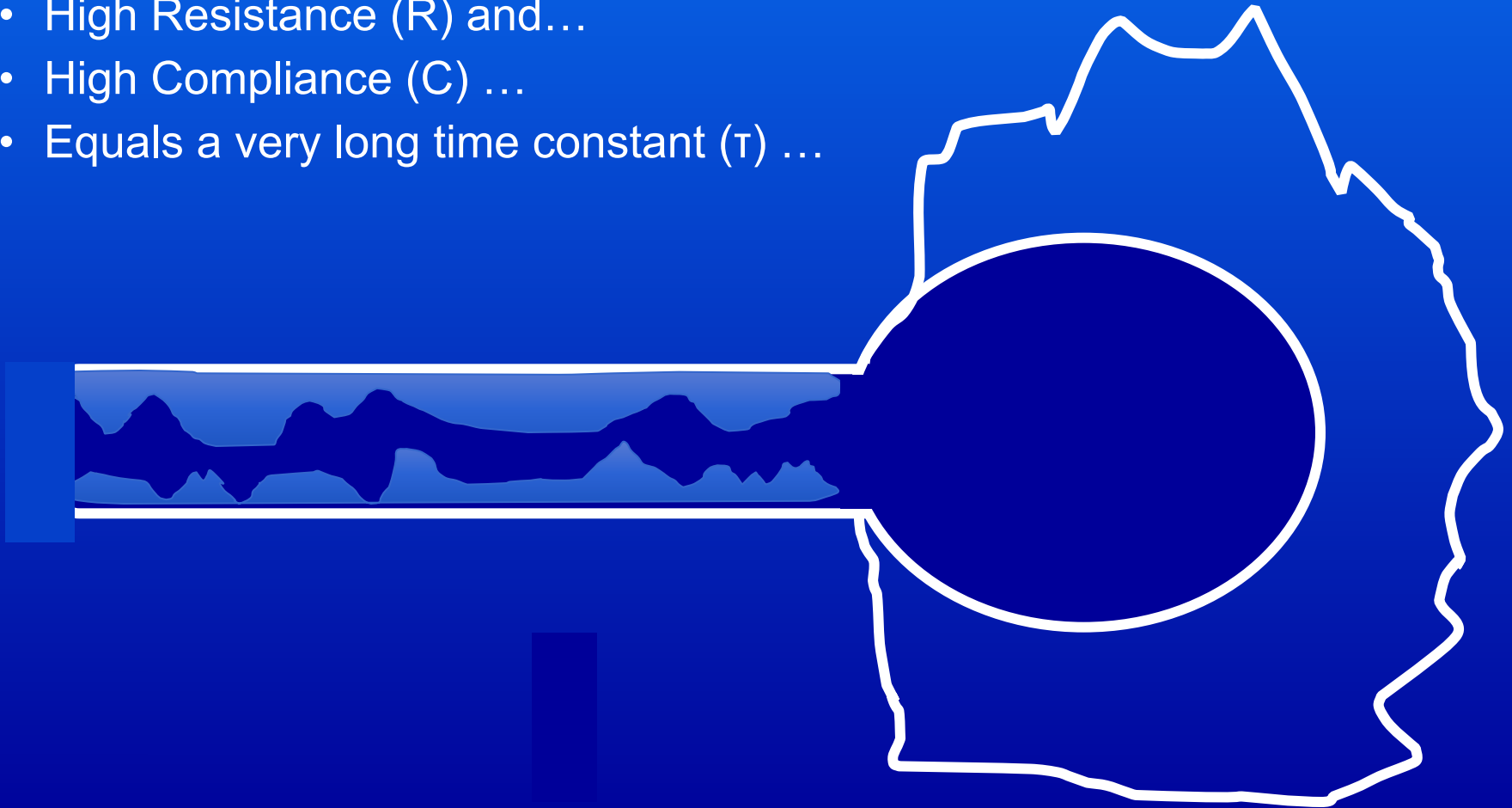
Originally Published in Press as DOI: 10.1164/rccm.201408-1492PP on October 29, 2014

Internet address: www.atsjournals.org

Why is High Airway Resistance combined with High Parenchymal Compliance a Problem?

Use?

- Time constant (τ) = Resistance (R) x Compliance (C)
- High Resistance (R) and...
- High Compliance (C) ...
- Equals a very long time constant (τ) ...



COPD Phenotypes by CT Scan

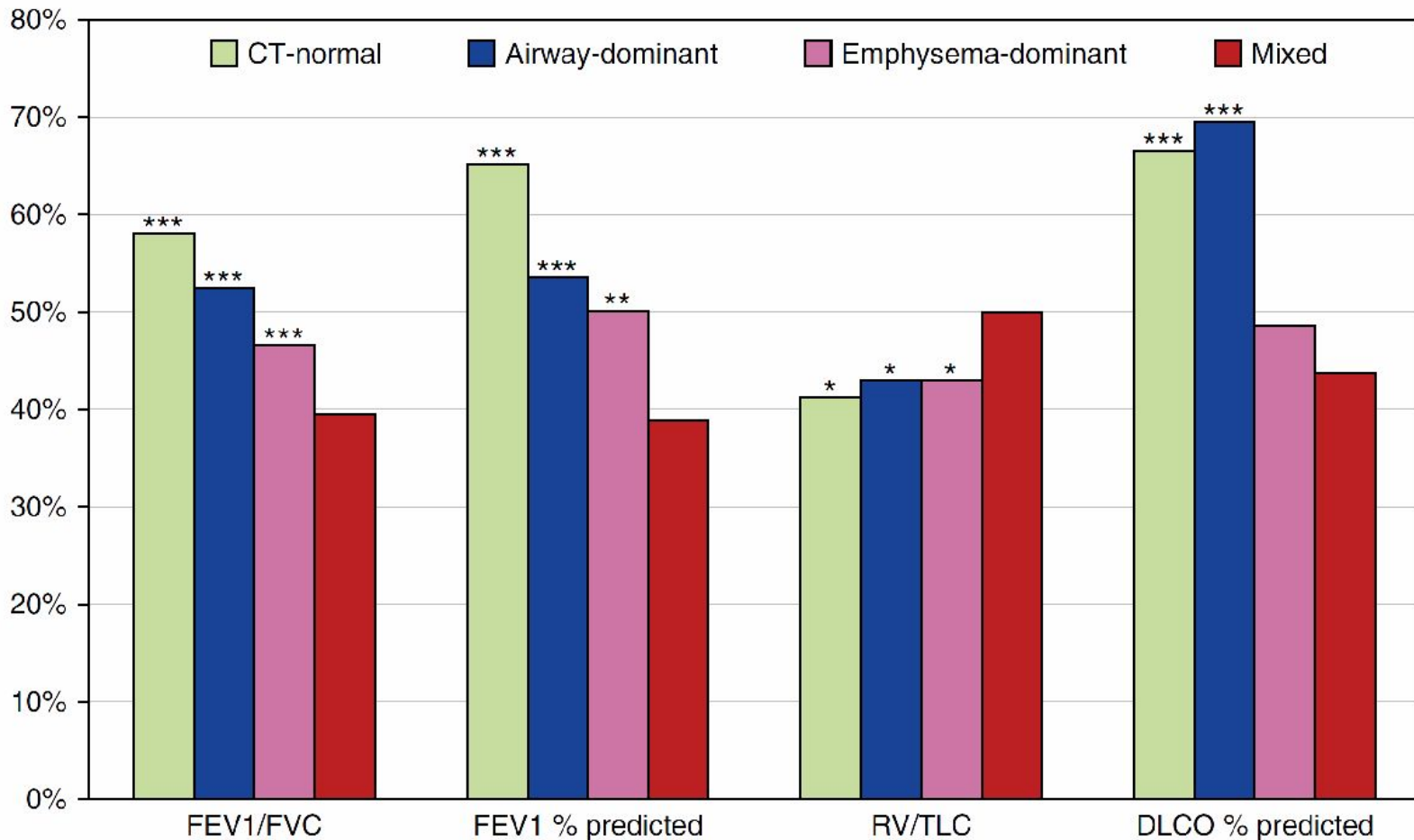
- **427** male smokers in Vietnam.
- CT Scans were used to place COPD patients into four categories:
 - CT-normal phenotype - 53 (21.7%)
 - airway-dominant phenotype - 39 (16.3%)
 - square root of wall area of a hypothetical airway with an internal perimeter of 10 mm (Pi10) were measured
 - emphysema-dominant phenotype - 103 (42.9%)
 - - percentage of low-attenuation volume at the threshold of -950 Hounsfield units (%LAV)
 - mixed phenotype - 46 (19.2%)
- Patients with COPD with the mixed phenotype were associated with more severe dyspnea than those with each of the remaining CT-based phenotypes ($P < 0.01$ for all comparisons). The number of hospitalizations for COPD exacerbations during the preceding year was 2.0 to 3.6 times higher in patients with the mixed phenotype than in those with each of the remaining CT-based phenotypes ($P < 0.05$ for all comparisons). Findings persisted after adjustment for age, pack-years of smoking, smoking status, body mass index, and FEV1.
- **Conclusions:** Patients with COPD with the mixed phenotype are associated with more severe dyspnea and more frequent hospitalizations than those with each of the remaining CT-based phenotypes. Thus, patients with COPD with the mixed phenotype may need more attention and interventions.

COPD Phenotypes by CT Scan

Table 2. Comparisons of characteristics among four computed tomography-based phenotypes in 240 patients with chronic obstructive pulmonary disease

Characteristics	CT-Normal (n = 52)	Airway-Dominant (n = 39)	Emphysema-Dominant (n = 103)	Mixed (n = 46)	P Value*
Age, yr	62.2 ± 9.6	58.1 ± 11.1	63.3 ± 9.2	63.0 ± 9.4	0.0351
Pack-years	37.4 ± 14.2	31.9 ± 13.4	39.8 ± 12.9	33.1 ± 14.1	0.0038
Current smokers	22 (42.3)	14 (35.9)	34 (33.0)	13 (28.3)	0.5098
Body mass index, kg/m ²	21.0 ± 3.1	21.7 ± 2.7	21.1 ± 3.7	21.4 ± 3.6	0.7681
mMRC grade ≥ 2	22 (42.3)	19 (48.7)	45 (43.7)	36 (78.3)	0.0004
No. of hospitalizations ≥ 1	12 (23.1)	12 (30.8)	27 (26.2)	15 (32.6)	0.7053
COPD duration, yr	1 (0.25–3)	2 (1–3)	2 (1–4)	3 (1.75–7.25)	0.0055
FVC, % predicted	82.4 ± 18.7	75.4 ± 17.5	78.2 ± 16.5	72.5 ± 18.0	0.0388
FEV ₁ /FVC, %	58.1 ± 7.3	52.5 ± 8.1	46.7 ± 10.6	39.5 ± 7.6	0.0001
FEV ₁ , % predicted	65.2 ± 19.2	53.6 ± 17.3	50.2 ± 17.3	39.0 ± 13.0	0.0001
FVC, % predicted	84.3 ± 14.0	74.3 ± 10.3	73.2 ± 11.4	73.0 ± 14.4	0.0001
DL _{CO} , % predicted [†]	66.6 ± 17.1	69.6 ± 17.9	48.6 ± 15.8	43.8 ± 16.4	0.0001
DL _{CO} /VA, % predicted [†]	67.5 ± 17.5	75.3 ± 17.1	49.6 ± 17.4	47.6 ± 19.0	0.0001
TLC, % predicted [†]	87.8 ± 18.8	82.4 ± 18.8	88.2 ± 18.8	88.8 ± 14.8	0.2225
RV, % predicted [†]	94.6 ± 27.8	98.6 ± 23.1	100.3 ± 35.0	112.3 ± 35.5	0.2587
RV/TLC, % [†]	41.3 ± 9.5	43.0 ± 8.8	43.0 ± 11.0	50.1 ± 9.1	0.0183
Bronchodilator reversibility	8/50 (16.0)	6/35 (17.1)	18/102 (17.7)	12/45 (26.7)	0.5556
White blood cell count, cells/μl	8,280 (7,102.5–9,822.5)	7,820 (6,160–9,330)	8,380 (7,097.5–10,875)	8,875 (7,672.5–10,697.5)	0.0450
Blood neutrophil count, cells/μl	4,537 (3,619–5,693)	4,307 (3,312–5,943)	5,072 (3,722–7,151)	5,604 (4,542–7,225)	0.0101
Blood eosinophil count, cells/μl	416 (209–579)	317 (178–536)	255 (130–397)	299 (150–483)	0.0289
C-reactive protein, mg/L	2.54 (1.18–5.05)	2.66 (1.23–8.21)	2.42 (1.14–5.11)	3.29 (1.60–6.86)	0.4992

COPD Phenotypes by CT Scan

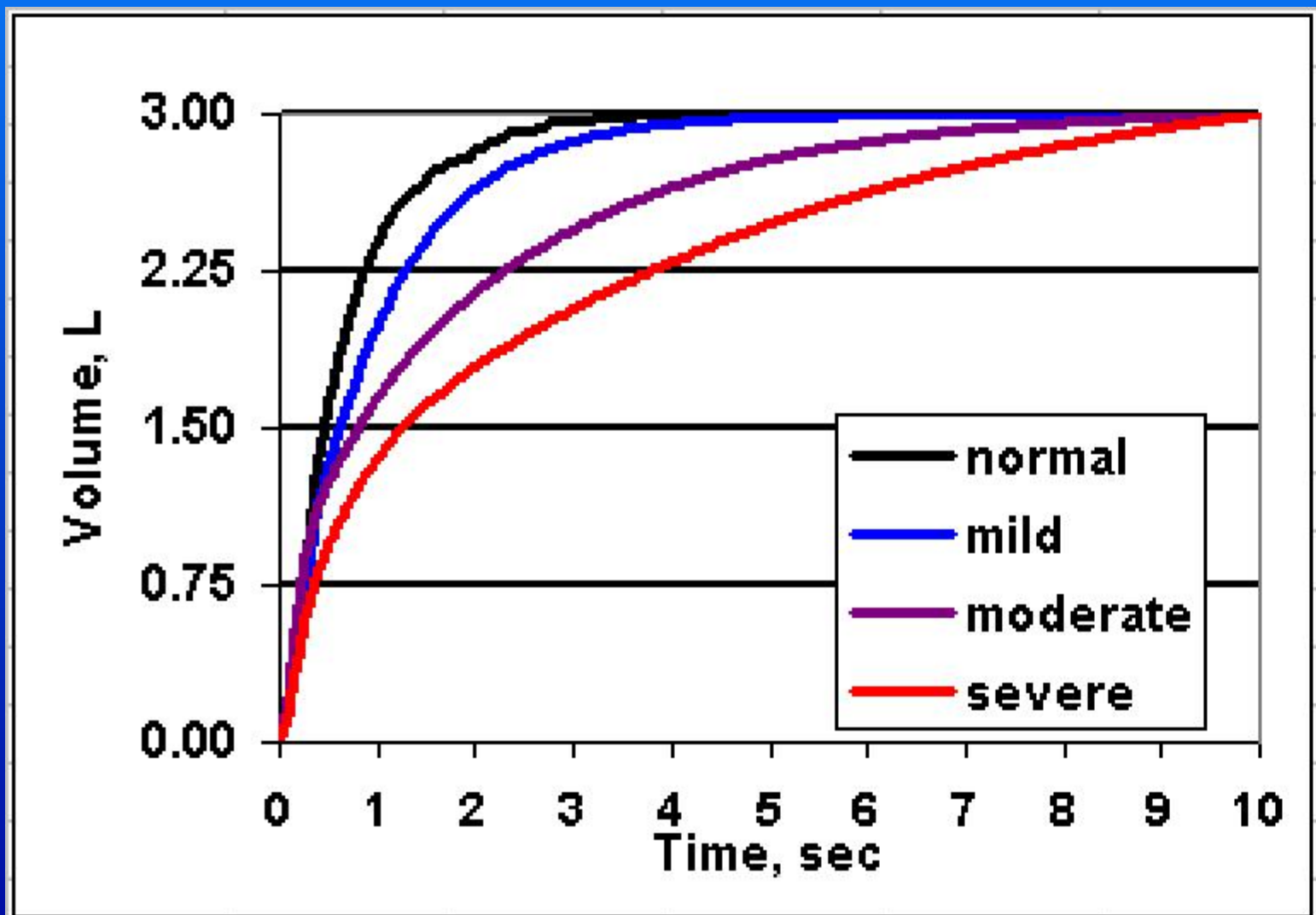


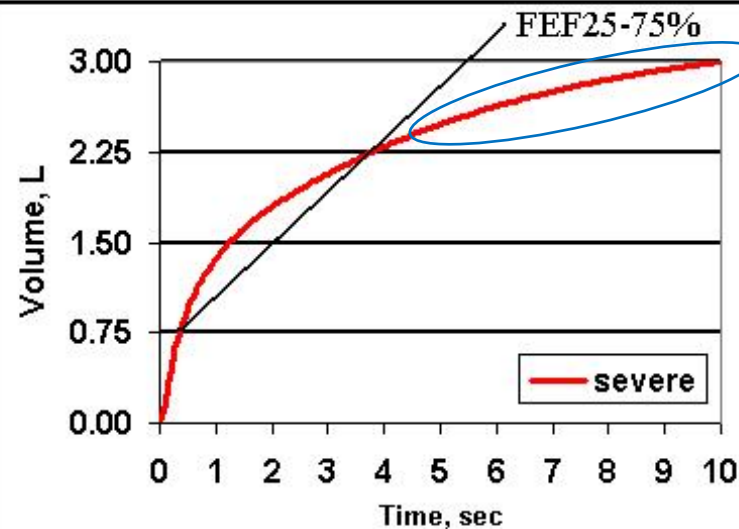
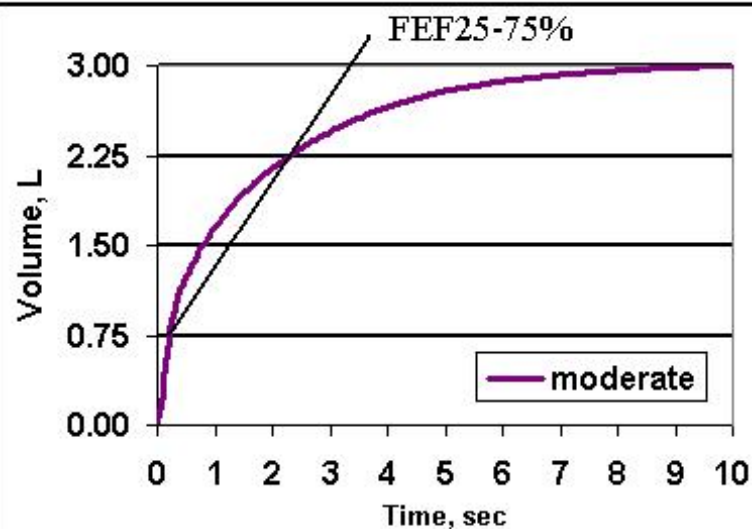
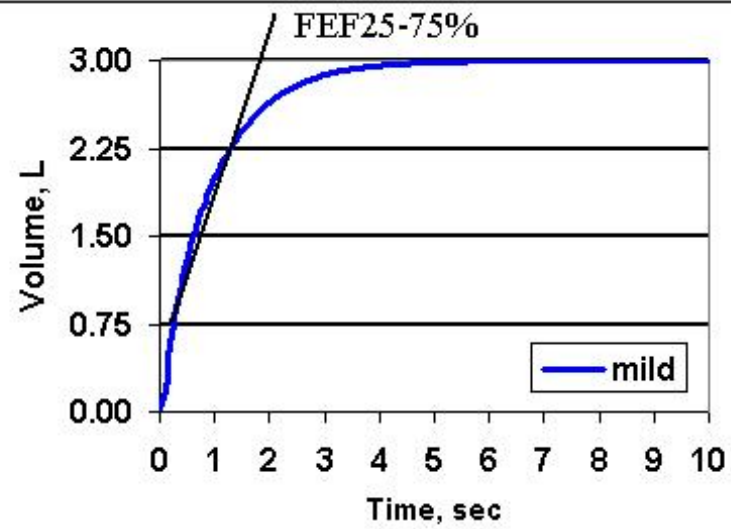
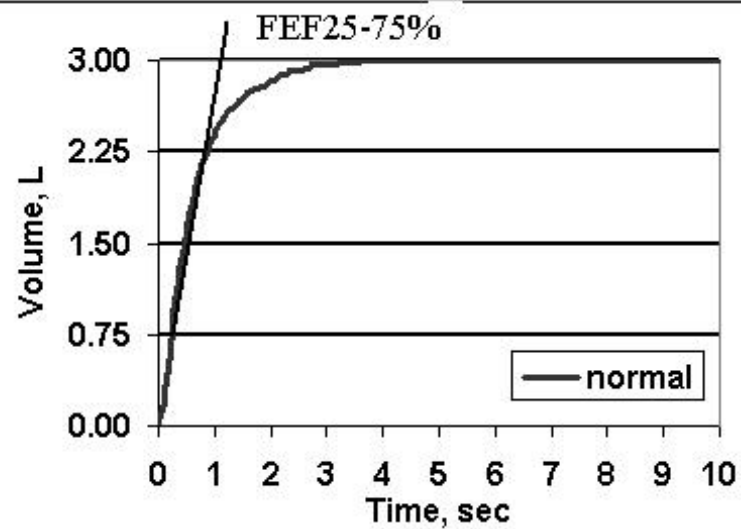
FEV3

Use?

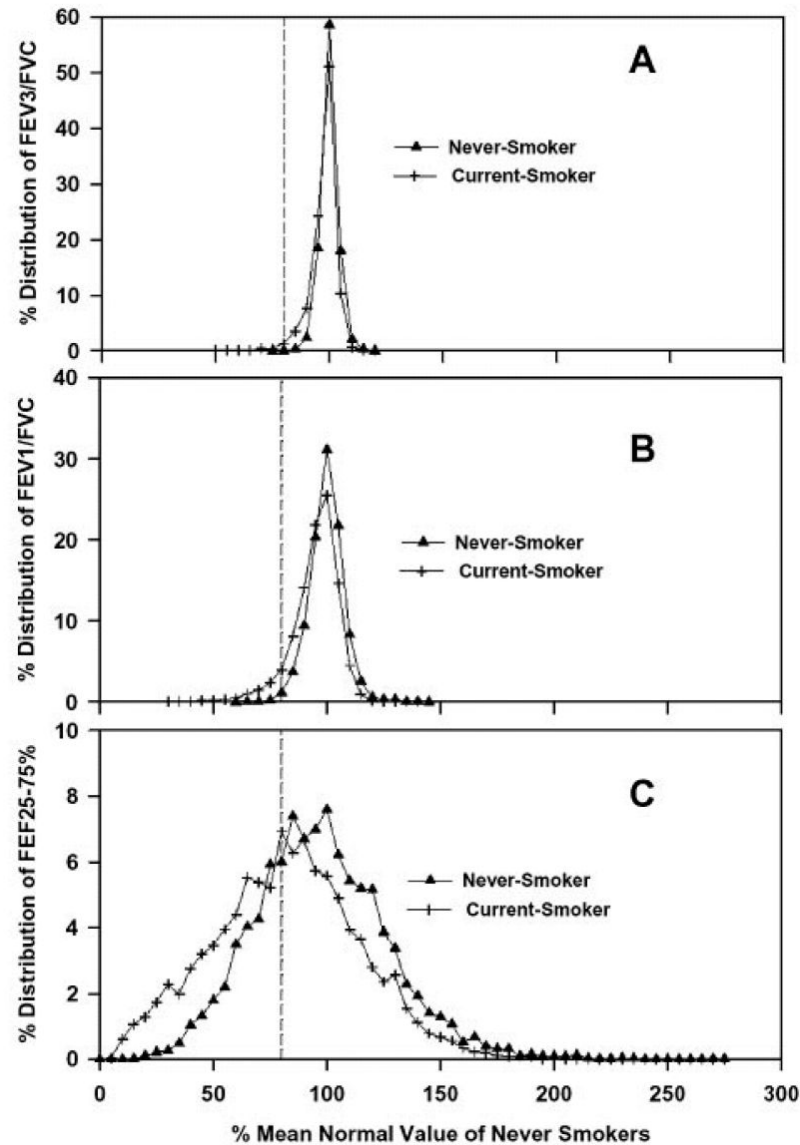
- Forced Expiratory Volume in 3 seconds.
- Better indicator of **lower airway function** as it assesses the sub-segmental and sub-sub-segmental airways.
- FEV_3/FVC or FEV_3/FEV_6 more reliable than FEV_1/FVC in airflow obstruction.

Mild, Moderate, Severe COPD



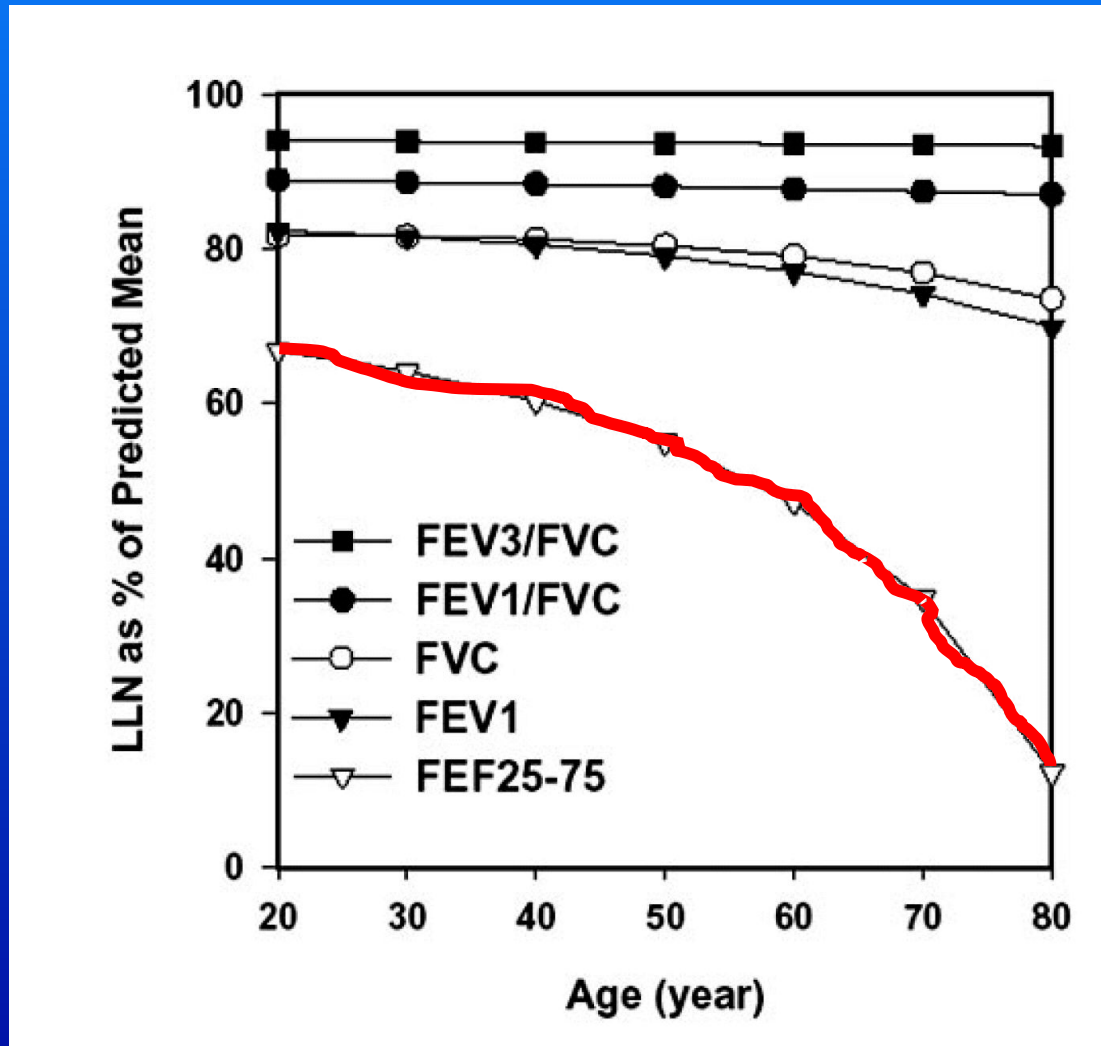


Controversies – FEV_3 vs FEF_{25-75}

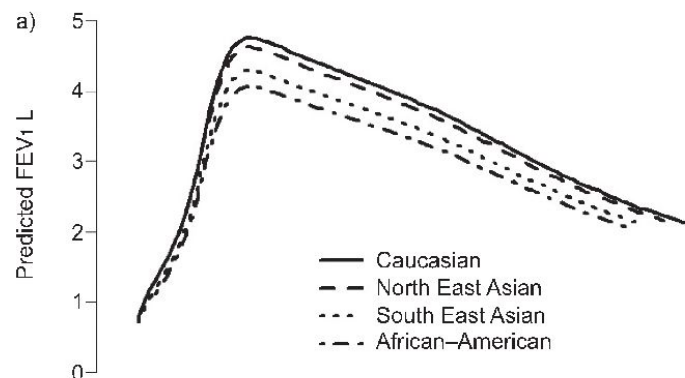


J Hansen, et al.
Chest 129:
369-377, 2006

Why FEF 25-75 Doesn't Belong on your PFT



J Hansen, et al. Chest 129: 369-377, 2006



Initiative (GLI)

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 ed#



NIH Public Access

Author Manuscript

Eur Respir J. Author manuscript; available in PMC 2013 September 30.

Published in final edited form as:

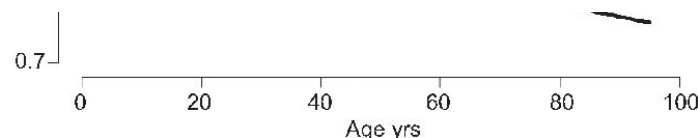
Eur Respir J. 2012 December ; 40(6): 1324–1343. doi:10.1183/09031936.00080312.

MULTI-ETHNIC REFERENCE VALUES FOR SPIROMETRY FOR THE 3–95 YEAR AGE RANGE: THE GLOBAL LUNG FUNCTION 2012 EQUATIONS:

Report of the Global Lung Function Initiative (GLI), ERS Task Force to establish improved Lung Function Reference Values

Philip H. Quanjer,

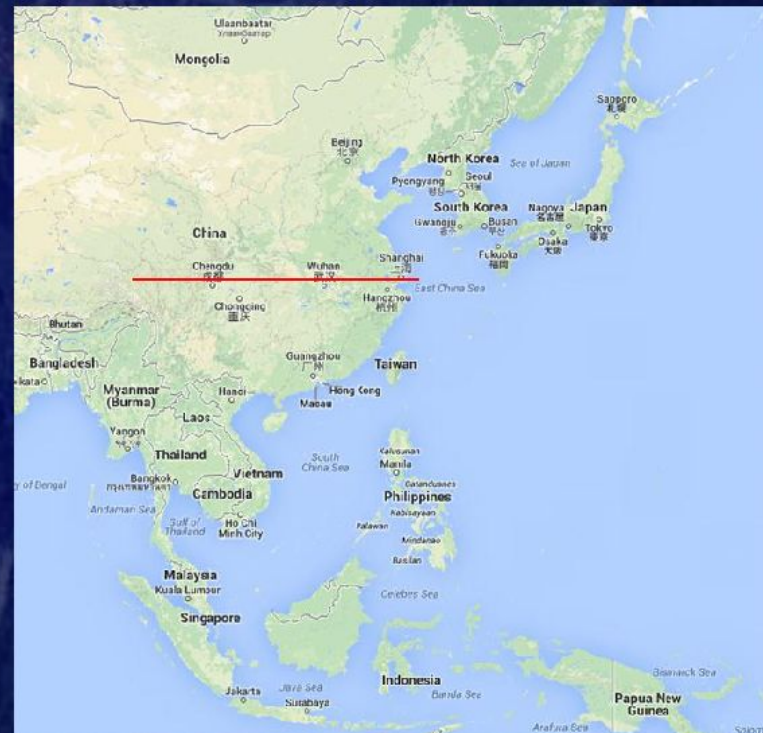
Department of Pulmonary Diseases and Department of Paediatrics, Erasmus Medical Centre, Erasmus University, Rotterdam, the Netherlands



E1 in the online supplementary data.

GLI

North vs South East Asian



Classification of Severity of Airflow Limitation in COPD*

Table 2. Spirometric Classification of the Severity of Chronic Obstructive Pulmonary Disease

Severity of Obstruction	Post-bronchodilator FEV ₁ /FVC	FEV ₁ % Predicted
At risk	>0.7	≥80
Mild COPD	≤0.7	≥80
Moderate COPD	≤0.7	50–80
Severe COPD	≤0.7	30–50
Very severe COPD	≤0.7	<30

Definition of abbreviation: COPD = chronic obstructive pulmonary disease.

At risk are (1) patients who smoke or have exposure to pollutants; (2) patients who have cough, sputum, or dyspnea; and (3) patients who have a family history of chronic respiratory disease.

*Based on **Post-Bronchodilator FEV₁**

AMERICAN THORACIC SOCIETY DOCUMENTS

An Official American Thoracic Society/European Respiratory Society Statement: Research Questions in Chronic Obstructive Pulmonary Disease

Bartolome R. Celli*, Marc Decramer*, Jacek A. Wedzicha*, Kevin C. Wilson*, Alvar Agusti, Gerard J. Criner, William MacNee, Barry J. Make, Stephen I. Rennard, Robert A. Stockley, Claus Vogelmeier, Antonio Anzueto, David H. Au, Peter J. Barnes, Pierre-Regis Burgel, Peter M. Calverley, Ciro Casanova, Enrico M. Ciri, Christopher B. Cooper, Harvey O. Coxson, Daniel J. Desser, Leonardo M. Fabbri, Bonnie Fahy, Gary T. Ferguson, Andrew Fisher, Monica J. Fletcher, Maurice Heyot, John R. Hurst, Paul W. Jones, Donald A. Mahler, François Maltais, David M. Mannino, Fernando J. Martinez, Marc Miravettes, Paula M. Meek, Alberto Papi, Klaus F. Rabe, Nicolas Roche, Frank C. Scurba, Sanjay Sethi, Nikos Siafakas, Don D. Sin, Joan B. Soriano, James K. Stoller, Donald P. Tashkin, Thierry Troosters, Geert M. Verkleiden, Johnny Verschakelen, Jorgen Vestbo, John W. Walsh, George R. Washko, Robert A. Wise, Ernie F. M. Wouters, and Richard L. Zúñiga, on behalf of the ATS/ERS Task Force for COPD Research

The official statement of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) was approved by the ATS Board of Directors, November 25, 2014, and by the ERS Science Council and Executive Committee, November 5 and November 27, 2014, respectively.

Novel Spirometric Measure (FEV₃/FEV₆) identifies COPD unidentified by standard criteria

[Original Research COPD]



A Novel Spirometric Measure Identifies Mild COPD Unidentified by Standard Criteria



Asli Gorek Dilektasli, MD; Janos Porszasz, MD, PhD; Richard Casaburi, PhD, MD; William H. Stringer, MD; Surya P. Bhatt, MD; Youngju Pak, PhD; Harry B. Rossiter, PhD; George Washko, MD; Peter J. Castaldi, MD; Raul San Jose Estepar, PhD; and James F. Hansson, MD; for the COPDGene investigators

BACKGROUND: In chronic obstructive pulmonary disease, both smaller and larger airways are affected. FEV₁ mainly reflects large airways obstruction, while the later fraction of forced exhalation reflects reduction in terminal expiratory flow. In this study, the objective was to evaluate the relationship between spirometric ratios, including the ratio of forced expiratory volume in 3 and 6 seconds (FEV₃/FEV₆), and small airways measures and gas trapping at quantitative chest CT scanning, and clinical outcomes in the Genetic Epidemiology of COPD (COPDGene) cohort.

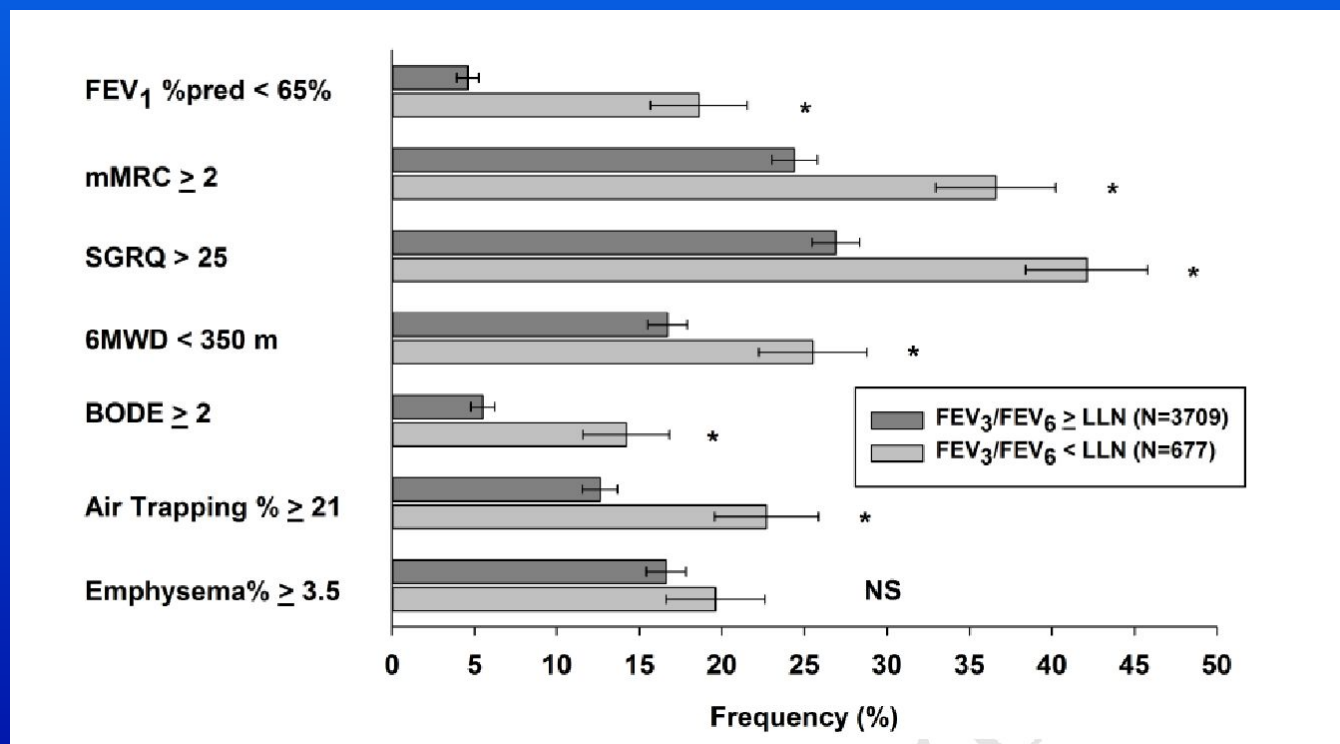
METHODS: Seven thousand eight hundred fifty-three current and ex-smokers were evaluated for airflow obstruction by using recently defined linear iteratively derived equations of Hansen et al to determine lower limit of normal (LLN) equations for prebronchodilator FEV₁/FVC, FEV₁/FEV₆, FEV₃/FEV₆, and FEV₃/FVC. General linear and ordinal regression models were applied to the relationship between prebronchodilator spirometric and radiologic and clinical data.

RESULTS: Of the 10,311 participants included in the COPDGene phase I study, participants with incomplete quantitative CT scanning or relevant spirometric data were excluded, resulting in 7,853 participants in the present study. Of 4,386 participants with FEV₁/FVC greater than or equal to the LLN, 15.4% had abnormal FEV₃/FEV₆. Compared with normal FEV₃/FEV₆ and FEV₁/FVC, abnormal FEV₃/FEV₆ was associated with significantly greater gas trapping; St. George's Respiratory Questionnaire score; modified Medical Research Council dyspnea score; and BMI, airflow obstruction, dyspnea, and exercise index and with shorter 6-min walking distance (all $P < .0001$) but not with CT scanning evidence of emphysema.

CONCLUSIONS: Current and ex smokers with prebronchodilator FEV₃/FEV₆ less than the LLN as the sole abnormality identifies a distinct population with evidence of small airways disease in quantitative CT scanning, impaired indexes of physical function and quality of life otherwise deemed normal by using the current spirometric definition.

CHEST 2016; 150(5):1080-1090

Novel Spirometric Measure (FEV₃/FEV₆) identifies COPD unidentified by standard criteria



Detecting SAD (Small Airways Disease)

www.medscape.com

COMMENTARY

Assess Those Small Airways With FEV₃

Aaron B. Holley, MD | September 13, 2016

Small Airway Disease

COPDGene was an observational study that enrolled more than 10,000 cigarette users with and without chronic obstructive pulmonary disease (COPD).^[1] The study was designed to explore genetic associations with COPD and to refine our

I have been writing a lot recently about small airway disease (SAD)—its measurement and significance in the setting of asthma or COPD. The *CHEST* Journal just published more data from COPDGene that evaluated markers for SAD.^[2] The study is important for several reasons. First, the investigators compared measures of SAD using more than one modality. They also expanded on what we already know about the forced expiratory volume in 3 seconds (FEV₃). Perhaps of greatest importance, they correlated small airway dysfunction with functional outcomes.

variability and overlap between normal and abnormal values.^[4] Impulse oscillometry (IOS), plethysmography, FEV₃, and CT imaging with air-trapping/mosaicism have all been used to establish SAD. Unfortunately, little in the way of comparative research between modalities has been done, and little correlation with clinical outcomes has been found.

FEV₃, the SAD Measure of Choice

Enter the most recent installment from the COPDGene study published in *CHEST*.^[2] The investigators compared FEV₃ with CT and established good correlation. It's reassuring that the two modalities are measuring the same phenomenon. In addition to what we already know about FEV₃ and SAD,^[5,6] they found that FEV₃/FVC₆ was superior to FEV₃/FVC for predicting clinical outcomes in patients with COPD. Among patients with otherwise normal spirometry, the 15.4% with a low FEV₃/FVC₆ had increased symptoms (St George's Respiratory Questionnaire and modified Medical Research Council [mMRC] dyspnea score) and BODE index score,^[7] as well as shorter 6-minute walk distance compared with those with normal FEV₃/FVC₆. The importance of the relationship with functional status and symptoms cannot be overstated. All of the modalities used to measure SAD are short on clinical outcomes data; without those data, how do we know whether the deficits we believe we are identifying are clinically relevant?

This is more evidence that SAD is clinically relevant and supports using FEV₃ as the small airway measure of choice. It's easy; it has already been reported with spirometry and, in my opinion, is backed by the best data.^[2,4,7] There is no radiation risk and it doesn't require advanced equipment like IOS or plethysmography. For all you pulmonologists out there, start looking at the FEV₃ when you get spirometry on your tobacco users and patients with unexplained dyspnea.

References

1. Regan E, Hokanson JE, Murphy JR, et al. Genetic epidemiology of COPD (COPDGene) study design. *COPD*. 2010;7:32-43. Abstract
2. Dilektaşlı A, Porszasz J, Casaburi R, et al; COPDGene Investigators. A novel spirometric measure identifies mild chronic obstructive pulmonary disease unidentified by standard criteria. *Chest*. 2016 Jul 21. [Epub ahead of print]
3. Mead J. The lung's "quiet zone". *N Engl J Med*. 1970;282:1318-1319. Abstract

PRISM (Preserved Ratio, Impaired Spirometry) & COPD Gene

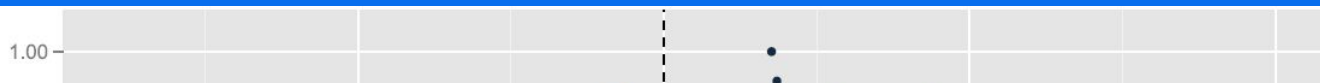
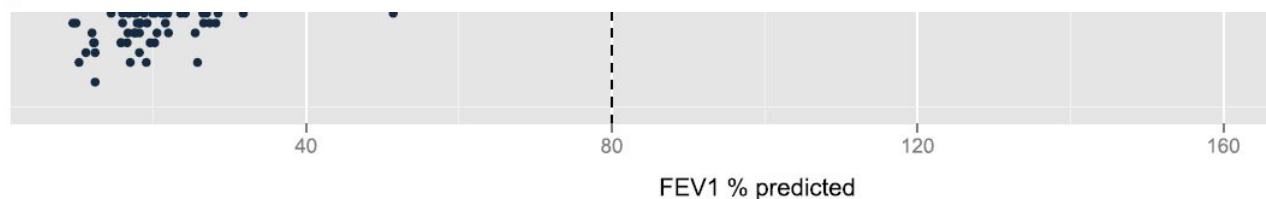


Table 1 Characteristics of Preserved Ratio Impaired Spirometry (PRISM), smoking control, and COPD subjects in COPDgene using fixed threshold criteria

	Control subjects	PRISM	COPD
n	4388	1257	3690
Age	56.7 (8.4)*	57.2 (8.2)	63.4 (8.5)*
Sex (% Male)	52.9*	46.1	55.6*
African American	41.2	43.1	22.7*
Current smoker	59.7*	63.8	40.7*
Pack-years	37.2 (20.2)*	42.7 (24.2)	53.0 (27.5)*
Body Mass Index	28.9 (5.8)*	31.8 (7.3)	28.1 (6.3)*
FEV ₁ % predicted	97.5 (11.5)*	70.2 (8.4)	50.2 (18.0)*
FVC% predicted	96.6 (11.9)*	71.5 (9.1)	76.3 (17.3)*
FEV ₁ /FVC	0.79 (0.05)*	0.77 (0.05)	0.50 (0.13)*
Bronchodilator Responsiveness [†]	10.0*	13.7	36.6*
Total Lung Capacity _{CT} % predicted	92.3 (14.6)*	79.9 (13.5)	101.5 (17.1)*



Jeffrey M. Drazen, M.D., *Editor*

The Asthma–COPD Overlap Syndrome

Dirkje S. Postma, M.D., Ph.D., and Klaus F. Rabe, M.D., Ph.D.

ACOS

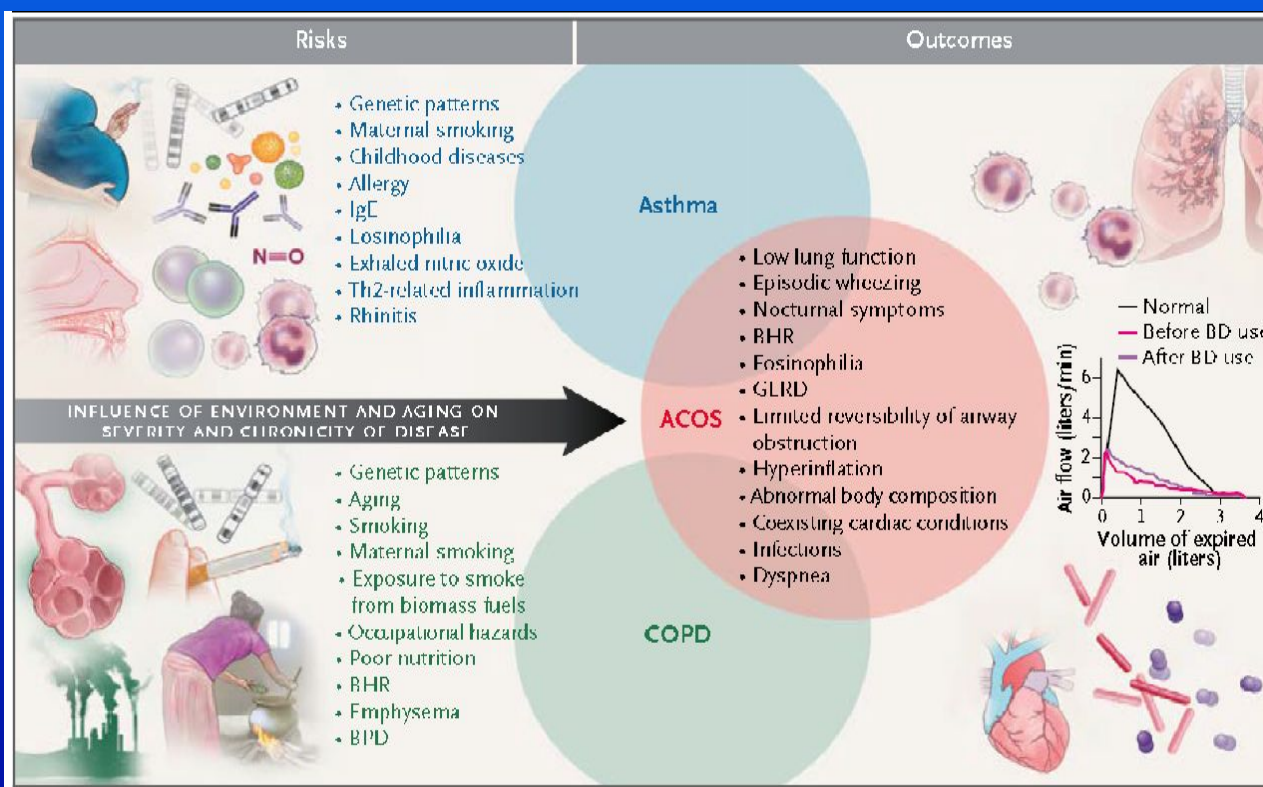
Table 1. Four Examples of Patients with Obstructive Airway Disease.*

Characteristic	Patient with “Easy” Asthma	Patient with “Easy” COPD	Patient with ACOS Stemming from Asthma	Patient with ACOS Stemming from COPD
Age (yr)	21	65	45	45
Atopy	Yes	No	Yes	Yes
Current smoker	No	Yes	No	Yes
Pack-years	0	95	0	20
Dyspnea	Recurrent	Chronic	Chronic with flares	Chronic with flares
Wheezing	Yes	No	Yes	Yes
Reversible airway obstruction	Yes	No	No	Yes
Bronchial hyperresponsiveness	Yes	No	Yes	Yes or no

Jeffrey M. Drazen, M.D., Editor

The Asthma-COPD Overlap Syndrome

Dirkje S. Postma, M.D., Ph.D., and Klaus F. Rabe, M.D., Ph.D.



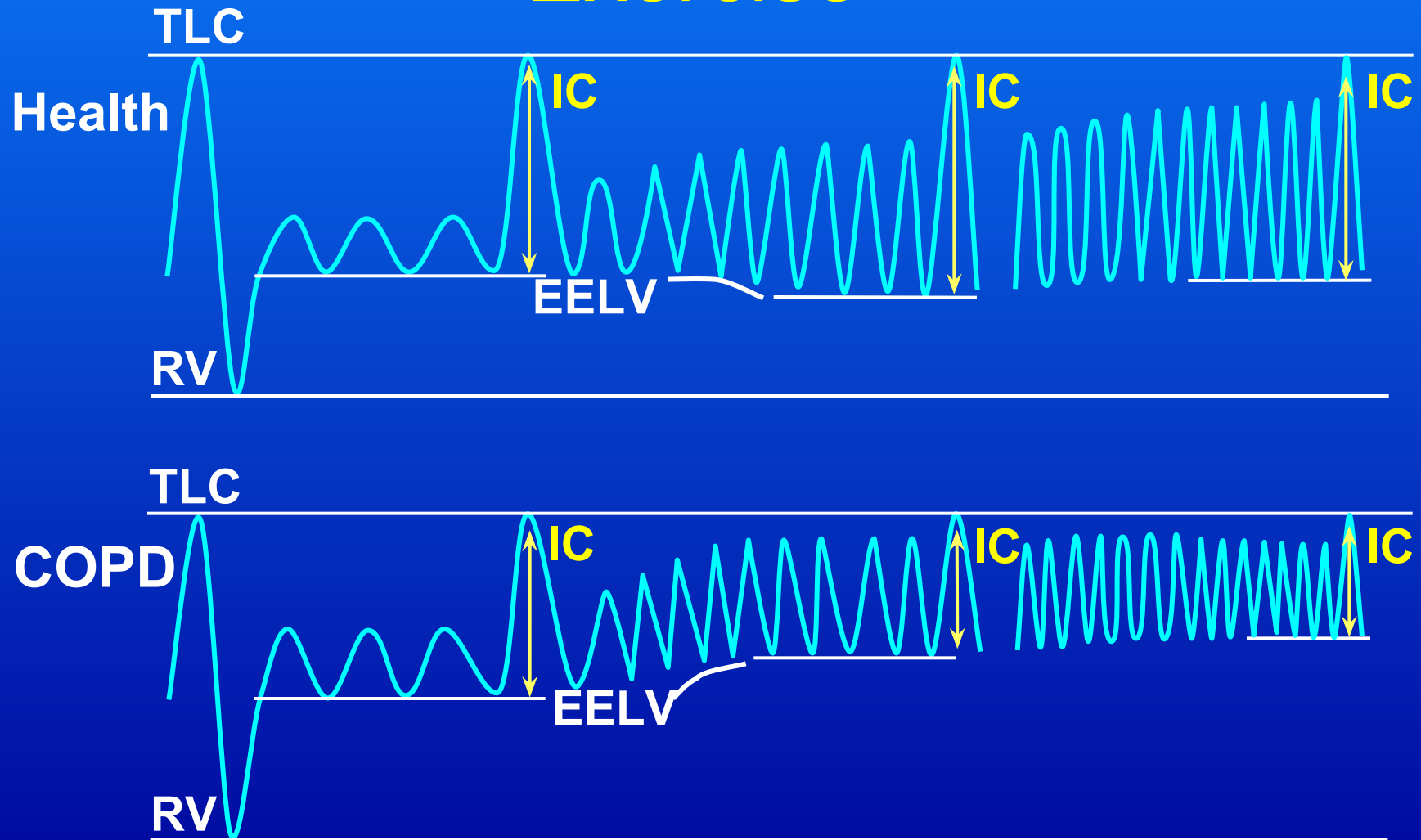
Exercise Testing in COPD Patients

- Assessing mechanisms of exercise limitation
- Defining contraindications to an exercise program
- Determining need for oxygen supplementation
- Providing an exercise prescription
- Measuring improvement from rehabilitation

Evaluating Exercise Limitation in Pulmonary Patients

- Defining Ventilatory Limitation
 - Breathing reserve
 - Assessment of hyperinflation
- Determining contributors to high ventilatory requirement
 - High V_D/V_T
 - Hypoxemia
 - Early onset of lactic acidosis
- Detecting Pulmonary Vascular Disease

Lung Volume Response to Exercise



Oxygen Prescription for Exercise

pulse oximetry
vs.
arterial blood gas

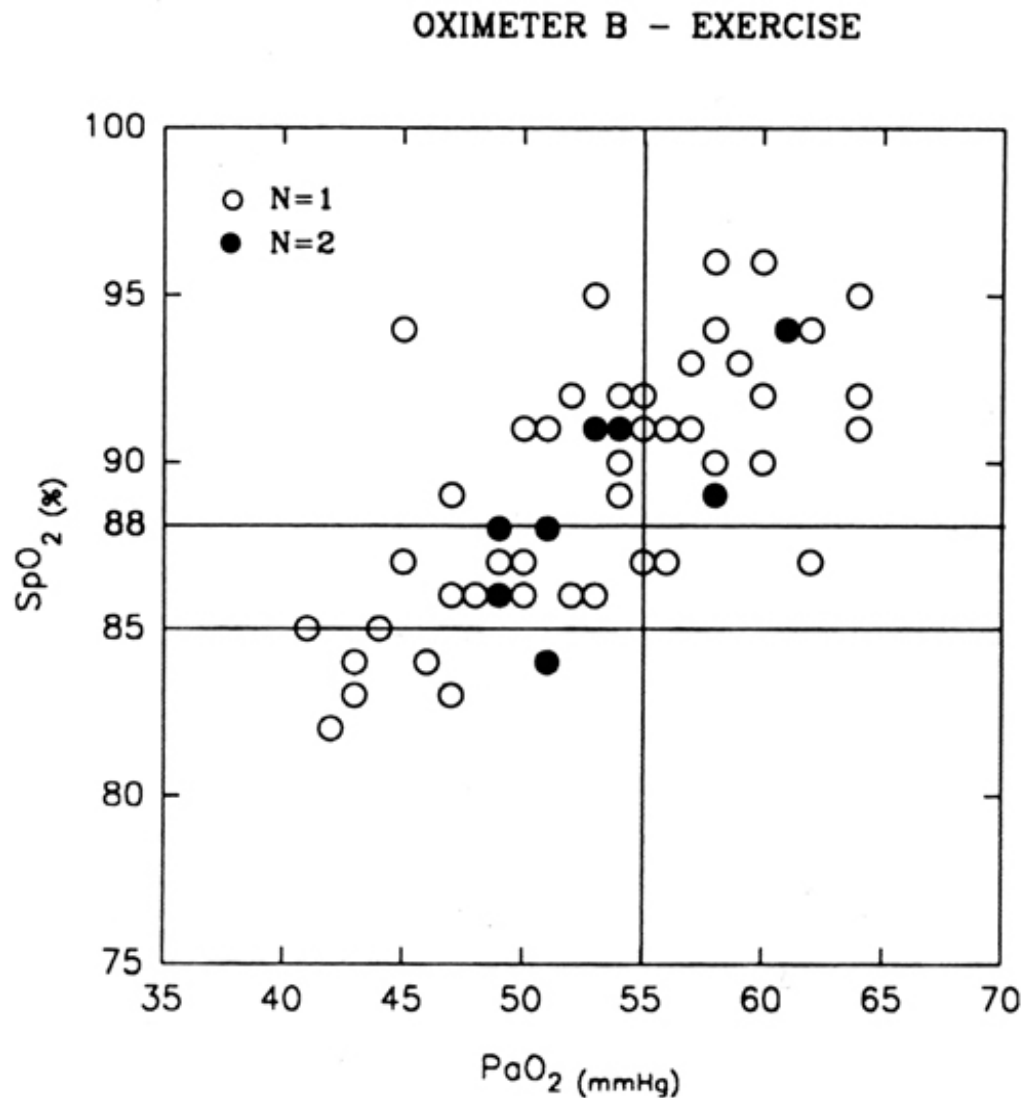


FIGURE 2. The relationship between SpO_2 and PaO_2 at end incremental exercise (oximeter B).

Carlin et al., Chest, 1988

Oxygen Prescription for Exercise

arterial blood
co-oximetry
vs.
arterial blood gas

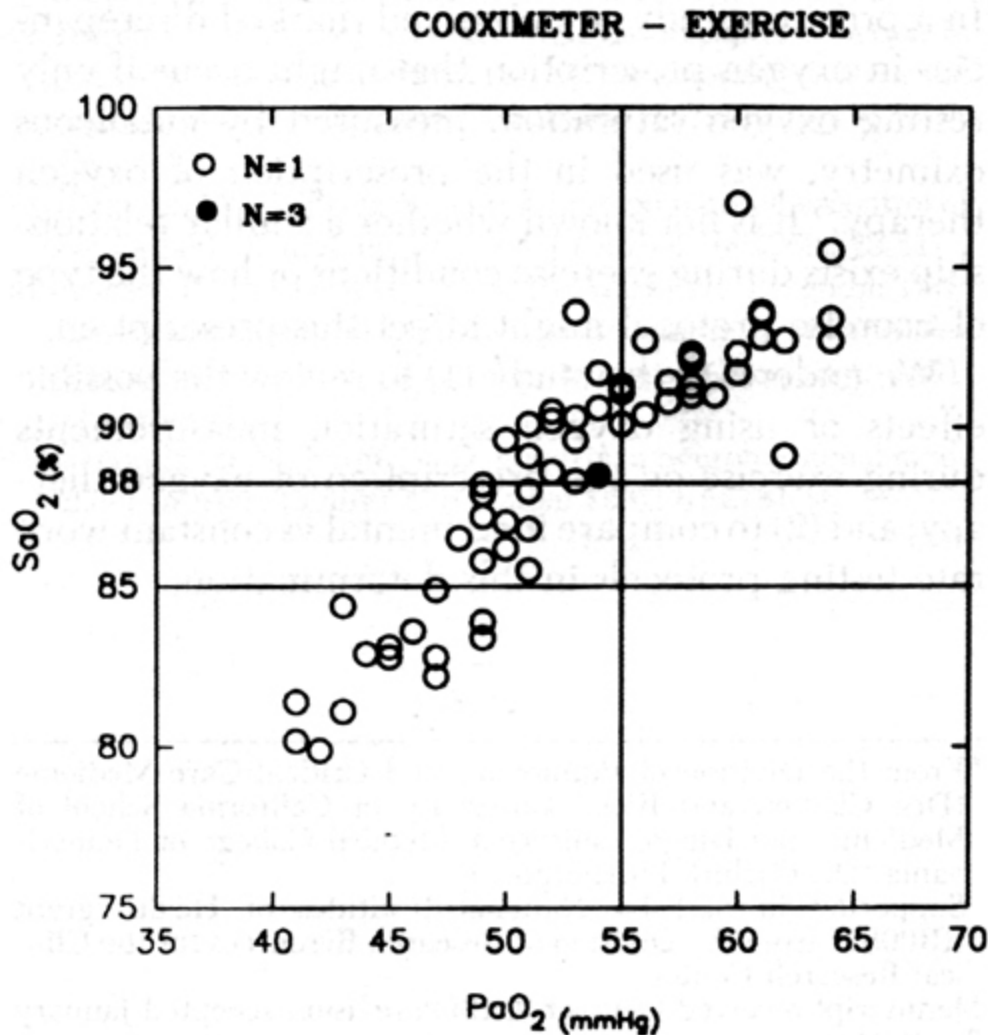
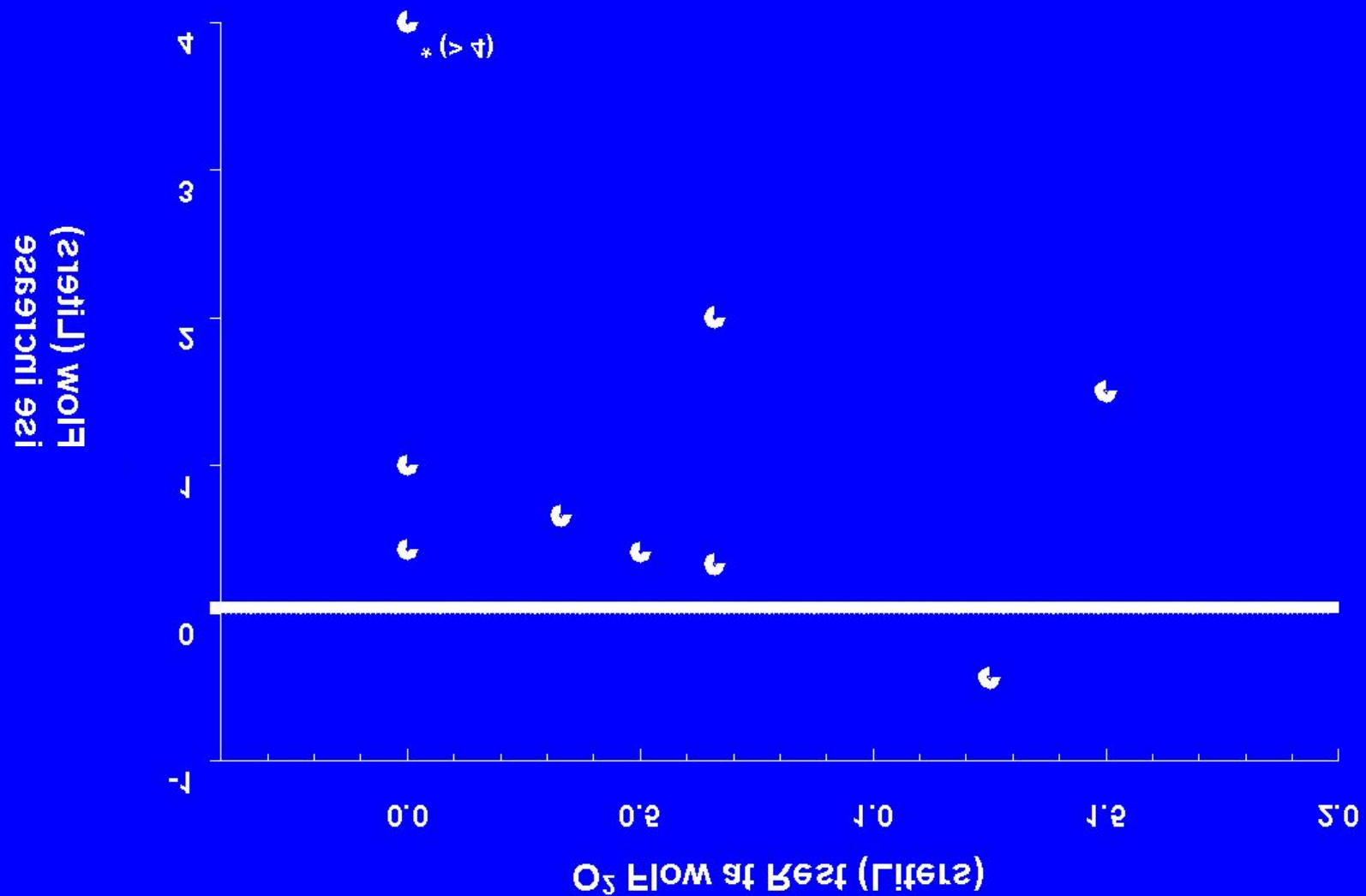


FIGURE 3. The relationship between SpO_2 and PaO_2 at end incremental exercise (co-oximeter).

Carlin et al., Chest, 1988

Oxygen Prescription For Exercise in COPD

Increase in Nasal O₂ Flow to Maintain O₂ Saturation at 95%



BODE Index

Table 4. Composite Prognostic Indexes in Chronic Obstructive Pulmonary Disease

Composite Index	Components	Reference
BODE	BMI, FEV ₁ , mMRC, 6MWD	43
mBODE	BMI, FEV ₁ , mMRC, peak V _{O2}	44
eBODE	BMI, FEV ₁ , mMRC, 6MWD, exacerbation rate	45
BODEx	BMI, FEV ₁ , mMRC, exacerbation rate	46
Inflammatory BODE	BODE, inflammatory biomarkers, age, and hospitalization history	47
ADO	Age, mMRC, FEV ₁	48
DOSE	mMRC, FEV ₁ , smoking status, exacerbation rate	49
CODEx	Comorbidity, obstruction, dyspnea, and previous severe exacerbations	50

Definition of abbreviations: 6MWD = 6-minute-walk distance; ADO = age, dyspnea, and airflow obstruction index; BMI = body mass index (kg/m²); BODE = body mass index, airflow obstruction, dyspnea, and exercise capacity index; BODEx = exacerbations replace 6MWD in the original BODE; CODEx = comorbidities, airflow obstruction, dyspnea, and exacerbations index; DOSE = dyspnea, airflow obstruction, smoking status, and exacerbations index; eBODE = exacerbations added to original BODE; FEV₁ = forced expiratory volume in 1 second (severity of airflow obstruction); inflammatory BODE = inflammatory markers added to original BODE; mBODE = modified BODE in which 6MWD is replaced by peak oxygen consumption; mMRC = level of dyspnea according to the Modified Medical Research Council questionnaire.

Exercise Testing for Pulmonary Rehabilitation

Characteristics of an Exercise Training Program

- Frequency
- Duration
- Intensity

Characteristics of an Exercise Training Program

- Frequency
 - sessions held 3-5 times per week
- Duration
 - sessions of 30-60 minutes length
 - program 6-8 weeks long

Characteristics of an Exercise Training Program

- Critical Training Intensity
 - there is an intensity of training below which no physiologic training effect will be obtained

“...studies demonstrating relatively convincing evidence of a physiologic training effect incorporated supervised exercise programs with a high intensity component.”

Pulmonary Rehabilitation
Evidence-Based Guidelines
Chest 1997

Selecting a High Intensity Exercise Target for COPD Patients

- Perform incremental exercise test
- Chose initial exercise intensity target as:
 - 75%-80% of peak work rate or
 - heart rate at 75%-80% of peak work rate

Exercise Prescription Guidelines

- Supervised group exercise program
- Adequate program duration, session frequency and session duration
- Individualized exercise intensity prescription based on cardiopulmonary exercise testing
- High intensity target based on work rate or heart rate target

Exercise Testing in Pulmonary Rehabilitation

- Measuring improvement from rehabilitation

Response to Bronchodilator in COPD

-Comparison of Exercise Testing Modalities

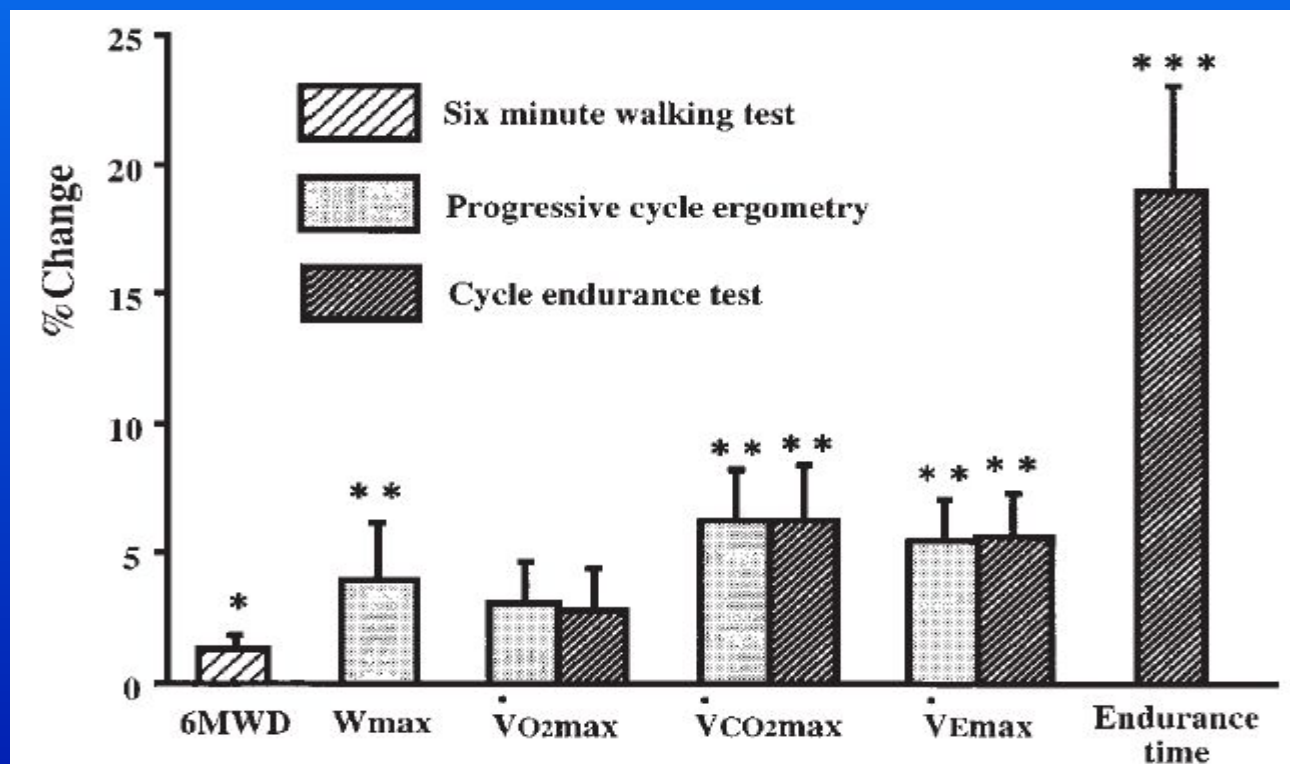
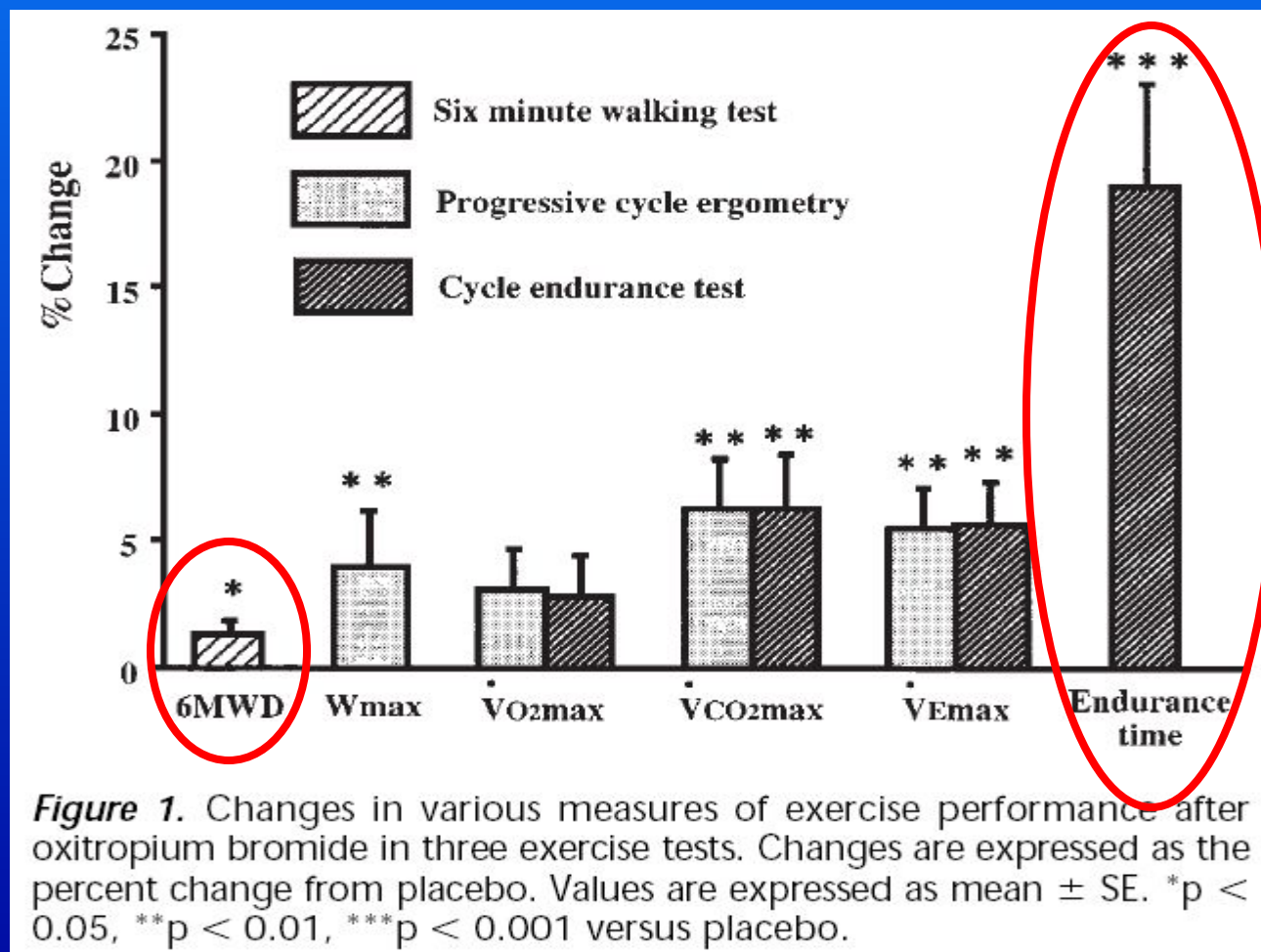


Figure 1. Changes in various measures of exercise performance after oxitropium bromide in three exercise tests. Changes are expressed as the percent change from placebo. Values are expressed as mean $\pm$ SE. *p < 0.05, **p < 0.01, ***p < 0.001 versus placebo.

Response to Bronchodilator in COPD

-Comparison of 6 minute walk and cardiopulmonary exercise testing-



Methodology for Utilizing Constant Work Rate Duration in Interventional Studies in COPD

- Goal: Predict a work rate that will yield a test whose duration will be in the 4 to 7 minute range
- Method: Perform an incremental exercise test. Utilize 85% of the peak work rate in the constant work rate test.

We Need an Exercise Testing Tool that Complements the Sophistication of our Approach to Exercise Training



6 Minute Walk Test



Cardiopulmonary Exercise Test

Accurately evaluate exercise intolerance

Cardiopulmonary Exercise Testing

- **Peak oxygen uptake** - well defined normal values
- **Anaerobic threshold** - *effort independent* measure of exercise tolerance



Accurately evaluate exercise intolerance

6 Minute Walk Test

- Very effort and motivation dependent
- Plateau effect: insensitive to mild exercise intolerance
- Expressing distance in relation to normal values seldom employed



Accurately evaluate exercise intolerance

6 Minute Walk Test

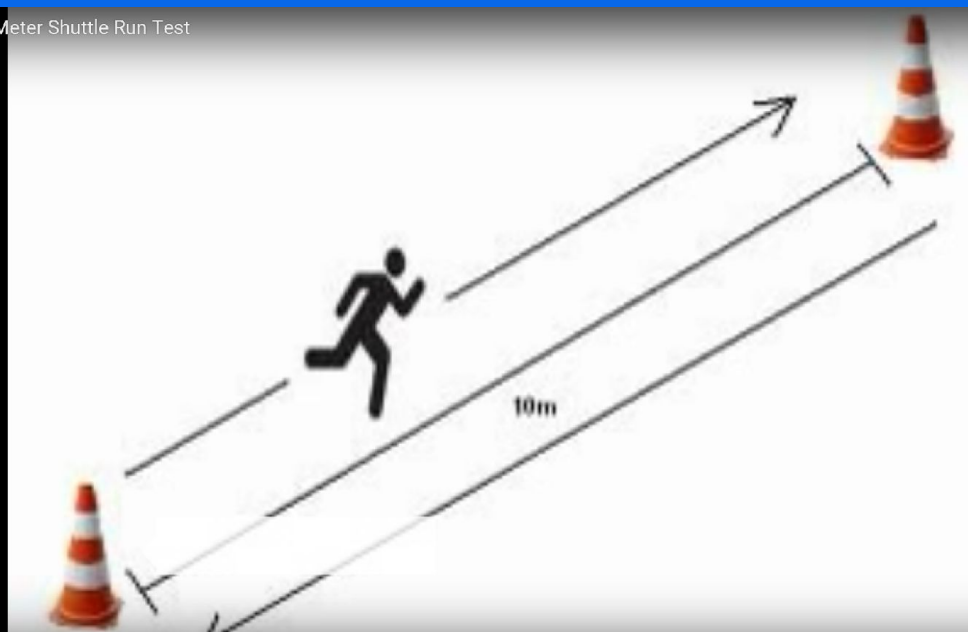
- Very effort and motivation dependent
- Plateau effect: insensitive to mild exercise intolerance
- Expressing distance in relation to normal values seldom employed

...with good reason



Shuttle Walk

10 Meter Shuttle Run Test



g
m

Table 1—Indications and Contraindications for Performing the 6MWT*

Indications

- Response to a medical intervention (pretreatment and posttreatment comparisons)
- Lung transplantation
- Lung resection
- Lung volume reduction surgery
- Pulmonary rehabilitation
- COPD
- Pulmonary arterial hypertension
- CHIF
- Single measurement of functional status
- COPD
- Cystic fibrosis
- CHF
- Peripheral vascular disease
- Fibromyalgia
- Predictors of morbidity and mortality
- CHIF
- COPD
- IPAH
- Idiopathic pulmonary fibrosis

Contraindications

- Absolute contraindications**
 - Unstable coronary disease
 - Myocardial infarction in the preceding month
- Relative contraindications**
 - Resting tachycardia > 120 beats/min
 - Systolic BP > 180 mm Hg
 - Diastolic BP > 100 mm Hg
 - Arthritis, skeletal, or neuromuscular disease limiting ambulation
 - Syncope during exercise (especially in pulmonary hypertension)

*Based on data from references 4, 5, 14 to 22, and 35.

American Thoracic Society

ATS Statement: Guidelines for the Six-Minute Walk Test

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY WAS APPROVED BY THE ATS BOARD OF DIRECTORS
MARCH 2002



CHEST

Topics in Practice Management

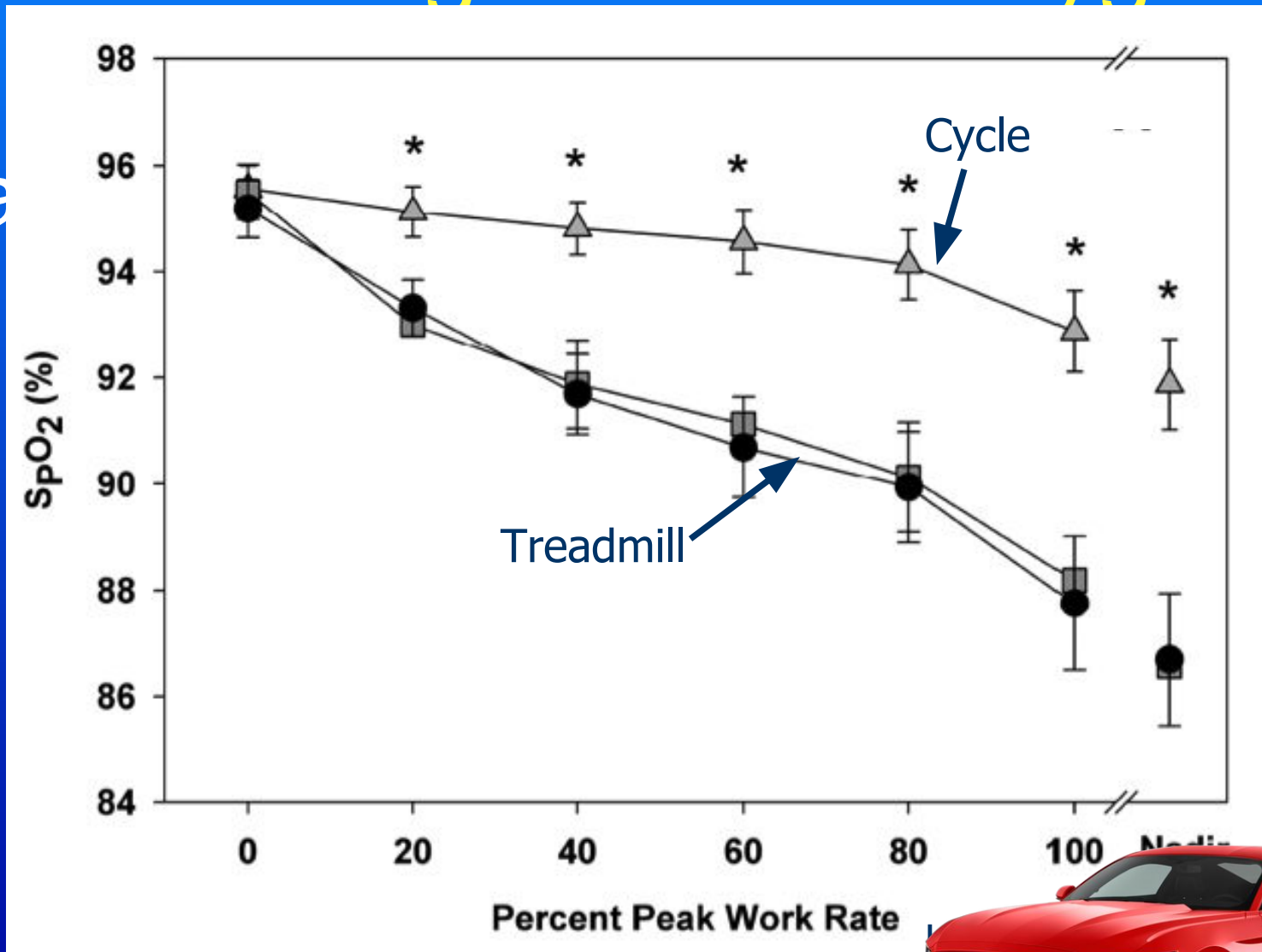
The 6-Min Walk Test*

Clinical and Research Role, Technique, Coding,
and Reimbursement

Steve H. Solomon, MD, FCCP

Determining Need for Oxygen

Ca



Determining Need for Oxygen Supplementation

6 Minute Walk Testing

Oximetry performed even
immediately after exercise will
lead to underestimates of
desaturation

“... motion artifact that prevents accurate readings during the walk.”

ATS 6MW Guidelines, 2002

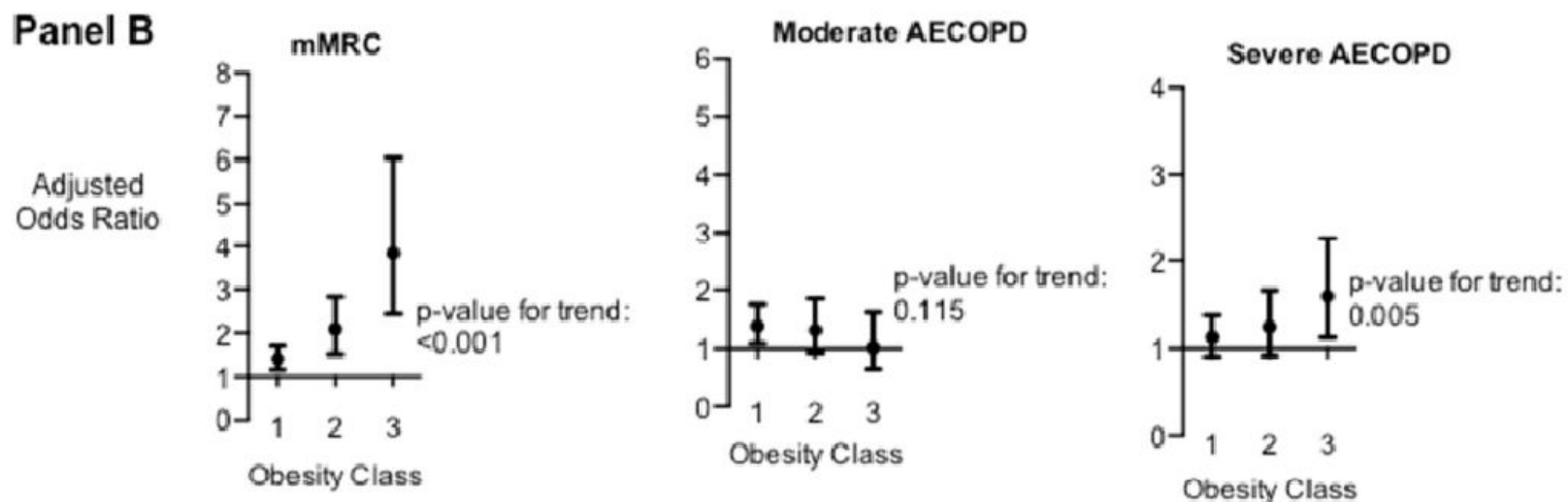
Some Recent Interesting Articles from the Literature

Obesity and COPD Gene Database

Panel A



Panel B



ACE Rx and COPD Rehab

ORIGINAL ARTICLE

Angiotensin-Converting Enzyme Inhibition as an Adjunct to Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease

Katrina J. Curtis¹, Victoria M. Meyrick^{1,2}, Bhavin Mehta¹, Gulam S. Haji¹, Kawah Li³, Hugh Montgomery³, William D.-C. Man^{1,4}, Michael I. Polkey¹, and Nicholas S. Hopkinson¹

¹National Institute for Health Research Respiratory Biomedical Research Unit, Royal Brompton & Harefield NHS Trust and Imperial College, London, United Kingdom; ²Department of Respiratory Medicine, King's College London NHS Foundation Trust, London, United Kingdom; ³Institute for Sport, Exercise and Health, University College London, London, United Kingdom; and ⁴Harefield Pulmonary Rehabilitation Unit, Harefield Hospital, London, United Kingdom

ORCID ID: 0000 0003 3235 0454 (N.S.H.).

Abstract

Rationale: Epidemiological studies in older individuals have found an association between the use of angiotensin-converting enzyme (ACE) inhibition (ACE-I) therapy and preserved locomotor muscle mass, strength, and walking speed. ACE-I therapy might therefore have a role in the context of pulmonary rehabilitation (PR).

Objectives: To investigate the hypothesis that enalapril, an ACE inhibitor, would augment the improvement in exercise capacity seen during PR.

Methods: We performed a double-blind, placebo-controlled, parallel-group randomized controlled trial. Patients with chronic obstructive pulmonary disease, who had at least moderate airflow obstruction and were taking part in PR, were randomized to either 10 weeks of therapy with an ACE inhibitor (10 mg enalapril) or placebo.

Measurements and Main Results: The primary outcome measurement was the change in peak power (assessed using cycle ergometry) from baseline. Eighty patients were enrolled, 78 were

randomized (age 67 ± 8 years; FEV₁ $48 \pm 21\%$ predicted), and 65 completed the trial (34 on placebo, 31 on the ACE inhibitor). The ACE inhibitor-treated group demonstrated a significant reduction in systolic blood pressure (Δ , -16 mm Hg; 95% confidence interval [CI], -22 to -11) and serum ACE activity (Δ , -18 IU/L; 95% CI, -23 to -12) versus placebo (between-group differences, $P < 0.0001$). Peak power increased significantly more in the placebo group (placebo Δ , $+9$ W; 95% CI, 5 to 13 vs. ACE-I Δ , $+1$ W; 95% CI, -2 to 4 ; between-group difference, 8 W; 95% CI, 3 to 13 ; $P = 0.001$). There was no significant between-group difference in quadriceps strength or health-related quality of life.

Conclusions: Use of the ACE inhibitor enalapril, together with a program of PR, in patients without an established indication for ACE-I, reduced the peak work rate response to exercise training in patients with chronic obstructive pulmonary disease.

Keywords: COPD; renin-angiotensin system; exercise; rehabilitation

Survival After Pulm Rehab (6MW and CPET)

Table 1 Baseline characteristics of subjects

Demographic characteristics	All subjects	Completed 3 months of PR			Groups according to 6MWDi and Δ6MWD				P-value
		Yes	No	P-value	6MWDi ≥350 m		6MWDi <350 m		
					Δ≥30 m; Group 1	Δ<30 m; Group 2	Δ≥30 m; Group 3	Δ<30 m; Group 4	
Number of patients	423	333	90		125	144	74	80	
Age (years)	65±8	66±8	65±8	0.7118	65±8	65±8	67±8	67±8	0.2380
Male sex, n (%)	335 (79)	265 (80)	70 (78)	0.7087	97 (77)	115 (80)	60 (81)	63 (79)	0.9400
BMI (kg.m ⁻²)	25±6	25±5	25±7	0.7913	26±5	26±5	24±6	25±6	0.5474
Lung function									
FEV ₁ (% predicted)	43±16	43±15	44±19	0.8367	46±16	47±16	37±12*†	37±16*†	<0.0001
FEV ₁ /FVC (%)	41±12	40±11	43±15	0.1643	42±11	42±11	37±11*†	39±15	0.0066
FRC (% predicted)	154±37	154±37	152±38	0.5906	152±35	150±34	166±40*†	153±39	0.0275
DL _{CO} (% predicted)	48±17	48±18	48±18	0.8556	53±17	52±17	41±13*†	40±17*†	<0.0001
Peripheral muscle force									
QF (Nm)	100±38	102±37	92±38	0.0232	113±35	110±35	79±30*†	80±35*†	<0.0001
QF (% predicted)	69±26	69±23	66±36	0.4644	75±21	78±28	57±23*†	58±25*†	<0.0001
Exercise capacity									
Oxygen uptake (% predicted)	48±19	49±19	44±18	0.0245	53±18	51±18	40±18*†	42±21*†	<0.0001
Oxygen uptake (mL.kg.min ⁻¹)	14±4	14±4	13±4*	0.0038	16±4	15±5	12±4*†	11±3*†	<0.0001
Max workload (% predicted)	48±20	49±19	45±20	0.0892	55±19	53±18	37±18*†	37±16*†	<0.0001
6MWD (m)	381±134	395±129	328±138	<0.0001	458±65	469±74	234±78*†	230±84*†	<0.0001
6MWD (% predicted)	59±21	61±20	52±22	<0.0001	71±10	73±11	37±13*†	37±14*†	<0.0001

CT Metrics and BODE / Health Status

Figure 1 Frequency distribution of BODE index scores

Distribution of BODE index scores

Distribution of SGRQ total scores

Table. Variables and cutoff values for points 0 to 3 in the BODE index computation.

	Point on BODE index*			
	0	1	2	3
FEV ₁ (% of predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 minutes (m)	≥350	250–349	150–249	≤149
Dyspnea scale score	0–1	2	3	4
Body mass index measure	>21	≤21	—	—

*Values range from 0 (best) to 10 (worst)

Source: Adapted from the Body-mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index in Chronic Obstructive Pulmonary Disease⁸



Figure 2 (A) Three dimensional plot demonstrating the relationship between increasing 10 mm luminal perimeter (pi10), emphysema percentage and St George's Respiratory Questionnaire (SGRQ) score. (B) Density plot of patients with chronic obstructive pulmonary disease (COPD) with SGRQ score approximately in the 90th percentile (score ≥64, n = 146) demonstrating degree of pi10 and emphysema in this subgroup. High density in red, low density in blue. (C) Three dimensional plot demonstrating the relationship between increasing pi10, emphysema percentage and BODE index score. (D) Density plot of patients with COPD with BODE score approximately in the 90th percentile (score ≥6, n = 142) demonstrating the degree of pi10 and emphysema in this subgroup. High density in red, low density in blue.

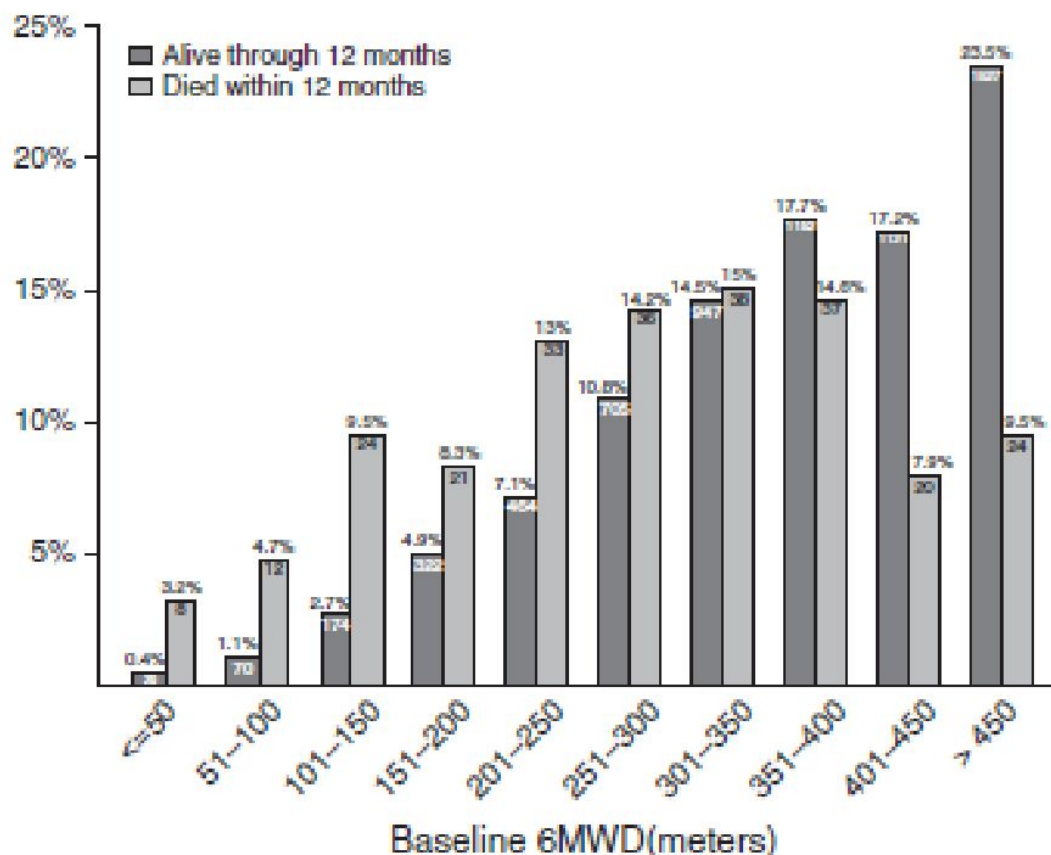
6 Minute Walk – COPD Stratification

Table 1. Baseline Characteristics

--

Age, yr, mean
Sex, females
Race, nonwhite
Region of the
Americas
European
Southeast
Western
African
GOLD COPD
0
1
2
3
4
Missing/un-
History of ex-
0
1
2
3 or more
Missing
Comorbidities
Hypertension
Cardiovascular
Diabetes
6MWD, m, mean

A



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

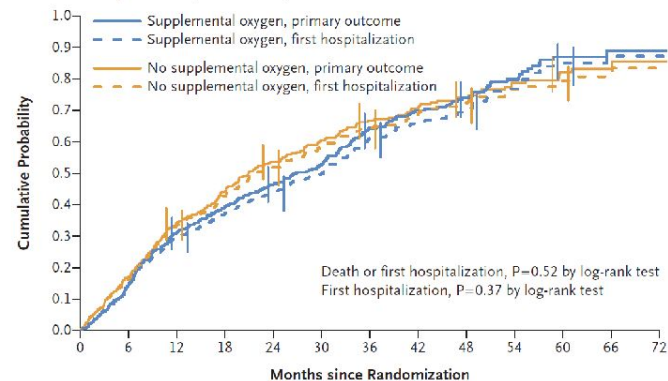
OCTOBER 27, 2016

VOL. 375 NO. 17

A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation

The Long-Term Oxygen Treatment Trial Research Group*

A Primary Outcome (Death or First Hospitalization) or First Hospitalization

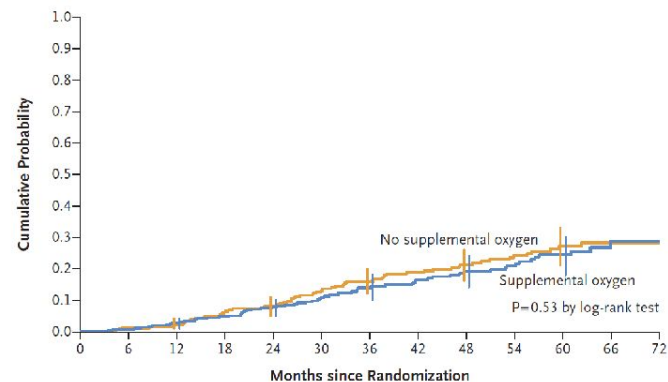


No. at Risk

No supplemental oxygen
Supplemental oxygen

370	304	232	181	139	102	76	59	43	29	21	7	1
368	314	243	198	158	125	86	61	44	24	13	6	1

B Death



The Role of Physiologic Testing in COPD Patients

- Standard Testing
 - PFTs – Review
 - Out with the Old (Lose the FEF 25-75...)
 - In with the new... (e.g. FEV3/FEV6, PRISM)
 - Tests of COPD Physiology
 - 6 minute walk (+/- oxygenation)
 - Shuttle Walk
 - Cardiopulmonary Exercise Testing
 - Assessing Exercise Induced Hyperinflation
 - Constant Work Rate Testing
 - Measuring improvement from rehabilitation
- Recent Articles of Interest

THE CLINICIAN'S GUIDE TO DIFFERENTIATING THE MANY FACES OF COPD

Vipul Jain, MD, MS
UCSF Fresno

Saturday September 30, 2017 – 9:40 a.m. – 10:20 a.m.

Vipul Jain, MD, MS, completed a MPH at the University of Iowa before starting his postdoctoral research in Asthma there and has continued on in Asthma and COPD over the past 15 years. He completed his Pulmonary and Critical Care fellowship at UCSD. Currently, Dr. Jain is an Associate Professor of Medicine at UCSF-Fresno and the medical director for the chronic lung disease program.

Clinician's Guide to COPD: Differentiating the Many faces of Obstructive Lung Disease

California Thoracic Society
3rd Annual COPD Symposium
Sep 30th, 2017, UC San Diego, CA

Vipul V. Jain, MD, MS
Medical Director, Chronic Lung Disease Program
Associate Clinical Professor of Medicine, UCSF Fresno



Disclosures

- Conflict of Interest Disclosure
 - Neither I, nor my spouse/partner has any financial relationships with commercial entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients relevant to the content I am planning, developing, presenting, or evaluating
- Content Attestation
 - I hereby declare that the content for this activity, including any presentation of therapeutic options, is well balanced, unbiased, and to the extent possible, evidence-based.

2



Disclosures

- Consultant and Speaker
 - Astra-Zeneca
 - Aerocrine
 - Paradigm Medical
- **I have no actual or potential conflict of interest in relation to this presentation**

3



Immunology of COPD

Animation Slide

4

COPD Phenotypes

“Driving Pathology” – COPD

5

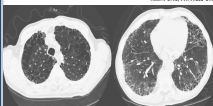
Phenotyping COPD

CHEST Recent Advances in Chest Medicine

Combined Pulmonary Fibrosis and Emphysema Syndrome

There is increasing clinical, radiologic, and pathologic recognition of the coexistence of emphysema and pulmonary fibrosis in the same patient, resulting in clinical syndromes known as combined pulmonary fibrosis and emphysema (CPFE). This is characterized by chronic, progressive respiratory, restrictive, fibrotic, and obstructive lung pathology. The clinical response is complicated by pulmonary hypertension, with long-term, unclear survival. The CPFE syndrome typically occurs in male smokers, and the overall survival with this condition compared to pulmonary hypertension is poorer. In addition, this review explores the current state of the literature and future challenges and clinical management of the CPFE syndrome.

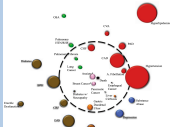
(CHEST 2012; 141(1):228-231)



Chronic Obstructive Pulmonary Disease Phenotypes: Past, Present, and Future

Pierre-Régis Burgel^{1,2}, Sanjay Sethi^{3,4}, and Victor Kim⁵

¹Hopital Cochin, Assistance Publique-Hôpitaux de Paris, France; ²Université Paris Descartes, St. Francis; ³University at Buffalo, State University of New York, New York; ⁴Veterans Affairs Western New York, Buffalo, New York; and ⁵Temple University School of Medicine, Philadelphia, Pennsylvania



Diagnosis of Diseases of Chronic Airway Limitation:

Asthma, COPD, and Asthma - COPD Overlap Syndrome (ACOS)

(J Allergy Clin Immunol 2012; 129:101-110)

Asthma-COPD Overlap

Clinical Relevance of Genomic Signatures of Type 2 Inflammation in Chronic Obstructive Pulmonary Disease

Stephanie A. Christenson^{1,2}, Katrina Stalling^{3,4}, Maarten van den Berge^{5,6}, Kalkrishnan Hiji⁷, Pieter S. Hiemstra⁸, Dhruv S. Poonia⁹, Marc E. Leirburg¹⁰, Arunim Sengupta¹¹, and Prescott G. Woodruff¹²

¹Department of Medicine, Division of Pulmonary, Critical Care, Allergy, and Sleep and Gastrointestinal Research Institute, University of California, San Francisco, San Francisco, California; ²Department of Biomedical Research Institute, University of California, San Francisco, San Francisco, California; ³Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; ⁴Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; ⁵Department of Pulmonary, Allergy, and Respiratory Medicine, Asthma and COPD, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; ⁶National Institute of Science and Technology, Hyderabad, India; ⁷Center for Molecular and Genomic Research, University of Groningen, Groningen, The Netherlands; ⁸Department of Pulmonary, Allergy, and Sleep and Gastrointestinal Research Institute, University of California, San Francisco, San Francisco, California; ⁹Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; ¹⁰Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; ¹¹Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; ¹²Department of Medicine, Boston University School of Medicine, Boston, Massachusetts

2

ACOS

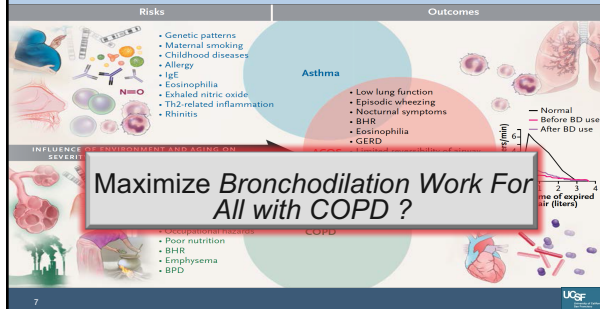
In their most typical forms, both Asthma and COPD can be readily distinguished

Risks	Outcomes
- Genetic patterns - Maternal smoking - Childhood diseases - Allergy ↑ IgE - Eosinophilia - Exhaled nitric oxide - Th2-related inflammation - Rhinitis	- Low lung function - Episodic wheezing - Nocturnal symptoms - BHR - Eosinophilia - GERD

Maximize Bronchodilation Work For All with COPD ?

• Poor nutrition
• BHR
• Emphysema
• BPD

- In their most typical forms, both Asthma and COPD can be readily distinguished



ACOS: Mechanisms

ORIGINAL ARTICLE

Asthma-COPD Overlap

Clinical Relevance of Genomic Signatures of Type 2 Inflammation in Chronic Obstructive Pulmonary Disease

Stephanie A. Christenson^{1,2}, Katrina Stelling^{3,4}, Maarten van den Berge^{5,6}, Kahkeshan Hijazi⁷, Pieter S. Hiemstra⁸, Dirkje S. Postma^{5,6}, Marc E. Lenburg⁴, Avrum Spira^{3,4,8}, and Prescott G. Woodruff^{1,2}

- Airway epithelial Gene expression overlap in a **Asthma cohort** (n=105) and **two COPD cohorts** (n=237, 171) by comparing microarray profiles
- Heatmap of the Gene signatures

Am J Respir Crit Care Med Vol 191, Iss 7, pp 758–766, Apr 1, 2015

UCSF

Asthma-COPD Overlap

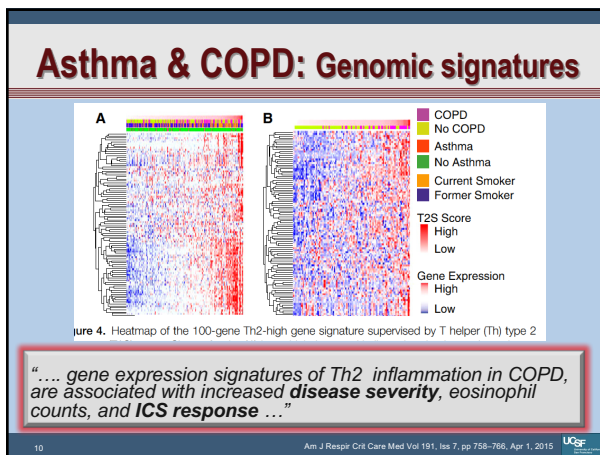
Stephanie A. Christenson^{1,2}, Katrina Steiling^{3,4}, Maarten van den Berge^{5,6}, Kahkeshan Hijazi⁷, Pieter S. Hiemstra⁸, Dirkje S. Postma^{5,6}, Marc E. Lenburg^{3,4,9}, Avrum Spira^{3,4,9}, and Prescott G. Woodruff^{1,2}

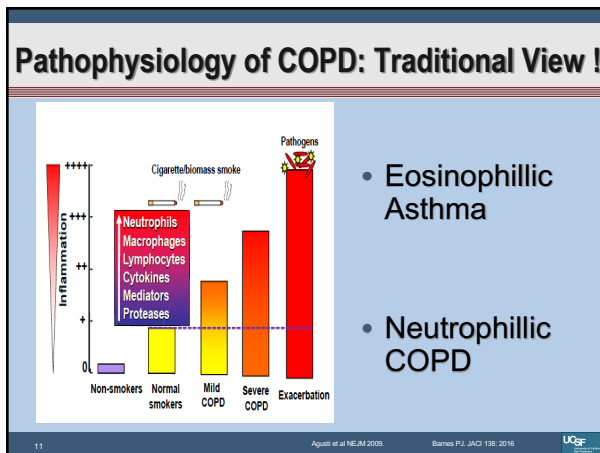
- Airway epithelial Gene expression overlap in a **Asthma cohort** (n=105) and **two COPD cohorts** (n=237, 171) by comparing microarray profiles
- Heatmap of the Gene signatures

Asthma & COPD: Genomic signatures

Gene	155000	155001	155002	155003	155004	155005	155006	155007	155008	155009	155010	155011	155012	155013	155014	155015	155016	155017	155018	155019	155020	155021	155022	155023	155024	155025	155026	155027	155028	155029	155030	155031	155032	155033	155034	155035	155036	155037	155038	155039	155040	155041	155042	155043	155044	155045	155046	155047	155048	155049	155050	155051	155052	155053	155054	155055	155056	155057	155058	155059	155060	155061	155062	155063	155064	155065	155066	155067	155068	155069	155070	155071	155072	155073	155074	155075	155076	155077	155078	155079	155080	155081	155082	155083	155084	155085	155086	155087	155088	155089	155090	155091	155092	155093	155094	155095	155096	155097	155098	155099	155100	155101	155102	155103	155104	155105	155106	155107	155108	155109	155110	155111	155112	155113	155114	155115	155116	155117	155118	155119	155120	155121	155122	155123	155124	155125	155126	155127	155128	155129	155130	155131	155132	155133	155134	155135	155136	155137	155138	155139	155140	155141	155142	155143	155144	155145	155146	155147	155148	155149	155150	155151	155152	155153	155154	155155	155156	155157	155158	155159	155160	155161	155162	155163	155164	155165	155166	155167	155168	155169	155170	155171	155172	155173	155174	155175	155176	155177	155178	155179	155180	155181	155182	155183	155184	155185	155186	155187	155188	155189	155190	155191	155192	155193	155194	155195	155196	155197	155198	155199	155200	155201	155202	155203	155204	155205	155206	155207	155208	155209	155210	155211	155212	155213	155214	155215	155216	155217	155218	155219	155220	155221	155222	155223	155224	155225	155226	155227	155228	155229	155230	155231	155232	155233	155234	155235	155236	155237	155238	155239	155240	155241	155242	155243	155244	155245	155246	155247	155248	155249	155250	155251	155252	155253	155254	155255	155256	155257	155258	155259	155260	155261	155262	155263	155264	155265	155266	155267	155268	155269	155270	155271	155272	155273	155274	155275	155276	155277	155278	155279	155280	155281	155282	155283	155284	155285	155286	155287	155288	155289	155290	155291	155292	155293	155294	155295	155296	155297	155298	155299	155300	155301	155302	155303	155304	155305	155306	155307	155308	155309	155310	155311	155312	155313	155314	155315	155316	155317	155318	155319	155320	155321	155322	155323	155324	155325	155326	1553
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Eosinophil or Neutrophil – Should we Care ?

ORIGINAL ARTICLE

Blood Eosinophils and Exacerbations in Chronic Obstructive Pulmonary Disease

The Copenhagen General Population Study

Signe Vedel-Krogh^{1,2,3}, Sune F. Nielsen^{1,2,3}, Peter Lange^{3,4,5}, Jørgen Vestbo⁶, and Berge G. Nordestgaard^{1,2,3}

¹Department of Clinical Biochemistry, Herlev and Gentofte Hospital; ²The Copenhagen General Population Study, Herlev and Gentofte Hospital; and ³Medical Unit, Respiratory Section, Hvidovre Hospital, Copenhagen University Hospital, Copenhagen, Denmark; ⁴Faculty of Health and Medical Sciences and ⁵Section of Social Medicine, Department of Public Health, University of Copenhagen, Copenhagen, Denmark; and ⁶Centre for Respiratory Medicine and Allergy, The University of Manchester and University Hospital South Manchester NHS Foundation Trust, Manchester, United Kingdom

[Original Research COPD]

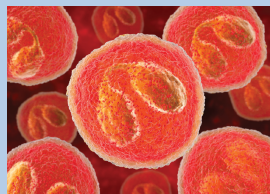
CHEST

Eosinophils in COPD Exacerbations Are Associated With Increased Readmissions

Simon Couillard, MD; Pierre Larivée, MD; Josiane Courteau, PhD; and Alain Vanasse, MD, PhD

12 Vedel-Krogh BLUJ Sep 2015 Couillard CHEST 2017; 151(2):366-373

COPD Exacerbations & Eosinophils

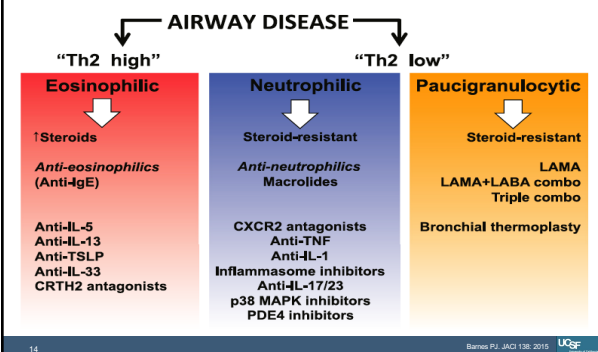


- UCSF- Fresno Data (add Figures 1 & 2)

13

Unpublished Data 2017 UCSF

Inflammatory Phenotypes: A New Paradigm ?



14

Barnes PJ, JACI 136 2015 UCSF

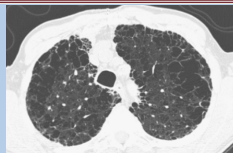
CPEF



CHEST Recent Advances in Chest Medicine

Combined Pulmonary Fibrosis and Emphysema Syndrome

- 98% of pts described as "CFPE" are Male smokers
- Upper lobe Emphysema and LL fibrosis in Smokers
- Frequently complicated by Acute lung injury, Lung CA, and PH
- Higher healthcare utilization and worse outcomes



15

CHEST / 141 / 1 / JANUARY, 2012 UCSF

COPD “Phenotypes”

“Driving Pathology” – Non-COPD

Smoking Related Lung Disease

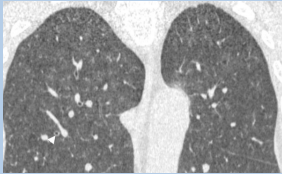
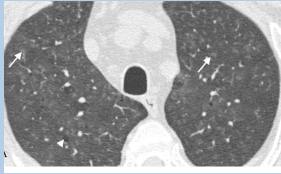
16


Smoking Related Lung Diseases: RBILD

- **RB-ILD** is defined by the presence of
 - Pathologic changes of RB in a smoker
 - Clinical evidence of interstitial lung disease
- **Cough/SOB**
- **PFTs**
 - Obstructive or Restrictive
 - Isolated increase in RV (Air Trapping)
 - Isolated decrease in DLCO

17
Ryu JH et al. Chest 2005; 127 (1): 178
Lynch O and King TE. J Comput Assist Tomogr. 2002;26(1):13


Smoking Related Lung Diseases: RBILD

- **RB-ILD Imaging**
 - GGOs
 - Poorly defined centrilobular nodules
- **SC alone** (without any other Rx) can lead to clinical, functional & radiographic improvement (ERJ, 2007)
 - Another study described a clinical and functional decline in 2/3rd patients with RB-ILD, despite SC
 - SC is likely to improve clinical outcomes in about a third to 2/3rd of patients with RB-ILD

18
Ryu JH et al. Chest 2005; 127 (1): 178
Lynch O and King TE. J Comput Assist Tomogr. 2002;26(1):13


Smoking Related Lung Diseases: DIP

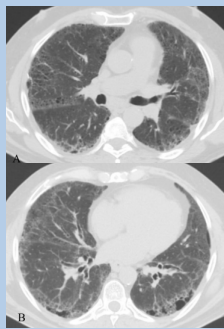
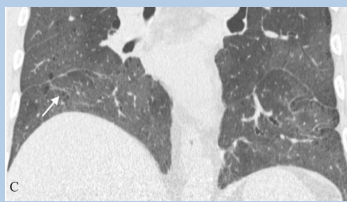
- **DIP** : Majority (>90%) of DIP is seen in smokers
 - About 5-15% of lung biopsies performed for ILD, some in CTD
 - Mortality is 6-30%
- **Cough/SOB**
- PFTs – Decreased DLCO +/- Restrictive
- Imaging:
 - Diffuse **GGO**
 - bilateral and symmetric (86 %)
 - basal and peripheral (60 %), patchy (20 %) and diffuse (20 %)
 - Irregular linear opacities. Microcysts (50 % of patients)

19

King TE, Schwarz MI, Schwarz MI. Chronic diffuse parenchymal lung disease. 1999. p.457



Smoking Related Lung Diseases: DIP



- **SC alone** can lead to improvement (~50%) but others have progressive disease despite cessation
- Glucocorticoids have been reported to be beneficial in case series, although improvement may be temporary (NEJM 1978, n=40 and Thorax 1997, n=5)

20

King TE, Schwarz MI, Schwarz MI. Chronic diffuse parenchymal lung disease. 1999. p.457



Smoking Related Lung Diseases: PLCH

- **PLCH** : Universal association with smoking
 - Multi-organ (extrapulmonary) NOT associated with smoking
 - Lung disease in multi-organ histiocytic disorders is commonly in children
- **Cough/SOB**
- PFTs
 - **Disproportionately** reduced DLCO & exercise intolerance
 - Minority with Obstruction and hyperinflation

21

Pulmonary Langerhans cell histiocytosis: a update. Eur Respir J. 2011;32(11):1459-15. [Epub 11-01-2011].
Pulmonary Langerhans cell histiocytosis: a review of the literature. Chest. 2008;133(5):1402-1412.
Am J Respir Crit Care Med. 2004;169(12):1501-1507.



Smoking Related Lung Diseases: PLCH

- **Imaging**
 - Moreso in Upper/Mid-Zones
 - Ill-defined or stellate nodules (2 to 10 mm in size)
 - Upper zone cysts or honeycombing
- SC is focus of therapy: **Complete recovery** in early and nodular cases of PLCH
- Immunosuppressive therapies, such as glucocorticoids and cytotoxic agents, are of **limited value**



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Pulmonary Langerhans cell histiocytosis in adults. Eur Respir J. 2011;32(11):1469-75. 2011 Feb 11.
Pulmonary Langerhans cell histiocytosis. Radiology. 2010;316(2):400-10. 2010 Oct 15.
Pulmonary Langerhans cell histiocytosis. Chest. 2009;135(5):1402-10. 2009 May 15.
Nag RS, et al. Histopathologic and clinical features of PLCH. J Clin Invest. 2005;115(12):3375-83.



Smoking Related Lung Diseases: IPF

- **IPF**
- **Cough/SOB**
- Mechanisms of IPF remain elusive
 - ? Fibrosis - Genetic predisposition (Telomerase, SP-A2 mutations)
 - Failure of Myofibroblasts to undergo apoptosis is typical of IPF
 - Smoke exposure (besides genetic alterations) is shown to inhibit apoptosis

Idiopathic Pulmonary Fibrosis Outcome in Relation to Smoking Status

Katherine M. Antoniou¹, David M. Hanzlik², Michael R. Palmer³, Katherine Martin⁴, Sadi R. Durr⁵,
Mikaela M. Sullivan⁶, Andrew G. Nicholson⁷, Richard M. de Blee⁸, and Athol U. Wells⁹

- A total of 249 patients with IPF were studied
 - Current smokers & Former smokers, n=186
 - Never-smokers, n = 63
- **Conclusions**
 - In IPF, survival and severity-adjusted **survival are higher** in nonsmokers than in former smokers or the combined group of former and current smokers

23

Sullivan N et al. Am J Respir Crit Care Med Vol 177, pp 190-194, 2008

Raghu et al. Am J Respir Crit Care Med. 2011;183(5):788



COPD “Phenotypes”

“Driving Pathology” – Non-COPD

Hypercapnea & Hypoventilation

24



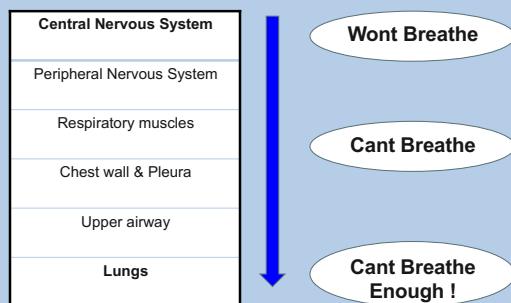
Clinical Features of Hypercapnea

- Mild to Moderate hypercapnea that develops slowly may be anxious, complain of dyspnea and fatigue with daytime somnolence
- Higher levels or rapidly developing hypercapnea with frank neurologic manifestations
- Acute Hypercapnea
 - Encountered in ER or inpatient settings
 - Symptoms mostly Neurologic and Pulmonary
 - Vary depending on level and rate of CO₂ accumulation in arterial blood

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Mechanisms of Hypercapnea



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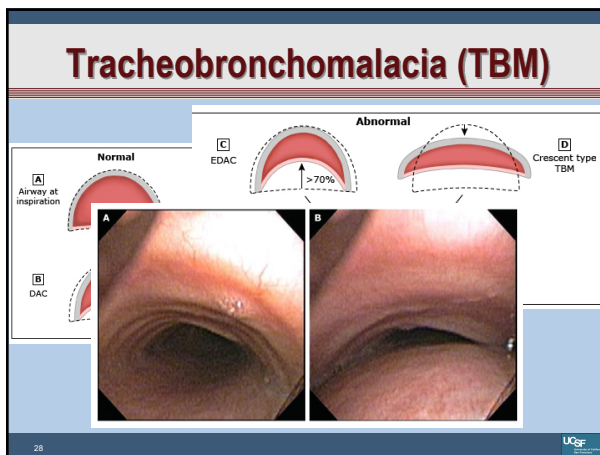
UCSF

Tracheobronchomalacia (TBM)

- Diffuse or segmental tracheal weakness
 - Anatomical (cartilagenous) with softening of cartilage
 - Membranous with excessive forward displacement of post-membrane (dynamic collapse)

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Tracheobronchomalacia (TBM)

- Asymptomatic if Mild
- Major symptoms are **Dyspnea, cough** and **sputum** retention
- Diagnosis with Bronchoscopy and dynamic CT

UCSF

OSA/OHS and Obesity

- Suspected in all who are at risk of hypoventilation
 - Physiologic dead space & limited pulmonary reserve (COPD)
 - Sedatives
 - Obesity and OSA/OHS
- Obesity presents a challenge in interpreting PFTs

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COPD “Phenotypes”

“Driving Pathology” – Non-COPD

Infection

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UCSF

Burden and trends of hospitalisations associated with pulmonary non-tuberculous mycobacterial infections in Germany, 2005–2011

Felix C Ringhausen^{1*}, Rosa-Marie Apel¹, Franz-Christoph Bange², André de Roux³, Mathias W Pletz⁴, Jessica Rademacher¹, Hendrik Suhling¹, Dirk Wagner² and Tobias Welte¹

Abstract

Background: Representative population-based data on the epidemiology of pulmonary non-tuberculous mycobacterial (PNTM) infections in Europe are limited. However, these data are needed in order to optimise patient care and to facilitate the allocation of healthcare resources. The aim of the present study was to investigate the current burden and the trends of PNTM infection-associated hospitalisations in Germany.

Methods: *International Classification of Diseases, 10th revision* (ICD-10) discharge diagnosis codes were extracted from the official nationwide diagnosis-related groups (DRG) hospital statistics in order to identify PNTM infection-associated hospitalisations (ICD-10 code A31.0) between 2005 and 2011. Poisson log-linear regression analysis was used to assess the significance of trends.

Results: Overall, 5,959 records with PNTM infection as any hospital discharge diagnosis were extracted from more than 125 million hospitalisations. The average annual age-adjusted rate was 0.91 hospitalisations per 100,000 population. Hospitalisation rates increased during the study period for both males and females, with the highest rate of 3.0 hospitalisations per 100,000 population among elderly men, but the most pronounced average increase of 6.4%/year among females, particularly those of young and middle age, and hospitalisations associated with cystic fibrosis. Overall, chronic obstructive pulmonary disease (COPD) was the most frequent PNTM infection-associated condition in 28.9% of hospitalisations and also showed a significant average annual increase of 4.8%.

Conclusions: The prevalence of PNTM infection-associated hospitalisations is steadily increasing in Germany. COPD is currently the most important associated condition. Our population-based study provides evidence of a changing epidemiology of PNTM infections and highlights emerging clinical implications.

Keywords: Atypical mycobacterial infection, Bronchiectasis, Clinical epidemiology, COPD epidemiology, Cystic fibrosis, Health services research, International classification of diseases, *Mycobacterium avium* complex, Non-tuberculous mycobacteria, Tuberculosis

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Ringhausen et al. BMC Infectious Diseases 2013, 13:231

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ICS & Nontuberculous Infections


CrossMark

ORIGINAL ARTICLE
RESPIRATORY INFECTIONS

The risk of mycobacterial infections associated with inhaled corticosteroid use

Sarah K. Brode^{1,2,3}, Michael A. Campitelli⁴, Jeffrey C. Kwong^{4,5,6,7}, Hong Lu⁴, Alex Marchand-Austin⁴, Andrea S. Gershon^{1,2,7,8}, Frances B. Jamieson^{2,7} and Theodore K. Marras^{1,2}

ABSTRACT Inhaled corticosteroid (ICS) use is associated with an increased risk of pneumonia. This study was performed to determine if ICS use is associated with an increased risk of nontuberculous mycobacterial pulmonary disease (NTM-PD) or tuberculosis (TB).

We conducted a population-based nested case-control study using linked laboratory and health administrative databases in Ontario, Canada, including adults aged ≥66 years with treated obstructive lung disease (i.e. asthma, chronic obstructive pulmonary disease (COPD) or asthma-COPD overlap syndrome) between 2001 and 2013. We estimated odds ratios comparing ICS use with nonuse among NTM-PD and TB cases and controls using conditional logistic regression.

Among 417,494 older adults with treated obstructive lung disease, we identified 2966 cases of NTM-PD and 327 cases of TB. Current ICS use was associated with NTM-PD compared with nonuse (adjusted OR (aOR) 1.86, 95% CI 1.60–2.15) and was statistically significant for fluticasone (aOR 2.09, 95% CI 1.80–2.43), but not for budesonide (aOR 1.19, 95% CI 0.97–1.45). There was a strong dose-response relationship between incident NTM-PD and cumulative ICS dose over 1 year. There was no significant association between current ICS use and TB (aOR 1.43, 95% CI 0.95–2.16).

This study suggests that ICS use is associated with an increased risk of NTM-PD, but not TB.

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Brode S et al. Eur Respir J 2017; 50: 1700037

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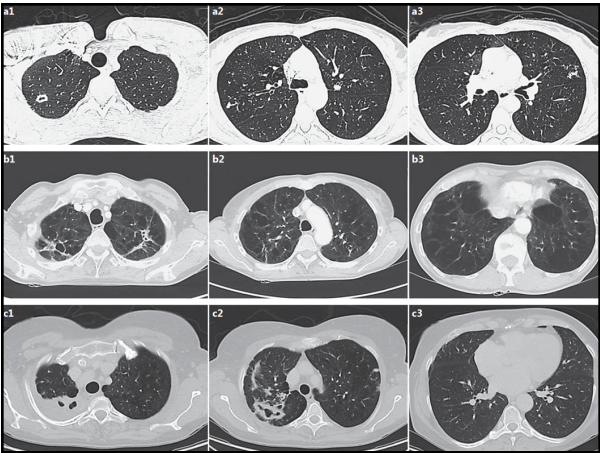
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Non-Tuberculous Infections

- SOB/Cough
- Constitutional symptoms
- Major predisposing factor to lung infection is COPD
 - Over 2/3rd of M *Kansasii* case have COPD
- Imaging characteristics may overlap with RB-ILD and other smoking-related lung disease

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Other Atypical Infections

- Chronic (Semi invasive) Pulmonary Aspergillosis
 - Especially in setting of chronic steroid use and relative immunosuppression
- Coccidioidomycosis

Predictors of mortality in chronic pulmonary aspergillosis

@ERSpublications
This article describes the world's largest experience of chronic pulmonary aspergillosis and its outcome <http://ow.ly/pG9X303Yw8L>

Cite this article as: Lowe D, Al-Shaib K, Newton PL, et al. Predictors of mortality in chronic pulmonary aspergillosis. *Eur Respir J* 2017; 49: 1601062. <https://doi.org/10.1183/13993003.01062-2016>.

ABSTRACT Chronic pulmonary aspergillosis (CPA) is a chronic progressive infection that destroys lung tissue in non-immunocompromised patients. Contemporary series suggest 50–85% 5-year mortality, with few prognostic factors identified.

A cohort of 387 CPA patients referred to the UK's National Aspergillosis Centre from 1992 to June 2012 was studied until June 2015. The impact of objective and subjective variables including age, sex, previous pulmonary conditions, dyspnoea score, quality of life, serum albumin and C-reactive protein and radiological appearances were assessed using Kaplan-Meier curves, log rank tests and Cox proportional hazards modelling. In a subset of patients, retrospective review of time from likely onset of CPA to referral and cause of death were also investigated.

Survival was 60%, 62% and 47% at 1, 5 and 10 years, respectively. Increased mortality was associated with nontuberculous mycobacterial infection (hazard ratio 2.07, 95% CI 1.22–3.52; $p<0.001$) and chronic obstructive pulmonary disease (1.57, 1.05–2.36; $p=0.02$) as well as higher age (1.03, 1.01–1.07 per year; $p<0.001$), lower albumin (0.92, 0.87–0.96 per $g\ L^{-1}$; $p<0.001$), lower activity (1.01, 1.01–1.03 per point increase in St George's Respiratory Questionnaire activity domain; $p<0.001$) and having one, and especially, bilateral aspergillomas ($p<0.001$).

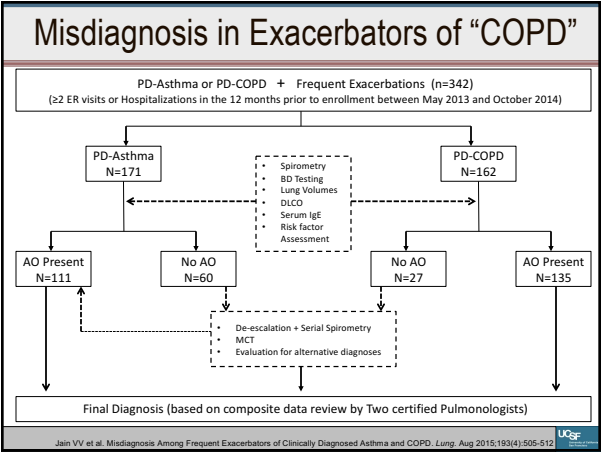
Several factors impact on mortality of CPA, and can be evaluated as tools to assess CPA prognosis.

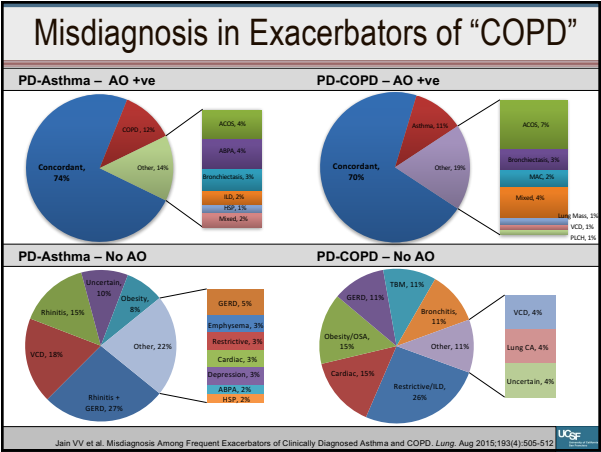
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Eur Respir J 2017; 49: 1601062

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Misdiagnosis among Frequent Exacerbators of COPD





Misdiagnosis in Exacerbators of “COPD”

- **Misdiagnosis was found in 26% (87 of 333 pts)**
- Another 12% had OLD other than Asthma/COPD
- **Spirometry utilization** was strongly associated with **reduced** risk of misdiagnosis
- **Smoking history increased** Risk of misdiagnosis

Table 4: Predictors of Misdiagnosis in patients with PD-Asthma and PD-COPD

Variable	PD-Asthma (n=171)			PD-COPD (n=162)		
	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Age	0.99	0.96-1.02	0.71	1.0	0.93-1.08	0.87
Gender	1.69	0.67-4.27	0.26	0.88	0.26-2.92	0.84
Ethnicity	1.10	0.72-1.68	0.64	0.56	0.29-1.05	0.07
Spirometry Underutilization	2.8	1.16-6.78	0.017 *	10.7	2.05-56.27	0.005 *
Obesity	0.86	0.36-2.09	0.75	2.92	0.83-10.2	0.09
Igt	1.0	0.99-1	0.57			
BNP				1.0	0.99-1.0	0.45
Smoking (Total pack Years)				1.05	1.01-1.11	0.033 *

Jain VV et al. Misdiagnosis Among Frequent Exacerbators of Clinically Diagnosed Asthma and COPD. *Lung*. Aug 2015;193(4):505-512



Misdiagnosis in Asthma & COPD ?

Misdiagnosis of COPD and Asthma in Primary Care Patients 40 Years of Age and Over

DAVID G. TINKELMAN, M.D.,¹ DAVID B. PRICE, M.D.,² ROBERT J. NORDYKE, PH.D.,³
AND R. J. HALBERT, M.D., M.P.H.¹

¹Health Initiatives, National Jewish Medical and Research Center, Denver, USA

²General Practice & Primary Care, University of Aberdeen, Aberdeen, Scotland, UK

³Center Health Insights, Beverly Hills, CA and UCLA School of Public Health, Los Angeles, CA

Research

JAMA | Original Investigation

Reevaluation of Diagnosis in Adults With Physician-Diagnosed Asthma

Shawn D. Aaron, MD; Katherine L. Vandemheen, MScN; J. Mark FitzGerald, MD; Martha Alnslie, MD; Samir Gupta, MD; Catherine Lemière, MD; Stephen K. Field, MD; R. Andrew McVie, MD; Paul Hernandez, MD; Irvin Mayers, MD; Sanita Muliyil, MD; Gonzalo G. Alvarez, MD; Smita Palchak, MD; Ranjesta Mallick, PhD; Louis-Philippe Boulet, MD, for the Canadian Respiratory Research Network

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Tinkelman et al. J Asthma 2008

Aaron S et al. JAMA 2017



Burden of COPD

- Over a Fifth of our Country has OLD

- 8-14% with Asthma
- 7-8% with COPD (10% when ≥ 40yrs)

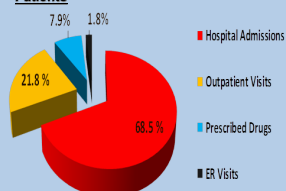
- COPD is the 3rd leading cause of death among adults in the US

- Expected to be 3rd worldwide by 2020

Annual COPD costs over **\$50 Billion & Rising**

Exacerbations account for 90% of the costs

Direct Medical Expenditures in COPD Patients



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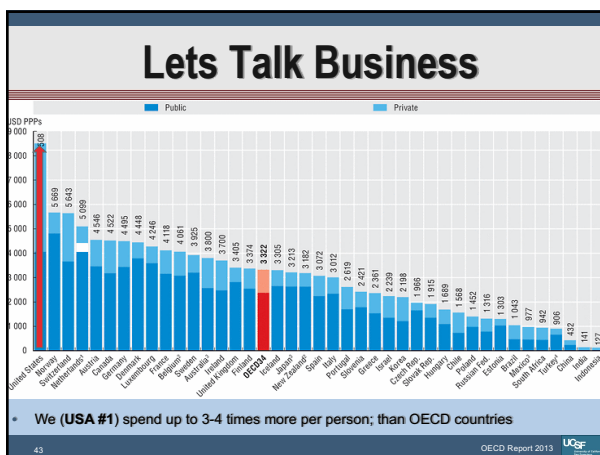
GINA 2014

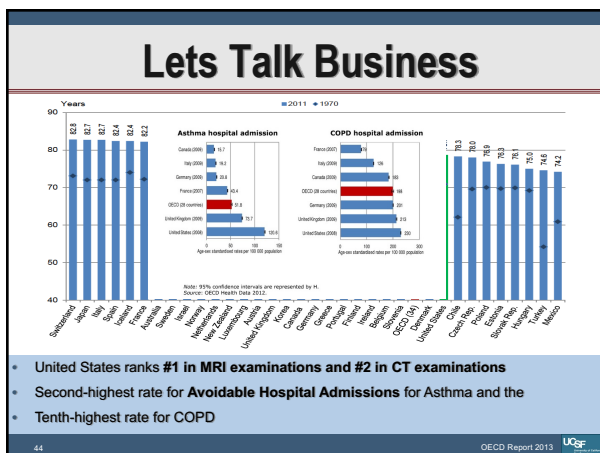
GOLD 2015

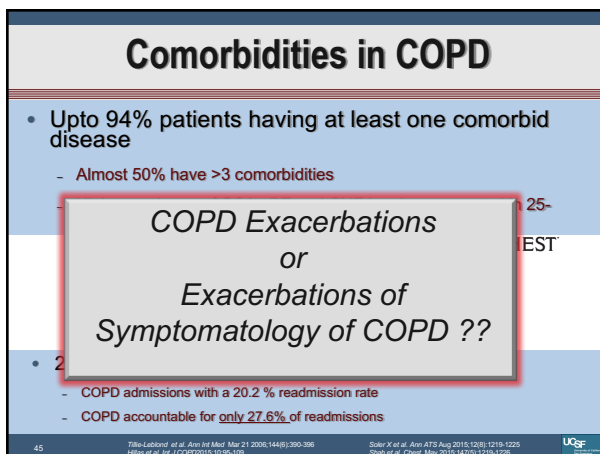
Oosterink, Rutten-van Molken, *Respir Med* 2004;98:883-891

CHEST 2015; 147(1): 31-45



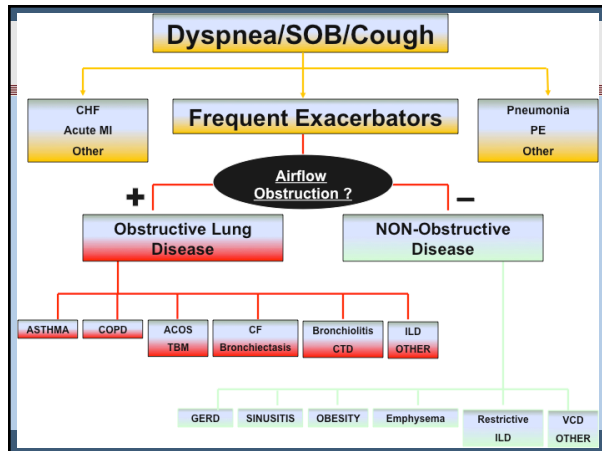






Animation Slide

UCsf



PFT Utilization in USA

CHEST PULMONARY FUNCTION TESTS
Spirometry Utilization for COPD*
How Do We Measure Up?
Melissa K. Han, MD, MS; Min Guepko Kim, MPP; Russell Mardon, PhD;
Phil Bower, MBA; Scott Sullivan, PharmD; Gregory B. Diette, MD, MHS; and
Fernando J. Martinez, MD, MS, FCCP

Choosing Wisely: Adherence by Physicians to Recommended Use of Spirometry in the Diagnosis and Management of Adult Asthma
Krislin C. Sakal, MD, MS, MPH; Gulshan Sharma, MD, MPH; Yu-Li Lin, MS; Randall R. Glickman, MD
*Division of Pulmonary, Allergy and Immunology, The University of Texas Medical Branch, Galveston; *Sack & South Department of Clinical

Long (2015) 115:508-512
DOI: 10.1016/j.chest.2015.07.014

Misdiagnosis Among Frequent Exacerbators of Clinically Diagnosed Asthma and COPD in Absence of Confirmation of Airflow Obstruction
Vigil V, Jain V, B. Richard Alkhamis, Sherry Andrews, Jamil Mejjad, Paul R. Nadeau, Michael W. Parnianpour

Han MK et al. Chest 2007; 132:402-409

- N=5039; newly diagnosed COPD
- 32% did not have a spirometry in prior 2 years
- N=134,208; diagnosis of Asthma
- 52% never had a spirometry
- N=342; Frequent exacerbators of Asthma/COPD
- 69% never had a spirometry

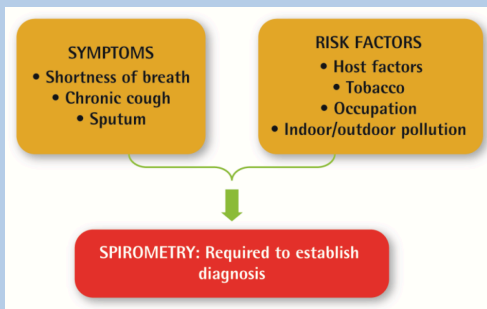
Current Trends: Diagnosis

- **Clinical diagnosis is the norm, Not the exception**
- Three out of every Four patients with a diagnosis of COPD have never had a spirometry test to confirm the “O” in COPD
- In the *real world*, it may be unrealistic to expect strategies to work in a population where the very diagnosis is in doubt !

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GOLD 2017

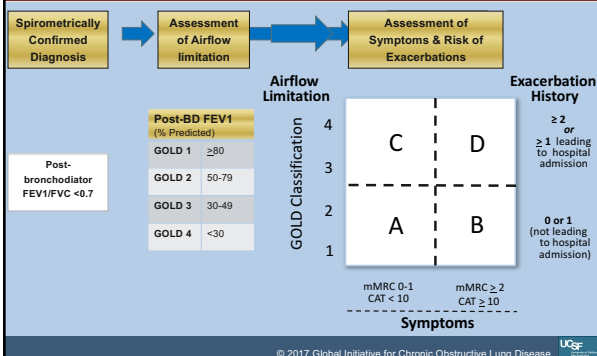


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GOLD Update Feb 2017

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GOLD 2017: Refined ABCD Assessment Tool



Eliminating Barriers: Access to Formal PFT Labs

The Clinical Respiratory Journal

ORIGINAL ARTICLE

Office spirometry correlates with laboratory spirometry in patients with symptomatic asthma and COPD

Gurpreet Bamra¹, Leena Jalota¹, Chandni Kapoor², Paul K. Mills², Jose Joseph Vempilly¹ and Vipul V. Jain¹

¹ Division of Pulmonary and Critical Care, University of California, San Francisco, Fresno, CA, USA

- 107 patients Symptomatic Asthma and COPD
- Two Office Spirometers compared to formal hospital based Lab Spirometry
- Performed by trained RT's
- Office spirometry may be accurate and reliable in Symptomatic Asthma and COPD patients (independent of the spirometer used).

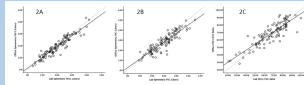


Table 1. Correlation between Ranges of Flows and Volumes

FVC Tertiles	FEV1: OS versus LS			FVC: OS versus LS		
	N	Pearson Coefficient	p-value	N	Pearson Coefficient	p-value
Tertile 1: <2.0 L	36	0.912	<0.001	36	0.948	<0.001
Tertile 2: 2.0 to 2.5 L	36	0.908	<0.001	36	0.932	<0.001
Tertile 3: >2.5 L	35	0.889	<0.001	35	0.748	<0.001

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Jalota L et al. Clin Respir J. 2015 Dec 1;12(419)



Eliminating Barriers: Can't do in ER/Hospital !

CHEST

Original Research

ASTHMA

FEV₁ Performance Among Patients With Acute Asthma

Results From a Multicenter Clinical Trial

Robert A. Simonson, MD, Edith R. Simonson, MD, Paul L. Bangle, MD, and Steven G. Simonson, MD, FCCP

Objective: To determine the ability of patients with acute asthma exacerbation to perform spirometry. **Design:** A multicenter, prospective, observational study. **Setting:** Academic medical centers. **Participants:** Patients with acute asthma exacerbation. **Measurements and Main Results:** Spirometry was performed in 107 patients. The mean FEV₁ was 1.2 L (SD, 0.4 L). The mean FVC was 2.0 L (SD, 0.6 L). The mean PEF was 3.5 L/min (SD, 1.2 L/min). The mean FEV₁/FVC ratio was 0.60 (SD, 0.05). The mean PEF/FEV₁ ratio was 0.85 (SD, 0.10). The mean FEV₁/FVC ratio was significantly lower than the normal range (0.80-1.00). The mean PEF/FEV₁ ratio was significantly lower than the normal range (1.00-1.50). The mean FEV₁/FVC ratio was significantly lower than the normal range (0.80-1.00). The mean PEF/FEV₁ ratio was significantly lower than the normal range (1.00-1.50). **Conclusion:** Spirometry is difficult to perform in patients with acute asthma exacerbation. **Keywords:** Spirometry, acute asthma, FEV₁, FVC, PEF.

RESEARCH ARTICLE

Open Access

Confirmatory spirometry for adults hospitalized with a diagnosis of asthma or chronic obstructive pulmonary disease exacerbation

William H. Lim, MD, PhD, David J. Nisenzon, MD, PhD, Carlos A. Castro, MD, PhD, Jeffrey Chalmers, MD, PhD, William H. Lim, MD, PhD, and Amy R. Kohnen, MD, PhD

Background: Spirometry is a key component of the diagnosis and management of asthma and chronic obstructive pulmonary disease (COPD). However, the ability to perform spirometry in the hospital setting is often limited. **Objective:** To determine the ability of patients with asthma or COPD to perform spirometry in the hospital setting. **Design:** A multicenter, prospective, observational study. **Setting:** Academic medical centers. **Participants:** Patients with asthma or COPD. **Measurements and Main Results:** Spirometry was performed in 107 patients. The mean FEV₁ was 1.2 L (SD, 0.4 L). The mean FVC was 2.0 L (SD, 0.6 L). The mean PEF was 3.5 L/min (SD, 1.2 L/min). The mean FEV₁/FVC ratio was 0.60 (SD, 0.05). The mean PEF/FEV₁ ratio was 0.85 (SD, 0.10). The mean FEV₁/FVC ratio was significantly lower than the normal range (0.80-1.00). The mean PEF/FEV₁ ratio was significantly lower than the normal range (1.00-1.50). **Conclusion:** Spirometry is difficult to perform in patients with asthma or COPD. **Keywords:** Spirometry, asthma, COPD, FEV₁, FVC, PEF.

Acute Asthma or COPD; ER or Inpatient

There are NO excuses for Not performing spirometry

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Improving COPD Outcomes

•Choosing Wisely: Spirometry

•Phenotypes-Comorbidities

•Customizing effective modalities & therapies

Physician Behavior:

Clinician

Patient Behavior

•Adherence vs Compliance

•Education vs Comprehension

•Delivery systems

•Nihilism

•Clinical Inertia

•Training: Role of Educator

Physician Behavior:

Educator

The Business of Medicine

•Resources

•Legislation

•Reimbursement



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Linda Kimura, PharmD

Fellows
John McClain, MD
Leena Jalota, MD
Gurpreet Bamba, MD
Sherry Andrews, MD

Thank You

Vipul Jain, MD
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vjain@fresno.ucsf.edu

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BREAK/EXHIBITORS

Saturday September 30, 2017 – 10:20 a.m. – 10:40 a.m.

THE ROLE OF RADIOGRAPHIC IMAGING IN COPD

Fereidoun Abtin, MD
UCLA

Saturday September 30, 2017 – 10:40 a.m. – 11:20 a.m.

Fereidoun Abtin, MD completed his fellowship training at UCLA and joined their Thoracic Imaging Section. He is currently an associate professor, director of a specialized outpatient interventional center and director of the Thoracic Imaging Fellowship at UCLA.

Dr. Abtin's work with COPD precedes his fellowship where he participated in developing quantitative imaging at UCLA. He has remained active with the program and currently directs the thoracic quantitative imaging lab.

The Role of Radiographic Imaging in COPD

Fereidoun Abtin M.D.
Thoracic Imaging
Department of Radiological Sciences
David Geffen School of Medicine at UCLA



COPD: Imaging Techniques

- Digital radiography (DR)
- Computed tomography (CT)
 - High resolution CT
 - Expiratory CT
 - Functional CT
 - Quantitative CT
- Magnetic Resonance Imaging (MRI)

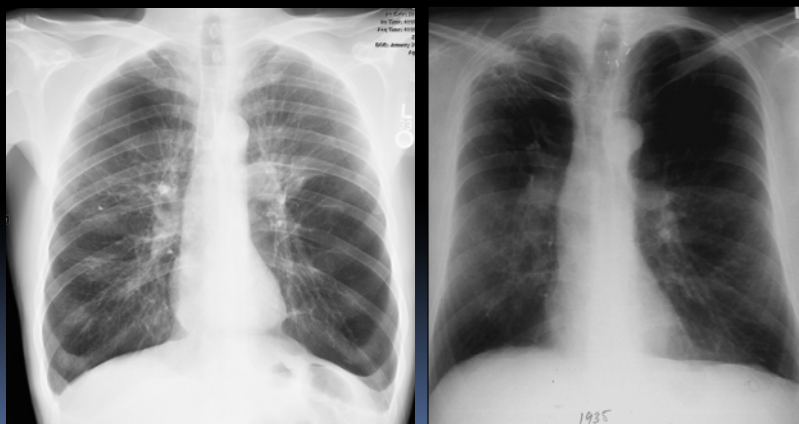
COPD: Imaging Techniques

- Digital radiography (DR)
 - Solid state photon detector
 - Direct conversion to digital image
 - 2 views (PA and lateral)
 - Upright imaging
 - 120 kVp
 - Half the dose of conventional radiography

UCLA

COPD: Imaging Techniques

- CXR Digital and Analog



UCLA

COPD: Imaging Techniques

- Digital radiography (DR)
- Computed tomography (CT)
 - High resolution CT
 - Expiratory CT
 - Functional CT
 - Quantitative CT
- Magnetic Resonance Imaging (MRI)

UCLA

COPD: Computed Tomography

- High Resolution CT (HRCT)
 - Ability to resolve small objects at close proximity
 - 1982: Term was coined by Todo et. Al
 - 1985: Naidich and Nakata first reports on HRCT of lung
 - Parameters: Slice thickness, KVP, mAs, FOV, collimation
 - Less than 2 mm, Lung/Sharp/Bone algorithm



UCLA

COPD: Computed Tomography

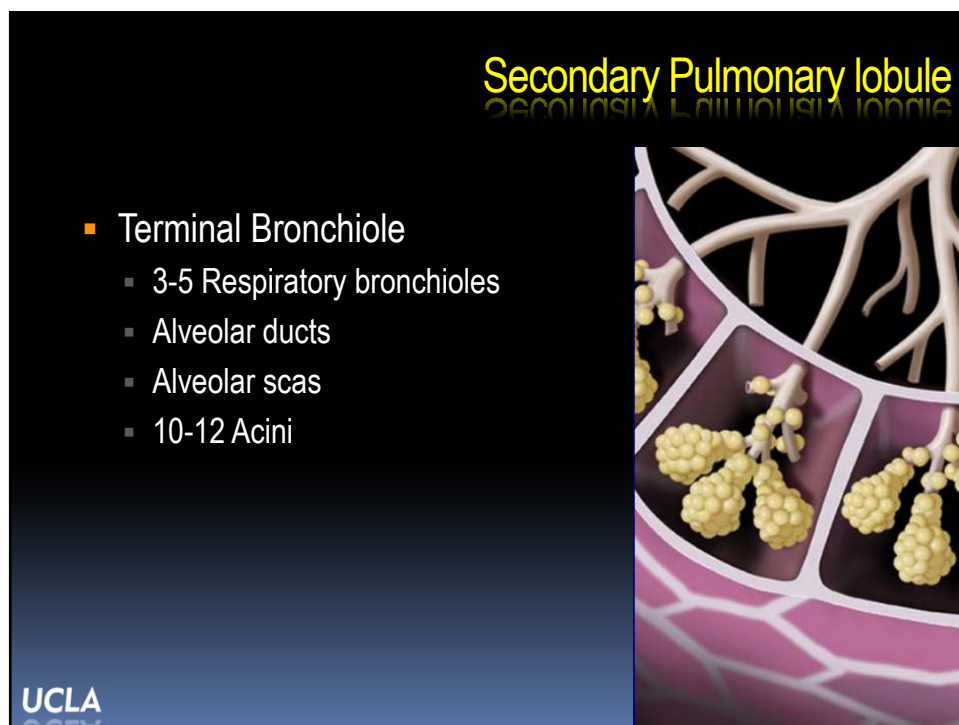
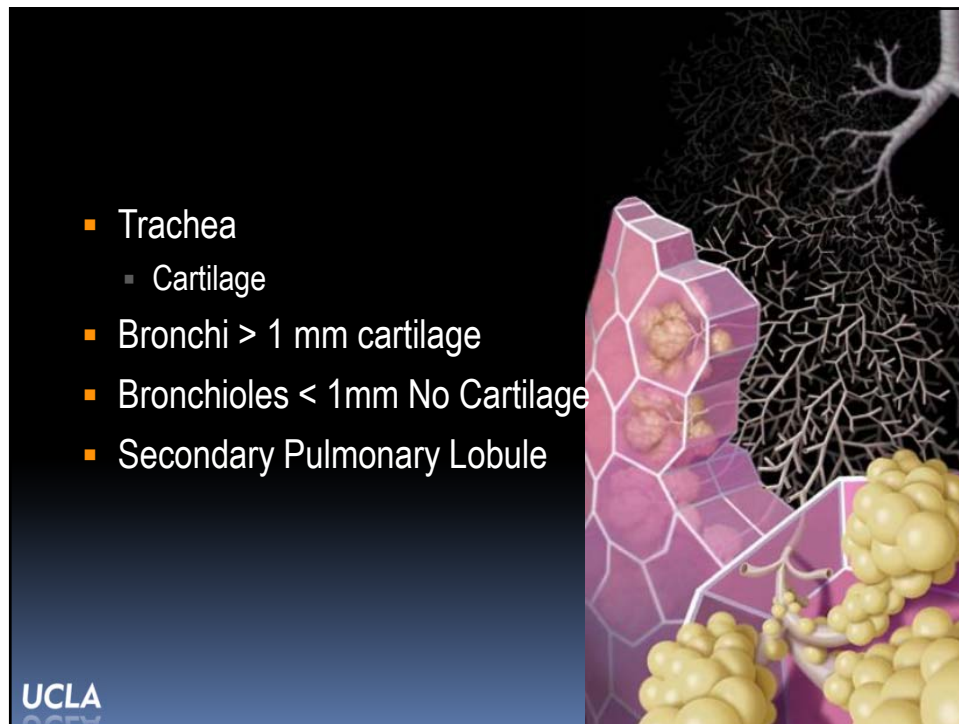
- High Resolution CT (HRCT)
 - Ability to resolve small objects at close proximity
 - 1982: Term was coined by Todo et. Al
 - 1985: Naidich and Nakata first reports on HRCT of lung
 - Parameters: Slice thickness, KVP, mAs, FOV, collimation
 - Less than 2 mm, Lung/Sharp/Bone algorithm
 - ALL lung CT scans can be HRCT

UCLA

COPD: Computed Tomography

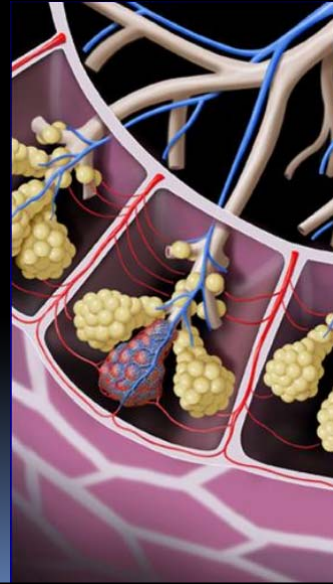
- High Resolution CT (HRCT)
- Multi-row detector – 16, 64, 256, 320, Flat panel detectors
- 16 cm in one rotation= Whole lung acquisition < 1 sec.
- 0.275 mm reconstruction
- TLC acquisition (inspiratory)
 - Prone for fibrosis

UCLA



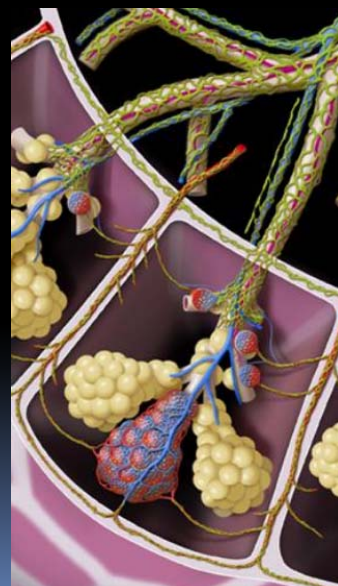
Secondary Pulmonary lobule

- Terminal Bronchiole
- Pulmonary arterioles
- Pulmonary venules



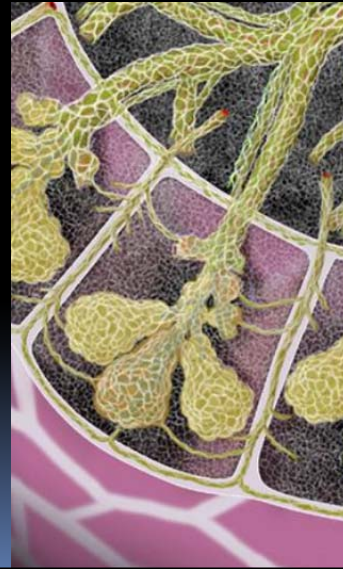
Secondary Pulmonary lobule

- Terminal Bronchiole
- Pulmonary arterioles
- Pulmonary venules
- Lymphatics



Secondary Pulmonary lobule

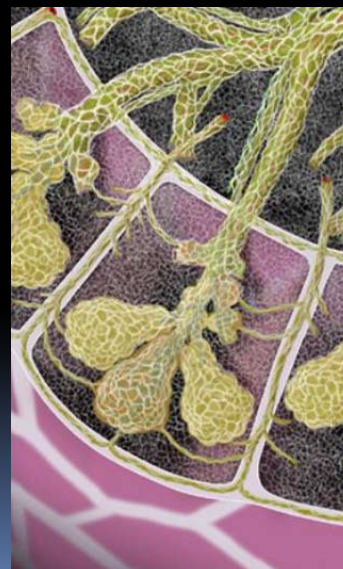
- Terminal Bronchiole
- Pulmonary arterioles
- Pulmonary venules
- Lymphatics
- Interstitium and connective tissue network



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Secondary Pulmonary lobule

- Terminal Bronchiole
- Pulmonary arterioles
- Pulmonary venules
- Lymphatics
- Interstitium and connective tissue network



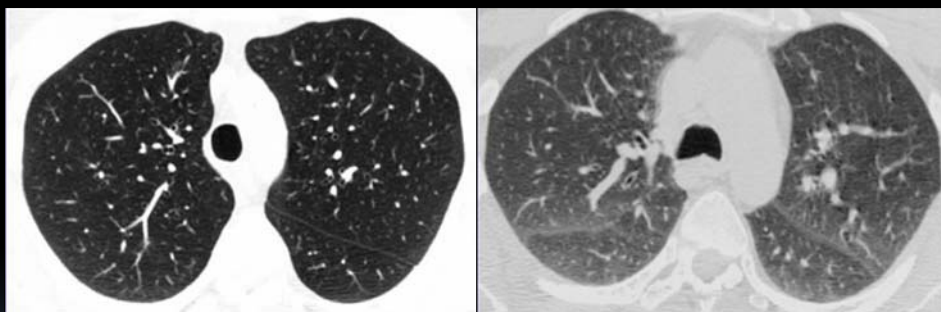
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COPD: Computed Tomography

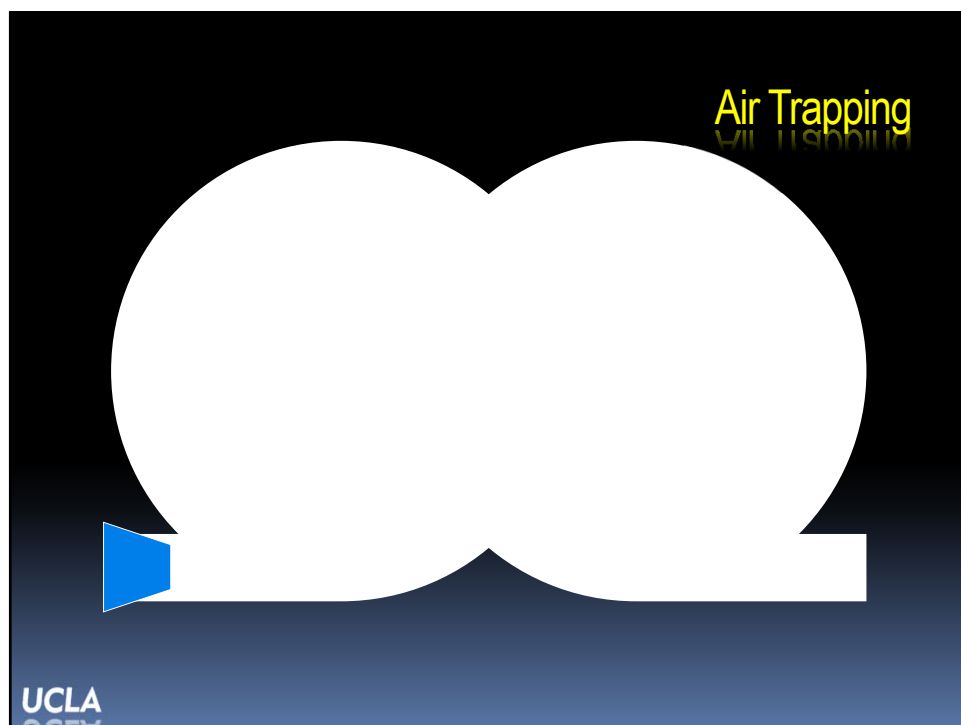
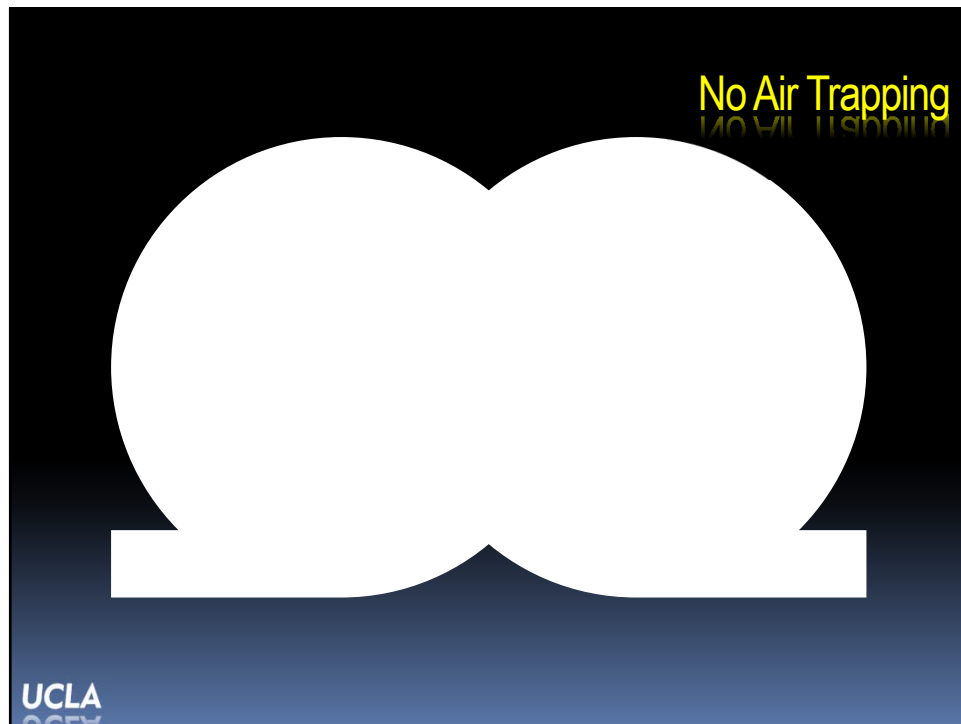
- High Resolution CT (HRCT)
- Multi-row detector – 16, 64, 256, 320, Flat panel detectors
- 16 cm in one rotation= Whole lung acquisition < 1 sec.
- 0.275 mm reconstruction
- TLC acquisition (inspiratory)
- RV acquisition (expiratory)

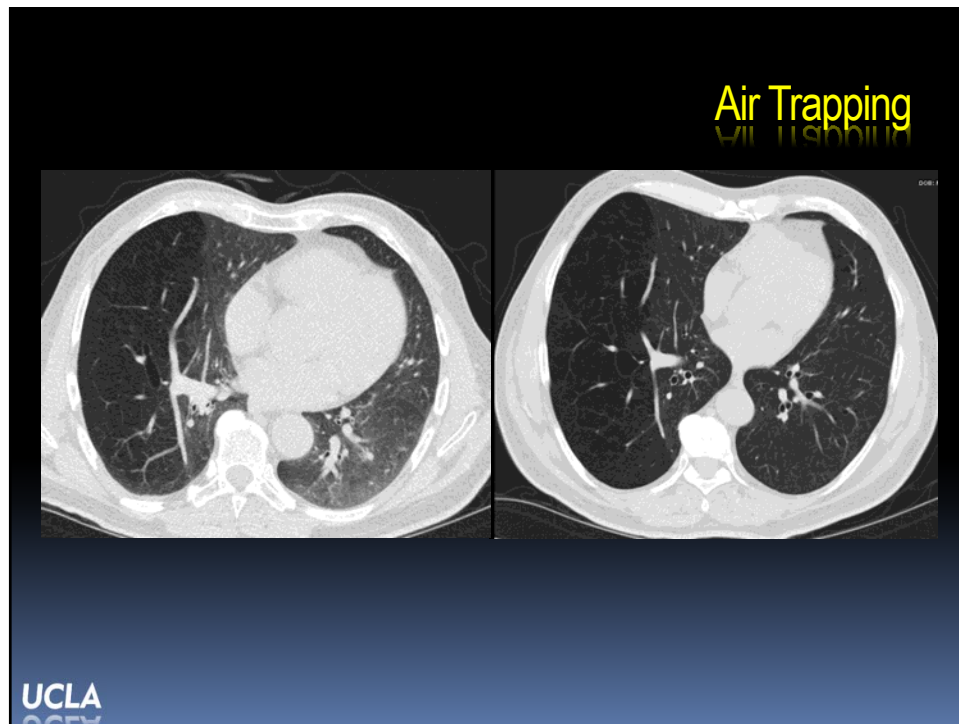
UCLA

Insp and Exp CT



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COPD: Computed Tomography

- High Resolution CT (HRCT)
- Multi-row detector – 16, 64, 256, 320, Flat panel detectors
- 16 cm in one rotation= Whole lung acquisition < 1 sec.
- 0.275 mm reconstruction
- TLC acquisition (inspiratory)
- RV acquisition (expiratory)
- 3D reconstruction

The UCLA logo is in the bottom left corner.

COPD: Computed Tomography



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COPD: Computed Tomography

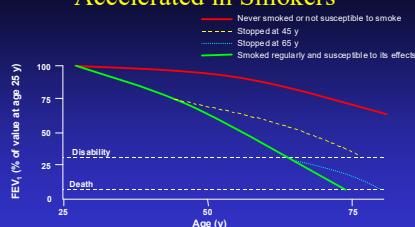
- High Resolution CT (HRCT)
- Multi-row detector – 16, 64, 256, 320, Flat panel detectors
- 16 cm in one rotation= Whole lung acquisition < 1 sec.
- 0.275 mm reconstruction
- TLC acquisition (inspiratory)
- RV acquisition (expiratory)
- 3D reconstruction
- 4D imaging

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COPD: Definition

- A disease state characterized by airflow limitation that:
 - is not fully reversible
 - is usually progressive
 - is associated with an abnormal inflammatory response of the lungs to noxious particles or gases

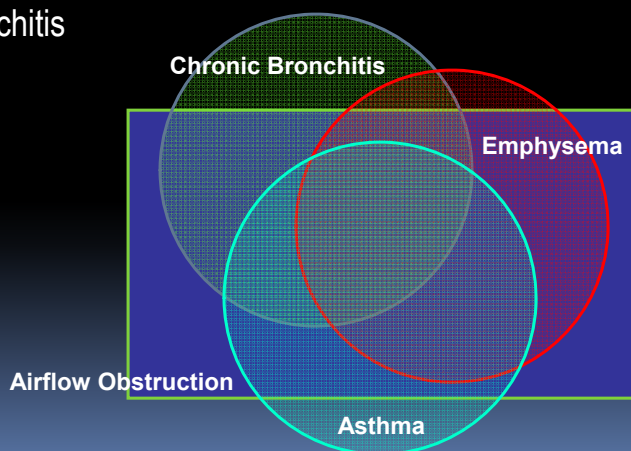
Age-Related Decline in FEV₁ Is Accelerated in Smokers



UCLA * <http://www.goldcopd.com> 2003

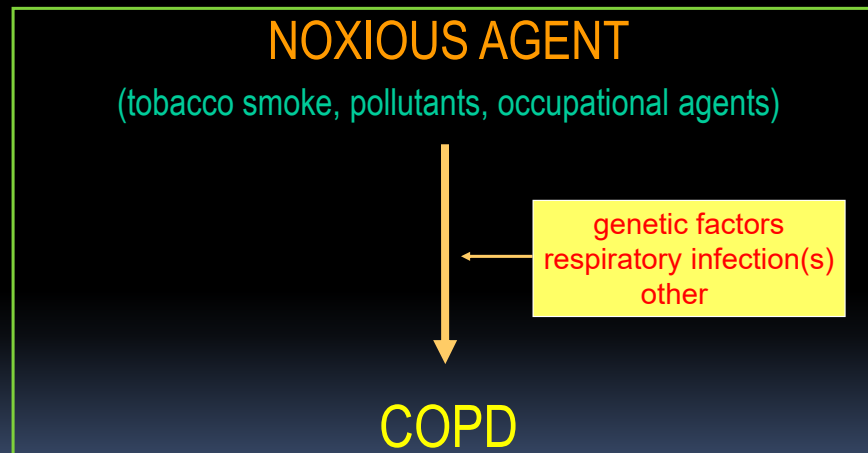
COPD: Types

- Asthma
- Chronic bronchitis
- Emphysema



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COPD: Pathogenesis



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Emphysema: Definition

- Defined pathologically
- Condition of the lung characterized by abnormal permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls, and without obvious fibrosis*

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*American Thoracic Society 1987

Emphysema: 2 Main Subtypes

- Centrilobular emphysema (CLE)
 - Centriacinar emphysema
- Panlobular emphysema (PLE)
 - Panacinar emphysema

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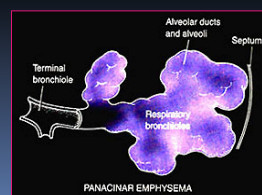
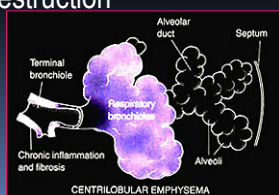
Emphysema: 2 Main Subtypes

- Centrilobular emphysema (CLE)
 - Centriacinar emphysema
 - More common than panlobular variety
 - Smokers
 - Upper lobes more involved
- Panlobular emphysema (PLE)
 - Panacinar emphysema
 - More common in women than centrilobular
 - Associated with α -1 antitrypsin deficiency
 - Lower lobes usually affected and more involved

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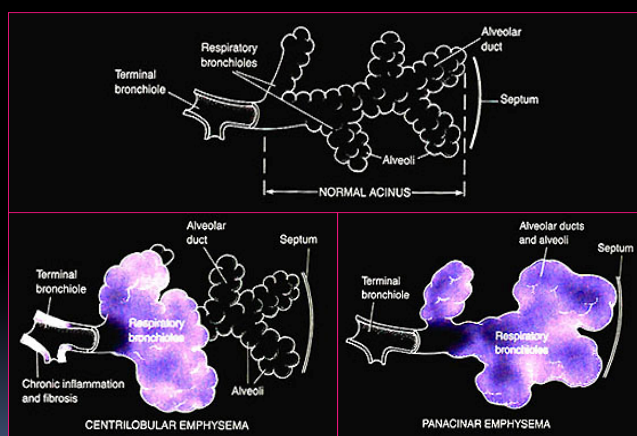
Emphysema: 2 Main Subtypes

- Centrilobular emphysema
 - Destruction and dilation distal to terminal bronchioles and respiratory bronchioles
 - Airflow obstruction and collapse due to loss of support and parenchymal destruction
- Panlobular emphysema
 - Distal to the terminal bronchiole
 - Overinflation and destruction of respiratory bronchioles, alveolar ducts and sacs



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Emphysema: 2 Main Subtypes



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Emphysema: Radiographic Patterns

- Hyper inflated lungs
- Arterial Deficiency pattern
 - More common
 - Easier to recognize
- Increased Markings pattern
 - Less common
 - More difficult to recognize

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Emphysema: Chest Radiograph

- Hyperinflation 29.5 cm
 - Hemidiaphragm flattening or inversion
 - CP angle blunting
 - Insertion of muscle slips on ribs
- Oligemia
- Bullae
- Decreased heart size < 11.5 cm (Tubular)
- Aorto-pulmonary Groove
- Retrosternal space enlargement
 - 3 cm, 2.5 - 4.5 cm

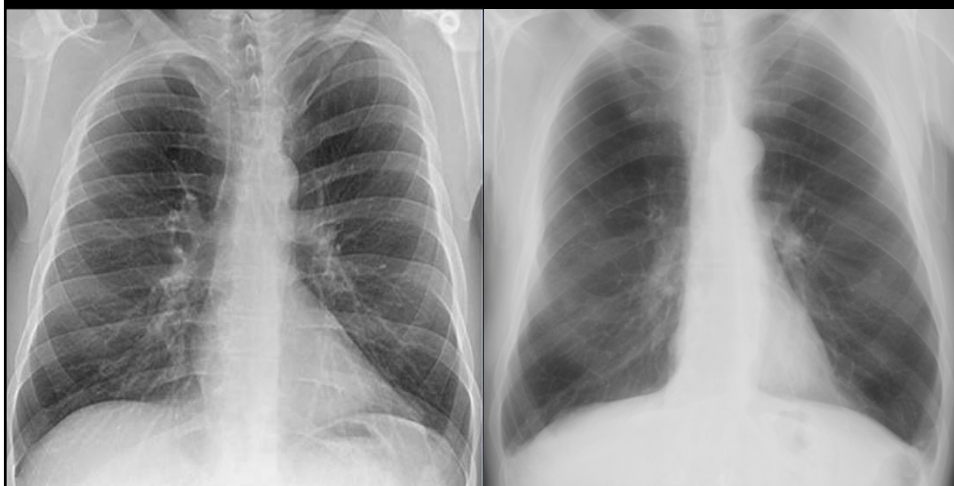
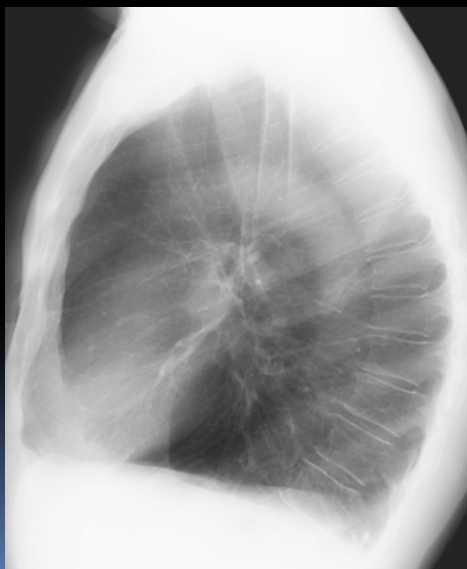


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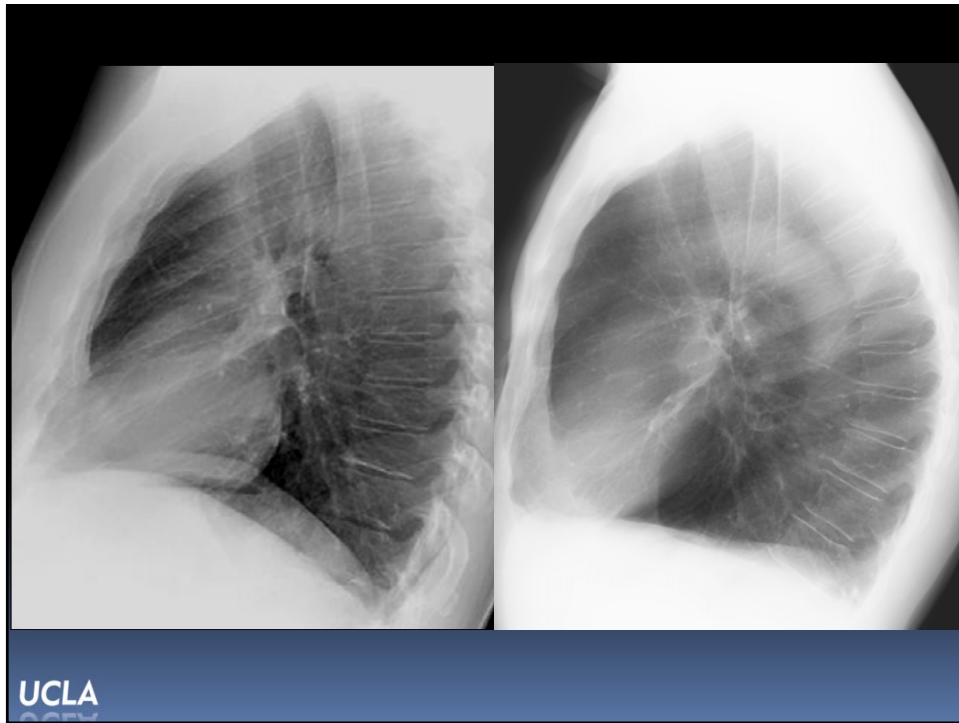
Emphysema: Chest Radiograph

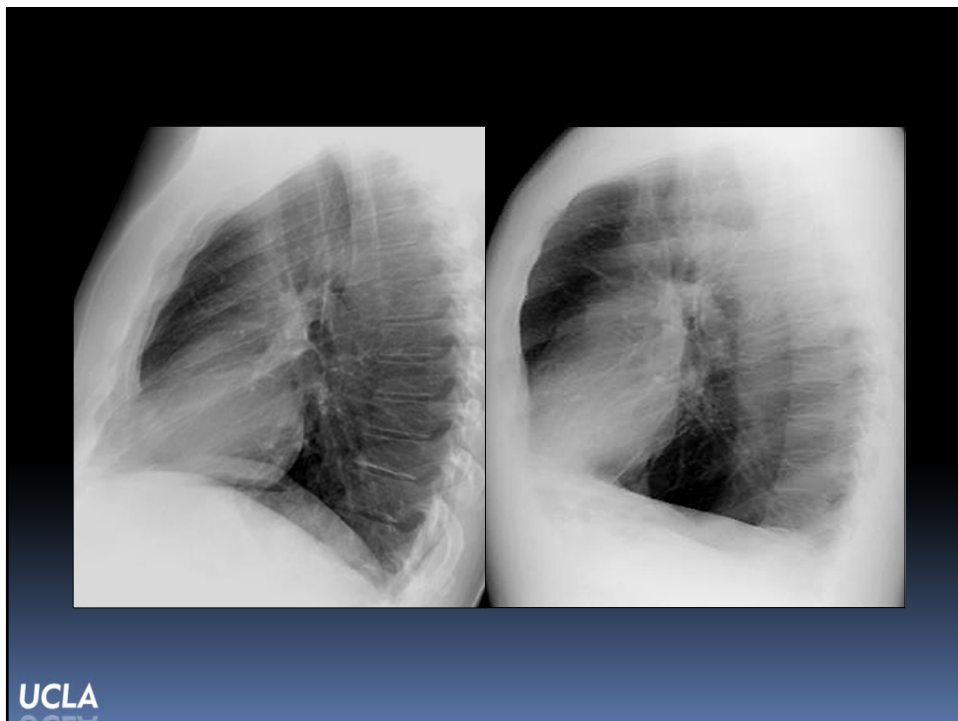
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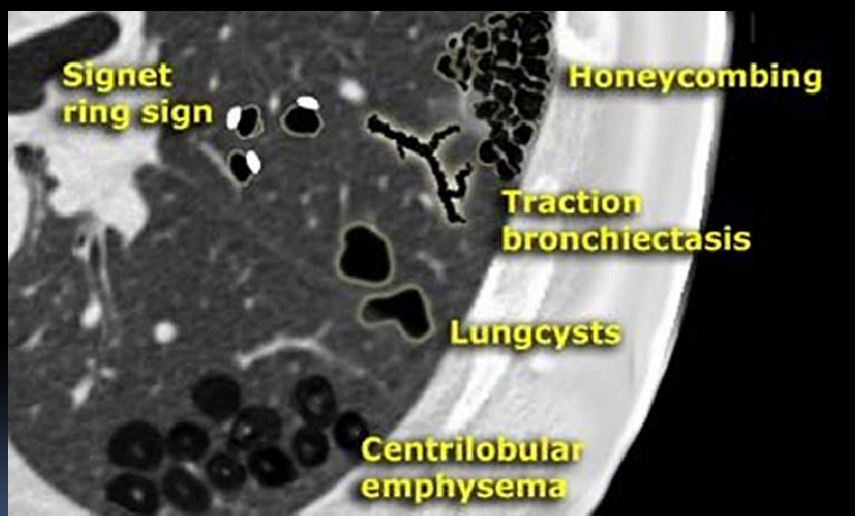




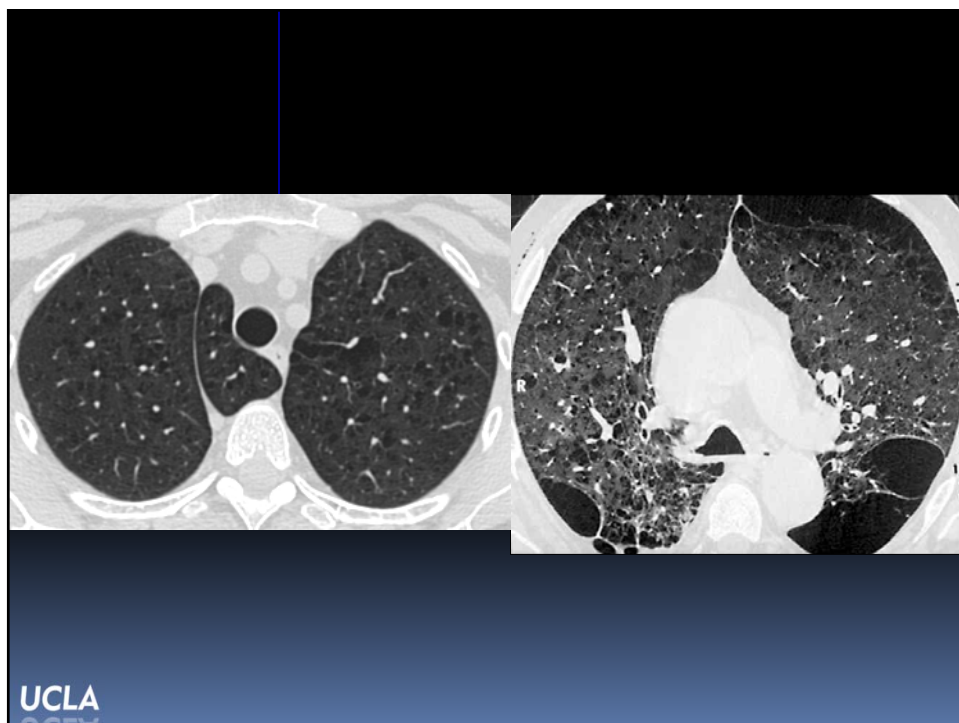
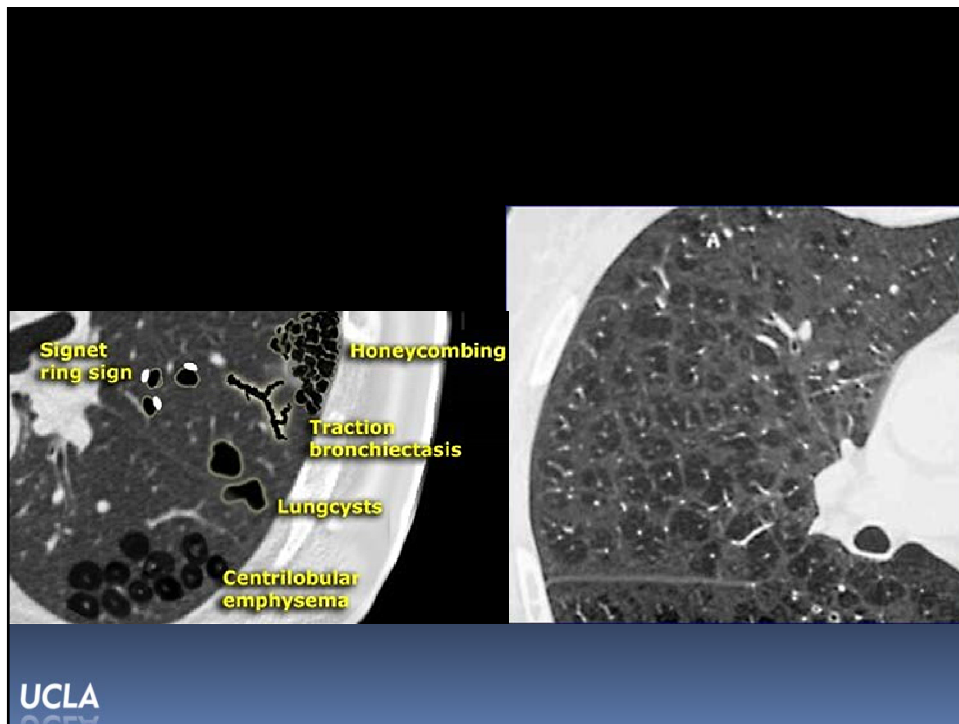
Emphysema: HRCT Findings

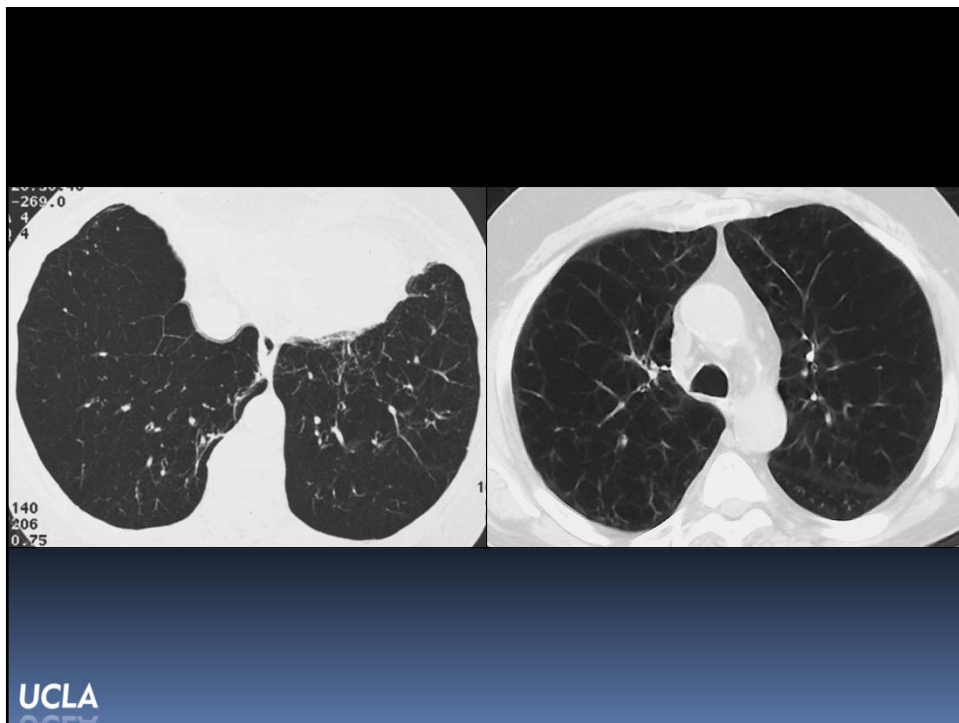
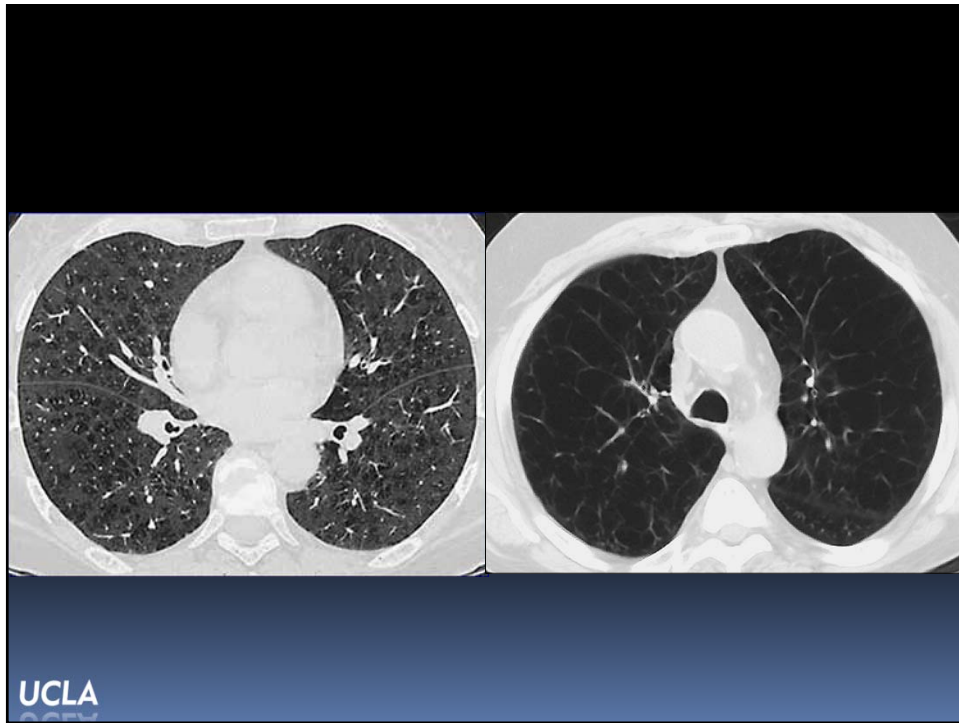
- Cysts with imperceptible or thin walls
 - Several millimeters in diameter
 - Central; surrounding the centrilobular core
 - Panlobular; entire lobule
- Bullae > 1 cm
 - Coalescent
- Vascular attenuation and distortion
- Upper versus lower lung involvement
 - Upper – centrilobular
 - Lower – panlobular

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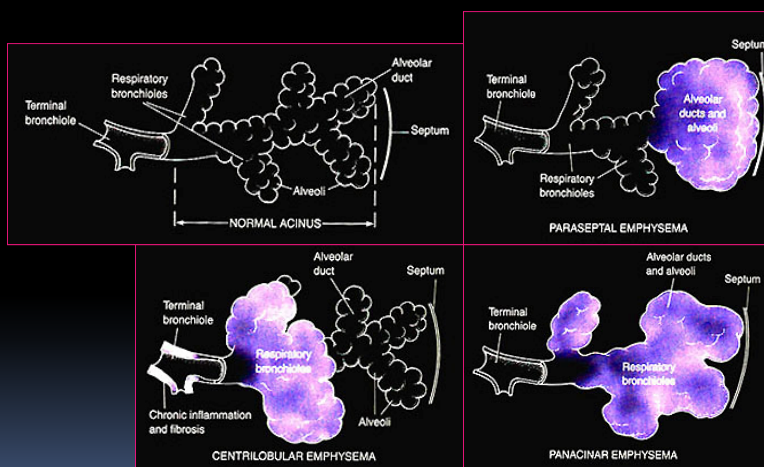
Paraseptal Emphysema

- Isolated or with CLE
- Often asymptomatic
 - Spontaneous pneumothorax in young adults
- Involvement of the distal part of the secondary lobule
- Subpleural in location
 - Bullae with thin and visible walls
 - Blebs, arising from outside the internal elastic layer of the lung



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Emphysema: Main Subtypes

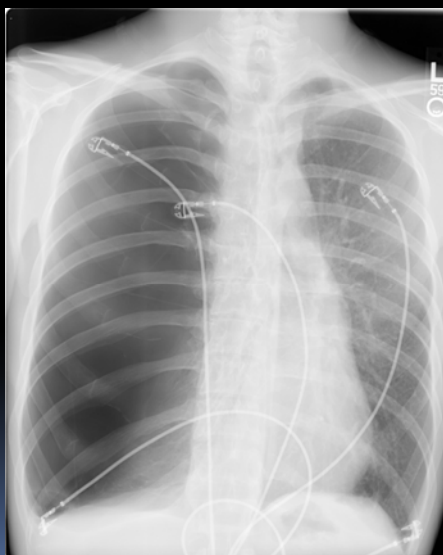


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Bullous Emphysema

- Not in itself a specific entity
- Generally in association with centrilobular or paraseptal emphysema
- “Idiopathic Giant Bullous Disease” or “Vanishing Lung Syndrome”
 - Young males
 - Most are cigarette smokers but may occur in non-smokers
 - Characterized by progressive, large upper lung bullae, occupying significant volume



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Bullous Emphysema

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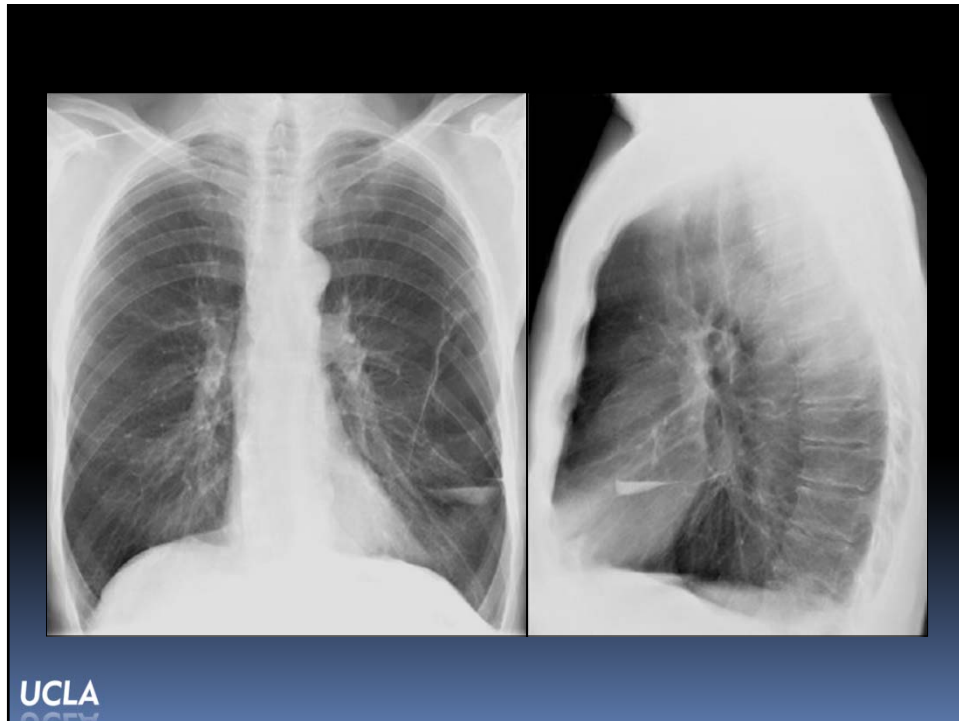
Emphysema: Additional Findings

- Pulmonary arterial hypertension
 - Increased thickness of intima and media
 - Reflex vasoconstriction
- Cor pulmonale
 - Associated more often with Increased Markings
- Infections
- Air leak complications
- Bronchogenic carcinoma

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Emphysema Differential Diagnosis

- Bronchiectasis
- Lymphangioma: LAM
- Pulmonary Langerhans cell histiocytosis: PLCH
- Bronchopulmonary Dysplasia
- Desquamate Interstitial pneumonia: DIP
- Lymphocytic Interstitial Pneumonia: LIP
- Cystic Cancers

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Congenital Bronchiectasis

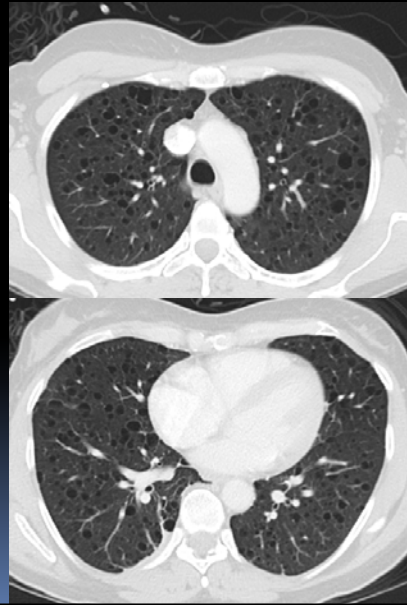
- William Campbell Syndrome
- Absence of Bronchial Cartilage
- Involves Trachea and Bronchi



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LAM

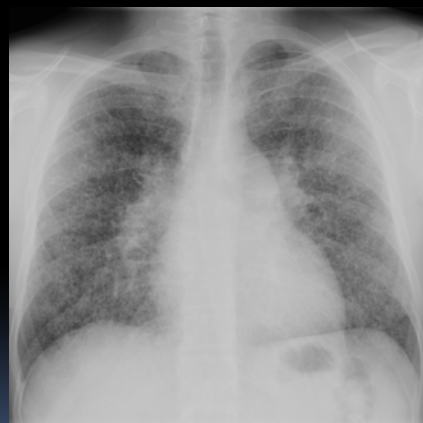
- Female, reproductive age
- Non-neoplastic hamartomatous proliferation of atypical muscle cells that lead to progressive cystic destruction of lung
- Thin walled Pericentimeter cysts
- Diffuse
- Chylous pleural effusion and enlarged thoracic duct
- PTX presentation in 50%, and 80% sometime



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Pulmonary Langerhans cell histiocytosis (PLCH)

- Smoking related lung disease
- Peribronchiolar proliferation of Langerhans cell infiltrates → Peribronchial nodules
- Cavitate and form thick or thin walled cysts → bizarre shaped cysts
- Fibrosis along the airways



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Pulmonary Langerhans cell histiocytosis (PLCH)

- Smoking related lung disease
- Peribronchiolar proliferation of Langerhans cell infiltrates → Peribronchial nodules
- Cavitate and form thick or thin walled cysts → bizarre shaped cysts
- Fibrosis along the airways



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Bronchopulmonary Dysplasia

- Teenage and adult manifestation of premature lung disease; Chronic respiratory morbidity
- New born Intubation
- High oxygen and positive pressures
- Kept on back for months
- Well-defined linear opacities radiating from the periphery toward the hilum
- Subpleural opacities, defined as small triangles with a pleural base and an internal apex
- Mosaic perfusion in inspiration
- Severity of air trapping in expiration



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Bronchiectasis

Desquamative Interstitial Pneumonia: DIP

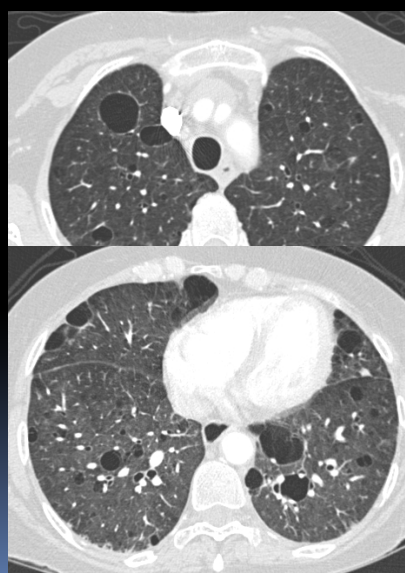
- Inflammation of alveolar epithelium and accumulation of Macrophages
- Peripheral GGO → 100%
- Upper lobe < Lower lobe → 73%
- Associated with cyst → 25%
 - True
 - CLE
- Minimal architectural distortion



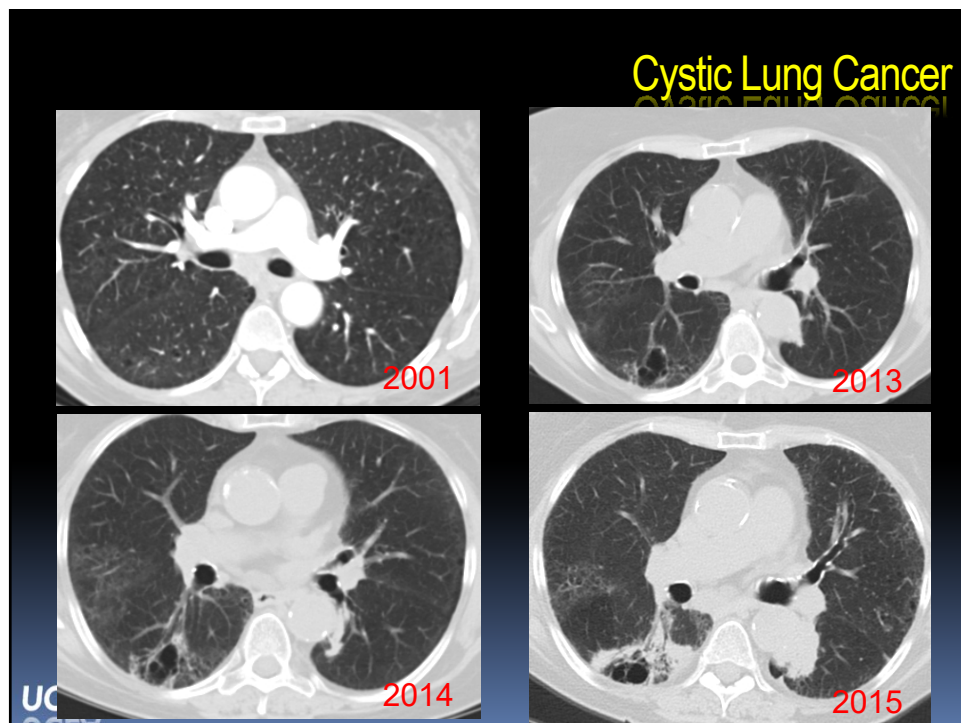
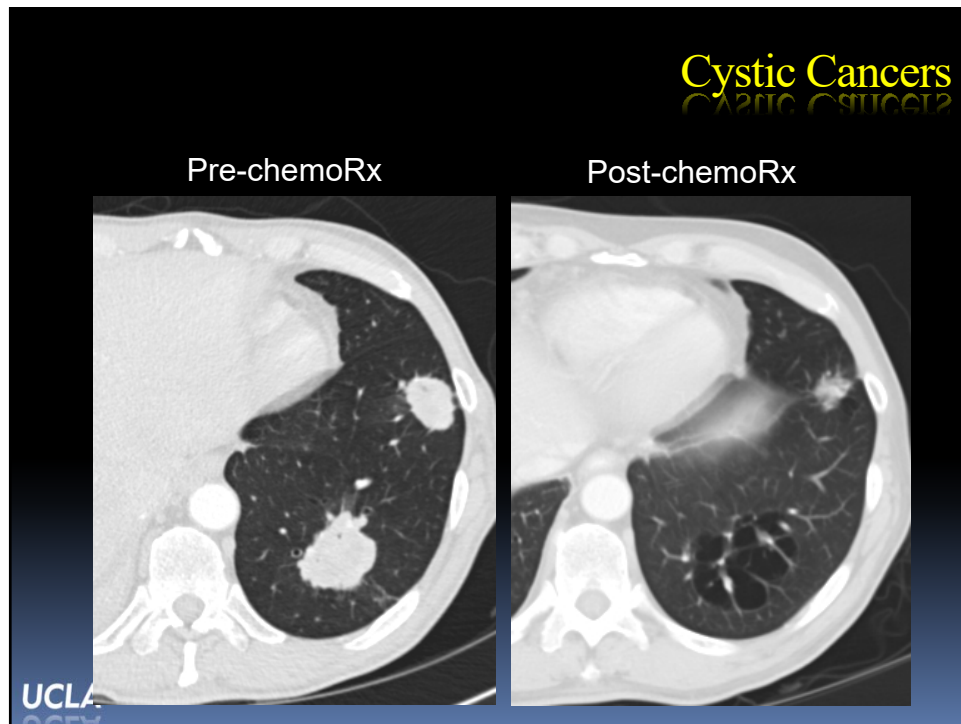
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Lymphocytic Interstitial Pneumonia: LIP

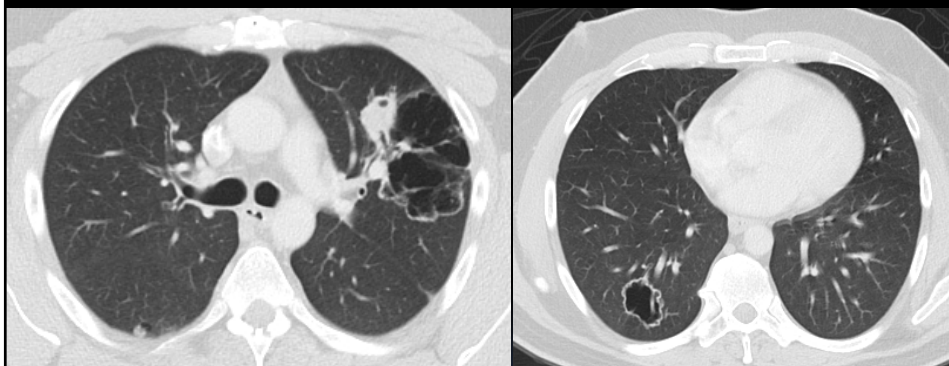
- Lymphocytic Interstitial Pneumonia
- Can progress to low-grade lymphoma, however this is rare
- LIP association:
 - HIV and AIDS
 - CTD, especially Sjögren's syndrome
- Radiology Findings
 - Ground-glass attenuation is the most common finding
 - Cysts in perivascular distribution
 - Perilymphatic nodularity
 - Cystic form of LIP is more common among patients with Sjögren's syndrome



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Recurrent Papillomatosis

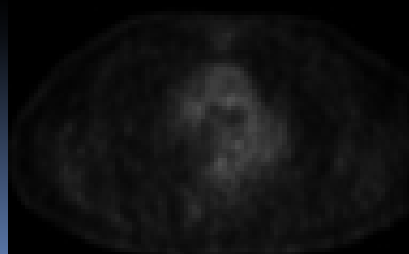


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65

Cystic mesenchymal Hamartoma

- Incidental case reports
- Biopsy was negative
- Resection for diagnosis



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Emphysema family of lung disease

- Combined pulmonary fibrosis and emphysema (CPFE)
- SRIF

Chronic Bronchitis: Definition

- Clinical diagnosis based on excessive mucous expectoration (3 months 2 consecutive years)
- Generally, not a radiographic diagnosis

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Chronic Bronchitis: Chest Radiograph

- Cannot be diagnosed radiographically
- > 50% have normal radiographs
- Thickened bronchial walls
 - Tram tracks or peribronchial thickening
 - Doughnuts, ring shadows or peribronchial cuffing
- Increased lung markings
 - “Dirty chest”
- Over inflation usually associated emphysema

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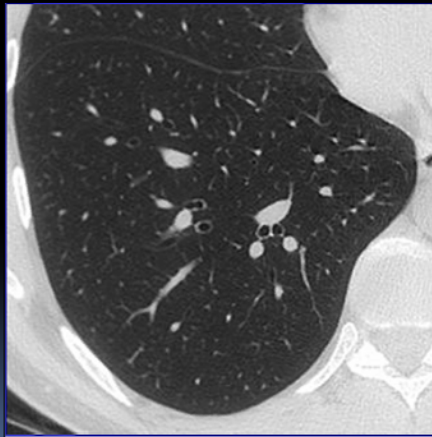
Chronic Bronchitis: HRCT

- Thickened bronchial walls
- Mucous plugs / impaction
- Centrilobular nodules
 - V, Y, O
 - Tree-in-bud
- Bronchiectasis
 - Irreversible airway dilation
- Mild air trapping

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Bronchoarterial Pairs

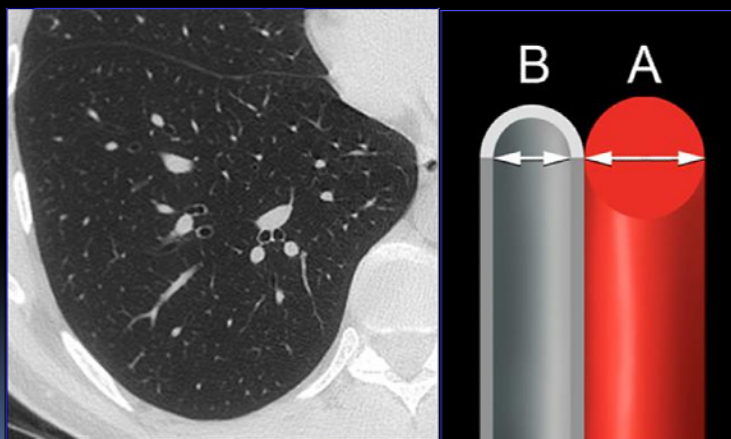
- Normal
- Diameter of bronchus = paired pulmonary artery



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Bronchoarterial (BA) Ratio

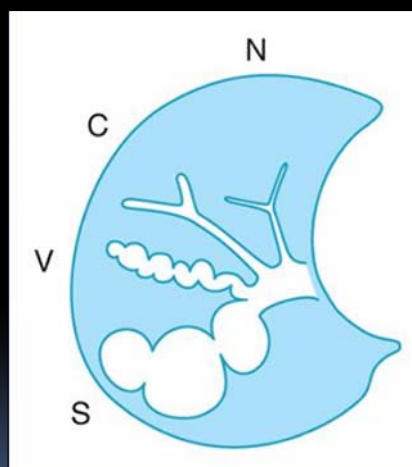
- Normal BA ratio = 0.65 – 0.70
- Bronchiectasis > 1.0



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Bronchiectasis: Grades of Severity

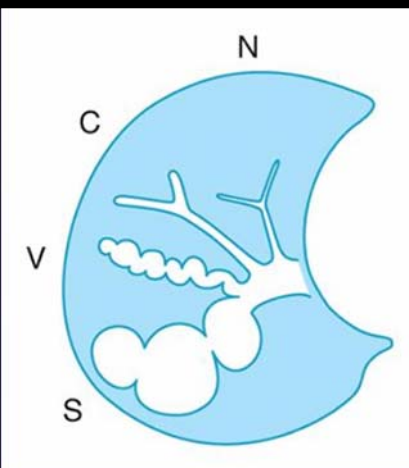
- Cylindrical
- Varicose
- Saccular / Cystic
- Normal



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Bronchiectasis: Grades of Severity

- Cylindrical = “Tram tracks”



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Bronchiectasis

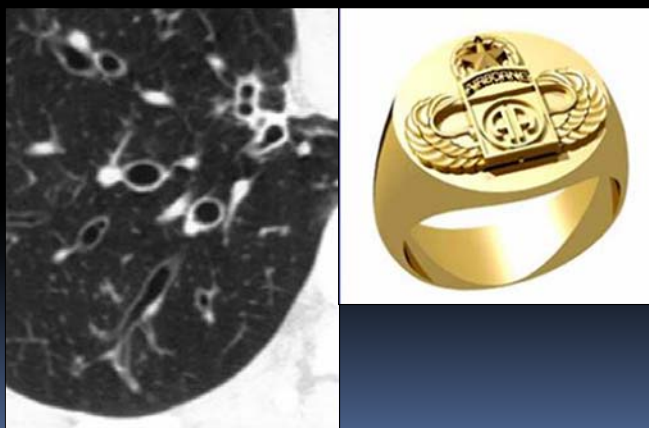
- Cylindrical when longitudinal



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Bronchiectasis

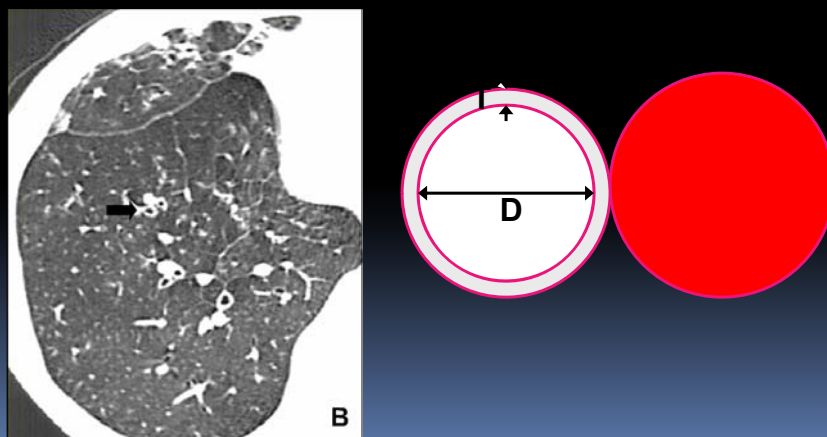
- Cylindrical when on cross-section
- “Signet ring” sign



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Bronchial Thickness

- Normal segmental airway thickness = 3 mm
- Airway thickness : diameter = 10 – 20%

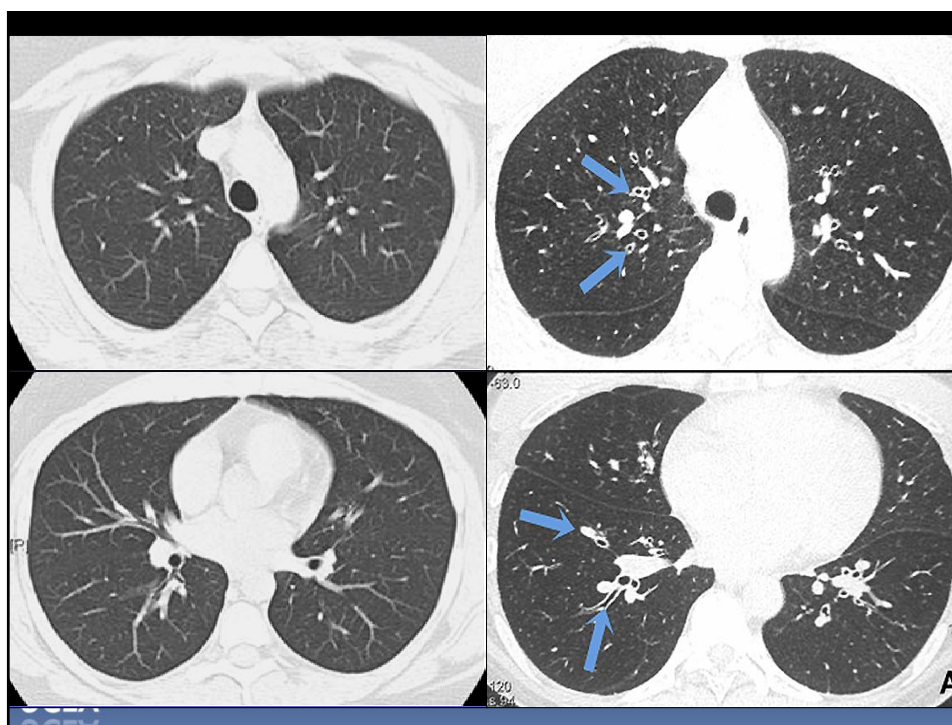
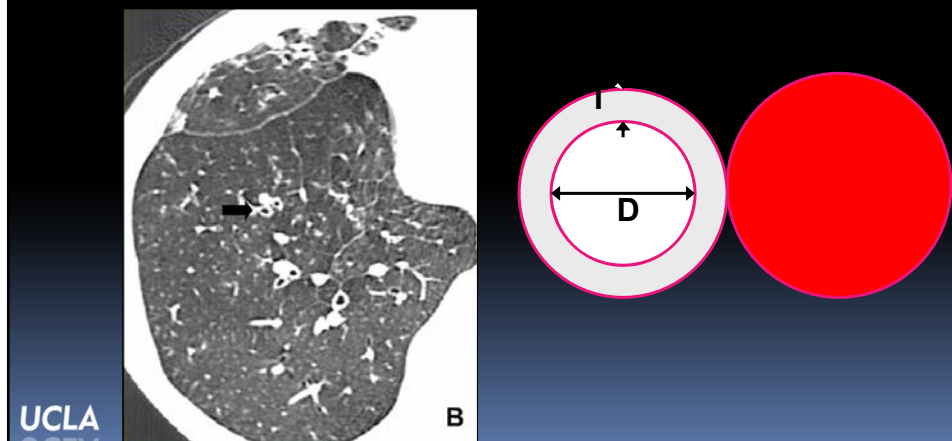


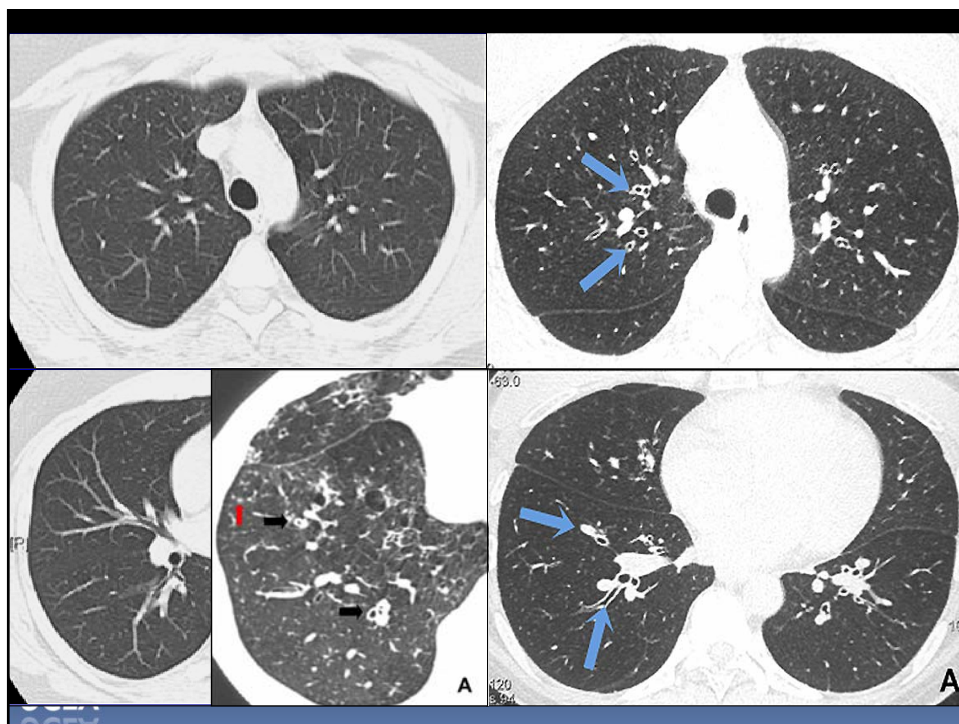
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B

Bronchial Thickness

- Normal segmental airway thickness = 3 mm
- Airway thickness : diameter = 10 – 20%





Asthma

- Reversible bronchoconstriction due to a variety of stimuli
- Technically, may not be considered COPD

Asthma: Types

- Intrinsic
- Extrinsic

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Intrinsic Asthma: General

- Middle aged
- Probably due to an auto-immune mechanism

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Extrinsic Asthma: General

- From antigens producing type I (immediate) hypersensitivity reaction
- Reagin sensitizes mast cells to secrete histamine
 - Increased vascular permeability
 - Edema
 - Smooth muscle contraction
 - Bronchoconstriction
- Inflammatory response

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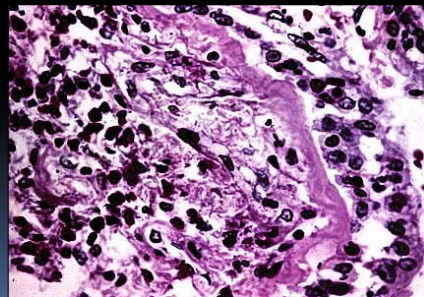
Extrinsic Asthma: Allergens

- Pollen, dog and cat fur
- Wood dust, flour, grain
- Castor bean, grain weevil
- Aspirin
- Nickel, platinum

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Asthma: Pathology

- Bronchial plugging
 - Mucous
 - Eosinophils
 - Charcot-Leyden crystals
- Hypertrophy of mucous glands and smooth muscle



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Acute Asthma: Chest Radiograph

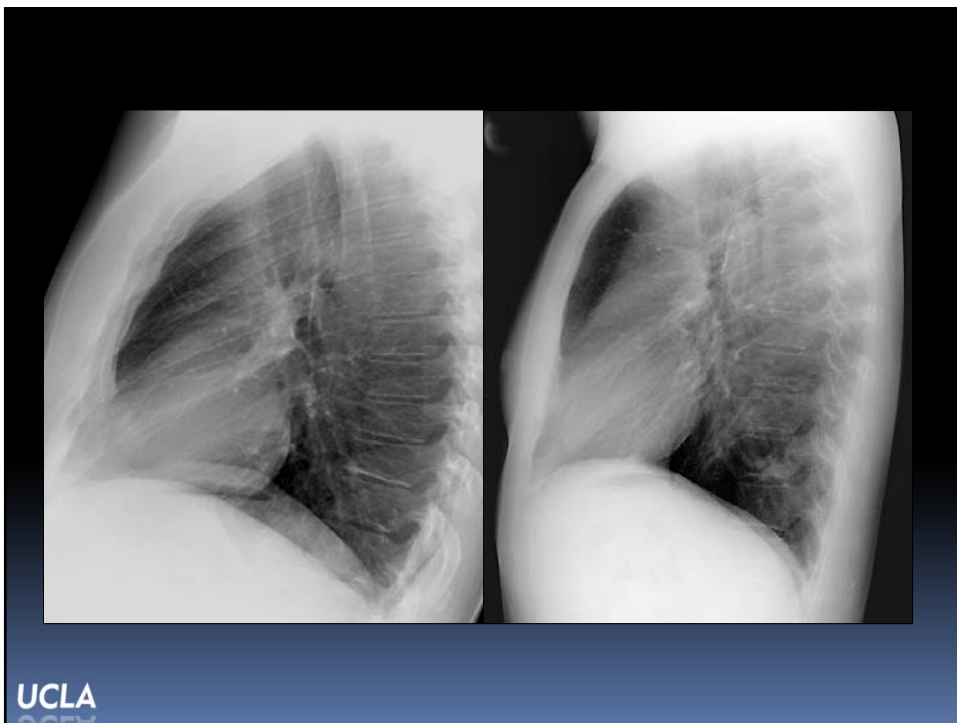
- Overaeration (< 24 hours)
- Hemidiaphragm flattening (20-39-70%)
- Increased retrosternal clear space
- Mucous plugs / impaction
- Peribronchial thickening and cuffing
- Hilar prominence (10%)
 - Lymph nodes or vascular enlargement
- Peripheral oligemia

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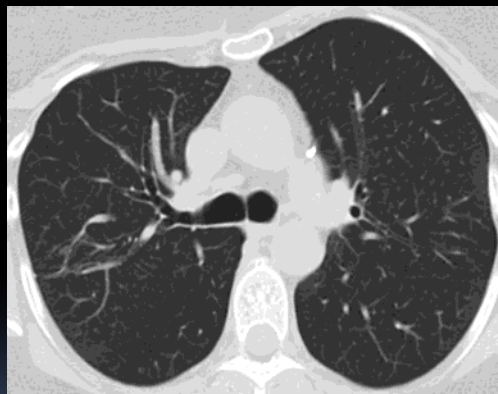
Chronic Asthma: Chest Radiograph

- Normal radiographs for most individuals
- Abnormal radiograph with early onset and severe disease
- Overinflation (19%)
- Bronchiectasis
- Postinflammatory pleuroparenchymal scarring



Asthma: HRCT Findings

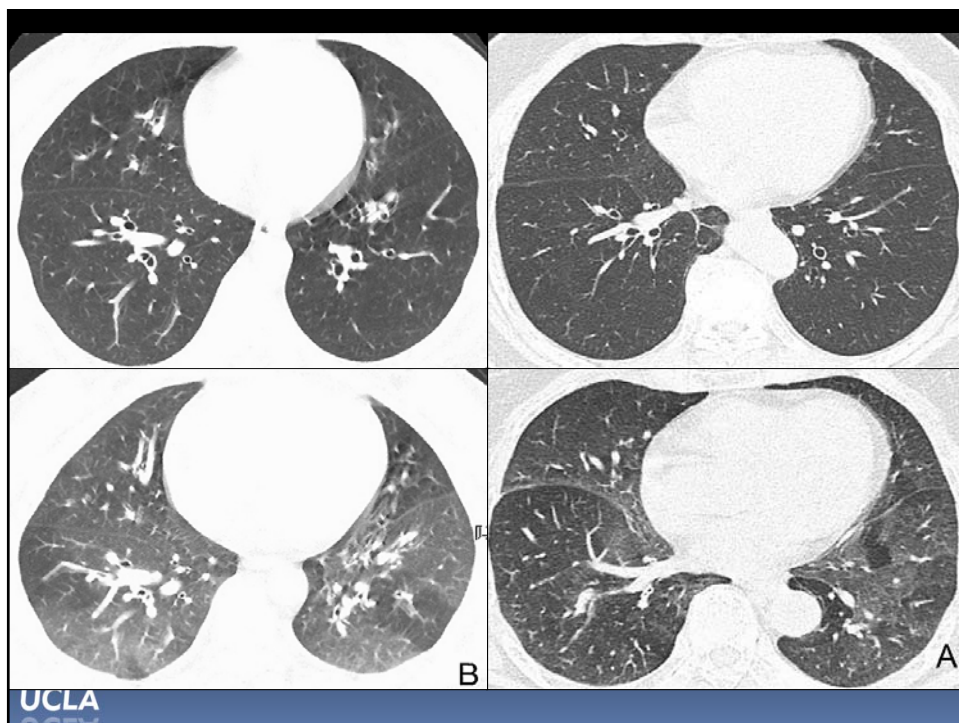
- Bronchial wall thickening (16-92%)
- Bronchial narrowing (70%)
- Bronchiectasis-cylindrical (56-77%)
- Air trapping
- Mucous plugs / impaction
- Centrilobular acinar nodules
- Atelectasis
- Pleuroparenchymal scarring



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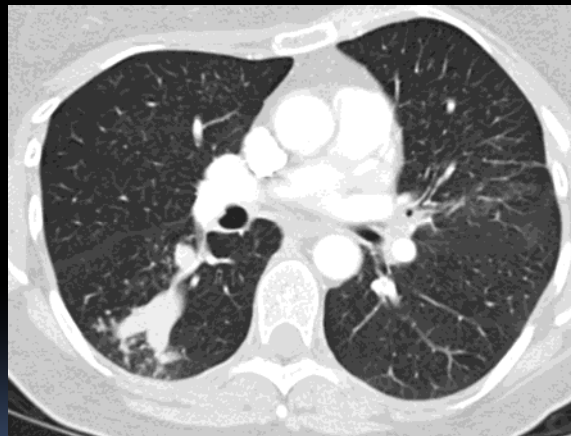
Asthma: Complications

- Pneumonia
 - Twice as frequent as in non-asthmatics
- Atelectasis
 - Related to mucous plugs
- Air leak (more common in children)
 - Pneumomediastinum
 - Pneumothorax
 - Pneumoperitoneum
 - Subcutaneous emphysema

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Asthma: Complications

- Allergic bronchopulmonary aspergillosis (ABPA)



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COPD: Summary

- HRCT is more sensitive than chest radiographs
 - Diagnosing emphysema
 - Determining extent and type
 - Measuring bronchial wall thickening and caliber
 - Determining air trapping
- HRCT carries a high specificity for diagnosing emphysema
 - Rarely overcalled in normal individuals or in those with over inflation from other causes
- Chronic bronchitis and asthma are generally not radiographic diagnoses

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Citations and References

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3. Fraser RS, Muller NL, Coleman N, Pare PD. Diagnosis of diseases of the chest. 4th edition. WB Saunders. 1999. Philadelphia.
4. Wright FW. Radiology of the chest and related conditions. Taylor and Francis. 2002. New York and London.
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6. Shah VNL. A user friendly multiscale lung modeling suite and application. Drexel University. 2007.
7. Smithus R, van Delden O, Schaefer-Prokop C. HRCT part I: basic interpretation. The Radiology Assistant. 2006. Radiological Society of the Netherlands. www.radiologyassistant.nl.
8. Abbott GF. Airways disease: anatomy-radiology-pathology correlation. Back to basics. 2007. Society of Thoracic Radiology. www.thoracicrad.org.

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Emphysema

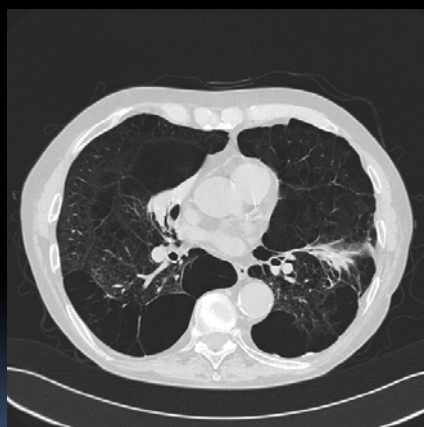


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Thoracic Radiology Research Group, David Geffen School of Medicine at UCLA

Bullae

- Distinct wall
- More than 10 mm
- Bullous emphysema

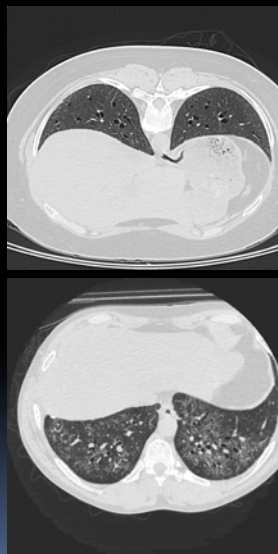


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Bronchiectasis

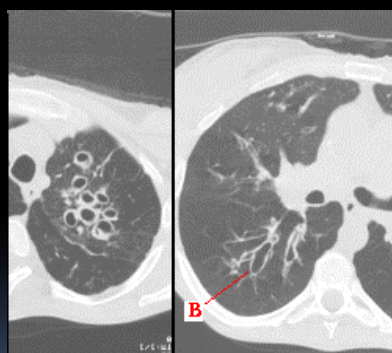
- Localized irreversible bronchial dilatation
- Caused by damage to the bronchial wall by infection, impacted mucus plugs or inherited abnormalities
- Cylindrical, Varicoid & Sacular (Cystic)
- Traction



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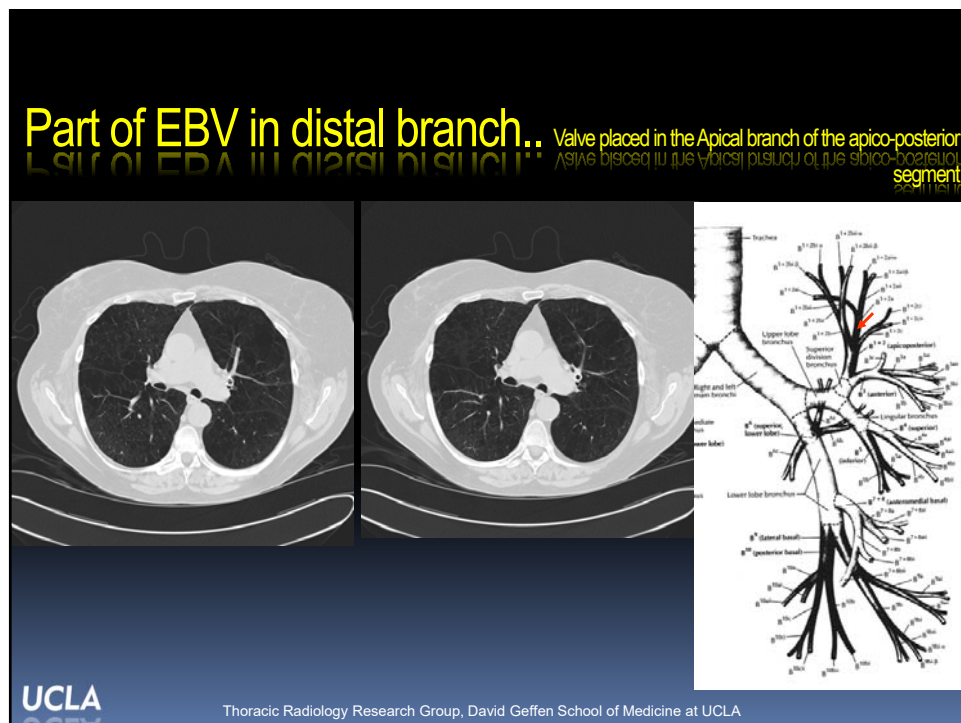
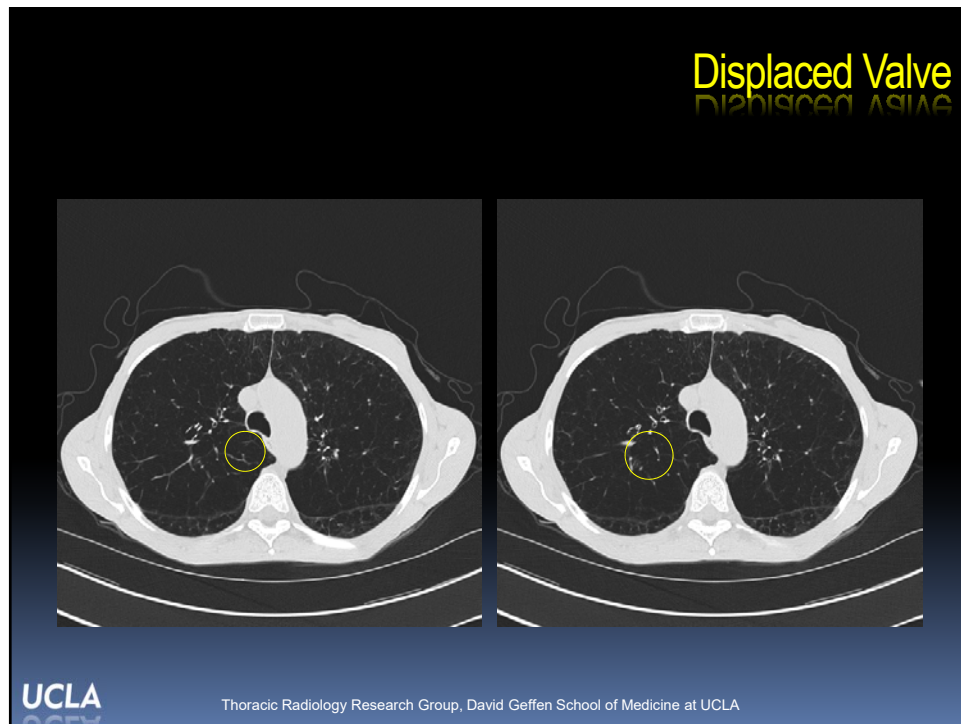
Thoracic Radiology Research Group, David Geffen School of Medicine at UCLA

Bronchiectasis

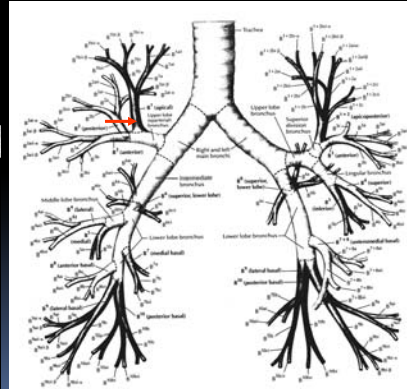
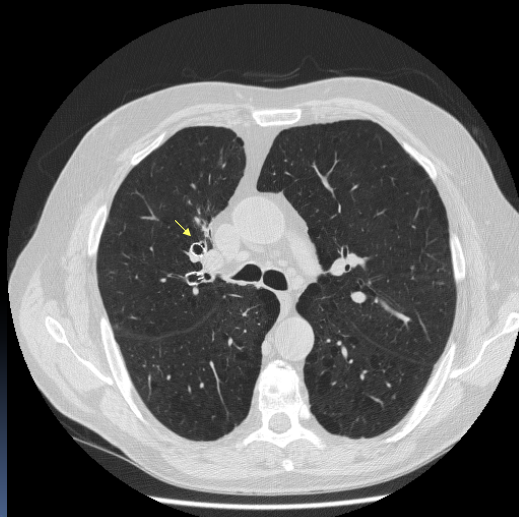


UCLA

Thoracic Radiology Research Group, David Geffen School of Medicine at UCLA



Part of EBV in distal branch... Distal to anterior segment division



UCLA

Thoracic Radiology Research Group, David Geffen School of Medicine at UCLA

COPD: BEHAVIOR CHANGE AND VALUED LIVING
Arpi Minassian, PhD
UCSD

Saturday September 30, 2017 – 11:20 a.m. – 11:40 a.m.

Dr. Minassian received her doctorate from the California School of Professional Psychology-San Diego. She completed her predoctoral internship in the UCSD Psychology Internship Training Program and continued in the NIMH Fellowship in Biological Psychiatry and Neuroscience. She joined the faculty of the Department of Psychiatry in July of 2004 and is currently a Clinical Professor. She serves as a faculty psychologist at the Medical Center, working on the Burn Service and the Pulmonary Rehabilitation Program. She is also a clinical supervisor in the Psychology Internship Training Program.

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COPD: Behavior Change and Valued Living

Arpi Minassian, Ph.D.
Clinical Professor of Psychiatry
University of California, San Diego



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**I have no conflicts of interest to
disclose.**



Agenda

- Depression and anxiety in COPD
- Cognitive Behavioral Therapy (CBT) in Pulmonary Rehabilitation
- Mindfulness and Psychological Flexibility
- Questions/Discussion



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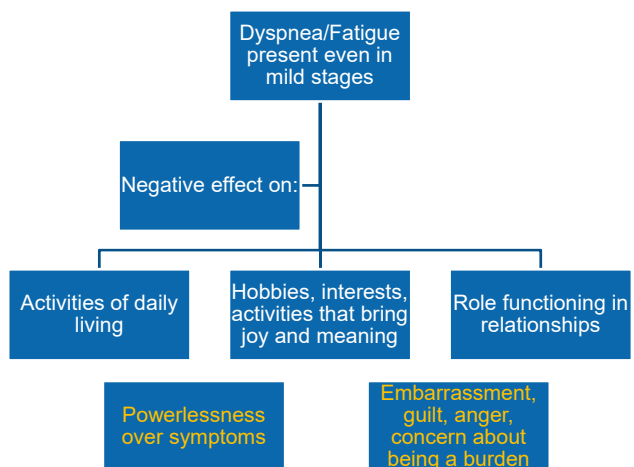
“You aren’t the person you used to be. You are someone else now.”

Ellison L, Gask L, Bakerly ND, Roberts J. Meeting the mental health needs of people with chronic obstructive pulmonary disease: a qualitative study. *Chronic illness* 2012;8(4):308-320.

4

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Loss of Identity in COPD



5

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"The Incredible Shrinking Man"



6

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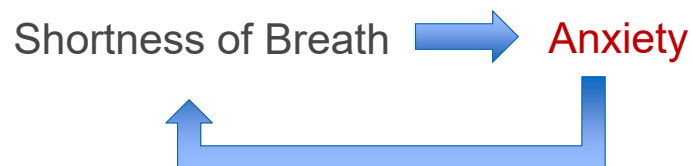
Depression and Anxiety in people with COPD

- 37-71% of people with severe COPD have depression
- Panic attacks are very common
- COPD patients with psychiatric diagnoses have worse functioning, more hospitalizations, and higher mortality

7

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The Fear-Dyspnea Cycle



8

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Psychological Treatments in Pulmonary Rehabilitation

Support groups



Complementary Medicine



Cognitive Behavioral therapy

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Cognitive behavioral therapy in pulmonary rehab

Cognitive

- Distorted/faulty thinking makes depression/anxiety worse. Changing thinking patterns will improve mood.

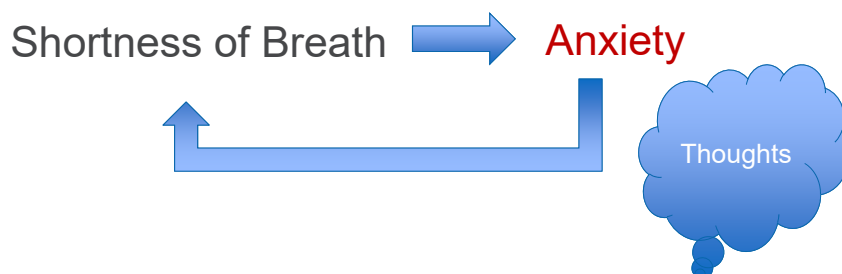
Behavioral

- Being active and engaging in hobbies will improve mood.

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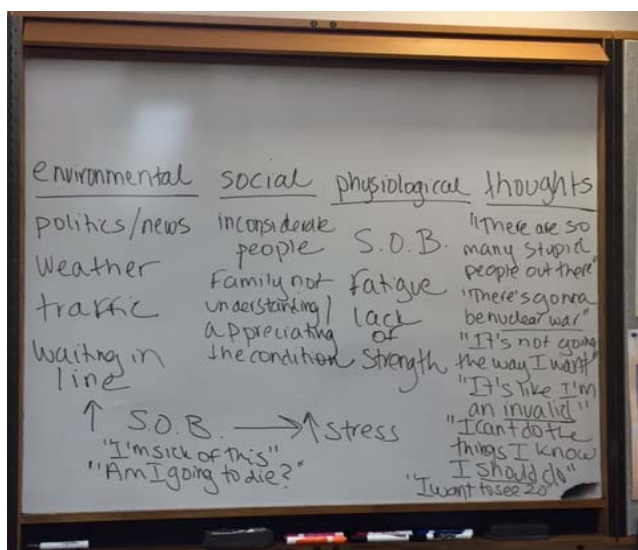
The Fear-Dyspnea Cycle: what drives it?



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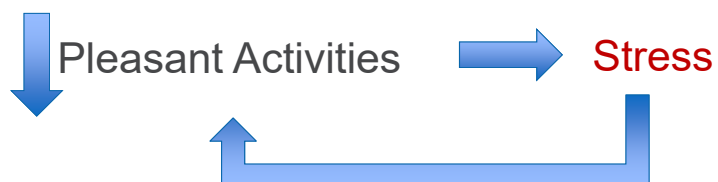
An example from our group: understanding where stress comes from, with emphasis on THOUGHTS



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Behavioral Activation: Importance of Pleasant Activities



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Encouraging Behavioral Activation

PULMONARY REHABILITATION PROGRAM
MY PLEASANT ACTIVITIES
(LIST AT LEAST 5)

- 1.
- 2.
- 3.
- 4.
- 5.

PULMONARY REHABILITATION PROGRAM
ACTIVITY TRACKING RECORD

Stress Scale: Rate your stress level from 0 (no stress) to 10 (the most stress you can imagine).

Activity	Thoughts Before	Stress Scale	Thoughts During	Stress Scale	Thoughts After	Stress Scale
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						

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Do Pulmonary Rehabilitation and psychological interventions decrease anxiety and depression?

- The short answer: **YES**
- The long answer: Yes, but not very much, and not for long.

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There's room for improvement...

Coventry
et al 2007

- Compared PR to education-only (6 studies). PR reduced anxiety/depression scores with a small effect size at 6 months, but not at 12 months.

Smith et al
2014

- Reviewed 7 studies with psych interventions (mostly CBT). Small improvements in anxiety/depression scores.

Coventry PA, Hind D. Comprehensive pulmonary rehabilitation for anxiety and depression in adults with chronic obstructive pulmonary disease: Systematic review and meta-analysis. *Journal of psychosomatic research* 2007;63(5):551-565.

Smith SM, Sonogo S, Ketcheson L, Larson JL. A review of the effectiveness of psychological interventions used for anxiety and depression in chronic obstructive pulmonary disease. *BMJ open respiratory research* 2014;1(1)

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Do psychological interventions decrease physical symptoms of COPD?

Some evidence that CBT is more effective for psychological symptoms (depression, anxiety) while “mind-body” interventions (relaxation, yoga, mindfulness) are more effective for physical symptoms (dyspnea, exercise capacity, fatigue, lung function).

Farver-Vestergaard I, Jacobsen D, Zachariae. Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Psychotherapy and Psychosomatics* 2015; 84: 37-50. **UC San Diego Health**

17

A twist on CBT...Psychological Flexibility and Acceptance and Commitment Therapy

Psychological inflexibility can lead to depression and anxiety

- Being “fused” with your thoughts, always accepting them as true
- Believing that you won’t be happy unless your problem is “fixed”

Mindfulness can help with psychological flexibility, especially with “defusing” from thoughts

Instead of focusing on trying to change thoughts or solve the problem, focus on VALUES

- Values are what we want our life to stand for
- Values exist despite lung disease or anything else

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Introducing Mindfulness Meditation

Your 5 senses

“Mindfulness means
paying attention
in a particular way;
On purpose, in
the present moment,
and non-judgmentally.”

Jon Kabat-Zinn

YOU



**Your thoughts,
worries, sadness**

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Your 5 senses

YOU

**Your thoughts,
worries, sadness**

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Effect of Mindfulness in Pulmonary Disease

- Mentioned in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 report as a recommended treatment
- Dr. Ni-Cheng Liang's UC San Diego study
 - Enrolling people with chronic lung disease into an 8-week Mindfulness-Based Stress Reduction Program
 - Initial results suggest positive effects on stress and quality of life
 - Trend towards improvement in 6-minute walk distance and dyspnea



Mindfulness Benefits Patients with Chronic Lung Disease

Ni-Cheng Liang, MD¹; Eleanore Bernadas, MD²; Rachel Jen, MD^{1,3}; Yanru Li, MD^{1,4}; Arpi Minassian, PhD¹; Atul Malhotra, MD¹; Andrew Ries, MD^{1,5}; Steven Hickman, PsyD^{1,4,6}

¹ Division of Pulmonary, Critical Care and Sleep Medicine, University of California San Diego (UCSD); ² UCSD Department of Medicine; ³ UCSD Department of Family Medicine and Public Health; ⁴ UCSD Department of Psychiatry; ⁵ Respiratory Division, University of British Columbia; ⁶ Department of Otolaryngology Head and Neck Surgery, Beijing Tongren Hospital, Capital Medical University

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“Acceptance” is a difficult word...



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“Wanting” versus “Willing”

Even though I didn't want my lung disease, am I willing to do what it takes to live a meaningful life?

Do I want to exercise today?

Am I willing to exercise today in the service of what's important to me?

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Accessing Patients' Values

“What do you want to be remembered for?”



The Party

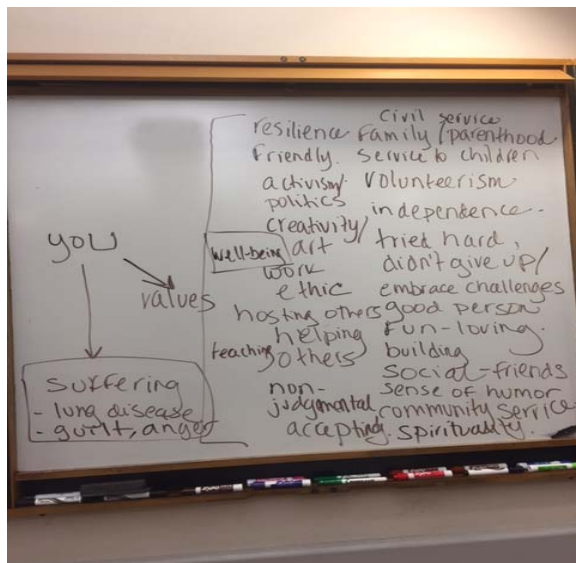


The Lifetime Achievement Award

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The Values Exercise in our group



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Summary

- People with COPD experience a sense of loss of identity.
- Depression and anxiety are very common, making it even more difficult to engage in activities and behaviors that are meaningful and promote health.
- Psychological interventions such as Cognitive Behavioral Therapy are useful in people with COPD, but there is room for improvement.
- Mindfulness approaches can help with psychological distress and perhaps the physical symptoms of COPD (breathlessness, fatigue).
- Orienting patients to their values may help them regain their identity.

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Arpi Minassian, Ph.D.
aminassian@ucsd.edu

PANEL

Richard Casaburi, PhD, MD; Vipul Jain, MD;
Fereidoun Abtin, MD; Arpi Minassian, PhD

Saturday September 30, 2017 – 11:40 a.m. – 12:00 p.m.

LUNCH

Saturday September 30, 2017 – 12:00 p.m. – 1:00 p.m.

ASTRAZENECA is sponsoring a non-CME lunch. The speaker will be:

Dr. Jill Ohar, MD

Professor of medicine

Department of Internal Medicine

Section on Pulmonary, Critical Care,

Allergy and Immunology

Wake Forest School of Medicine

O2 ASSESSMENT/DELIVERY DEVICE SELECTION

Trina Limberg, RRT, UCSD

Chris Garvey, NP, UCSF

(20 minutes each)

Saturday September 30, 2017 – 1:00 p.m. – 2:35 p.m.

Trina M. Limberg, BS, RRT, FAARC, MAACVPR, is the Director for the Pulmonary Rehabilitation Department for UC San Diego Health System. As a respiratory therapist, she has been working and practicing in the field of pulmonary rehabilitation for more than 30 years. She has been recognized for distinguished service and has been awarded a Master credential from the American Association of Cardiovascular and Pulmonary Rehabilitation and fellowship from the American Association of Respiratory Care. She serves on the AACVPR Board of Directors. Trina has been nationally recognized for excellence in patient education. She has served as a committee member and officer to state and national professional organizations for over 25 years. She has contributed to research in pulmonary rehabilitation and provided numerous training sessions for healthcare professionals. She is a contributing author on COPD exercise and clinical practice guidelines for post- acute care publications.

Christine Garvey, FNP, MSN, MPA, MAACVPR, is a nurse practitioner at the UCSF Sleep Disorders Center at Mount Zion where she cares for patients with sleep and pulmonary conditions. Under the supervision of a doctor, she provides assessments, orders diagnostic tests, interprets test results and makes recommendations for treatment. Her research interests include the areas of pulmonary rehabilitation, asthma and congestive heart failure.

Garvey earned a bachelor's degree in nursing and a master's degree in public administration at the University of San Francisco and a master's of science and nursing degree from Holy Names College in Oakland. She has authored chapters in the Lippincott Manual of Nursing Practice and has been published in several national professional journals. She has served as chair and as a member of many national and state committees, including co-chair of the American Thoracic Society's Pulmonary Rehabilitation Section. Her awards include the Mary Burns Award for Pulmonary Rehabilitation Services and the American Lung Association of California Research Program Scholarship. She is currently President of the California Thoracic Society.

Oxygen Therapy: Assessment, Compatible Equipment and Education (ACE)

Assessment

CMS Requirements

Reasonable and necessary oxygen items and equipment for home use must meet all of the following criteria:

1) Treating physician examines patient & determines he/she has one of the following conditions that might be expected to improve with oxygen therapy:

- A severe lung disease, COPD, ILD (known or unknown etiology), cystic fibrosis, bronchiectasis, and widespread pulmonary neoplasm; or
- Hypoxia-related symptoms or findings - PH, CHF due to cor pulmonale, erythrocytosis, impairment of cognitive process, nocturnal restlessness, and morning headache;

2) The treating physician or a qualified provider or supplier of laboratory services conducts the qualifying blood gas study. A qualified provider or supplier of laboratory services is:

- Certified to conduct blood gas studies; or
- A hospital certified to conduct blood gas studies;

3) The qualifying blood gas study value was obtained under the following conditions:

During an inpatient hospital stay – Closest to, but no earlier than, 2 days prior to the hospital discharge date, with home oxygen therapy beginning immediately following discharge; or

During an outpatient encounter – Within 30 days of the date of Initial Certification while the patient is in a chronic stable state. A chronic stable state is when the patient is not in a period of acute illness or an exacerbation of his or her underlying disease;

4) The treating physician tried or considered alternative treatments & they were deemed clinically ineffective; and

5) For Initial Certifications, the patient's blood gas study (either an arterial blood gas or an oximetry test) values meet specified criteria.

Oxygen Therapy: Assessment, Compatible Equipment and Education (ACE)

GROUP I Criteria	Group II Criteria
RA (awake) at rest O₂ arterial sat. $\leq 88\%$ or $\leq$ PaO₂ 55 mm Hg	<i>Includes portable oxygen systems if patient is mobile within the home & qualifying blood gas study performed at rest while awake or during exercise.</i> RA - 89% at rest (awake); or PaO₂ of 56-59 mm Hg; and a. Dependent edema suggesting CHF b. PH or cor pulmonale, determined by measurement of PAP, gated blood pool scan, "P" pulmonale on EKG (P wave > than 3 mm in standard leads II, III, or AVF) c. Erythrocythemia with a hematocrit > 56 %
Tested during exercise and, if during the day while at rest, arterial PO₂ is ≥ 56 mm Hg or oxygen saturation is $\geq 89\%$: - Arterial PO₂ is ≤ 55 mm Hg or arterial sat. $\leq 88\%$; and - Documented improvement of hypoxemia during exercise with oxygen	During exercise w. a saturation of 89% or PaO₂ of 56-59 mm Hg; and a. Dependent edema suggesting congestive heart failure; b. Pulmonary hypertension or cor pulmonale, determined by measurement of PAP, gated blood pool scan, "P" pulmonale on EKG (P wave > than 3 mm in standard leads II, III, or AVF); or c. Erythrocythemia with a hematocrit greater than 56%
Tested during sleep- if PaO₂ ≥ 56 mm Hg or arterial sat. is $\geq 89\%$ while awake, or - Decrease in PaO₂ of > than 10 mm Hg or a drop in sat. > than 5% at least 5 minutes associated w. s/s more than 5 percent from baseline saturation for at least 5 minutes taken during sleep; associated w. s/s reasonably attributable to hypoxemia. Symptoms: impairment of cognitive processes and (nocturnal restlessness or insomnia). Signs: cor pulmonale, "P" pulmonale on EKG, documented PH, & erythrocytosis reasonably attributable to hypoxemia <i>Initial coverage of Group I home oxygen therapy is limited to 12 months or the treating physician-specified length of need.</i>	Tested during sleep for at least 5 minutes: - 89%; or PaO₂ of 56-59 mm Hg; and a. Dependent edema suggesting congestive heart failure; b. PH or cor pulmonale, by measurement of pulmonary artery pressure, gated blood pool scan, echocardiogram, or "P" pulmonale on EKG (P wave greater than 3 mm in standard leads II, III, or AVF); or c. Erythrocythemia with a hematocrit greater than 56 percent; or <i>Initial coverage of Group II home oxygen therapy is limited to 3 months or the treating physician-specified length of need for oxygen, whichever is shorter.</i>

Adopted from: <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/Home-Oxygen-Therapy-Text-Only.pdf> Accessed 12_18_16.

Oxygen Therapy: Assessment, Compatible Equipment and Education (ACE)

Compatible Equipment

Stationary Systems	Ambulatory Options
Standard Concentrators	Portable Oxygen Concentrators (POCs) < 10 #
Transfillable Concentrators	Transportable Oxygen Concentrators (TOCs) > 10#
Liquid Oxygen	Liquid Oxygen
Compressed Gas cylinders	Compressed Gas Cylinders

Follow this link to the American Association for Respiratory Care website to access the Guide to Portable Oxygen Concentrators

www.aarc.org/resources/oxygen_resources/portable_oxygen_concentrators_guide.pdf

Oxygen Flow Delivery Devices	Oxygen Interface Administration Options
Standard regulator Electronically powered intermittent (pulse dose) Non-electronic (ie. pneumatic) pulse dose	Nasal cannula Reservoir cannula High flow nasal cannula Non-Rebreathing Mask Trans-tracheal oxygen catheter Ventilation support device – portable High flow humidification system

Commonly Used Oxygen Interface Characteristics

Standard nasal cannula	provides 24-40% oxygen up to 6 L/min	Influenced by breath rate Tidal volume Pathophysiology *the slower the inspired flow the higher the FIO ₂
High flow nasal cannula	Provides up to 15 L/min	
Reservoir nasal cannula	Provides 6-8 L/min	
Non-rebreathing mask	Provides FIO ₂ 40-90% with 8-10 L/min	Mask must be securely fastened Reservoir bag must be inflated

Adapted from the ATS Oxygen Delivery Method website www.ats.org and the AARC Clinical Practice Guideline: Oxygen Therapy in the Home and Alternate Site Care Facility- 2007.
<http://www.rcjournal.com/cpgs/> .

Take Aways:

1. Pulse dose bolus delivery may vary with increased respiratory rates.
2. There is no standardization between numbered continuous flow and pulse dose settings with any device.

Oxygen Therapy: Assessment, Compatible Equipment and Education (ACE)

3. In general, the smaller the POC the lower the production capability.
4. Patients should be tested using the prescribed device and the prescribed setting to assure SpO₂ >88% with exercise/activity.



Education and Adherence

- Several studies have evaluated compliance to LTOT showing rates ranging from **45 to 70%**.
- 20% of patients used oxygen less than prescribed due to treatment difficulties, lack of breathlessness, or fear of oxygen addiction.
- Non-adhering patients were primarily males and were ashamed of their therapy and the associated stigma.
- Patient complaints were related to restricted autonomy (50%), the delivery device (41%), and feeling ashamed (38%).

Source: [Katsenos, S. and Constantopoulos, S. Pulm Med. 2011; 2011: 325362. Published online 2011 Sep 15. doi: 10.1155/2011/325362](#)
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3175397>

Considerations for Educating Patients:

- Unclear prescriptions –many may not be able to articulate prescriptions
- Assessing patient expectations for reducing dyspnea
- Addressing underlying myths about O₂:
 - closer to death
 - now grounded to home
 - public embarrassment
 - the logistics of storage and portage – “range anxiety”

To Improve Therapy Acceptance:

- Provide information about **why** oxygen therapy is needed
- Provide written prescriptions
- Use rehab exercise sessions to help demonstrate use and benefits
- Be supportive, for many this is a difficult reality and often very embarrassing
- Be a resource on delivery options such as POCs

SPIROMETRY USE, INTERPRETATION

Vipul Jain, MD, UCLA

George Su, MD, ZSFGH

Garner Faulkner, RRT, UCSD

Saturday September 30, 2017 – 1:00 p.m. – 2:35 p.m.

Vipul Jain, MD, MS, completed a MPH at the University of Iowa before starting his postdoctoral research in Asthma there and has continued on in Asthma and COPD over the past 15 years. He completed his Pulmonary and Critical Care fellowship at UCSD. Currently, Dr. Jain is an Associate Professor of Medicine at UCSF-Fresno and the medical director for the chronic lung disease program.

George Su, MD, received his medical degree from the University of California at Los Angeles. He trained in internal medicine at the University of California at San Diego, then did his pulmonary and critical care fellowship at the University of California at San Francisco. Dr. Su is currently an Associate Professor in the UCSF School of Medicine. He serves as Medical Director of the Healthy San Francisco Asthma/COPD and Sleep Programs at San Francisco General Hospital and as Medical Director at the Telehealth Program for the San Francisco Health Network. Dr. Su also serves as a member of the ATS Quality Improvement and Implementation Committee.

George Faulkner II, BSRC, RRT, AE-C, graduated in 2002 with a BS in Respiratory Care. He has worked at University of California San Diego since 2005. Garner serves as the supervisor for the Exercise and Pulmonary Function Lab at UCSD. Garner is also an active member in the American Association for Respiratory Care.

INTERPRETATION CASE 1

CLOVIS COMMUNITY MEDICAL CENTER

2755 Herndon
Clovis, CA, 93612

Name: [REDACTED]	ID: [REDACTED]	Acct: 235541018	Date: 01/07/2015
Tech: ONG, ARLENE RRT	Height: 180.20	Age: 75	Room: OP
Doctor: JAIN, VIPUL	Weight: 119.40	Sex: Male	Race: Caucasian

Diagnosis: DYSPNEA ON EXERTION

Dyspnea: After any exertion Cough: Productive Wheeze: Frequent
Tbco Prod: Never Smoked Yrs Smk: Pks/Day: Yrs Quit:

Medications: Has Ventolin and Symbicort 160-4.5 but hasn't used in about 1 month

Pre Test Comments: Last ate around 0730.

Post Test Comments:

Calibration performed at: 1000 Software: BreezeSuite v.8.1 sp3 Predicted module: NHANES III & ITS
Test time: 1030

EXPOSURES: Second-hand smoke from father (very heavy smoker - 4 PPD) x 18 years. Was a mechanic all his life, includes exposure to asbestos. Grew up on a ranch (vineyard) and includes direct exposure to DDT.

The patient was seated. Good patient effort & cooperation. Coughing was noted mostly during pre-bronchodilator testing. He complained of being light-headed, beginning in the middle of DICO testing but especially during post-bronchodilator testing. The results of this test meet the ATS standards for acceptability and repeatability. Four puffs (360mcg) of Albuterol MDI were given using a valved holding chamber 15 minutes before the post test. The patient took the valved holding chamber with him upon completion of the test. Verbal instructions were given on the proper use of MDIs.

Arleene Ong, RCP, RRT
Arleene Ong, RCP, RRT

	Pre-Bronch				Post Bronch		
	Actual	Pred	%Pred	SD	LLN	Actual	%Chng
--- SPIROMETRY ---							
FVC (L)	3.46	4.36	79	0.58	3.40	3.55	+2
FEV1 (L)	2.39	3.16	75	0.49	2.35	2.49	+4
FEV1/FVC (%)	69	72	96	6	62	70	+1
FEV3 (L)	2.97					3.10	+4
FEV3/FEV6 (%)	90					90	+0
FEV6 (L)	3.28	4.10	80	0.57	3.16	3.43	+4
FEV1/FEV6 (%)	73	77	94	5	69	73	+0
FEF 25-75% (L/sec)	1.38	2.28	60	1.00	0.63	1.69	+22
FEF Max (L/sec)	6.42	7.96	80	1.45	5.57	6.81	+5
FIVC (L)	3.42					3.57	+4
FIF Max (L/sec)	3.43					5.30	+54
--- LUNG VOLUMES ---							
SVC (L)	3.54	4.62	76				
IC (L)	2.92	3.34	87				
ERV (L)	0.62	1.28	48				
FRC(pl) (L)	3.60	3.90	92	0.72	2.46		
RV (Pleth) (L)	2.98	2.62	113	0.37	1.88		
TLC (Pleth) (L)	6.52	7.24	90	0.79	5.66		
RV/TLC (Pleth) (%)	46	37	123	4	29		


235541018
PULMONARY FUNCT CONC 4/23/1939
PCP: COPELAND, GREGORY, DO
REF MD: JAIN, VIPUL
75 M PL: BLUE SHIELD HMO SAN*

CLOVIS COMMUNITY MEDICAL CENTER

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Doctor: JAIN, VIPUL	Weight: 119.40	Sex: Male	Race: Caucasian

	Pre-Bronch				Post Bronch	
	<u>Actual</u>	<u>Pred</u>	<u>%Pred</u>	<u>SD</u>	<u>LLN</u>	<u>%Chng</u>
Trapped Gas (L)						
--- DIFFUSION ---						
DLCOunc (ml/min/mmHg)	16.74	32.03	52	4.83	22.37	
DLCOcor (ml/min/mmHg)		32.03		4.83	22.37	
DL/VA (ml/min/mmHg/L)	3.22	4.43	72			
VA (L)	5.20	7.24	71	0.79	5.94	
--- AIRWAYS RESISTANCE ---						
Raw (cmH2O/L/s)		1.45		0.48	0.66	
Gaw (1/s/cmH2O)		1.03				
sRaw (cmH2O*s)		4.76				
sGaw (1/cmH2O*s)		0.20		0.07	0.08	



235541018

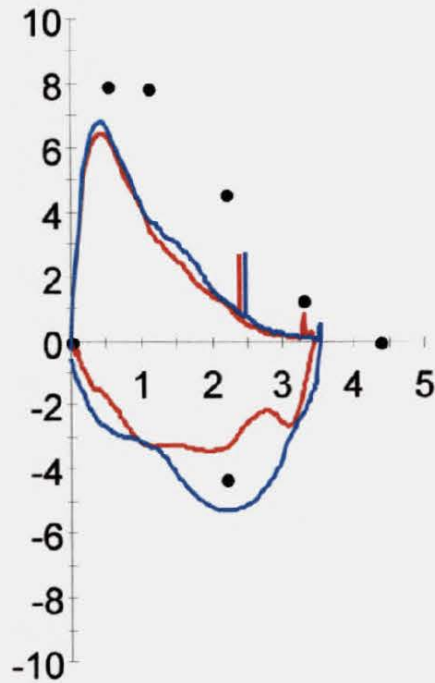
PULMONARY FUNCT. CONC 4/23/1939

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• Pred — Pre — Post

Pre

E



REF MD: JAIN, VIPUL
75 M PL: BLUE SHIELD HMO SAN*

CLOVIS COMMUNITY MEDICAL CENTER

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Tech: ONG, ARLENE RRT	Height: 180.20	Age: 75	Room: OP
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Time Select I-Lp Test M ATS

			FVC absolute	FVC % p/c	FEV1 absolute	FEV1 % p/c	FEF Max absolute
Pre							
10:48:14	*	*	3.35	76	2.26	71	6.42
10:49:54	*		3.45	79	2.39	75	6.38
10:51:39	*		3.46	79	2.35	74	6.12
ATS		Pre/Ba	3.46	79	2.39	75	6.42
Post							
12:13:54	*	*	3.49	+1	2.48	+3	6.81
12:14:28	*		3.55	+2	2.49	+4	6.76
12:16:01	*		3.40	-1	2.44	+1	6.79
ATS		Post	3.55	+2	2.49	+4	6.81

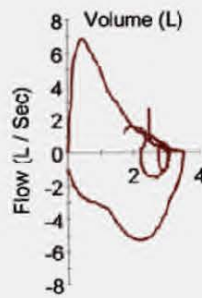
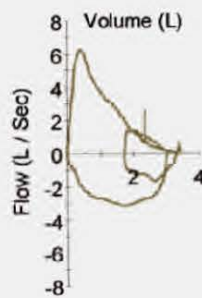
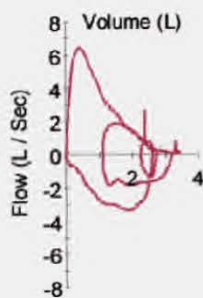
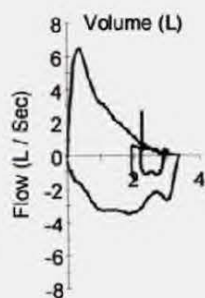
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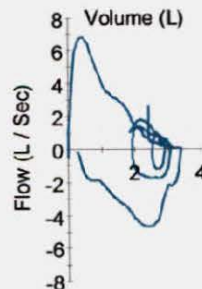
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12:13:54

12:14:28



12:16:01



235541018
 PCP: COPELAND, GREGORY, DO
 REF MD: JAIN, VIPUL
 75 M PL: BLUE SHIELD HMO SAN*

Patient: [REDACTED]

Encounter: 235541018

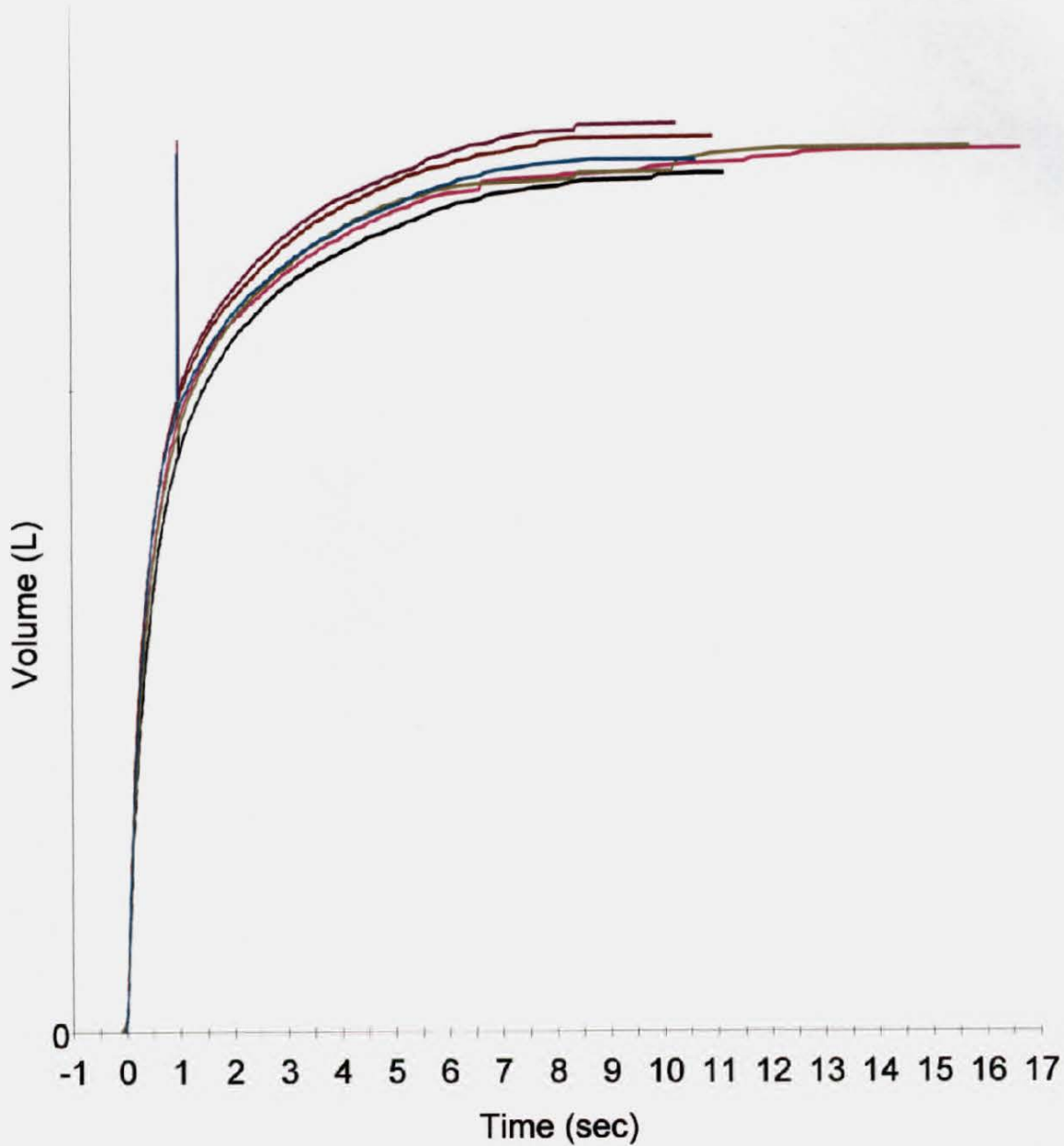
Page 4 of 5

CLOVIS COMMUNITY MEDICAL CENTER

2755 Herndon

Clovis, CA, 93612

Name: [REDACTED]	ID: [REDACTED]	Acct. 235541018	Date: 01/07/2015
Tech: ONG, ARLENE RRT	Height: 180.20	Age: 75	Room: OP
Doctor: JAIN, VIPUL	Weight: 119.40	Sex: Male	Race: Caucasian



235541018
PULMONARY FUNCT CCRC 4/3/1939

REF MD: JAIN, VIPUL
75 M PL: BLUE SHIELD HMO SAN*

INTERPRETATION CASE 2

COMMUNITY REGIONAL MEDICAL CENTER
2823 FRESNO ST
FRESNO, CA, 93715

Name: [REDACTED]	ID: [REDACTED]	Acct: 232712005	Date: 05/16/2014
Tech: REVILLA, BILL	Height: 178	Age: 64	Room: OP
Doctor: HANSEN-SMITH, KAREN J	Weight: 88	Sex: Male	Race: Caucasian

Diagnosis: ASTHMA

Dyspnea: On hills and stairs

Cough: Non-Productive

Wheeze: No Wheeze

Tbco Prod: Cigarette

Yrs Smk: 20.0

Pks/Day: 0.5

Yrs Quit: 30.0

Medications: Advair, taken yesterday; Ventolin, taken last week.

Pre Test Comments: The patient last ate a meal at 0700 PM yesterday.

Post Test Comments:

Calibration performed at: 0700 Software: BreezeSuite v. 7.1 SP4 Predicted module: NHANES III & ITS
Test time: 0810

The patient was seated. Good patient effort & cooperation. The results of this test meet the ATS standards for acceptability and repeatability. Verbal and written instructions were given on the proper use of MDIs and DPIs. Four puffs (360mcg) of Albuterol MDI were given using a valved holding chamber 15 minutes before the post test. The patient took the valved holding chamber with him upon completion of the test.

Bill Revilla, RRT, CPFT

5/16/14
920

	Pre-Bronch				Post Bronch		
	Actual	Pred	%Pred	SD	LLN	Actual	%Chng
--- SPIROMETRY ---							
FVC (L)	4.25	4.65	91	0.57	3.71	4.55	+7
FEV1 (L)	3.57	3.48	102	0.48	2.69	4.00	+12
FEV1/FVC (%)	84	75	111	6	65	*88	+4
FEV3 (L)	4.05					4.38	+8
FEV3/FEV6 (%)	96					96	+0
FEV6 (L)	4.24	4.41	96	0.55	3.50	4.55	+7
FEV1/FEV6 (%)	84	78	107	5	69	*88	+4
FEF 25-75% (L/sec)	4.19	2.77	151	0.97	1.17	*6.27	+49
FEF Max (L/sec)	*12.43	8.91	*139	1.41	6.58	*13.12	+5
FIVC (L)	4.03					4.45	+10
FIF Max (L/sec)	9.02					7.58	-15
--- LUNG VOLUMES ---							
SVC (L)	4.90	4.65	105	0.57	3.71		
IC (L)	3.52	3.33	105				
ERV (L)	1.38	1.32	104				
FRC(pl) (L)	3.63	3.69	98	0.72	2.25		
RV (Pleth) (L)	2.25	2.33	96	0.37	1.59		
TLC (Pleth) (L)	7.15	7.02	101	0.79	5.44		
RV/TLC (Pleth) (%)	31	34	92	4	25		
Trapped Gas (L)							



232712005
PULMONARY FUNCT. CMHC 3/8/1990

REF MD: HANSEN SMITH, KAREN J
64 M PL: BLUE CROSS ANTHEM P*

COMMUNITY REGIONAL MEDICAL CENTER
2823 FRESNO ST
FRESNO, CA, 93715

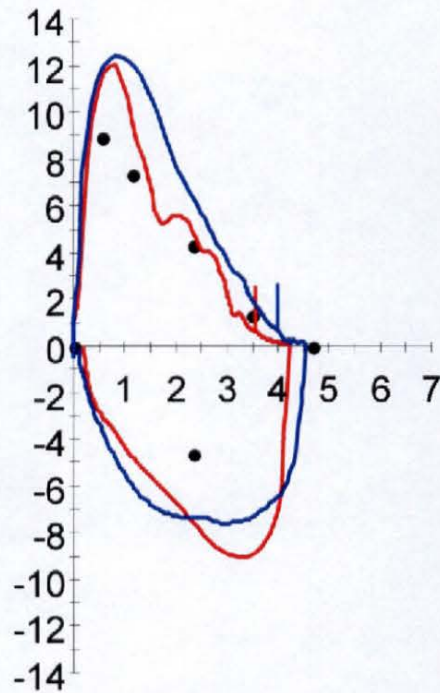
Name: [REDACTED] S	ID: [REDACTED]	[REDACTED]	Date: 05/16/2014
Tech: REVILLA, BILL	Height: 178	Age: 64	Room: OP
Doctor: HANSEN-SMITH, KAREN J	Weight: 88	Sex: Male	Race: Caucasian

	Pre-Bronch			Post Bronch		
	Actual	Pred	%Pred	SD	LLN	%Chng
--- DIFFUSION ---						
DLCOunc (ml/min/mmHg)	35.19	33.65	104	4.83	23.99	
DLCOcor (ml/min/mmHg)		33.65		4.83	23.99	
DL/VA (ml/min/mmHg/L)	5.23	4.81	108			
VA (L)	6.73	7.02	95	0.79	5.72	
--- AIRWAYS RESISTANCE --						
Raw (cmH2O/L/s)		1.45		0.48	0.66	
Gaw (L/s/cmH2O)		1.03				
sRaw (cmH2O*s)		4.76				
sGaw (1/cmH2O*s)		0.20		0.07	0.08	



COMMUNITY REGIONAL MEDICAL CENTER
2823 FRESNO ST
FRESNO, CA, 93715

Name:	[REDACTED]	ID:	[REDACTED] 6	Acct:	232712005	Date:	05/16/2014
Tech:	REVILLA, BILL	Height:	178	Age:	64	Room:	OP
Doctor:	HANSEN-SMITH, KAREN J	Weight:	88	Sex:	Male	Race:	Caucasian



• Pred — Pre — Post

Pre

E



J. *
REF MD: HANSEN SMITH, KAREN J
64 M PL: BLUE CROSS ANTHEM P*

COMMUNITY REGIONAL MEDICAL CENTER
2823 FRESNO ST
FRESNO, CA, 93715

Name: [REDACTED] Acct. 232712005 Date: 05/16/2014
Tech: REVILLA, BILL Height: 178 Age: 64 Room: OP
Doctor: HANSEN-SMITH, KAREN J Weight: 88 Sex: Male Race: Caucasian

Time Select I-L Test Mode ATS

			FVC absolute	FVC % Predicted	FEV1 absolute	FEV1 % p/c	FEF Max absolute
Pre							
08:13:52	*		3.83	82	3.45	99	*11.59
08:14:44	*	*	4.25	91	3.55	102	*12.43
08:15:07	*		4.24	91	3.57	102	*12.01
ATS		Pre/Ba	4.25	91	3.57	102	*12.43
Post							
08:58:50	*		4.53	97	3.94	+10	*12.84
08:59:13	*		4.47	96	3.98	+11	*13.12
08:59:50	*	*	4.55	97	4.00	+12	*12.31
ATS		Post	4.55	97	4.00	+12	*13.12

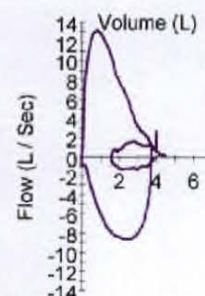
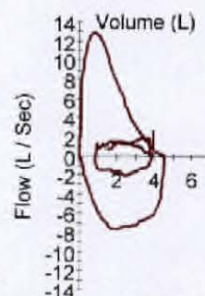
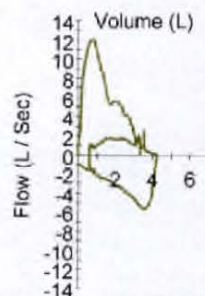
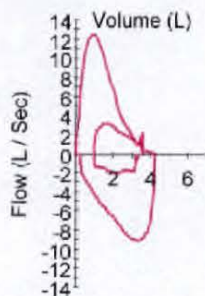
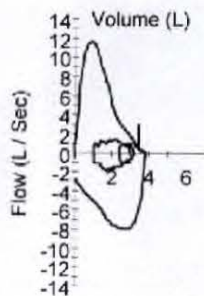
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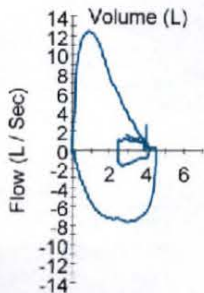
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08:58:50

08:59:13



08:59:50



232712005

PULMONARY FUNCTION TEST 3/8/1950

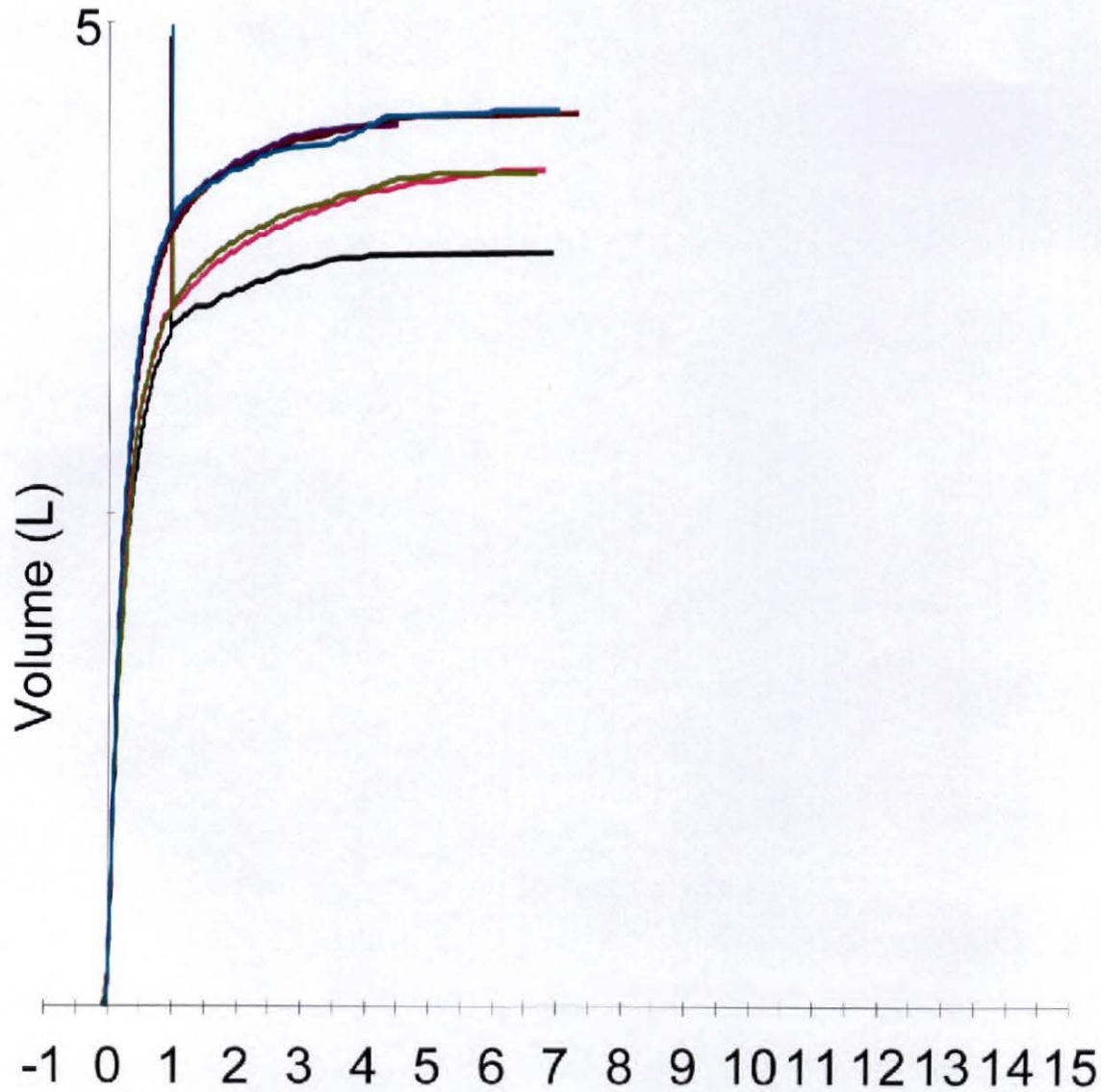
[REDACTED]

REF MD: HANSEN SMITH, KAREN J

64 M PL: BLUE CROSS ANTHEM P*

COMMUNITY REGIONAL MEDICAL CENTER
2823 FRESNO ST
FRESNO, CA, 93715

Name:	[REDACTED]	ID:	[REDACTED]	Acct:	232712005	Date:	05/16/2014
Tech:	REVILLA, BILL	Height:	178	Age:	64	Room:	OP
Doctor:	HANSEN-SMITH, KAREN J	Weight:	88	Sex:	Male	Race:	Caucasian



INTERPRETATION CASE 3

Community Medical Center, Fresno
PO Box 1232
Fresno, CA, 93715

Name: [REDACTED]	ID: [REDACTED]	Acct: 232379826	Date: 03/31/2014
Tech: PETERSON, PATTIE	Height: 188	Age: 69	Room: OP
Doctor: JAIN, VIPUL	Weight: 98.0	Sex: Male	Race: Caucasian

Diagnosis: ASTHMA

Dyspnea: After any exertion

Cough: Productive

Wheeze: Frequent

Tbco Prod: Never Smoked

Yrs Smk:

Pks/Day:

Yrs Quit:

Medications: SPRIVIA & ADVAIR 100/50 last taken yesterday AM
SINGULAIR - taken last night

Pre Test Comments: Pre and Post testing ordered

Post Test Comments:

Calibration performed at: 1500 Software: BreezeSuite v. 7.1 SP4 Predicted module: NHANES III & ITS Test time: 1600

The patient was seated. Good patient effort & cooperation. The results of this test meet the ATS standards for acceptability and repeatability. Four puffs (360mcg) of Albuterol MDI were given using a valved holding chamber 15 minutes before the post test. The patient took the valved holding chamber with him upon completion of the test. Verbal instructions were given on the proper use of MDIs and DPIs. EXPOSURES: Patient was a fireman for 18 yrs. Has been hospitalized for smoke inhalation 3 times. He has farmed all his life.

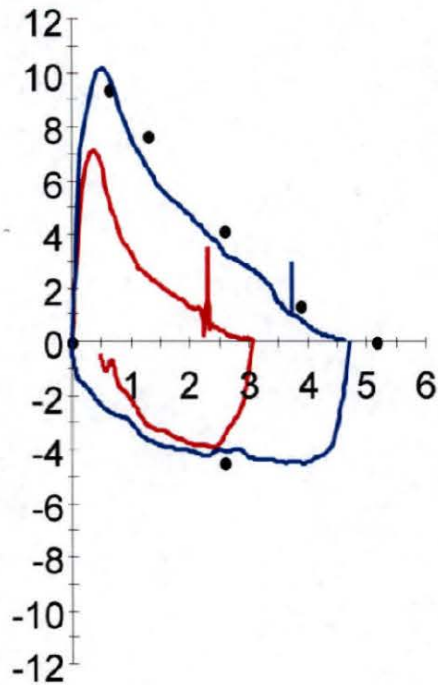
Pattie Peterson 1705
Pattie Peterson, RPFT 3-31-14

	Pre-Bronch			Post Bronch			
	Actual	Pred	%Pred	SD	LLN	Actual	%Chng
--- SPIROMETRY ---							
FVC (L)	3.06	5.15	59	0.63	4.11	4.60	+50
FEV1 (L)	2.31	3.81	60	0.54	2.92	3.75	+62
FEV1/FVC (%)	75	74	101	6	64	82	+8
FEV3 (L)	2.83					4.43	+56
FEV3/FEV6 (%)	93					96	+3
FEV6 (L)	3.06	4.89	62	0.62	3.87	4.60	+50
FEV1/FEV6 (%)	74	78	94	5	69	81	+9
FEF 25-75% (L/sec)	1.66	2.90	57	1.09	1.10	5.62	+239
FEF Max (L/sec)	7.11	9.38	75	1.57	6.79	10.12	+42
FIVC (L)	2.57					4.70	+82
FIF Max (L/sec)	3.93					4.51	+14


 232179826
 PULMONARY FUNCT. TEST 2/17/1845
 PCP: GROMIS, MICHAEL W. MD
 REF MD: JAIN, VIPUL
 69 M PL: BLUE SHIELD PPO 130*

Community Medical Center, Fresno
PO Box 1232
Fresno, CA, 93715

Name: [REDACTED]	ID: [REDACTED]	Acct. 232379826	Date: 03/31/2014
Tech: PETERSON, PATTIE	Height: 188	Age: 69	Room: OP
Doctor: JAIN, VIPUL	Weight: 98.0	Sex: Male	Race: Caucasian



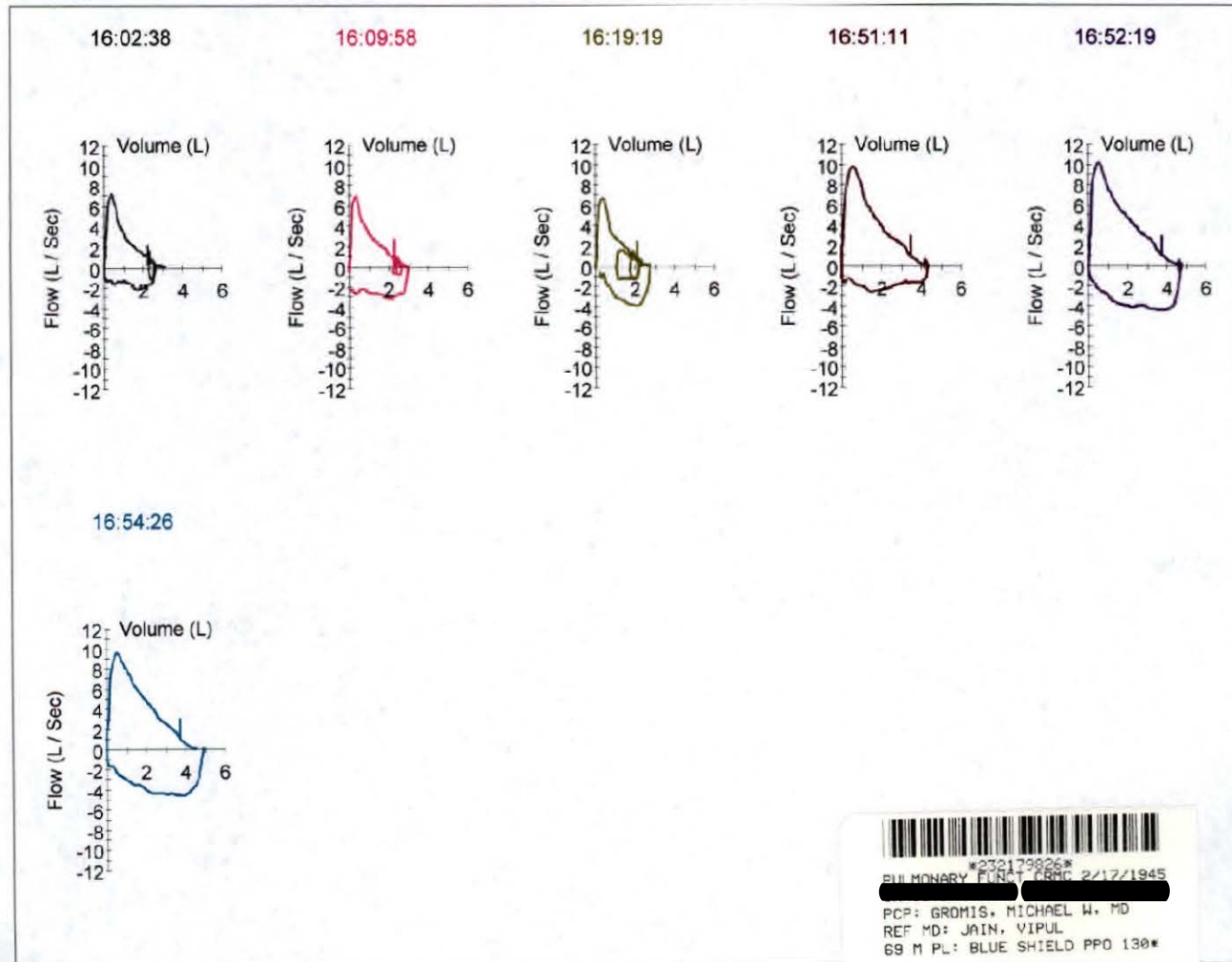
• Pred — Pre — Post

232179826*
232179826 2/17/1945
PCP: GROMIS, MICHAEL W. MD
REF MD: JAIN, VIPUL
69 M PL: BLUE SHIELD PPQ 130*

Community Medical Center, Fresno
PO Box 1232
Fresno, CA, 93715

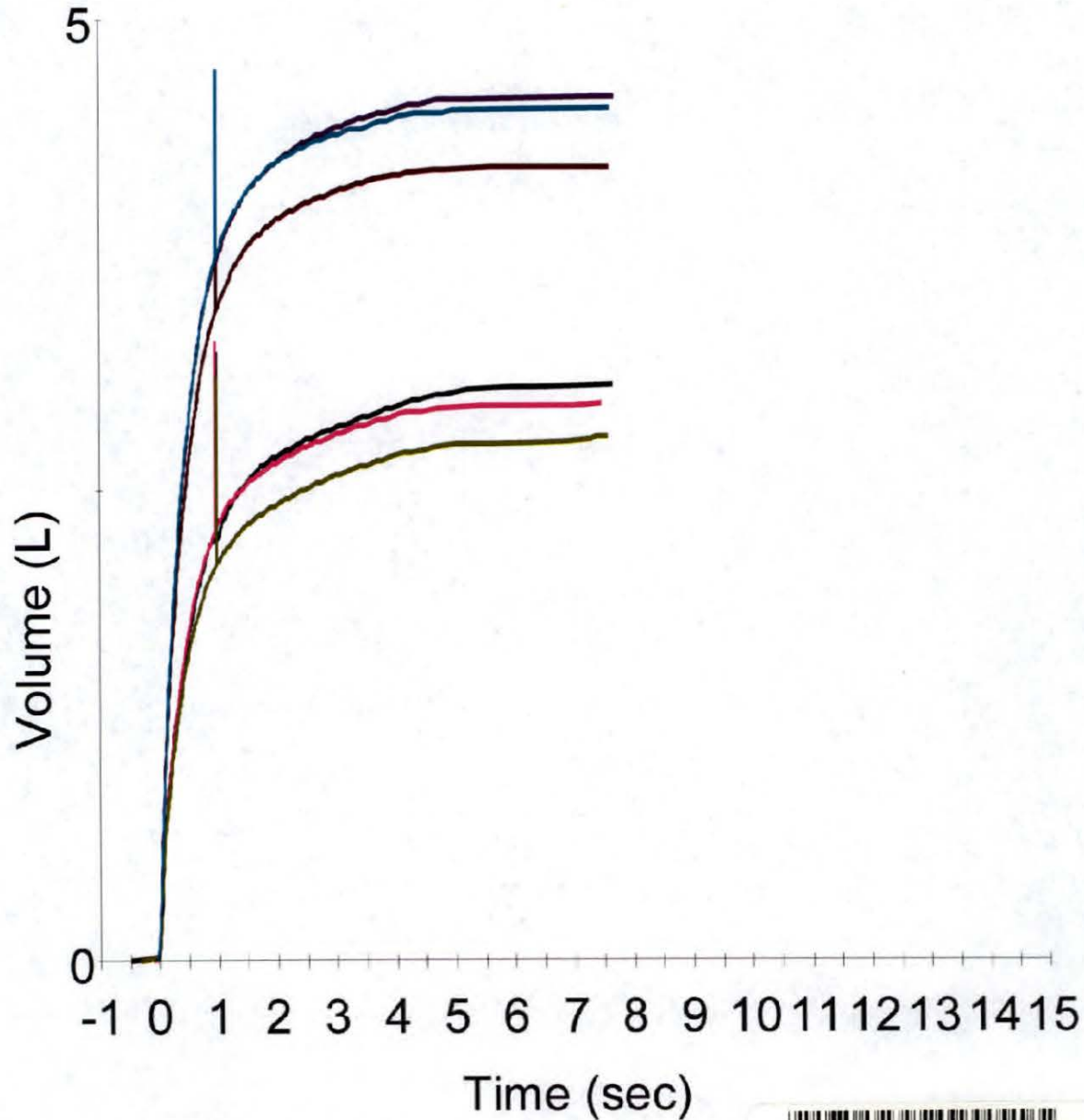
Name: [REDACTED]	ID: [REDACTED]	Acct: 232379826	Date: 03/31/2014
Tech: PETERSON, PAITIE	Height: 188	Age: 69	Room: OP
Doctor: JAIN, VIPUL	Weight: 98.0	Sex: Male	Race: Caucasian

Time	Select	I-Lp Test Mode	ATS	FVC absolute	FVC % Predicted	FEV1 absolute	FEV1 % p/c
Pre							
16:02:38	*			3.06	59	2.26	59
16:09:58	*			2.96	57	2.31	60
16:19:19	*	*		2.78	54	2.12	55
ATS		Pre/Baselin		3.06	59	2.31	60
Post							
16:51:11	*			4.22	82	3.47	+50
16:52:19	*			4.60	89	3.73	+61
16:54:26	*			4.53	87	3.75	+62
ATS		Post		4.60	89	3.75	+62



Community Medical Center, Fresno
PO Box 1232
Fresno, CA, 93715

Name: [REDACTED] A	ID: [REDACTED]	Acct. 232379826	Date: 03/31/2014
Tech: PETERSON, PATTIE	Height: 188	Age: 69	Room: OP
Doctor: JAIN, VIPUL	Weight: 98.0	Sex: Male	Race: Caucasian



232179826

PULMONARY FLOWMETER 2/12/1945

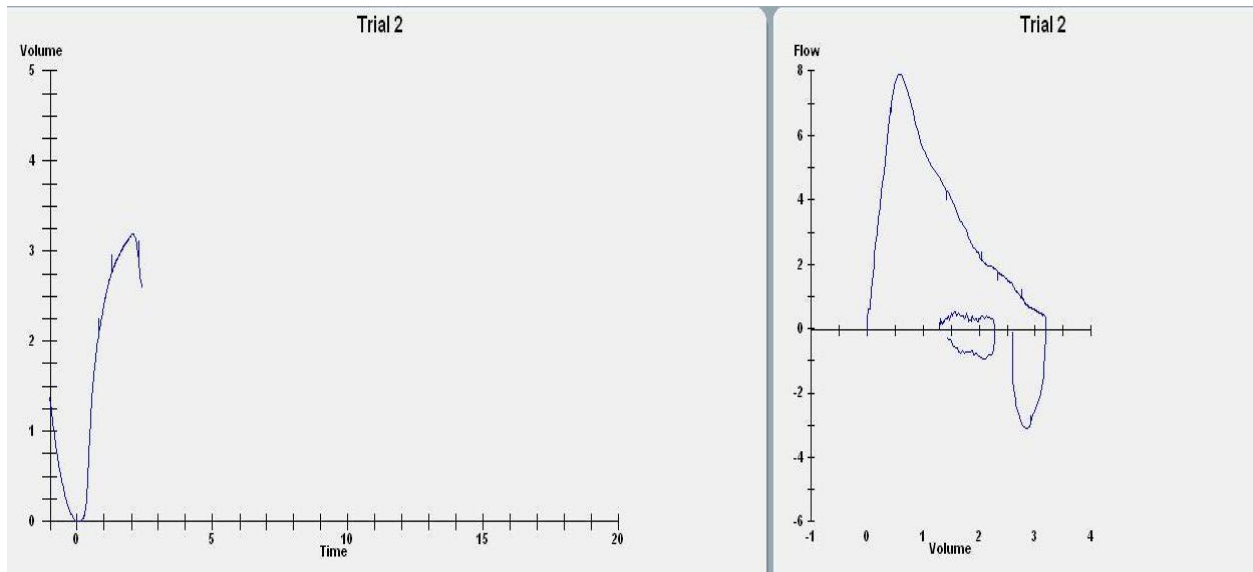
PCP: GROMIS, MICHAEL W, MD

REF MD: JAIN, VIPUL

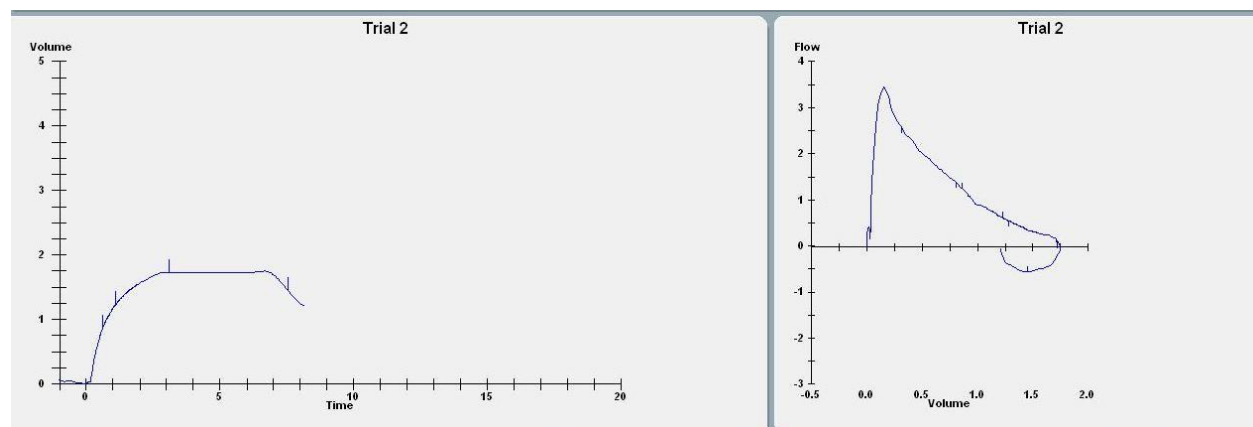
69 M PL: BLUE SHIELD PPO 130*

FVC Maneuver Quality Cases

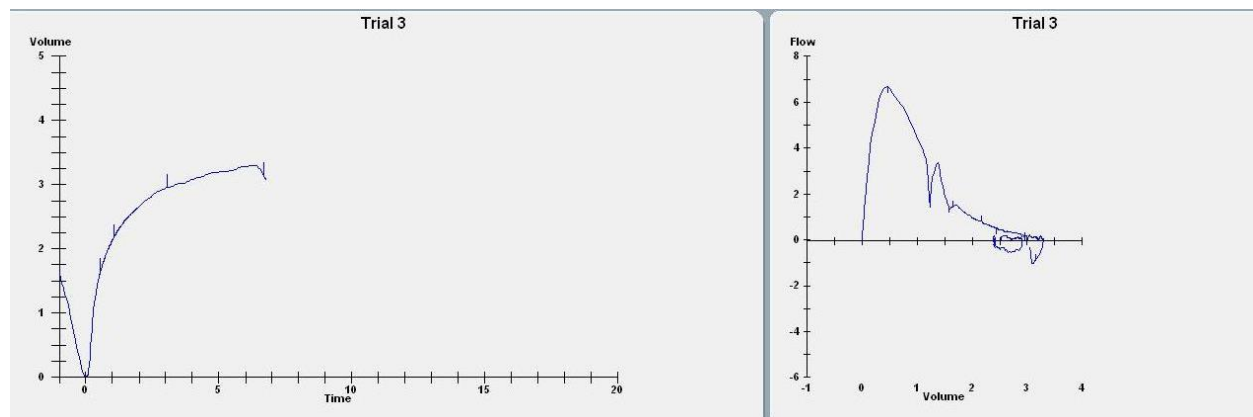
Case 1



Case 2



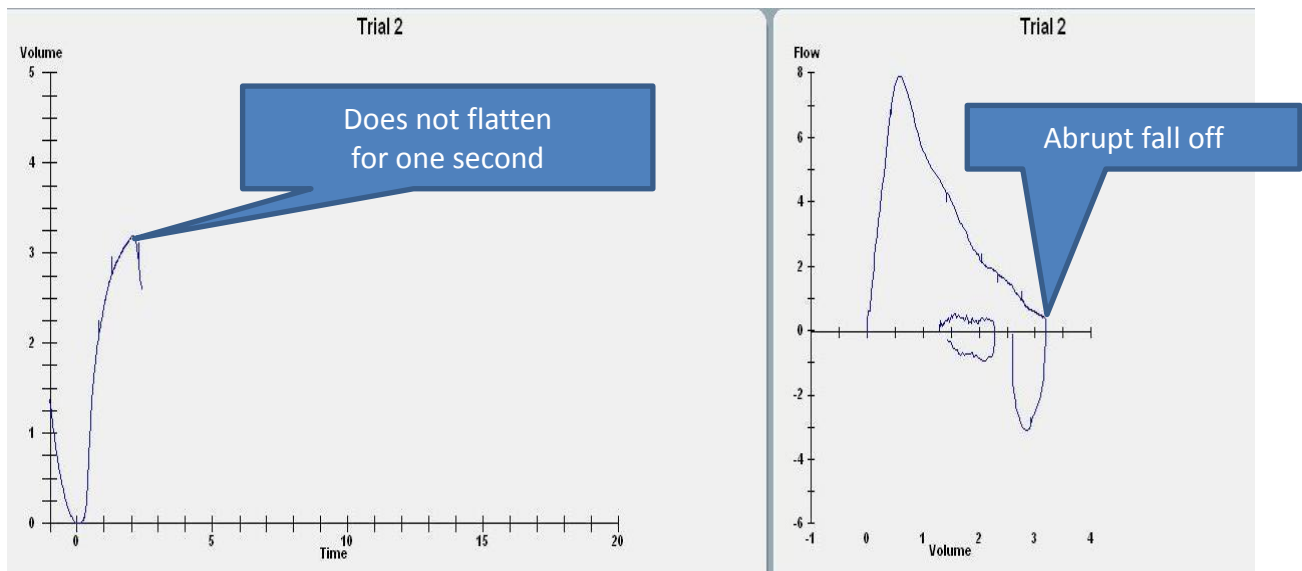
Case 3



Acceptability criteria summary

- **Good start**
 - Initial portion of the curve (most effort dependent) should be free from artifact AND
 - Extrapolated volume (Vext) should be < 5% of FVC
- **Satisfactory expiratory time**
 - Duration of exhalation is ≥ 6 s or at least a 1 second plateau is reached (volume-time curve)
- **Freedom from artifacts including:**
 - Cough during the 1st second of exhalation
 - Closure of the glottis
 - Early termination or cut-off
 - Submaximal effort throughout
 - Air leak
 - Obstructed mouthpiece

Case 1



Early Termination

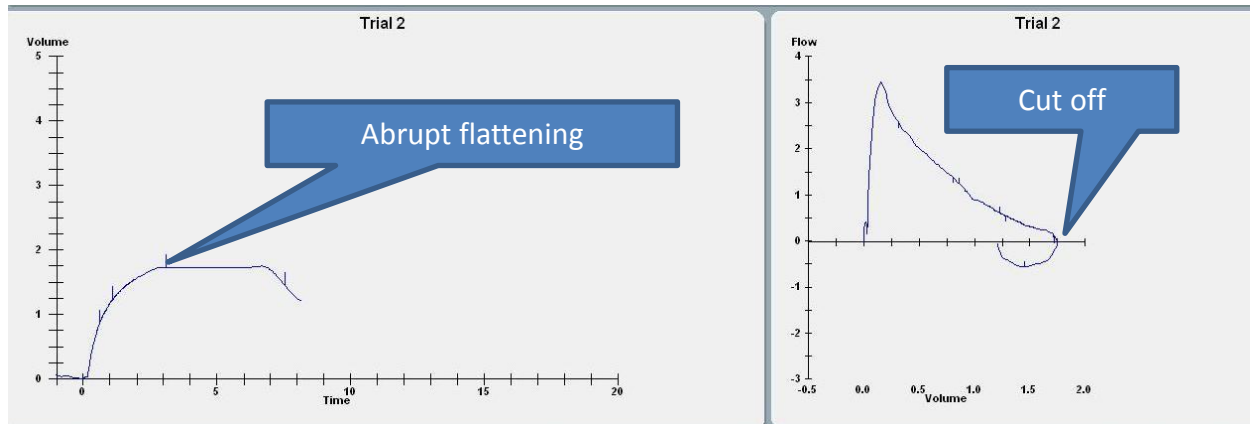
- VT curves with short or absent plateaus
- FV curves show abrupt drop off at the end
- The FET (forced expiratory time) under 6 seconds
- *Exception, known restrictive lung disease, one second plateau is acceptable
-

Correcting Early Termination

- Focus on END of TEST, blowing long and hard
- Coach patient to make a sustained effort
- Make sure the patient understands to empty lungs

- Cue the patient counting with six fingers “1...2...3...4...5...6”
- Use incentive screen

Case 2



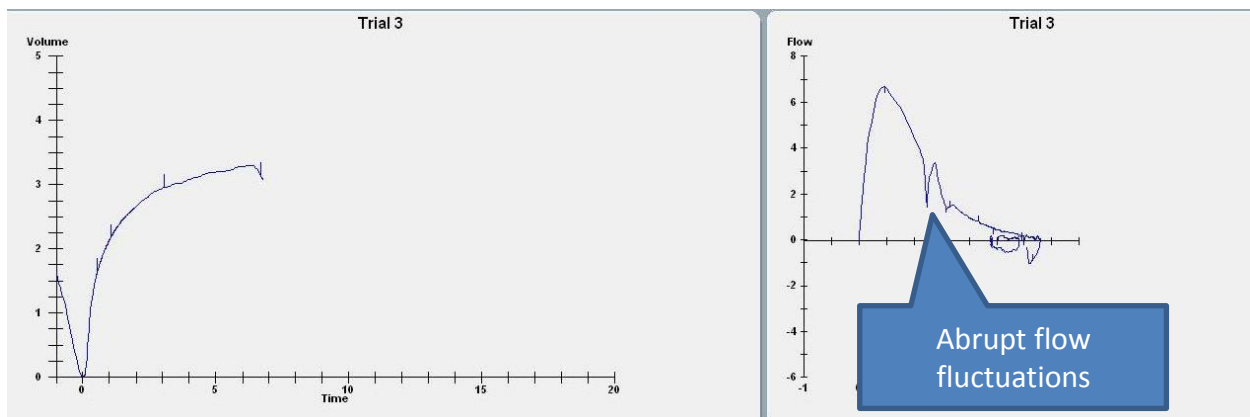
Glottic closure

- Appears like early termination on FV curve
- VT curve looks like it is drawn with a ruler
- FET very short despite patient sustained effort
- FET may not match the VT curve
- Patient may report sudden tightening near larynx

Correcting glottic closure

- Instruct patient to try to relax upper airway
- Instruct patient to relax, holding their head in a slight sniff position
- The patient should continue to blow until being told to stop

Case 3



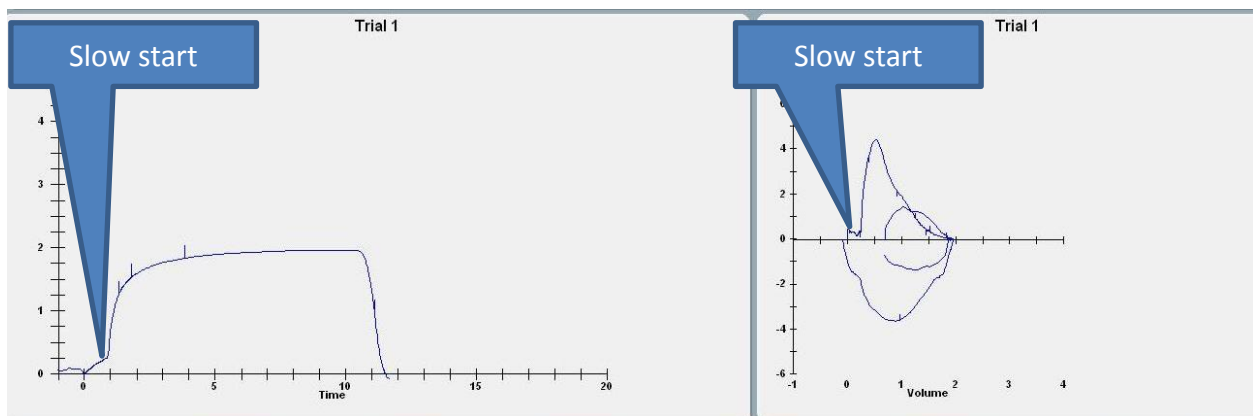
Cough

- Cough in first second invalidates effort
- Stop and reassess (patient may be unable to continue)
- Some efforts may still be valid (if cough occurs > 1 second after start)

Cough in first second

- Deflection on the FV curve will be seen as well as dips in the VT curve at the one second mark
- On the FV curve note the volume where the deflection occurs. Then go to the VT curve and look for a dip at the volume noted from the FV curve

Case 4



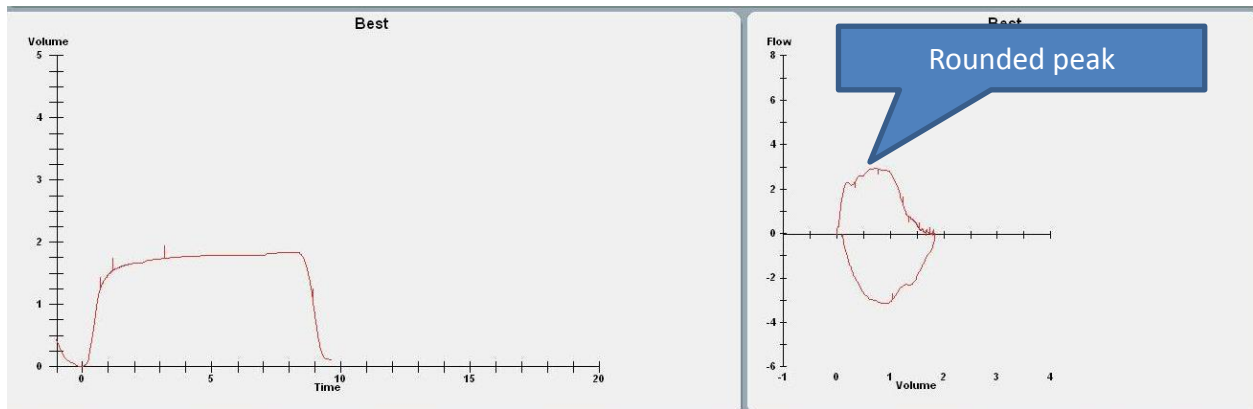
Slow start and hesitation

- FV Curve will be leaning or shifted to the right without a brisk incline
- VT Curve will display a slow take off
- Back extrapolated volume will be too high

Correcting slow start

- Concentrate on a fast blast immediately after a full inhalation
- Be enthusiastic and don't settle on a poor effort!

Case 5

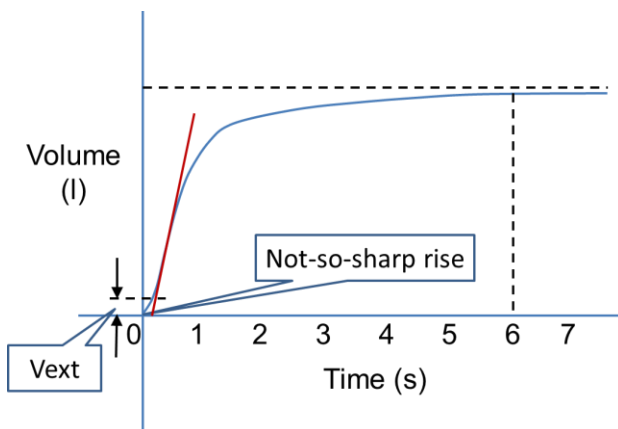


Poor initial blast/submaximal effort

- FV Curve will display a rounded or flat peak
- VT Curve will display decreased rise/slope

Correcting poor initial blast

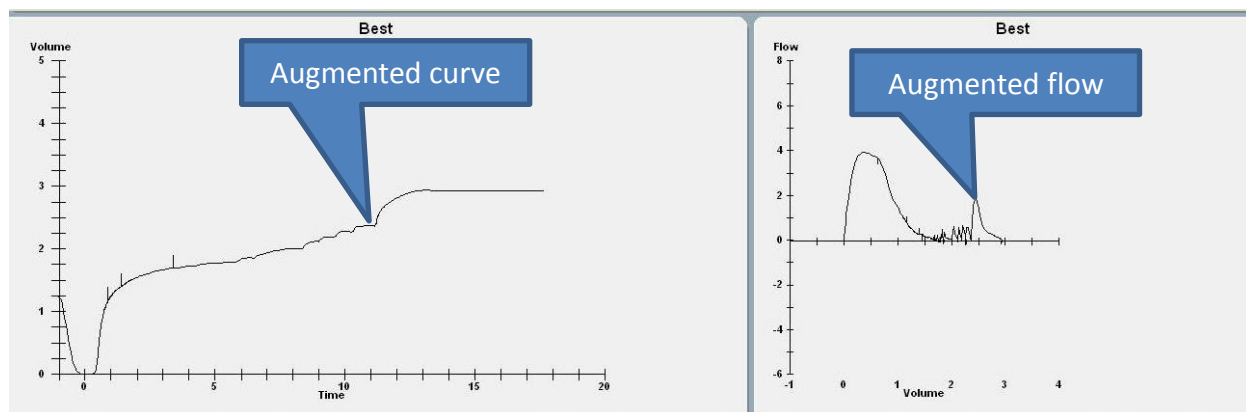
- Reinstruct and demonstrate
- “As hard and as fast as you can...”
- Use examples



Extrapolated volume (Vext)

- Quantification of “delay” to reach linear portion of volume-time upstroke
- Considered unacceptable if it exceeds 0.15 liters or 5% of the FVC, whichever is larger

Case 6



Extra breath

- VT: will see the start of a plateau and then another rapid rise
- FV: will see the flow start to increase again after it is first declining

Correcting extra breaths

- Instruct the patient to fully exhale in one long maneuver without stopping to pull more air in
- A nose clip may also be necessary to prevent the patient from breathing in through their nose and breathing out through their mouth

Case 7

Reproducibility criteria

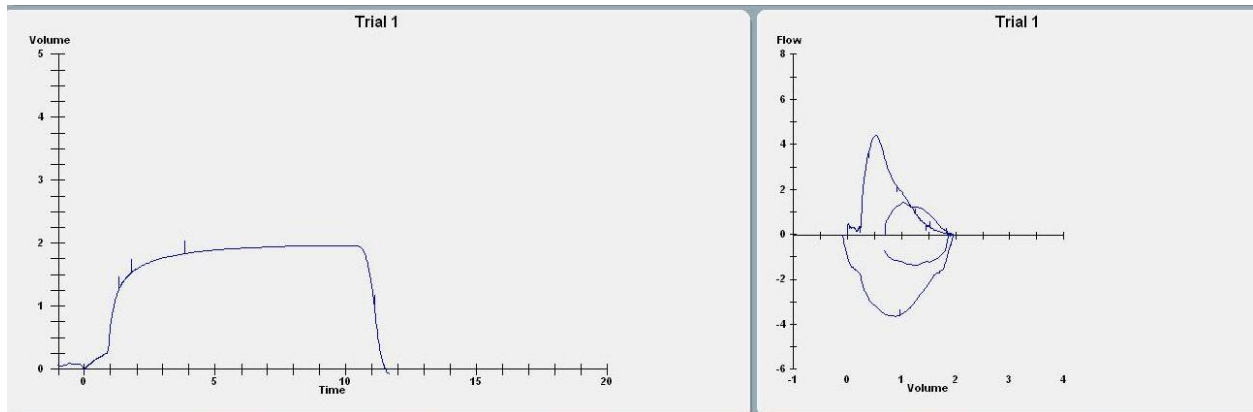
- After 3 acceptable maneuvers have been obtained, assess whether the following reproducibility criteria are met:
- The 2 largest FVC values are within 0.15 L of each other
- Or, the 2 largest FEV1 values are within 0.15 L of each other
- Spirometry Pre-test
- FVC (L)

1.33	1.38	1.33
.80	.81	.79
- FEV1 (L)

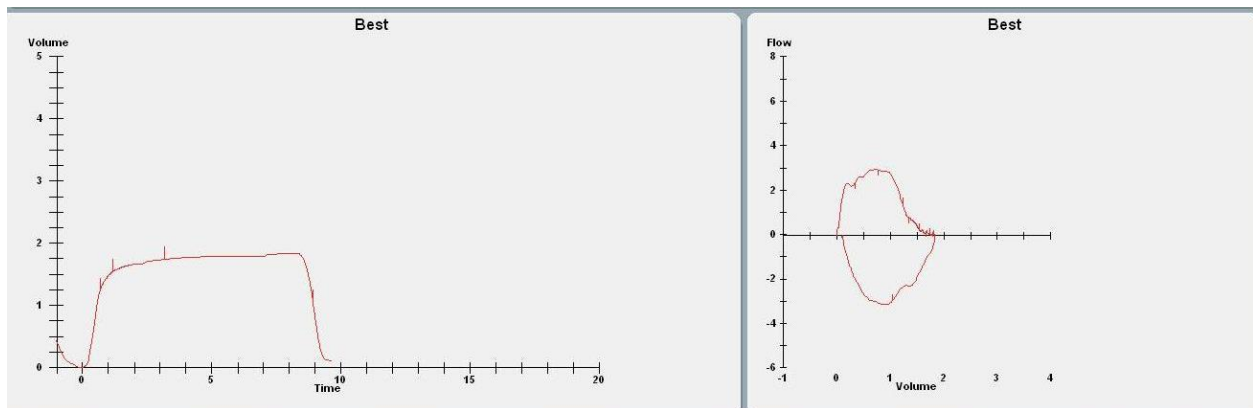
1.33	1.38	1.33
.80	.81	.79
- The two largest of either the FVC or FEV1 values are within 0.15 L of each other

1. Miller M R, Hankinson J, Brusasco V et al. Standardisation of Spirometry. European Respiratory Journal 2005;26(2)319-38.
2. American Thoracic Society. Guidelines for the measurement of respiratory function. Respiratory Medicine 1994 (88)165-194.
3. Spirometry 360 Learning Laboratory. <http://www.spirometry360.org/spiro360resources/>

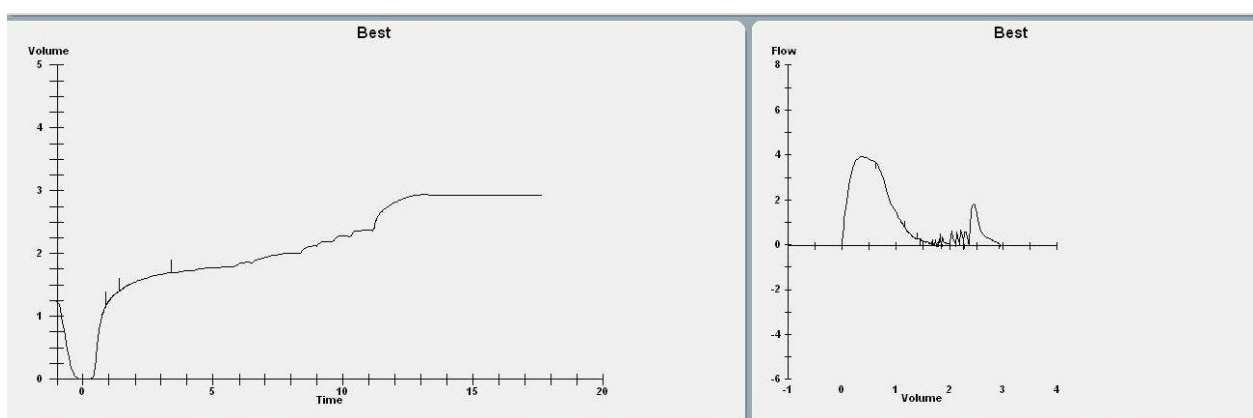
Case 4



Case 5



Case 6



Case 7

- Three **acceptable** efforts were obtained. Are these efforts considered **reproducible**?
- FVC (L) 1.33 1.38 1.33
- FEV1 (L) .80 .81 .79

INHALER USE

Stephanie Tsao, MSN, RN, ANP-BC, ZSFGH
Ni-Chang Liang, MD, UCSD

Saturday September 30, 2017 – 1:00 p.m. – 2:35 p.m.

Stephanie Tsao, MSN, RN, ANP-BC is the Program Director for the Healthy San Francisco Asthma/COPD Program, which aims to develop innovative ways to improve the quality of asthma and COPD care delivered within the SF safety net system. She is the lead clinician for the Asthma-COPD Clinic based at Zuckerberg San Francisco General Hospital.

Ni-Cheng Liang, MD, is an Assistant Clinical Professor at UCSD and is the Medical Director of Pulmonary Services at the UCSD Center for Pulmonary and Sleep Medicine. She is also the Executive Director for the UCSD Center for Mindfulness, and serves as Co-Chair of the American Thoracic Society Integrative Therapies Interest Group. She runs the multidisciplinary Airway Clinic for patients with obstructive lung disease. She is a member of the UCSD COPD Committee and is passionate about improvement in healthcare delivery for patients with COPD. She also has a special interest in integrative medicine, particularly using mindfulness based practices to improve the quality of life for patients with chronic lung disease.

Table 1: Inhaler types and critical steps for correct use

Type	Need for coordination	Speed of inhalation
Metered dose inhaler (MDI)	Yes	Slow 3-5 seconds
Dry powder inhaler (DPI)	No, but sufficient inspiratory flow is needed	Fast 1-2 seconds
Soft mist inhaler (SMI) Respimat®	Yes	Slow 3-5 seconds

Table 2: Strategies to ensure effective use of inhaler devices

CHOOSE

- Choose the most appropriate inhaler for the patient before prescribing. Consider patient physical barriers (e.g. arthritis), patient skills, medication options, the available devices, and cost.
- Avoid use of multiple different inhaler types to minimize confusion.
- If options are available, encourage patient participation in the choice.
- For MDIs, use of a spacer improves delivery and reduces the potential for side effects.

COACH

- Build knowledge and skills (Educate patient about action of medication, role (controller vs. rescue), dosing and frequency, correct inhaler technique, device care, priming, and knowing when to get refills)
- Engage and motivate

CHECK

- Check inhaler technique at every opportunity.
- Ask the patient to demonstrate how they use their inhaler.
- Identify any errors using a device-specific checklist.

CORRECT

- Show the patient how to use the device correctly with a physical demonstration.
- Check technique again. You may need to repeat this process multiple times and over multiple visits.
- Consider an alternative device if the patient cannot use the inhaler correctly after repeated training.
- Errors in technique often occur within 4-6 weeks of initial training.

CONFIRM

- Clinicians should be able to demonstrate correct technique for each of the inhalers they prescribe.
- Pharmacists, nurses, and respiratory therapists can provide highly effective inhaler skills training.

Adapted from Box 3-11. Global Strategy for Asthma Management and Prevention. Updated 2016.

Inhaler Device Training - Checklist

MDI	MDI with spacer	Respimat®	Key Education Points to Review
1. Check dose counter before each use. 2. Take off cap. 3. Shake inhaler 10 times. 4. Stand or sit up straight. 5. Breathe out all the way. 6. Seal lips tightly around mouthpiece. 7. Start breathing in slowly and press down on the canister one time. Keep breathing in SLOWLY and DEEPLY. 8. When lungs are full, take inhaler out of mouth. 9. Hold breath for 10 seconds or as long as one can. Breathe out normally. 10. If another puff is needed, wait one minute. Then repeat steps 3-9. 11. Put cap back on inhaler.	1. Check dose counter before each use. 2. Take off cap. Put mouthpiece into back of spacer. 3. Shake inhaler 10 times. 4. Stand or sit up straight. 5. Breathe out all the way. 6. Seal lips tightly around spacer mouthpiece. 7. Press down on canister one time. Then, breathe in SLOWLY and DEEPLY through mouth. If the spacer whistles like a harmonica, inhalation was too fast. 8. When lungs are full, take spacer out of your mouth. 9. Hold breath for 10 seconds or as long as one can. Breathe out normally. 10. If another puff of medicine is needed, wait one minute. Then repeat steps 3-9. 11. Put cap back on inhaler.	1. Check dose counter before each use. 2. Hold inhaler upright. Keep cap closed. 3. Turn clear base in the direction of the white arrows on the label until it clicks (half a turn). 4. Flip cap open. 5. Stand or sit up straight. 6. Breathe out all the way. 7. Seal lips tightly around mouthpiece. Do not cover air vents. 8. Start breathing in slowly and press down on the dose release button. Keep breathing in SLOWLY and DEEPLY. 9. When lungs are full take inhaler out of mouth. 10. Hold breath for 10 seconds or as long as one can. 11. Breathe out normally. 12. If another puff of medicine is needed, repeat steps 5-11. 13. Close cap over the mouthpiece after each use.	- Action of medication - Identify controller vs. rescue - Reinforce prescribed dose and frequency - Anticipatory guidance about what to expect. - Potential adverse effects. Instruct to rinse mouth, gargle, and spit after use of inhaled corticosteroids. - Correct inhaler technique - Inhaler and spacer care. - Priming. See inhaler grid for inhaler-specific instructions. - Knowing when to get refills.
Handihaler®	Ellipta®	Respiclick®	Notes:
1. Pull up cap. 2. Pull up mouthpiece. 3. Put capsule in chamber. 4. Close mouthpiece until it clicks. Hold inhaler so mouthpiece faces up. 5. Push green button ONE time. 6. Stand or sit up straight. 7. Breathe out all the way. Do NOT breathe into mouthpiece. 8. Seal lips tightly around mouthpiece. 9. Breathe in FAST and DEEP through mouth. Capsule should be heard "rattling" in the chamber. 10. When lungs are full take inhaler out of mouth. 11. Hold breath for at least 10 seconds or as long as one can. 12. Breathe out normally. Repeat steps 6-12. 13. Lift up mouthpiece. Shake capsule out of chamber. Do not touch capsule.	1. Check dose counter before each use. 2. Slide cover down until it "clicks". This loads one dose of medicine to breathe in. 3. Stand or sit up straight. 4. Breathe out all the way. Do NOT breathe into mouthpiece. 5. Seal lips tightly around mouthpiece. 6. Breathe in FAST and DEEP through mouth. Do not block air vents with fingers. 7. When lungs are full take inhaler out of mouth. 8. Hold breath for at least 3-4 seconds. 9. Breathe out normally. 10. Slide cover back over mouthpiece.	1. Check dose counter before each use. 2. Make sure cap is closed before each dose is taken. 3. Hold inhaler straight up. 4. Pull cap all the way back until it "clicks". 5. Stand or sit up straight. 6. Breathe out all the way. Do NOT breathe into mouthpiece. 7. Seal lips tightly around the mouthpiece. 8. Breathe in FAST and DEEP through mouth. Do NOT block vent above mouthpiece. 9. When lungs are full take inhaler out of mouth. 10. Hold breath for 10 seconds or as one can. 11. Breathe out normally. 12. Check dose counter to make sure dose was breathed in. 13. Close cap over mouthpiece after each use.	

 Healthy Kids Program National QIG Program	Short-acting bronchodilators							This document is intended for clinical use only.	
	Short-acting beta ₂ -agonist					Short-acting anticholinergic	Combination short-acting bronchodilator	Notes:	
Name	ProAir® HFA <i>albuterol sulfate</i> 	ProAir® Respiclick <i>albuterol sulfate inhalation powder</i> 	Proventil® HFA <i>albuterol sulfate</i> 	Ventolin® HFA <i>albuterol sulfate</i> 	Xopenex HFA® <i>levalbuterol tartrate</i> 	Atrovent® HFA <i>ipratropium bromide</i> 	Combivent® Respimat® <i>ipratropium bromide and albuterol</i> 	Sources: 1. National Institutes of Health. Estimated Comparative Daily Doses of Inhaled Corticosteroids. Guidelines from the National Asthma Education and Prevention Program: Expert Panel Report 3. 2. Global Initiative for Asthma. Low, medium, and high daily doses of inhaled corticosteroids (mcg). Global Strategy for Asthma Management and Prevention: Updated 2016.	
Type of inhaler	MDI	MDI	MDI	MDI	MDI	MDI	SMI		
Dose counter	Yes	Yes	No	Yes	No	Yes	Yes; counts down by 30		
Adult standard daily dosing	1-2 inh Q4-6 hrs PRN	1-2 inh Q4-6 hrs PRN	1-2 inh Q 4-6 hrs PRN	1-2 inh Q 4-6 hrs PRN	1-2 inh Q 4-6 hrs PRN	2 inh 4x/d. Not to exceed 12 inh/d	1 inh up to 4x/d. Not to exceed 6 inh/d		
Shaking and priming	Shake well and spray 3 times before first use or after 2 weeks of no use	N/A	Shake well and spray 4 times before first use or after 2 weeks of no use	Shake well and spray 4 times before first use or after 2 weeks of no use or after dropping	Shake well and spray 4 times before first use or after 3 days of no use	Shake well and spray 2 times before first use or after 3 days of no use	Do not shake. Spray 4 times before first use or after 21 days of no use. Spray once after 3 days of no use.		
Inhaled corticosteroids (ICS)									
Name	Aerospan® 80 mcg <i>flunisolide</i> 	Alvesco® HFA 80 mcg, 160 mcg <i>ciclesonide</i> 	Arnuity™ Ellipta® 100 mcg, 200 mcg <i>fluticasone furoate</i> 	Flovent® Diskus® 50 mcg, 100 mcg, 250 mcg <i>fluticasone propionate inhalation powder</i> 	Flovent® HFA 44 mcg, 110 mcg, 220 mcg <i>fluticasone propionate</i> 	Pulmicort Flexhaler™ 90 mcg, 180 mcg <i>budesonide inhalation powder</i> 	QVAR® HFA 40 mcg, 80 mcg <i>beclomethasone dipropionate</i> 	Asmanex® Twisthaler® 110mcg, 220mcg <i>mometasone furoate inhalation powder</i> 	Asmanex® HFA 100 mcg, 200 mcg <i>mometasone furoate</i> 
Type of inhaler	MDI	MDI	DPI	DPI	MDI	DPI	MDI	DPI	MDI
Dose counter	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adult standard daily dosing ^{1,2}	Low: 2 puffs BID Med: 3-4 puffs BID High: >4 puffs BID	Low: 80-160 mcg Medium: > 160-320mcg High > 3200 mcg	Initial: 100mcg 1 inh QD Max: 200mcg 1 inh QD	Low: 100 - 300 mcg Medium: 300 - 500 mcg High: > 500 mcg	Low: 88 - 264 mcg Medium: 264 - 440 mcg High: > 440 mcg	Low: 180 - 600 mcg Medium: 600 - 1200 mcg High > 1200 mcg	Low: 80 - 240 mcg Medium: >240 - 480 mcg High: > 480 mcg	Low: 200 mcg Medium: 400mcg High: > 400 mcg	Low: 100mcg 1 puff BID Med: 200 mcg 1 puff BID High: 200mcg 2 puffs BID
Shaking and priming	Shake well and spray 2 times before first use or after 2 weeks of no use.	Shake well and spray 3 times before first use or after 10 days of no use.	N/A	N/A	Spray 4 times before first use. Spray 1 time after 7 days of no use or after dropping. Shake well for 5 seconds before each spray.	Do not shake. To prime, twist and click 2 times before first use.	Shake well and spray 2 times before first use or after 10 days of no use.	N/A	Shake well and spray 4 times before first use or 5 days of no use.

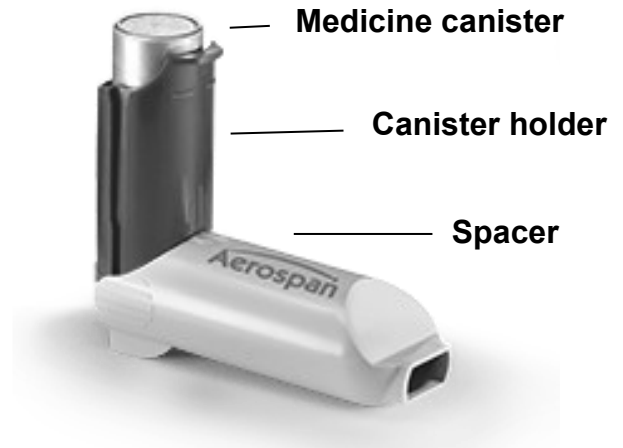
 	Long-acting bronchodilators									
	Long-acting beta ₂ -agonist (LABA)				Long-acting anticholinergic					
Name	Arcapta™ Neohaler™	Foradil® Aerolizer®	Serevent® Diskus®	Striverdi®Respimat®	Incruse® Ellipta®	Seebri™ Neohaler®	Spiriva® Handihaler®	Spiriva® Respimat® 1.25mcg, 2.5 mcg	Tudorza® Pressair®	
	<i>indacaterol inhalation powder</i>	<i>formoterol fumarate inhalation powder</i>	<i>salmeterol xinafoate inhalation powder</i>	<i>olodaterol</i>	<i>umeclidinium</i>	<i>glycopyrrolate</i>	<i>tiotropium bromide</i>	<i>tiotropium bromide</i>	<i>aclidinium bromide</i>	
										
Type of inhaler	DPI	DPI	DPI	SMI	DPI	DPI	DPI	SMI	DPI	
Dose counter	No	No	Yes	Yes	Yes	No	No	Yes	Yes	
Adult standard daily dosing	1 inh once daily	1 inh Q12 hr	1 inh Q12 hr	2 inh once daily	1 inh once daily	1 inh Q12 hr	1 cap once daily	Asthma: 1.25mcg COPD 2.5mcg 2 inh once daily	1 inh Q12 hr	
Shaking and priming	N/A	N/A	N/A	Do not shake. Spray 4 times before first use or after 21 days of no use. Spray once after 3 days of no use.	N/A	N/A	N/A	Do not shake. Spray 4 times before first use or after 21 days of no use. Spray once after 3 days of no use.	N/A	
	Combination medications									
	Inhaled corticosteroid and long-acting beta ₂ -agonist					Long-acting beta ₂ -agonist and long-acting anticholinergic				
Name	Advair Diskus® 100/50 250/50 500/50	Advair® HFA 45/21 115/21 230/21	Breo® Ellipta® 100/25 200/25	Dulera® HFA 100/5 200/5	Symbicort® HFA 80/4.5 160/4.5	Anoro® Ellipta®	Bevespi Aerosphere™	Stiolto™ Respimat®	Utibron™ Neohaler®	
	<i>fluticasone propionate and salmeterol inhalation powder</i>	<i>fluticasone propionate and salmeterol</i>	<i>fluticasone furoate and vilanterol</i>	<i>mometasone and formoterol</i>	<i>budesonide and formoterol</i>	<i>umeclidinium and vilanterol</i>	<i>glycopyrrolate and formoterol fumarate</i>	<i>tiotropium bromide and olodaterol</i>	<i>glycopyrrolate and indacaterol</i>	
										
Type of inhaler	DPI	MDI	DPI	MDI	MDI	DPI	MDI	SMI	DPI	
Dose counter	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	
Adult standard daily dosing	Low: 100/50 1 inh Q12 hr Med: 250/50 1 inh Q12 hr High: 500/50 1 inh Q12 hr	Low: 45/21 2 inh Q12 hr Med: 115/21 2 inh Q12 hr High: 230/21 2 inh Q12 hr	Asthma: 100/25, 200/25 COPD: 100/25 1 inh once daily	Med: 100/5 2 puffs Q12 hr High: 200/5 2 puffs Q12 hr	Low: 80/5 2 puffs Q12 hr Med: 160/4.5 2 puffs Q12hr	1 inh once daily	2 inh Q12 hr	2 inh once daily	1 capsule Q12 hr	
Shaking and priming	N/A	Spray 4 times before first use. Spray 2 times after 4 weeks of no use or after dropping. Shake well for 5 seconds before each spray.	N/A	Shake well and spray 4 times before first use or after 5 days of no use.	Shake for 5 seconds and spray 2 times before first use or after 7 days of no use or after dropping	N/A	Shake well and spray 4 times before first use. Shake well and spray 2 times after each cleaning or if after 7 days of no use.	Do not shake. Spray 4 times before first use or after 21 days of no use. Spray once after 3 days of no use.	N/A	

How to Use Your Aerospan®

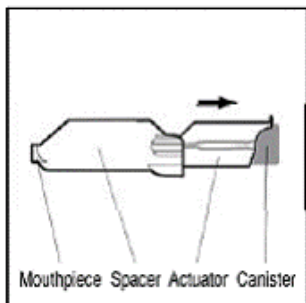
What do I need to know about this inhaler before first use?

This inhaler is made of 3 parts

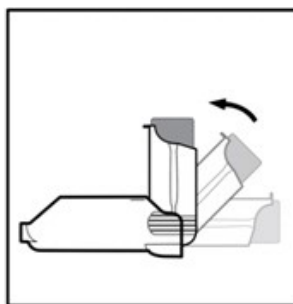
- Medicine canister
 - Canister holder (purple)
 - Spacer (gray)
- Do not separate the canister holder from the spacer.
 - Do not use the canister holder and spacer with any other medicine canisters.
 - Do not use the medicine canister with any medicine holders from other inhalers.
 - Do not use this inhaler with any other spacers.



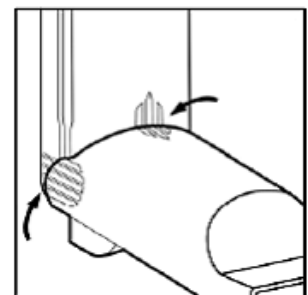
How do I open and position this inhaler for first use?



1. Pull the canister holder out from the spacer.



2. Grip the spacer. Pull the lip at the top of the medicine canister. Snap the inhaler into an "L" shape.



3. Make sure the guide lines on the canister holder and spacer line up. The inhaler is now ready to use.

Updated: 9/2017

How to Use Your Aerospan®

1. Open and position your inhaler. Pull the canister holder out from the spacer. Snap into an “L” shape.
2. Shake the inhaler 10 times.
3. Stand up or sit up straight.
4. Turn your head away from the inhaler. Breathe out all the way.
5. Seal your lips tightly around the mouthpiece.
6. As you start breathing in, press down on the canister one time. Keep breathing in SLOWLY (3-5 seconds) and DEEPLY through your mouth.
7. When your lungs are full take the inhaler out of your mouth.
8. Hold your breath for 10 seconds or as long as you can.
9. Breathe out slowly.
10. If you need to take another puff of medicine, wait 1 minute and repeat steps 2-8.



Note:

After using steroid inhalers like Aerospan®:

- Rinse your mouth
- Gargle
- Spit the water out
- DO NOT SWALLOW THE WATER

Updated: 9/2017

Aerospan® Tips

What is priming?

- Priming gets your inhaler ready to release full doses of medicine.

When do I prime my inhaler?

- Prime your inhaler when it is brand new or has not been used for 2 weeks.

How do I prime my inhaler?

1. Open and position your inhaler. Pull the canister holder out from the spacer. Snap into an “L” shape.
2. Shake the inhaler 10 times.
3. Point the mouthpiece away from you.
4. Push down on the canister 2 times to release 2 sprays.

How do I care for my inhaler?

- Keep your inhaler at room temperature.

How do I know when I need a refill of my inhaler?

- This inhaler dose not have a dose counter. You will need to keep track of the doses you use.
- Divide the starting number of doses by the number of doses used per day.
- This gives you the number of days your inhaler will last for. Mark your calendar with the date your inhaler runs out on.
- Contact the pharmacy to get a refill before your medicine runs out. Ask for a refill when you have 5 days of medicine left.
- You can also talk to your pharmacy about getting automatic refills.
- Do not use the inhaler past the expiration date. If expired, throw the inhaler away and ask for a refill.

Adapted from:

Meda Pharmaceuticals, Inc. (2017). *Aerospan®: Highlights of prescribing information*. Somerset, NJ: Author.

**Talk to your health care provider
if you have questions
about your Aerospan®.**

Updated: 9/2017

Aerospan® Tips

How do I know when I need a refill?

- When this inhaler is brand new, it has either 60 or 120 doses.
 - This inhaler does not have a dose counter. Track your doses so you know when your inhaler is running low and you need a refill.
 - Since this inhaler is to be used regularly, you can track your doses by using either one of these methods:
 1. Divide the starting number of doses by the number of doses used per day. This gives you the number of days your inhaler will last. Mark your calendar when your inhaler runs out. About 5 days before this date, contact your pharmacy to get a refill.
 2. Use a check off chart.
- If your canister has 60 sprays, use the Aerospan® 60 sprays check off chart.
 - If your canister has 120 sprays, use the Aerospan® 120 sprays check off chart.

P = prime

Dosing Sprays

P	P	60	59	58	57	56	55	54	53	52	51
		50	49	48	47	46	45	44	43	42	41
		40	39	38	37	36	35	34	33	32	31
		30	29	28	27	26	25	24	23	22	21
		20	19	18	17	16	15	14	13	12	11
		10	9	8	7	6	5	4	3	2	1

P = prime

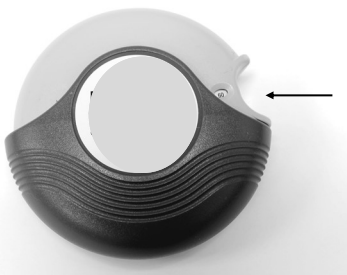
Dosing Sprays

P	P	120	119	118	117	116	115	114	113	112	111
		110	109	108	107	106	105	104	103	102	101
		100	99	98	97	96	95	94	93	92	91
		90	89	88	87	86	85	84	83	82	81
		80	79	78	77	76	75	74	73	72	71
		70	69	68	67	66	65	64	63	62	61
		60	59	58	57	56	55	54	53	52	51
		50	49	48	47	46	45	44	43	42	41
		40	39	38	37	36	35	34	33	32	31
		30	29	28	27	26	25	24	23	22	21
		20	19	18	17	16	15	14	13	12	11
		10	9	8	7	6	5	4	3	2	1

**Talk to your health care provider
if you have questions
about your Aerospan®.**

Updated: 10/7/2016

How to Use Your Diskus®



1. Check the dose counter before each use.



2. Hold the inhaler and push the thumb grip all the way back until it clicks.



3. Hold the inhaler flat and slide the lever back until it clicks.



4. Stand or sit up straight. Turn your head away from the inhaler. Breathe out all the way. DO NOT breathe into the inhaler.



5. Seal your lips tightly around the mouthpiece. Breathe in FAST (1-2 seconds) and DEEP through your mouth.



6. When your lungs are full take the inhaler out of your mouth. Hold your breath for 10 seconds or as long as you can.



7. Breathe out normally. Put your thumb in the grip.



8. Slide the thumb grip to the starting position to close the inhaler.

After using steroid inhalers like Advair® or Flovent Diskus®:

- Rinse your mouth
- Gargle
- Spit the water out
- DO NOT SWALLOW THE WATER

Diskus® Tips

Do I need to prime the Diskus®?

- This inhaler does not need to be primed.

How do I care for my Diskus®?

- Store this inhaler in the foil pouch and only open when you are ready to use it.
- Write the date you opened the foil pouch on the first blank line on the label.
- Write the “use by” date on the second line. This date is 1 month after first opened. Do not use after this date.
- Keep this inhaler in a dry place.
- Keep this inhaler at room temperature.
- Do not wash or take this inhaler apart.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.

How do I know when I need a refill?

- The dose counter shows the number of doses left in the inhaler.
- When this inhaler is brand new, it has 60 doses.
- The dose counter counts down by 1.
- When the dose counter reaches 5, it will turn red. Contact the pharmacy to get a refill.
- When the dose counter reaches “0”, it is empty. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw it away and ask for a refill.



*The Diskus® is a dry powder inhaler.
When you breathe in a dose,
you may or may not feel or taste the
medicine.*

Adapted from:

GlaxoSmithKline. (2017) *Advair® Diskus®: Highlights of prescribing information*. Research Triangle Park, NC: Author.



**Talk to your
health care provider
if you have questions
about your Diskus®.**

Updated: 9/2017



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Healthy
San Francisco
National COPD Program



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How to Use Your Ellipta®

1. Check the dose counter before each use.
2. Slide the cover down. You should hear a “click”. This loads one dose of medicine for you to breathe in. The dose counter will count down by one.
3. Stand or sit up straight.
4. Turn your head away from the inhaler. Breathe out all the way. DO NOT breathe into the inhaler.
5. Seal your lips tightly around the mouthpiece. DO NOT block the air vent with your fingers.
6. Breathe in FAST (1-2 seconds) and DEEP through your mouth.
7. When your lungs are full, take the inhaler out of your mouth.
8. Hold your breath for 3-4 seconds or as long as you can.
9. Breathe out normally.
10. Slide the cover back over the mouthpiece.

After using steroid inhalers like the Arnuity® or Breo® Ellipta®:

- Rinse your mouth
- Gargle
- Spit the water out
- DO NOT SWALLOW THE WATER



*The Ellipta® is a dry powder inhaler.
When you breathe in a dose,
you may or may not feel or taste
the medicine.*

Note:

If you open and close the cover without inhaling a dose of medicine, you will lose the dose.

The lost dose will be held inside the inhaler but will not be available for you to breathe in.

Updated: 9/2017

Ellipta® Tips

Do I need to prime the Ellipta®?

- This inhaler does not need to be primed.

How do I care for my Ellipta®?

- Keep this inhaler in the foil tray and only open when you are ready to use it.
- Write the date you opened the foil tray on the inhaler label.
- Write the “Discard” date on the inhaler label. This is 6 weeks after the tray is opened. Do not use the inhaler past the “Discard” date.
- Keep this inhaler in a dry place.
- Keep this inhaler at room temperature.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.

How do I know when I need a refill?

- The dose counter shows the number of doses left in the inhaler.
- When this inhaler is brand new, it has 30 doses.
- The dose counter counts down by 1.
- When there are fewer than 10 doses left, the dose counter turns red. Contact the pharmacy to get a refill.
- When the dose counter reaches “0” the inhaler is empty. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw the inhaler away and ask for a refill.

Adapted from:

GlaxoSmithKline. (2017). *Breo® Ellipta®: Highlights of prescribing information*. Research Triangle Park, NC: Author.

**Talk to your health care provider
if you have questions
about your Ellipta®.**

Updated: 9//2017



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Asthma/COPD Program



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How to Use Your Flexhaler®

1. Check the dose counter before each use.
2. Twist the cap off.
3. Hold the inhaler straight up. Twist the brown grip in one direction as far as it will go. Then twist the brown grip in the other direction as far as it will go. You will hear a “click” during one of the twists. This loads one dose of medicine for you to breathe in. DO NOT shake the inhaler.
4. Stand or sit up straight.
5. Turn your head away from the inhaler. Breathe out all the way. DO NOT breathe into the inhaler.
6. Hold the inhaler on its side. Seal your lips tightly around the mouthpiece.
7. Breathe in FAST and DEEP (1-2 seconds).
8. When your lungs are full, take the inhaler out of your mouth.
9. Hold your breath for 10 seconds or as long as you can.
10. Breathe out normally.
11. If more than one dose is prescribed, repeat steps 3-8.
12. Twist the cap back onto the inhaler.



*The Flexhaler® is a dry powder inhaler.
When you breathe in a dose,
you may or may not feel or taste
the medicine.*

After using steroid inhalers like the Flexhaler®:

- Rinse your mouth
- Gargle
- Spit the water out
- DO NOT SWALLOW THE WATER

Flexhaler® Tips

What is priming?

- Priming gets your inhaler ready to release full doses of medicine.

When do I need to prime the Flexhaler®?

- Prime this inhaler before you use it for the first time.

How do I prime the Flexhaler®?

- 1) Twist the cap off.
- 2) Hold the inhaler straight up. Twist the brown grip in one direction as far as it will go. Then twist the brown grip in the other direction as far as it will go. You will hear a “click” during one of the twists.
- 3) Repeat step 2. The inhaler is now primed. It is ready for loading your first dose of medicine.
- 4) You do not have to prime this inhaler again, even if you do not use it for a long period of time.

How do I care for my Flexhaler®?

- Keep this inhaler in a dry place with the cap tightly in place.
- Keep this inhaler at room temperature.
- Do not wash or take this inhaler apart.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.

How do I know when I need a refill?

- The dose counter shows the number of doses left in the inhaler.
- When this inhaler is brand new, it has 120 doses.
- The dose counter counts down by 10 doses.
- When the dose counter reaches 20, contact the pharmacy to get a refill.
- When the dose counter reaches “0” it is empty. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw the inhaler away and ask for a refill.

Adapted from:

AstraZeneca (2016). *Pulmicort Flexhaler®: Highlights of prescribing information*. Wilmington, DE: Author:

**Talk to your health care provider
if you have questions
about your Flexhaler®.**

Updated: 9/20/2017



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How to Use Your Handihaler®



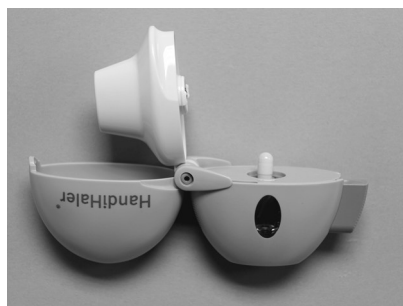
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Hospital and Trauma Center



UCSF RCS



1. Pull up the cap.



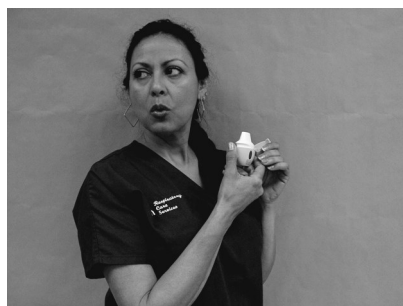
2. Pull up the mouthpiece so the chamber shows.
Put the capsule in the chamber.



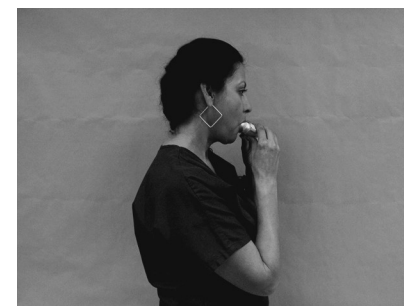
3. Close the mouthpiece until you hear a click.
Hold the inhaler so the mouthpiece faces up.



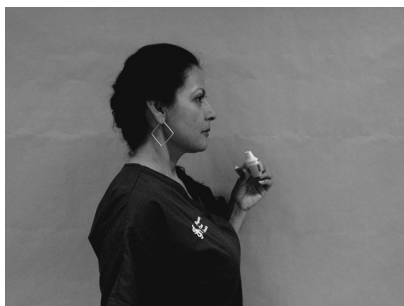
4. Push the green button once. Do not press
the green button more than one time.



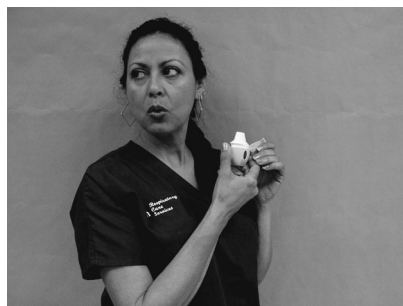
5. Stand or sit up straight. Turn your head away
from the inhaler. Breathe out all the way.
DO NOT breathe into the inhaler.



6. Seal your lips tightly around the mouthpiece.
Breathe in FAST and DEEP through your mouth.
You should hear the capsule rattle or feel it vibrate.



7. When your lungs are full take the inhaler
out of your mouth. Hold your breath for
10 seconds or as long as you can.



8. Breathe out normally.
Then, repeat steps 5-7.



9. Lift up the mouthpiece. Shake the capsule
out of the chamber. Do not touch the capsule.
After each use, close the cap over the mouthpiece.

HandiHaler® Tips

Do I need to prime the HandiHaler®?

- This inhaler does not need to be primed.

How do I get the most out of my HandiHaler®?

- DO NOT SWALLOW THE CAPSULES.
- A brand new box will have a new inhaler and 30 capsules. Use a new inhaler each month.
- Take the capsules out of the foil pouch when you are ready to take a dose.
- The capsules are to be breathed in using your Handihaler®.
- Breathe in fast enough through your mouth to hear the capsule rattling in the chamber.
- If you do not hear this rattling sound, tap the inhaler against a hard surface. Then breathe in fast again.

Can I touch the capsule after I breathe in the medicine?

- Do not touch the capsule.
- If you touch the capsule, wash your hands right away.

How do I know when I need a refill?

- When there are 5 capsules left, contact the pharmacy to get a refill.
- Do not use the capsules past the expiration date. If expired, throw away. Ask for a refill.



How do I clean my HandiHaler®?

- If the mouthpiece needs to be cleaned, wipe off with a clean, damp cloth.
- Clean the inhaler as needed.
- Clean right after you take your dose. It takes 24 hours for the inhaler to dry.
- Open the cap and mouthpiece.
- Open the base by lifting the green button.
- Look in the chamber for capsule pieces or powder buildup. If seen, tap out.
- Rinse the inhaler with warm water. Press the green button a few times as the chamber and piercing needle are rinsed.
- Dry the inhaler. Tip the excess water out. Leave the cap, mouthpiece, and base open fully spread out. Let air dry.

Adapted from:

Boehringer-Ingelheim Pharmaceuticals, Inc. (2016). *Spiriva® Handihaler®: Highlights of prescribing information*. Ridgefield, CT. Author.



**Talk to your
health care provider
if you have questions
about your HandiHaler®.**

Updated: 9/2017



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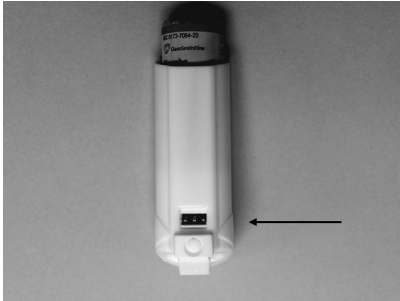


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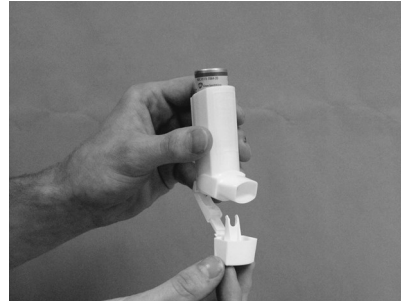


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How to Use Your Mist Inhaler with a Closed Mouth



1. Check the dose counter before each use.



2. Take off the cap.



3. Shake the inhaler 10 times.



4. Stand or sit up straight. Turn your head away from the inhaler. Breathe out all the way.



5. Seal your lips tightly around the mouthpiece. As you start breathing in, press down on the canister one time. Keep breathing in SLOWLY and DEEPLY (3-5 seconds) through your mouth.



6. When your lungs are full take the inhaler out of your mouth. Hold your breath for 10 seconds or as long as you can. Breathe out normally.



7. If you need to take another puff of medicine, wait one minute. Then repeat steps 3-6.

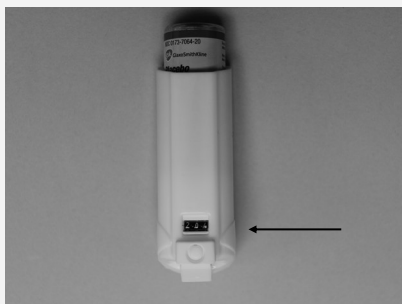


8. Put the cap back on.

REMINDERS:

- Timing when you press down on the canister with your breath in will get more medicine to your lungs.
- After using inhalers with steroids:
 - ◆ Rinse your mouth, gargle, and then spit the water out
 - ◆ DO NOT SWALLOW THE WATER

How to Use Your Mist Inhaler with a Spacer



1. Check the dose counter before each use.



2. Take off the cap.



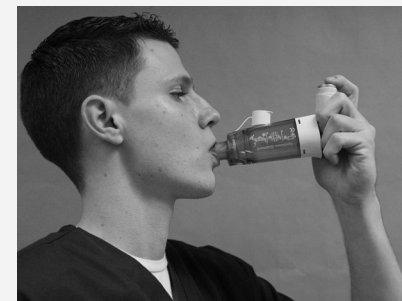
3. Put the mouthpiece into the back of the spacer.



4. Shake the inhaler 10 times.



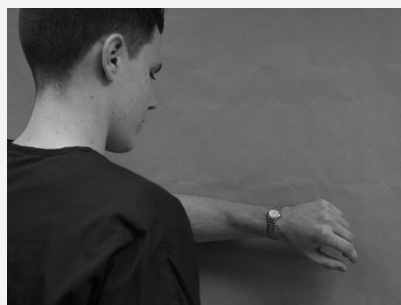
5. Stand or sit up straight.
Turn your head away from the inhaler.
Breathe out all the way.



6. Seal your lips tightly around the spacer mouthpiece. Press down on the canister one time. Then breathe in SLOWLY and DEEPLY (3-5 seconds) through your mouth.



7. When your lungs are full take the spacer out of your mouth. Hold your breath for 10 seconds or long as you can. Then, breathe out slowly.



8. If you need to take another puff of medicine, wait one minute and repeat steps 4-7.

REMINDERS:

- Some spacers whistle to let you know you are breathing in too fast. Slow down as you breathe in the medicine.
- After using inhalers with steroids:
 - ◆ Rinse your mouth, gargle, and spit the water out
 - ◆ DO NOT SWALLOW THE WATER

Mist Inhaler Tips

What is priming?

- Priming gets your inhaler ready to release full doses of medicine.

When do I prime my inhaler?

- Prime your inhaler before you use it for the first time or if it has not been used for a period of time.

How do I prime my inhaler?

1. Remove the cap
2. Shake the inhaler 10 times
3. Point the mouthpiece away from you
4. Push down on the canister to release a spray
5. For medicines with an (*) shake well before each spray.

Use the chart below to find out how many sprays are needed to prime your inhaler and when this needs to be done.

Medicine	Advair® HFA *	Aerospan®	Alvesco® HFA	Asmanex® HFA	Atrovent® HFA	Bevespi Aerosphere™	Dulera® HFA
Number of sprays before first use	4	2	3	5	2	4	4
Number of sprays after period of no use	2 after 4 weeks	2 after 2 weeks	3 after 10 days	5 after 5 days	2 after 3 days	2 after 1 week	4 after 5 days
Medicine	Flovent® HFA *	Pro Air® HFA	Proventil® HFA	QVAR® HFA	Symbicort® HFA	Ventolin® HFA	Xopenex® HFA
Number of sprays before first use	4	3	4	2	2	4	4
Number of sprays after period of no use	1 after 1 week	3 after 2 weeks	4 after 2 weeks	2 after 10 days	2 after 1 week	4 after 2 weeks	4 after 3 days



If you have questions about
priming your mist inhaler,
talk to your health care provider.

Updated: 9/2017



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Mist Inhaler Tips

How do I care for my mist inhaler and spacer?

- Keep your inhaler at room temperature.
- Before use, make sure the mouthpieces of the inhaler and spacer are clean and not blocked.

Clean your mist inhaler once a week to keep it from getting clogged*:

1. Take off the cap.
2. Take the canister out of the mouthpiece.
3. Rinse the mouthpiece with warm water.
4. Shake off the extra water.
5. Let the mouthpiece air-dry over night.
6. Put the canister back into the mouthpiece for use.

* Aerospan, Alvesco, Asmanex, Advair, Dulera, Flovent, QVAR, and Symbicort do not need to be cleaned.

How do I know when I need a refill?

- If your inhaler has a dose counter, check it before each use.
- If your inhaler does not have a dose counter:
 - ♦ Find out how many doses your inhaler starts with when it is brand new.
 - ♦ For inhalers that you do not use regularly:
 - Keep track of how many doses you use. Subtract the number of doses used from the starting number of doses. This tells you how many doses are left.
 - ♦ For inhalers that you use regularly:
 - Divide the starting number of doses by the number of doses used per day.
 - This gives you the number of days your inhaler will last for. Mark your calendar with the date your inhaler runs out on.
- Contact the pharmacy to get a refill before your medicine has run out. Ask for a refill when you have 5 days of medicine left.
- You can also talk to your pharmacy about getting automatic refills.
- Do not use the inhaler past the expiration date. If expired, throw away. Ask for a refill.



Clean the spacer once a week:

1. Follow the spacer manufacturer's cleaning instructions.

Updated: 9/2017



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Hospital and Trauma Center



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AutomatedCOPI Program



UCSF UCSF

Mist Inhaler References

How to Use Your Mist Inhaler with a Closed Mouth

1. National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma, August 2007 (NIH Publication No. 07-4051)

How to Use Your Mist Inhaler with a Spacer

1. National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma, August 2007 (NIH Publication No. 07-4051)

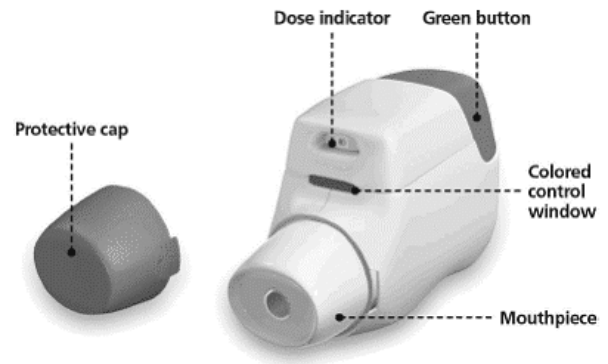
Mist Inhaler Tips

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14. Sunovion Pharmaceuticals, Inc. (2015). *Xopenex® HFA: Highlights of prescribing information*. Retrieved from <https://www.xopenexhfa.com/XOPENEX-HFA-Prescribing-Information.pdf>

Updated: 9/14/2017

How to Use Your Pressair®

1. Check the dose counter before each use.
2. Remove the cap by squeezing the arrows on each side of the cap and pulling off.
3. Hold the inhaler with the mouthpiece facing you. The green button should face straight up.
4. Press the green button all the way down and release.
5. Check the control window to make sure your dose is ready. When the control window is green, your medicine is ready to be breathed in. If the control window is red, press the green button all the way down and release. Repeat this until the control window is green. Now the dose is ready.
6. Stand or sit up straight.
7. Turn your head away from the inhaler. Breathe out all the way. DO NOT breathe into this inhaler.
8. Seal your lips tightly around the mouthpiece.
9. Breathe in FAST and DEEP (1-2 seconds) through your mouth. Breathe in until you hear a “click”. Keep breathing in even after you have heard the “click” to be sure you get a full dose.
10. When your lungs are full, take the inhaler out of your mouth.
11. Hold your breath for 10 seconds or as long as you can.



*The Pressair® is a dry powder inhaler.
When you breathe in a dose,
you may or may not feel or taste
the medicine.*

12. Breathe out normally.
13. Check the control window. If it is red you have breathed in a full dose of medicine. If the control window is still green, repeat steps 6-9.
14. Put the cap over the mouthpiece after each use.

Updated: 9/2017

Pressair® Tips

Do I need to prime the Pressair®?

- This inhaler does not need to be primed.

How do I care for my Pressair®?

- Store this inhaler in the foil pouch and only open when you are ready to use it.
- Write the date you opened the foil pouch on your calendar.
- Write the “Discard” date on your calendar. This is 45 days after the date you opened the foil pouch. Do not use the inhaler past the “Discard” date.
- Keep this inhaler in a dry place.
- Keep this inhaler at room temperature.
- Do not wash or take this inhaler apart.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.

How do I know when I need a refill?

- The dose counter shows the number of doses left in the inhaler.
- When this inhaler is brand new, it has 60 doses.
- The dose counter counts down by 10.
- When the dose counter turns red, there are few doses left. Contact the pharmacy to get a refill.
- When the dose counter reaches “0”, it is empty. The device will lock. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw the inhaler away and ask for a refill.

Adapted from:

AstraZeneca Pharmaceuticals LP. (2015). *Tudorza® Pressair®: Highlights of prescribing information*. Wilmington, DE: Author.

**Talk to your health care provider
if you have questions
about your Pressair®.**

Updated: 9/2017

How to Use Your Respiclick®

1. Check the dose counter before each use.
2. Make sure the cap is closed before you take a dose.
3. Hold the inhaler straight up. Pull the cap all the way back until you hear a “click”.
4. Stand or sit up straight.
5. Turn your head away from the inhaler. Breathe out all the way. DO NOT breathe into the inhaler.
6. Seal your lips tightly around the mouthpiece. DO NOT block the vent above the mouthpiece.
7. Breathe in FAST and DEEP (1-2 seconds) through your mouth.
8. When your lungs are full, take the inhaler out of your mouth.
9. Hold your breath for 10 seconds or as long as you can.
10. Breathe out normally.
11. Check the dose counter to make sure you breathed in the dose.
12. Close the cap over the mouthpiece after each use.
13. If you need another dose, repeat steps 1-10.



*The Respiclick® is a dry powder inhaler.
When you breathe in a dose,
you may or may not feel or taste
the medicine.*

Updated: 9/2017

Respiclick® Tips

Do I need to prime the Respiclick®?

- This inhaler does not need to be primed.

How do I care for my Respiclick®?

- Store this inhaler in the foil pouch and only open when you are ready to use it.
- Keep this inhaler in a dry place.
- Keep this inhaler at room temperature.
- Do not wash or take this inhaler apart.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.

How do I know when I need a refill?

- The dose counter shows the number of doses left in the inhaler.
- When this inhaler is brand new, it has 200 doses.
- The dose counter counts down by 2.
- When the dose counter reaches 20, it will turn red. Contact the pharmacy to get a refill.
- When the dose counter reaches “0”, it is empty. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw the inhaler away and ask for a refill.

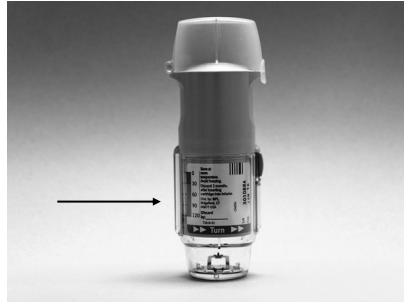
Adapted from:

Teva Respiratory LLC. (2017). *ProAir® Respiclick®: Highlights of prescribing information*. Horsham, PA: Author.

**Talk to your health care provider
if you have questions
about your Respiclick®.**

Updated: 9/2017

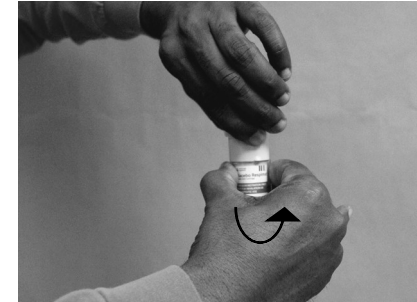
How to Use Your Respimat®



1. Check the dose counter before each use.



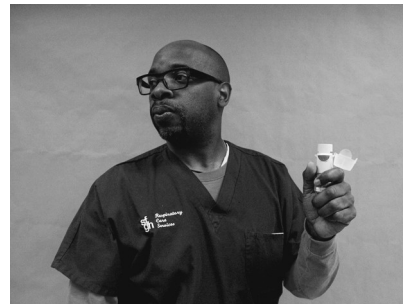
2. Hold the inhaler upright.
Keep the cap closed.



3. Turn the clear base in the direction of the white
arrows on the label until it clicks (half a turn).



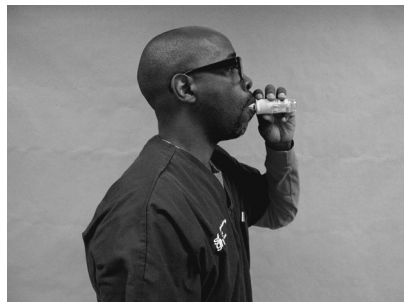
4. Flip the cap open.



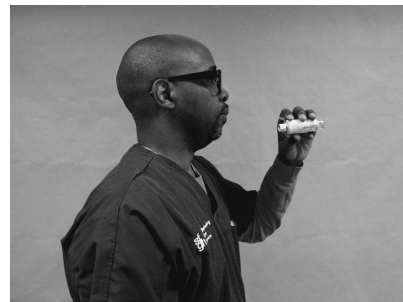
5. Stand or sit up straight. Turn your head away
from the inhaler. Breathe out all the way.



6. Seal your lips tightly around the mouthpiece.
Do not cover the air vents.



7. As you start breathing in slowly, press down on
the dose release button. Keep breathing in
SLOWLY and **DEEPLY** (3-5 seconds).



8. When your lungs are full take the inhaler
out of your mouth. Hold your breath for
10 seconds or as long as you can.



9. Breathe out normally. Close the cap over the
mouthpiece after each use.

Respimat® Tips

How do I prepare my Respimat® for first time use?

This inhaler needs to be prepared before you use it the first time. You can ask your pharmacist for help.

1. With the cap closed, press the safety catch while pulling off the clear base. Do not touch the piercing element at the bottom of the clear base.
2. Write the **discard by** date on the inhaler label. The **discard by** date is 3 months from the date the cartridge is inserted. Throw the inhaler away on the discard date.
3. Take the cartridge out of the box.
4. Push the narrow end of the cartridge into the inhaler. The base of the cartridge will stick out 1/8 of an inch when the cartridge is correctly inserted. The cartridge can be pushed against a firm surface to ensure it is correctly inserted. Do not remove the cartridge once it has been inserted into the inhaler.
5. Put the clear base back into place. Do not remove the clear base again. After you have inserted the cartridge, your inhaler should not be taken apart.



Talk to your pharmacist or health care provider if you have questions about how to prepare your Respimat® for first time use.

Updated: 9/2017

Respimat® Tips

What is priming?

- Priming gets your inhaler ready to release full doses of medicine.

When do I prime the Respimat®?

- Prime this inhaler before first use or if it has not been used for a period of time.

How do I prime the Respimat®?

If this inhaler is brand new or has not been used in more than 21 days, prime this inhaler by following these steps:

1. Hold the inhaler straight up with the cap closed. This keeps the inhaler from releasing a full dose of medicine.
2. Turn the clear base in the direction of the white arrows on the label until it clicks (half a turn).
3. Flip the cap open.
4. Point the mouthpiece away from you. Press down on the dose release button. Close the cap.
5. Repeat Steps 1-4 until a spray is seen.
6. Once the spray is seen, repeat Steps 1-4 three more times to make sure the inhaler is prepared for use.

If your Respimat® has not been used for more than 3 days, follow Steps 1-5 to release one dose of medicine.



How do I care for my Respimat®?

- Keep this inhaler clean and dry.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.
- Keep this inhaler at room temperature.

How do I know when I need a refill?

- The dose counter shows the number of doses left in the inhaler.
- When this inhaler is brand new, it has 120 doses.
- When the pointer enters the red area of the scale, there are about 30 doses left. Contact the pharmacy to get a refill.
- When the dose counter reaches the end of the scale, the inhaler is empty and will lock. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw away. Ask for a refill.

Adapted from:

Boehringer Ingelheim. (2017). *Combivent Respimat®: Highlights of prescribing information*. Ridgefield, CT: Author.



**Talk to your health care provider
if you have questions
about your Respimat®.**

Updated: 9/2017



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How to Use Your Twisthaler®

1. Check the dose counter before each use.
2. Hold the inhaler straight up with the colored base at the bottom.
3. Twist the white cap off. This loads one dose of medicine for you to breathe in. The dose counter will count down by one.
4. Stand or sit up straight.
5. Turn your head away from the inhaler. Breathe out all the way. DO NOT breathe into the inhaler.
6. Hold the inhaler on its side. Seal your lips tightly around the mouthpiece.
7. Breathe in FAST and DEEP (1-2 seconds) through your mouth. DO NOT cover the air vents while breathing in.
8. When your lungs are full, take the inhaler out of your mouth.
9. Hold your breath for 10 seconds or as long as you can.
10. Breathe out normally.
11. Twist the cap back onto the inhaler. Be sure the arrow on the white cap lines up with the dose counter. Turn until you hear a “click”. The arrow on the white cap should line up with the window on the pink base.
12. If a second dose is prescribed, repeat steps 1-10.



*The Twisthaler® is a dry powder inhaler.
When you breathe in a dose,
you may or may not feel or taste
the medicine.*

After using steroid inhalers like the Twisthaler®:

- Rinse your mouth
- Gargle
- Spit the water out
- DO NOT SWALLOW THE WATER

Updated: 4/14/2016



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Twisthaler® Tips

Do I need to prime the Twisthaler®?

- This inhaler does not need to be primed.

How do I care for my Twisthaler®?

- Store this inhaler in the foil pouch and only open when you are ready to use it.
- Write the date you opened the foil pouch on the cap.
- Write the “use by” date on the cap. This is 45 days after first opened. Do not use the inhaler past the “use by” date.
- Keep this inhaler in a dry place.
- Keep this inhaler at room temperature.
- Do not wash or take this inhaler apart.
- If the mouthpiece needs to be cleaned, wipe off with a dry cloth.

How do I know when I need a refill?

- The dose counter shows the number of doses left in this inhaler.
- When this inhaler is brand new, it has 120 doses.
- The dose counter counts down by 1.
- When the dose counter reaches 20, contact the pharmacy to get a refill.
- When the dose counter reaches “0”, it is empty. Throw it away.
- Do not use the inhaler past the expiration date. If expired, throw the inhaler away and ask for a refill.

Reference:

Merck. (). *Asmanex Twisthaler®. Highlights of prescribing information.* : Author.

**Talk to your health care provider
if you have questions
about your Twisthaler®.**

Updated: 4/14/2016

USING AND INTERPRETING EXERCISE TESTS

William Stringer, MD

Harbor UCLA

Saturday September 30, 2017 – 1:00 p.m. – 2:35 p.m.

Dr. William Stringer received his undergraduate and medical degree from the University of California, San Diego. He is currently an attending at Harbor-UCLA Medical Center in Torrance, California and a Professor of Medicine in the David Geffen School of Medicine at UCLA. He is a board certified in Internal Medicine, Pulmonary, and Critical Care Medicine, and is active in patient care, teaching, administration, and research. His research interests are in Chronic Obstructive Lung Disease (COPD), exercise physiology, pulmonary function testing, and rehabilitation science. He is married and has four college age children. His hobbies include cycling, playing a banjo, and the humanities.

Using and Interpreting Exercise Tests

William Stringer, MD, FACP, FCCP

Los Angeles Biomedical Research Institute (LABIOMED)
at Harbor-UCLA Medical Center
Torrance, California, USA

CALIFORNIA THORACIC SOCIETY

Advanced Clinical Training in COPD

September 30th, 2017 (1:00 – 2:35 pm)

Using and Interpreting Exercise Tests

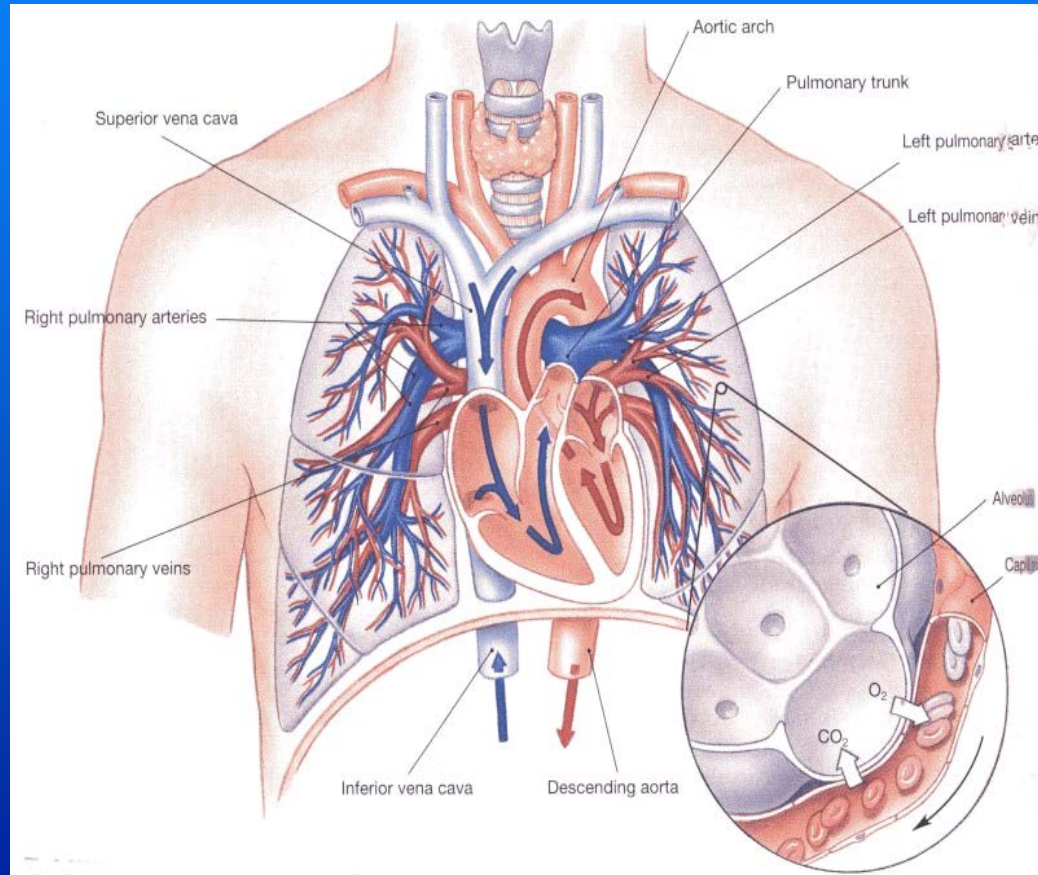
- Review of Important CPET Physiology
- Definitions
 - Gas Exchange:
 - VO_2 max, LAT, VO_2/WR , VE/VCO_2 , VE vs VCO_2 slope, Standard Testing
 - Cycle vs Treadmill
 - Out with the Old (Lose the FEF 25-75...)
 - In with the new... (e.g. FEV3/FEV6, PRISM)
 - Ramp/Progressively Increasing vs CWR/Endurance
- Exercise Phenotypes
 - COPD
 - HF
 - ILD
 - Pulm HTN

Disclosures

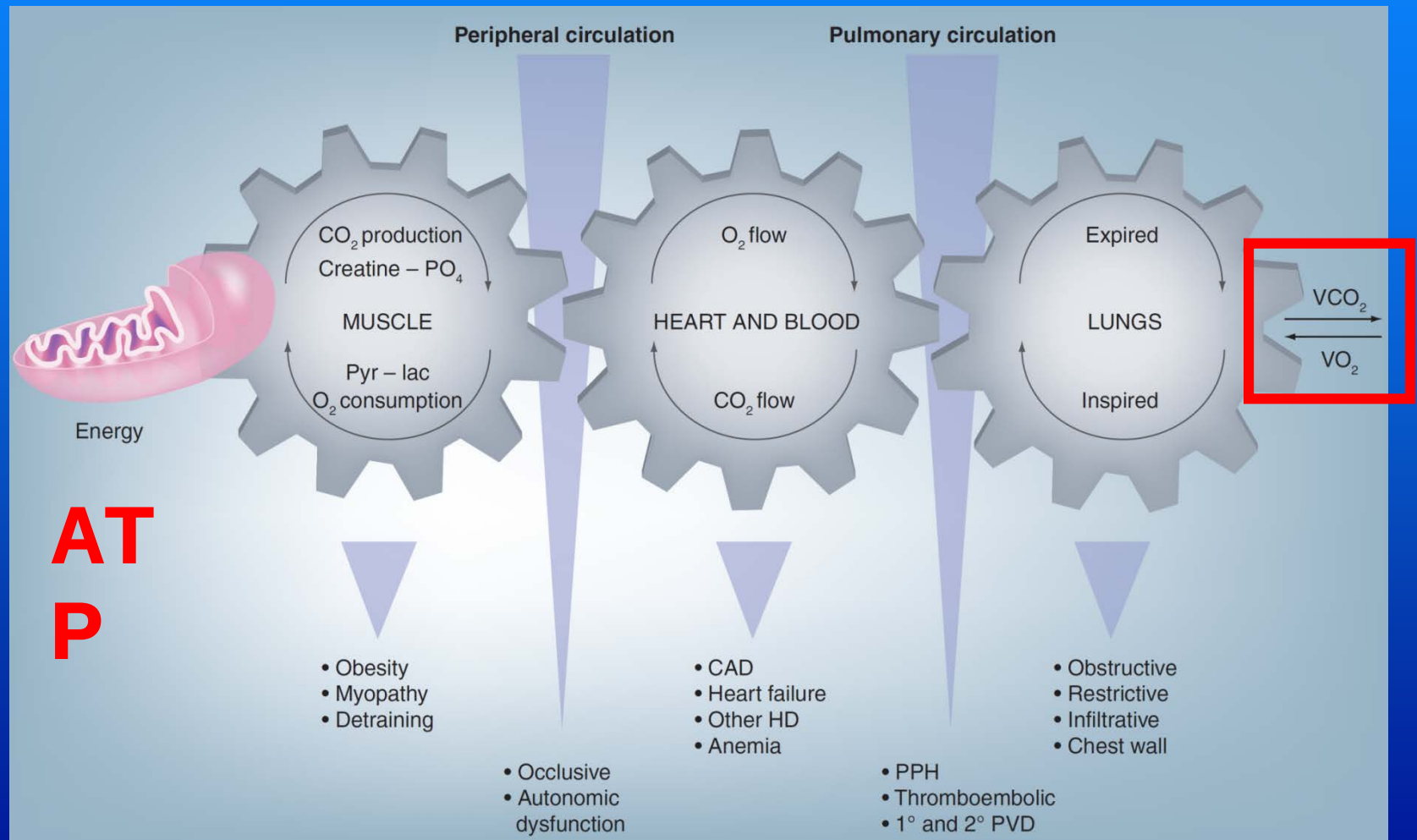
William W. Stringer, MD

William W. Stringer ,MD	Updated	September-17
Disclosure		
	<u>What is Received</u>	<u>Type of Financial Relationship</u>
<u>Company / Entity</u>		
NIH	Grant/Research Support	Research Grant in COPD
Department of Defense	Grant/Research Support	Research Grant in COPD
AstraZenica	Grant/Research Support	Research Grant in COPD
Boehringer-Ingelheim	Grant/Research Support	Research Grant in COPD
Astellas	Grant/Research Support	Research Grant in COPD
<u>Publishing</u>		
Walters Kluwer - Lippincott Williams & Wilkins - CPET Book	Royalties	Authorship
<u>Leadership Positions</u>		
California Thoracic Society	Past President	Volunteer
American College of Chest Physicians - ACCP Simulation Group (PFT and CPET)	Member	Volunteer
Director - ABG, PFT, and CPET Laboratory - Harbor-UCLA Medical Center	Employment	Employment
Pulmonary Rehabilitation - Medical Director - LCM Hospital - Torrance, California	Medical Director	Stipend
	Ö	= COI (Conflict of Interest)

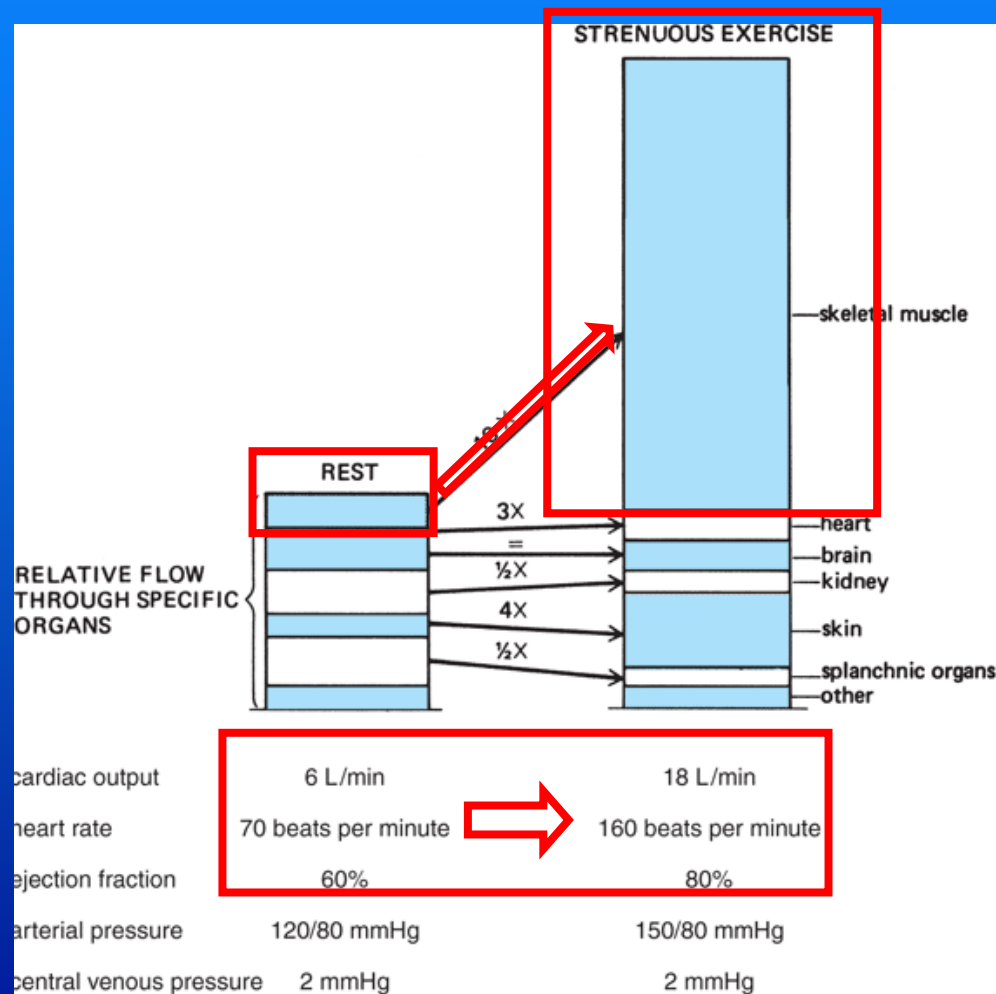
Cardio-Pulmonary Anatomy



Oxygen Flow Mouth to Muscle/Mitochondria



Relationship of METs & VO_2 to Exercise



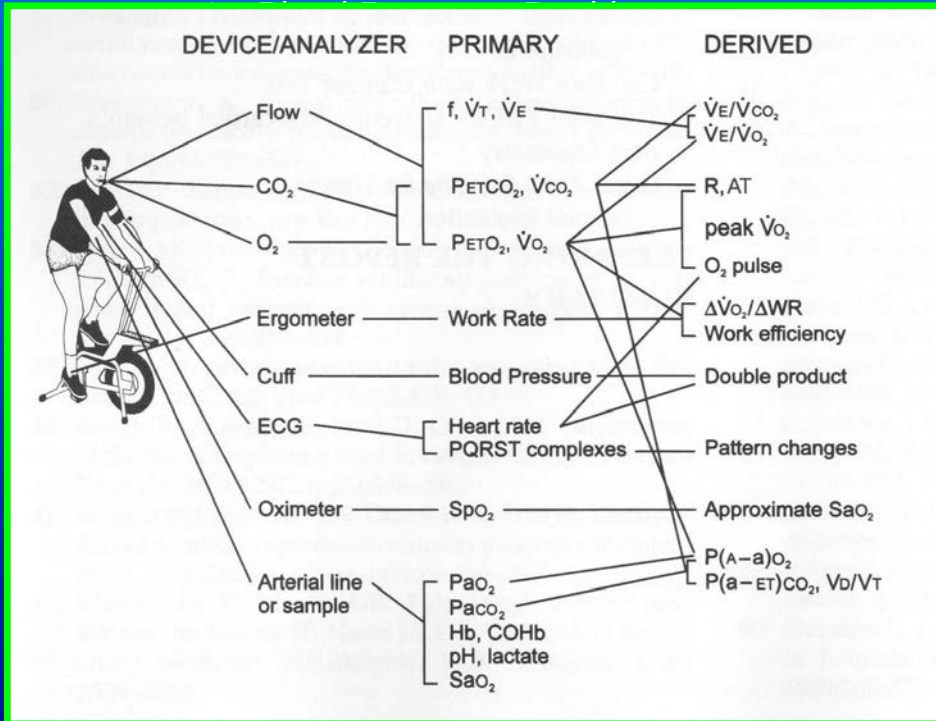
Source: Mohrman DE, Heller LJ: *Cardiovascular Physiology*, 5th Edition: <http://www.accessmedicine.com>

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Why use CPET?

• EKG Treadmill

- ★ Ischemia / 12 lead EKG
- ★ Heart Rate / HRR

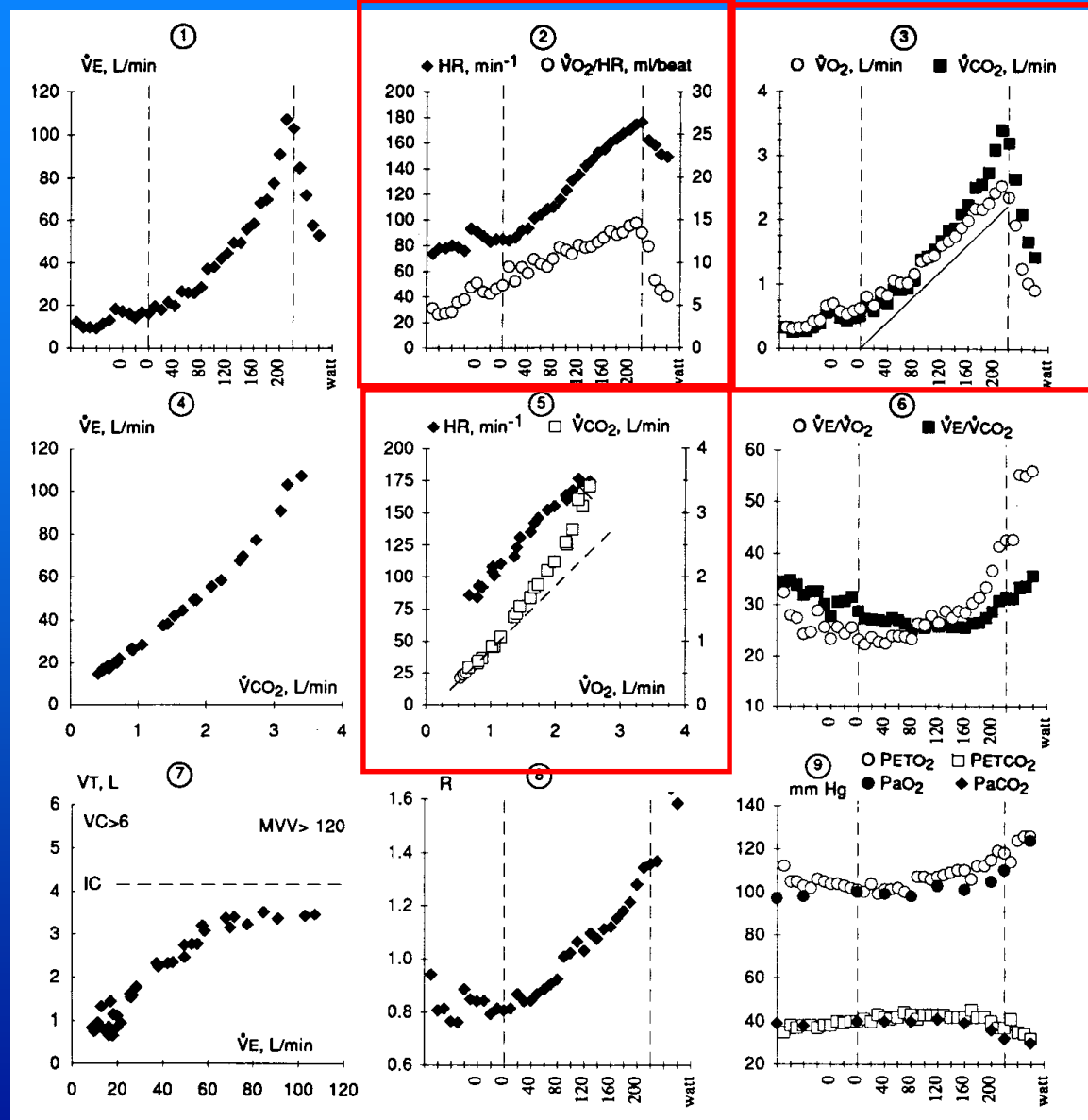


• CPET

- ★ Ischemia / 12 lead EKG
- ★ Heart Rate / HRR
- ★ Blood Pressure, Double Product
- ★ Measured Work Rate
- ★ Symptoms / Reason For Stopping
- ★ Oxygen Saturation
- ★ Maximal Oxygen Uptake (VO₂ max)
- ★ Lactic Acidosis Threshold (LAT)
- ★ Carbon Dioxide Output (VCO₂)
- ★ Minute Ventilation (V_E), TV, RR / BR
- ★ Ventilatory Equivalents (V_E/VO₂, V_E/VCO₂)
- ★ VO₂ / Work Rate Relationship ($\Delta\dot{V}_{O_2}/\Delta WR$)
- ★ O₂ Pulse (SV x C(a-v)O₂ Difference)
- ★ Respiratory Exchange Ratio (RER),
- ★ End Tidal O₂, CO₂
- ★ Blood Gases / COHg
- ★ Vd/Vt
- ★ P(A-a) O₂ ⇒ Low V_A/Q,
- ★ P(a-ET)CO₂ ⇒ High V_A/Q

Normal 9 Panel Plot for CPET

Cardiovascular



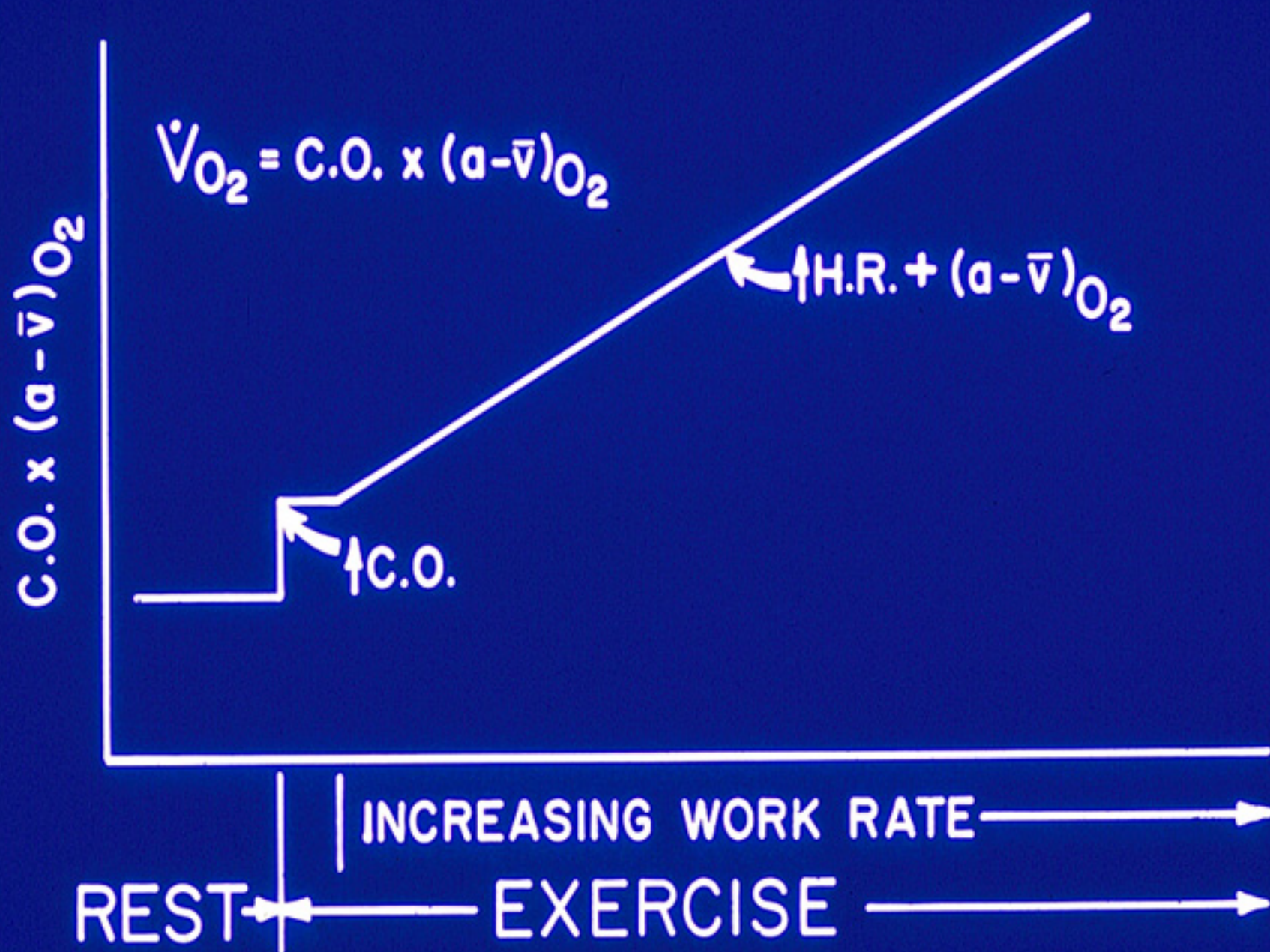
Fick Equation: $\dot{V}O_2$ Relationship to Cardiac Output

$$\dot{V}O_2 = C.O. \times C(a-v) O_2$$

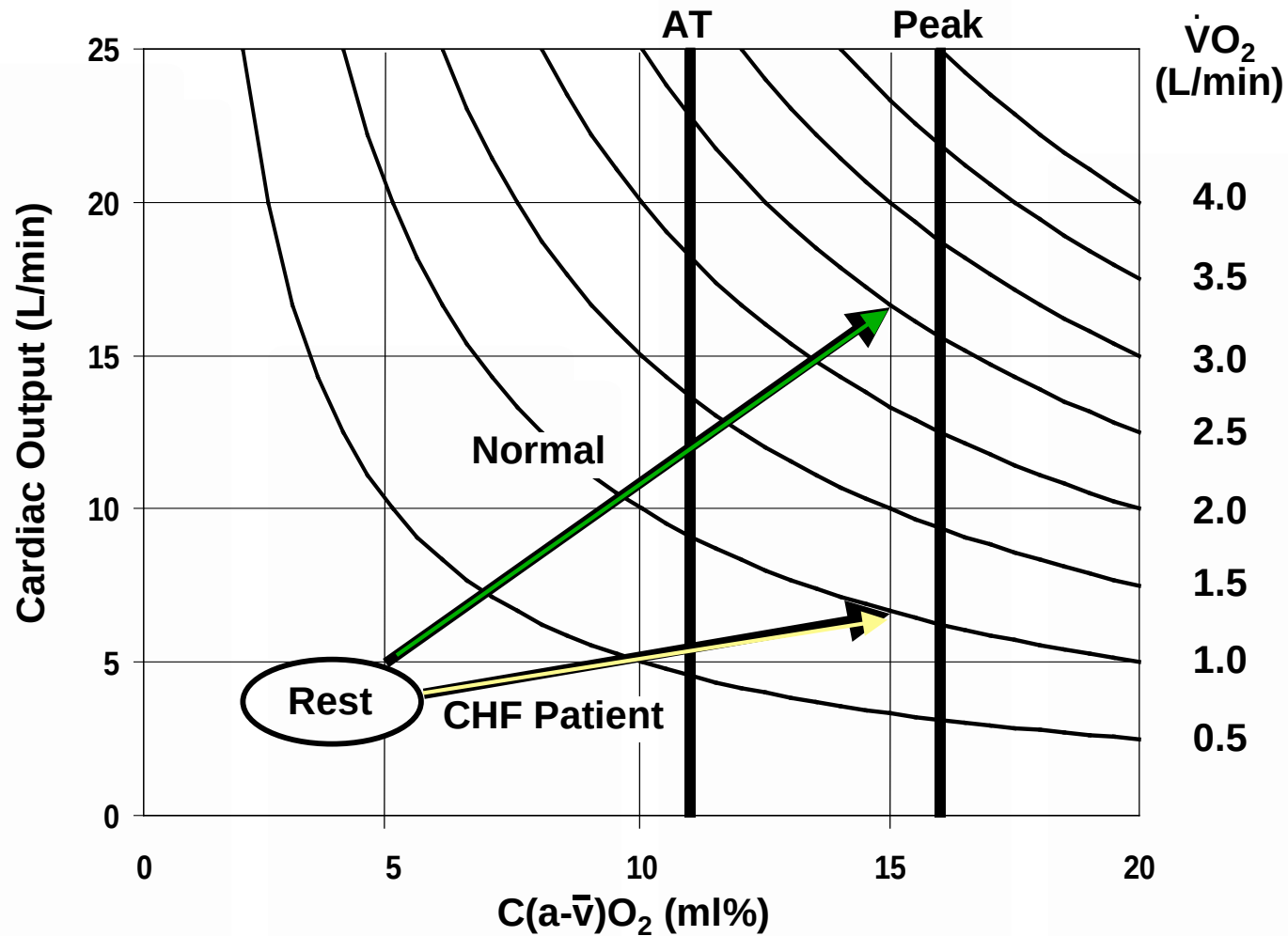

$$C.O. = HR \times SV$$


$$C = 1.34 \times \text{Sat } O_2 \times [Hb]$$


$$\dot{V}O_2 = HR \times SV \times C(a-v) O_2$$

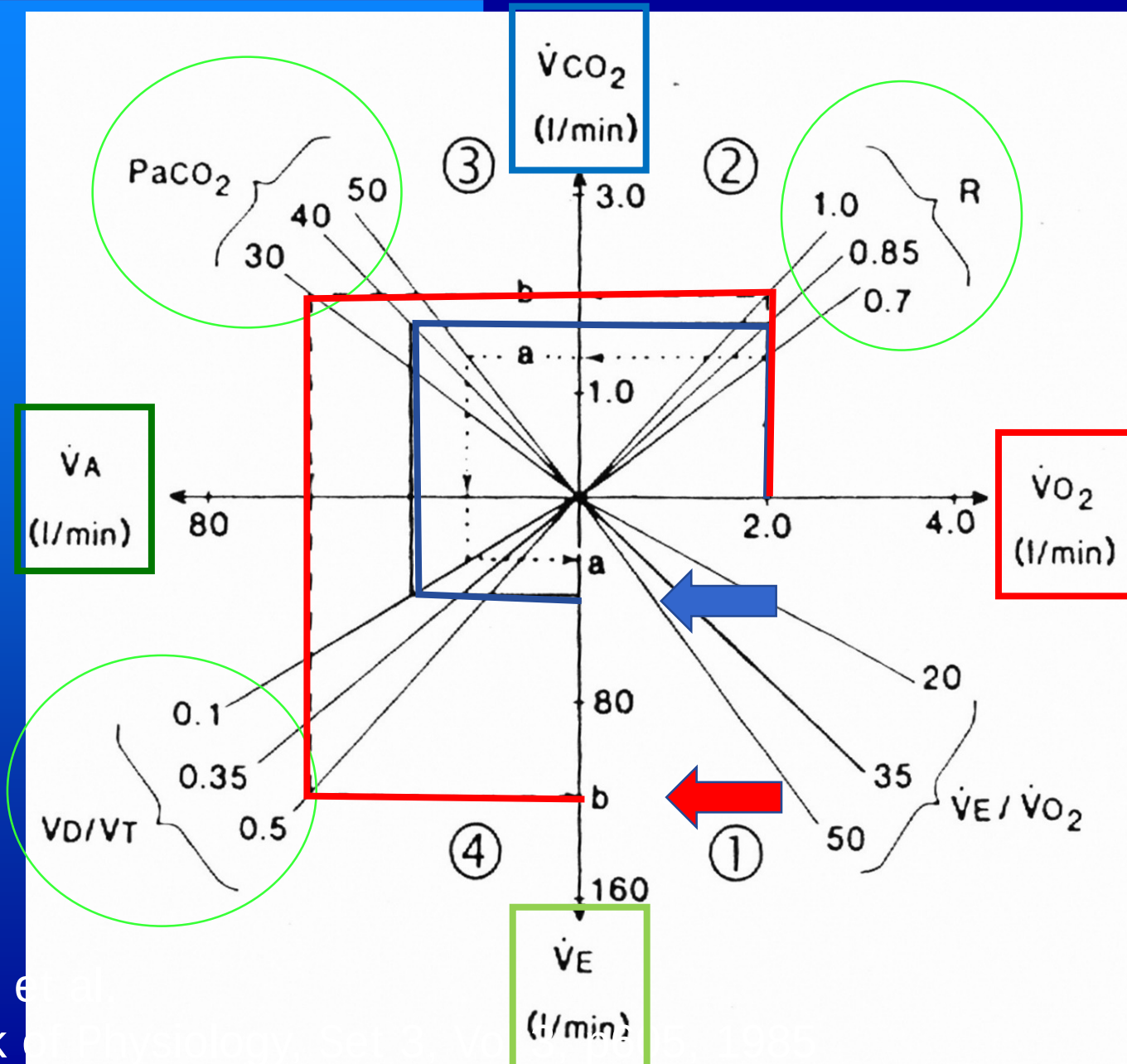


$$C.O. \times C(a-\bar{v})O_2 = \dot{V}O_2$$



$$\dot{V}O_2 = C.O. \times C(a-v) O_2$$

Determinants of the Ventilatory Response to Exercise



CPET Case Studies

- Cases:
 - Pulmonary Arterial Hypertension
 - Heart Failure
 - Interstitial Lung Disease
 - COPD

Pulmonary Arterial Hypertension

Case # 1

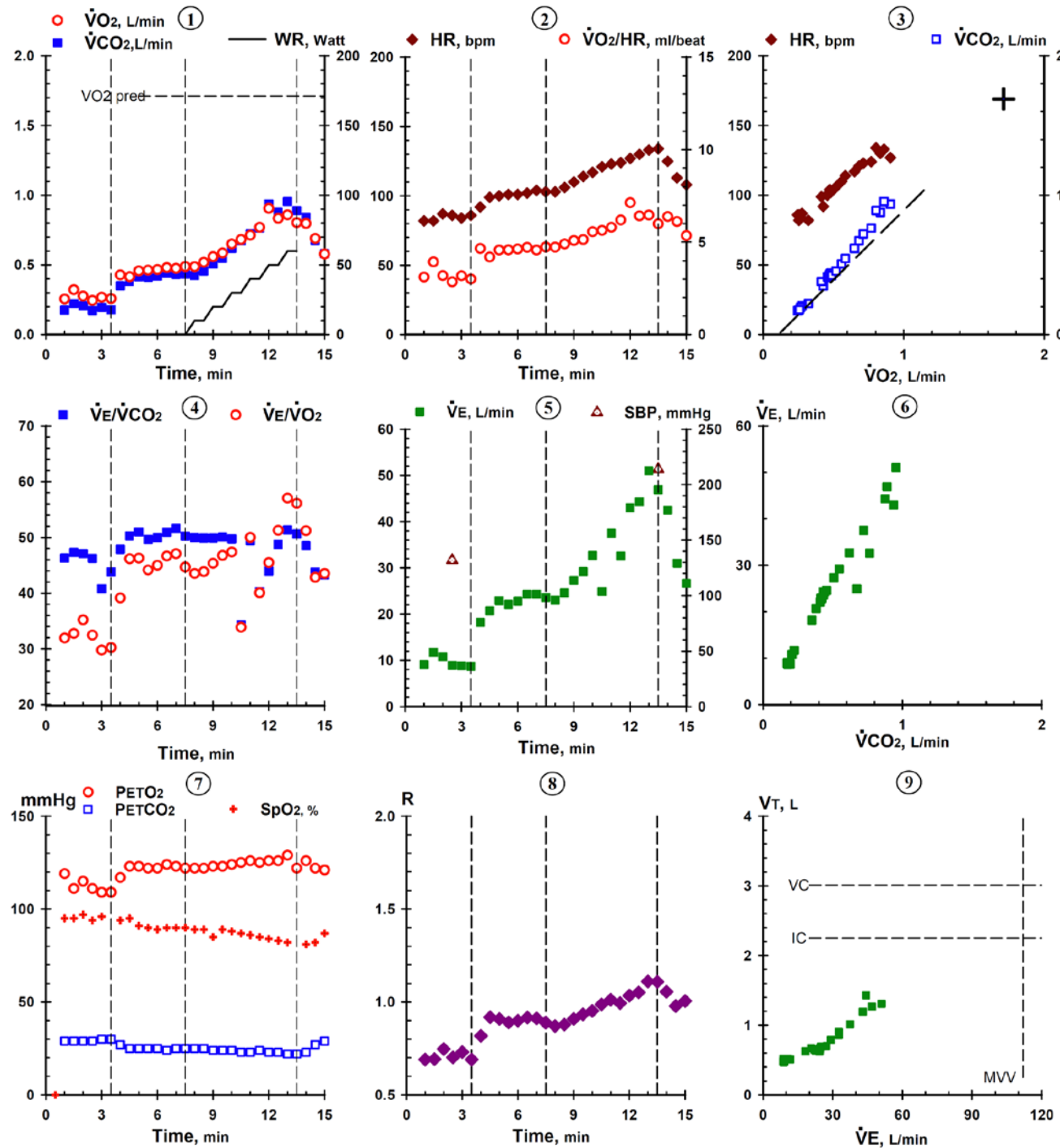
Pulmonary Arterial Hypertension

- 51 year old female, exertional dyspnea x 2-3 years.
- Fen-Phen (fenfluramine/phentermine) for 7 months 5 years ago.
- Systemic HTN as well.
- Medications: Verapamil, Benazapril, Atorvastatin, ASA.
- Physical Examination was normal except for a loud P2.
- CXR: Enlarged pulmonary arteries.
- EKG: RVH with strain.
- PFT's: FEV₁ 2.68 (105% predicted), FVC 3.20 (115% predicted), FEV1/VC 82%, DLCO 22.7 (89% of predicted)

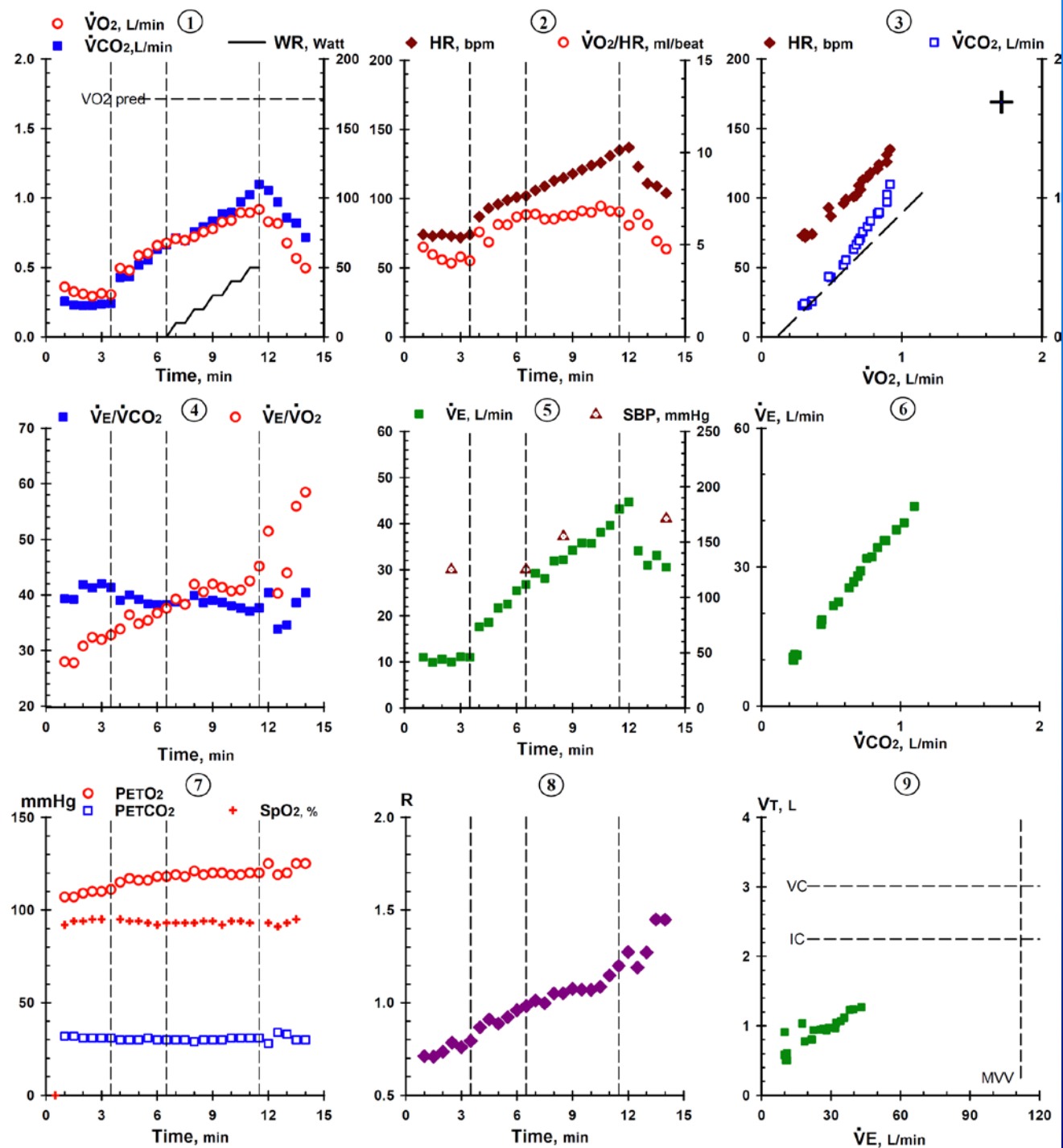
Exercise Indices - PAH

Measurement	Predicted	Pre Rx	Post Rx
Max Work Rate		60	50
Peak VO ₂	1.80	0.86	0.93
Max HR	168	134	136
Max O ₂ Pulse	10.0	6.4	6.8
Max VE		51	45
VE/VCO ₂ at AT	28.5	45.9	37.9

Initial CPET



endothelin-1
receptor
antagonist
after just 6 weeks



PAH – CPET Conclusions

- Very Low Peak VO_2
- High Ventilatory Equivalents
- Flat and Fixed O_2 Pulse
- Poor HR Response
- Right to Left Shunt Physiology
- Marked Improvement with an endothelin-1 receptor antagonist after just 6 weeks. Reversal of shunt physiology. Reduction in the ventilatory requirements of exercise.

Heart Failure

Case # 2

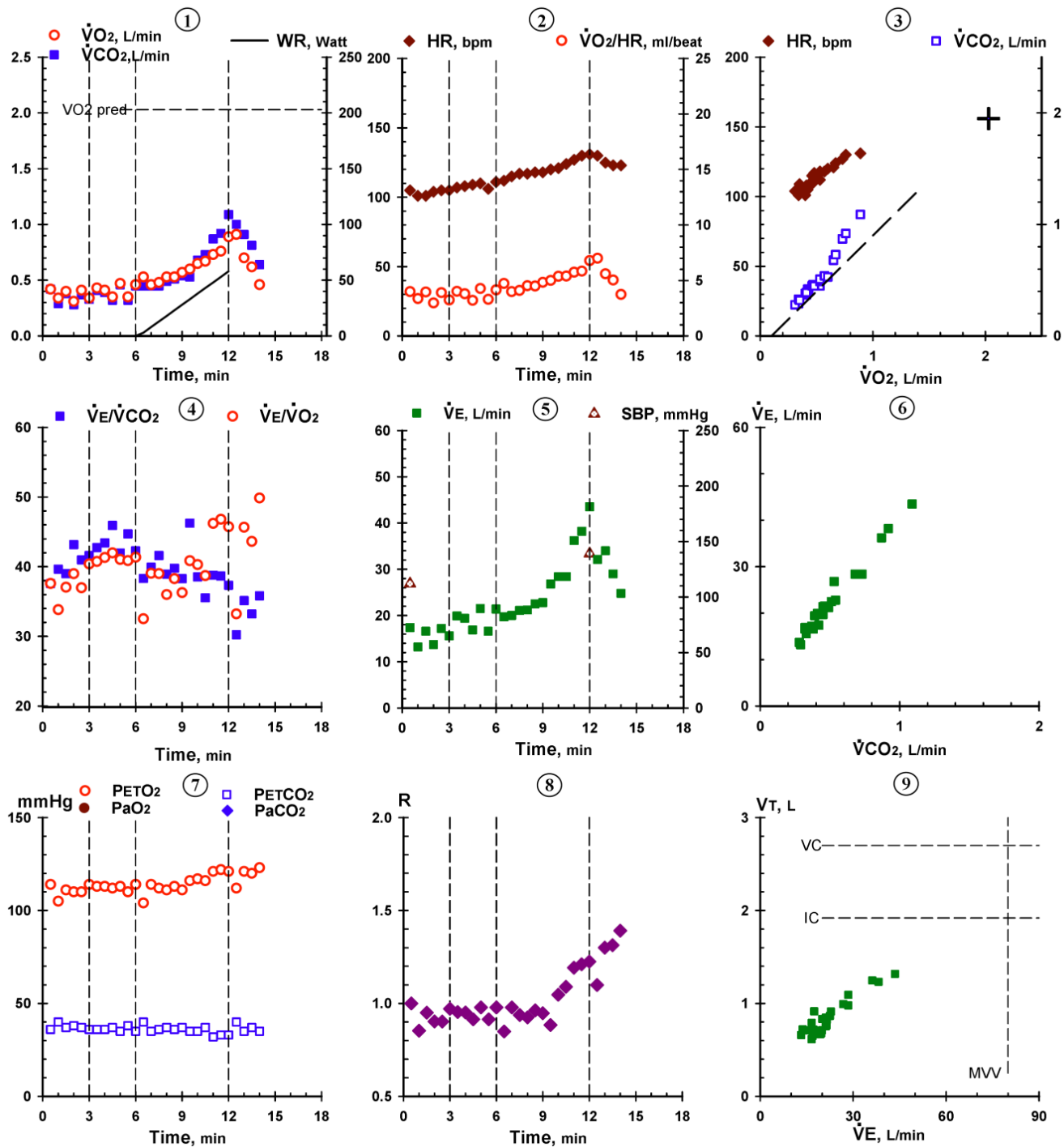
Heart Failure - HFrEF

- 64 year old male, shortness of breath and exertional dyspnea x 11 years. Multiple “CHF” admissions
- No prior MI’s or valvular disorders
- Medications: digoxin, furosemide, hydralazine (later ACE), KCL, ranitidine.
- Physical Examination S3, few rales, no peripheral edema.
- CXR: Cardiomegaly and Kerley B lines.
- EKG: LAE, LVH.
- PFT’s: FEV₁ 2.01 (69% predicted), FVC 2.70 (75% predicted), FEV₁/VC 74%, DLCO 22 (96% of predicted)

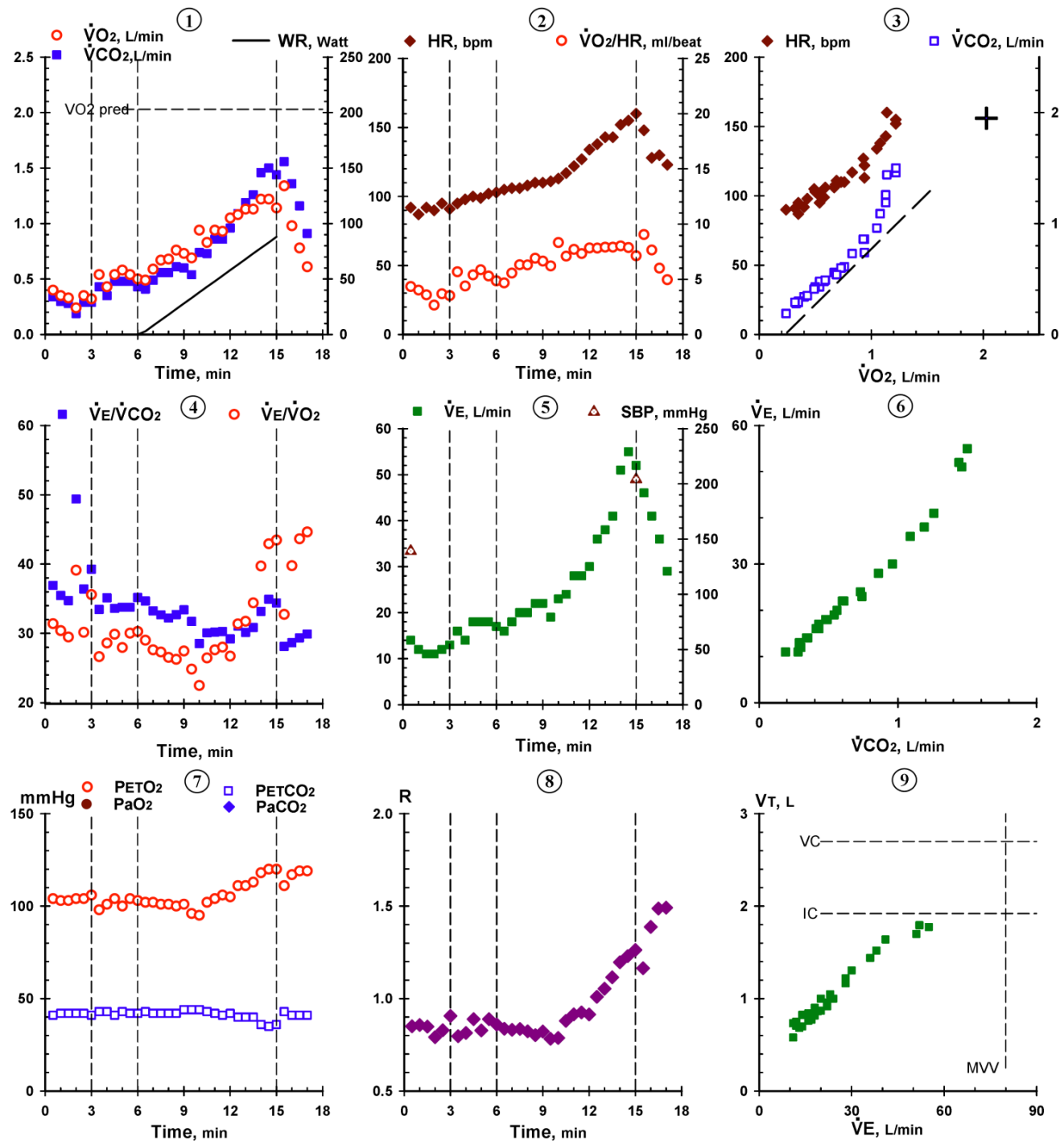
Exercise Indices - HF

Measurement	Predicted	Study # 1	Study # 2
Max WR		58	88
Peak VO ₂	2.03	0.91	1.34
AT	> 0.89	0.6	1.0
Max HR	156	131	160
O ₂ Pulse	13.0	7.0	9.0
Δ VO ₂ / Δ WR	10.3	8	9.2
Max VE		44	55
VE/VCO ₂ at AT	28.6	37.6	30.2
Breathing Reserve	> 15	36	25

First CPET



Second CPET



HF – CPET Conclusions

- Very Low VO_2
- Very Low AT
- Low O_2 pulse
- Low VO_2 / WR
- High Ventilatory Equivalents
- Marked Improvement in VO_2 and AT with ACE

Interstitial Lung Disease

Case # 3

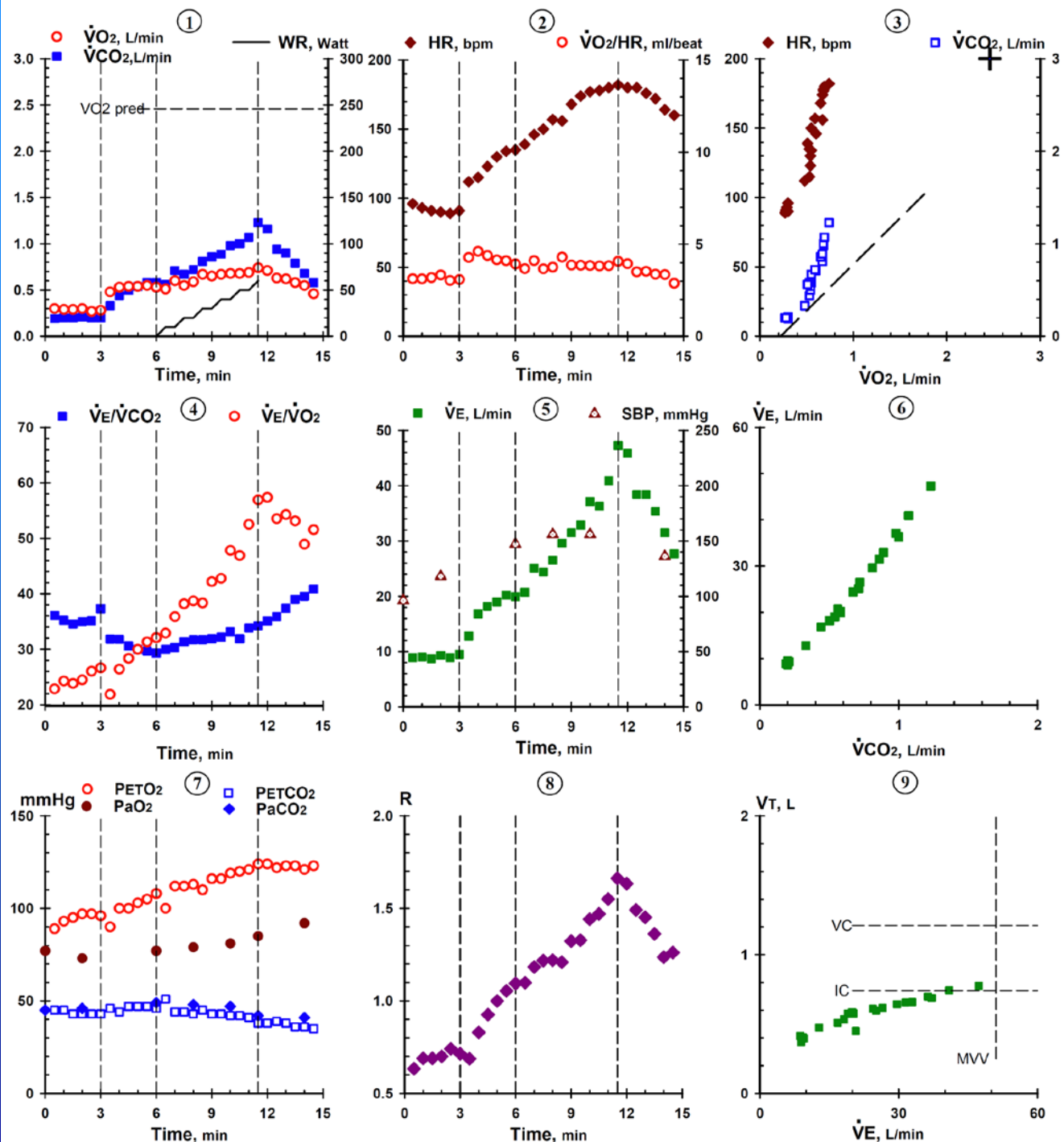
Interstitial Lung Disease

- 20 year old man with a prior history of exposure to crop dusting chemicals.
- Interstitial Lung Disease on Lung Biopsy with Mica deposits.
- Severe Dyspnea with walking one block or two flights of stairs.
- Medications: Prednisone.
- Physical Examination: Velcro Rales throughout both lung fields.
- CXR: Honeycombing.
- EKG: Normal.
- PFT's: FEV₁ 1.21 (41% predicted), FVC 1.24 (34% predicted), FEV1/VC 99%, MVV 51, DLCO 7 (23% of predicted)

Exercise Indices - ILD

Measurement	Predicted	Pre- Rehab
Max WR		60
Peak VO_2	2.46	0.74
AT	> 0.98	< 0.55
Max HR	200	182
Max VE		47
VE/VCO_2 at AT	24.4	30.1
RR at peak exercise		61
Breathing Reserve	> 15	4
VD/VT at LAT	< 0.3	0.36

CPET



ILD - CPET Conclusions

- Severe Restrictive Lung Disease with a Low DLCO
- Very Low Peak $\dot{V}O_2$
- Low Gas Exchange $\dot{V}A_{T}$
- Low stroke volume and cardiac output
- High $\dot{V}E/\dot{V}CO_2$ at AT

Chronic Obstructive
Pulmonary Disease (COPD)
Pre-Post Pulmonary Rehab

Case # 4

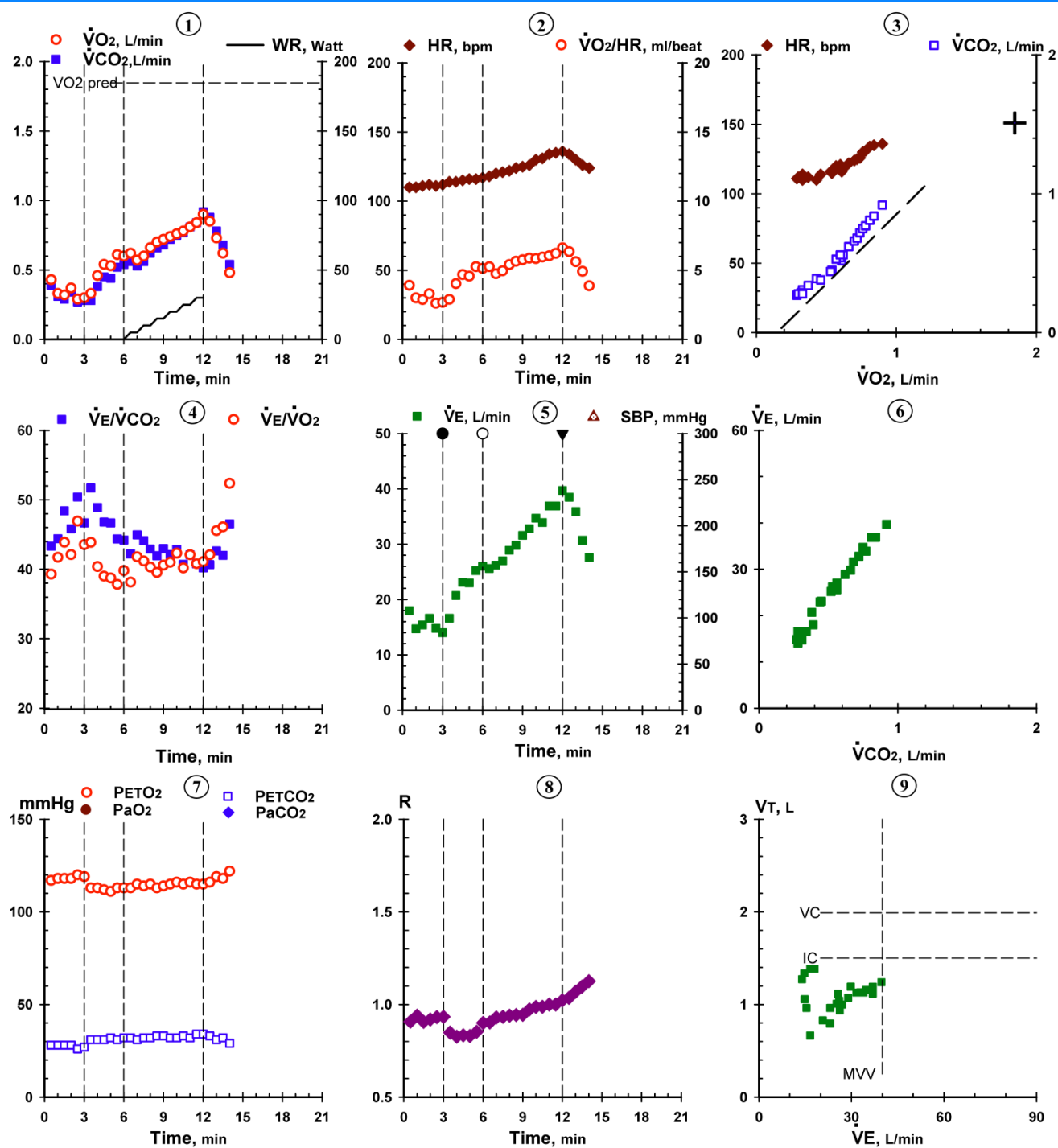
Chronic Obstructive Pulmonary Disease

- 69year old male with COPD. Lifelong smoker. Recently quit. F/U for Pulmonary Rehabilitation.
- Medications: theophylline, SABA, SAMA.
- Physical Examination: I:E 1:4
- CXR: Hyperinflated.
- EKG: Non-Specific ST and T wave changes.
- PFT's: FEV₁ 0.99 (35% predicted), FVC 1.99 (55% predicted), FEV1/VC 50%, MVV 40, DLCO 10 (45% of predicted)
- Post Rehab #'s (FEV1 1.11, FVC 2.19, MVV 44).

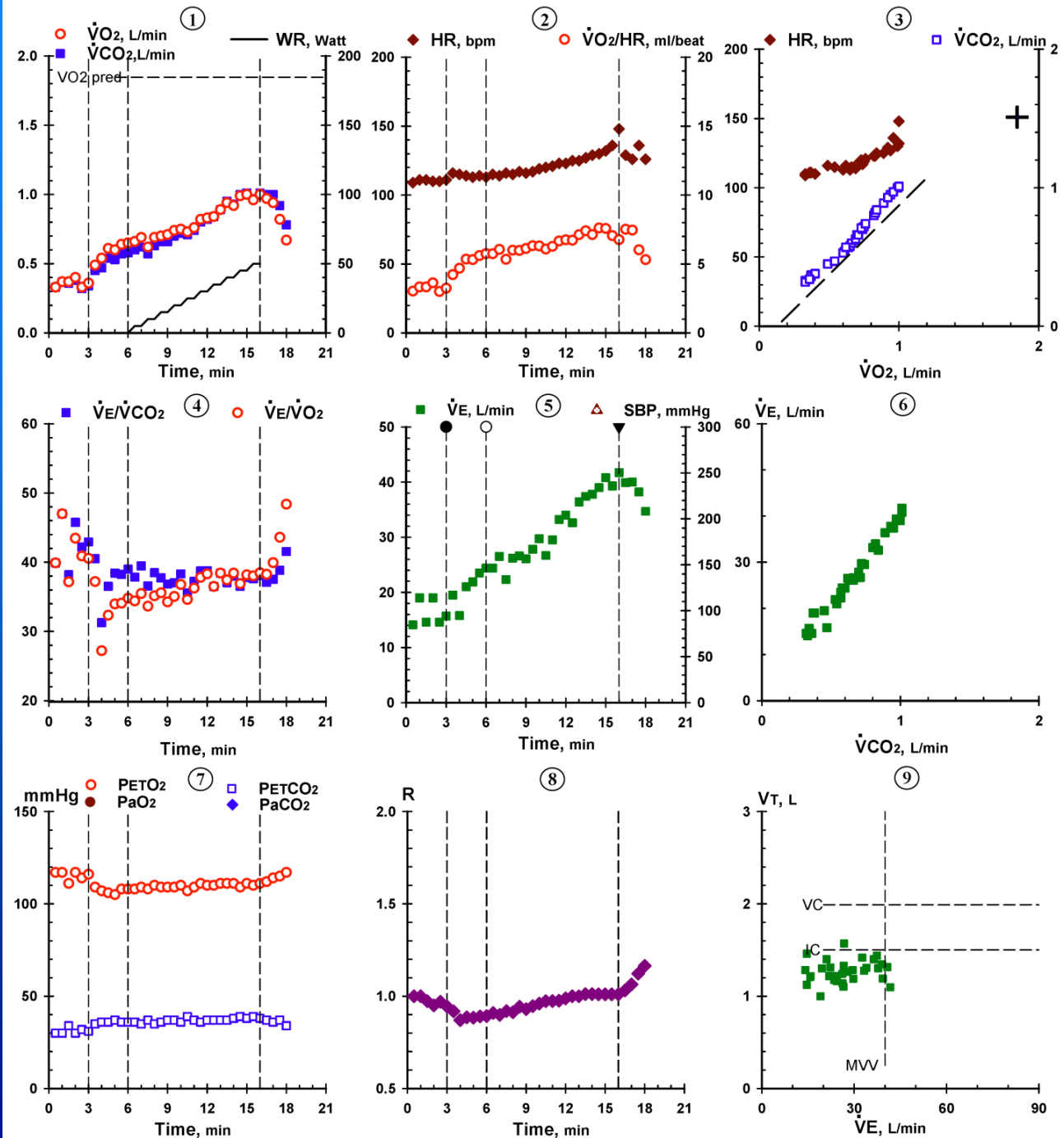
Exercise Indices - COPD

Measurement	Predicted	Pre- Rehab	Post- Rehab
Max WR		30	50
Peak VO2	1.67	0.90	1.0
AT	> 0.75	0.75	Indeterminant
Max HR	151	136	140
Max VE		40	42
VE/VCO2 at AT	29.1	41.5	37.4
RR at peak exercise		32	38
Breathing Reserve	> 15	0	2
Peak Lactate		3.0	2.3

First CPET Pre REHAB



Second CPET Post REHAB



COPD - CPET Conclusions

- Very Low peak VO_2
- Low AT
- High VE/VCO_2 at AT
- Low breathing reserve Δ
- Rehab:
 - PFT's about the same, although slightly better.
 - VE/VCO_2 decreased slightly
 - Training Effect – Lower Lactate

Using and Interpreting Exercise Tests

- Review of Important CPET Physiology
- Definitions
 - Gas Exchange:
 - VO_2 max, LAT, VO_2/WR , VE/VCO_2 , VE vs VCO_2 slope, Standard Testing
 - Cycle vs Treadmill
 - Out with the Old (Lose the FEF 25-75...)
 - In with the new... (e.g. FEV3/FEV6, PRISM)
 - Ramp/Progressively Increasing vs CWR/Endurance
- Exercise Phenotypes
 - COPD
 - HF
 - ILD
 - Pulm HTN

Hoc opus, hic labor est.

Virgil



“There is the task, and there is the toil.”

Dr. Brian Whipp (1937 – 2011)

THANK YOU!!

BREAK/EXHIBITORS

Saturday September 30, 2017 – 2:35 p.m. – 2:50 p.m.

RECOGNIZING AND MANAGING ACUTE EXACERBATIONS

Ni-Chang Liang, MD
UCSD

Saturday September 30, 2017 – 2:50 p.m. – 3:30 p.m.

Ni-Cheng Liang, MD, is an Assistant Clinical Professor at UCSD and is the Medical Director of Pulmonary Services at the UCSD Center for Pulmonary and Sleep Medicine. She is also the Executive Director for the UCSD Center for Mindfulness, and serves as Co-Chair of the American Thoracic Society Integrative Therapies Interest Group. She runs the multidisciplinary Airway Clinic for patients with obstructive lung disease. She is a member of the UCSD COPD Committee and is passionate about improvement in healthcare delivery for patients with COPD. She also has a special interest in integrative medicine, particularly using mindfulness based practices to improve the quality of life for patients with chronic lung disease.

Recognizing and Managing Acute Exacerbations of COPD (AECOPD)

September 30, 2017

Ni-Cheng Liang, MD

Medical Director, Pulmonary Services

UCSD Center for Pulmonary and Sleep Medicine

Executive Director, Center for Mindfulness

Assistant Clinical Professor of Medicine



Conflict of Interest Disclosure

I, Ni-Cheng Liang, MD, hereby declare that the content for this activity, including any presentation of therapeutic options, is well balanced, unbiased, and to the extent possible, evidence-based.

Astra-Zeneca Sub-Investigator

Actelion Sub-Investigator



Outline

- Definition of COPD Exacerbation (AECOPD)
- Symptoms
- Consequences of AECOPD
- Etiologies of AECOPD
- Risk factors for AECOPD
- Treatment of AECOPD
- Preventing COPD Exacerbations
- What you can do

Main Reference

- From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: <http://goldcopd.org>.
- Unless otherwise stated

GOLD Definition of AECOPD

"an acute worsening of respiratory symptoms that result in additional therapy."

- Mild- Short acting bronchodilators only (SABA)
- Moderate- SABA+ antibiotics and/or steroids
- Severe- hospitalization/ED/respiratory failure

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Table 3
Presenting features of chronic obstructive pulmonary disease exacerbation

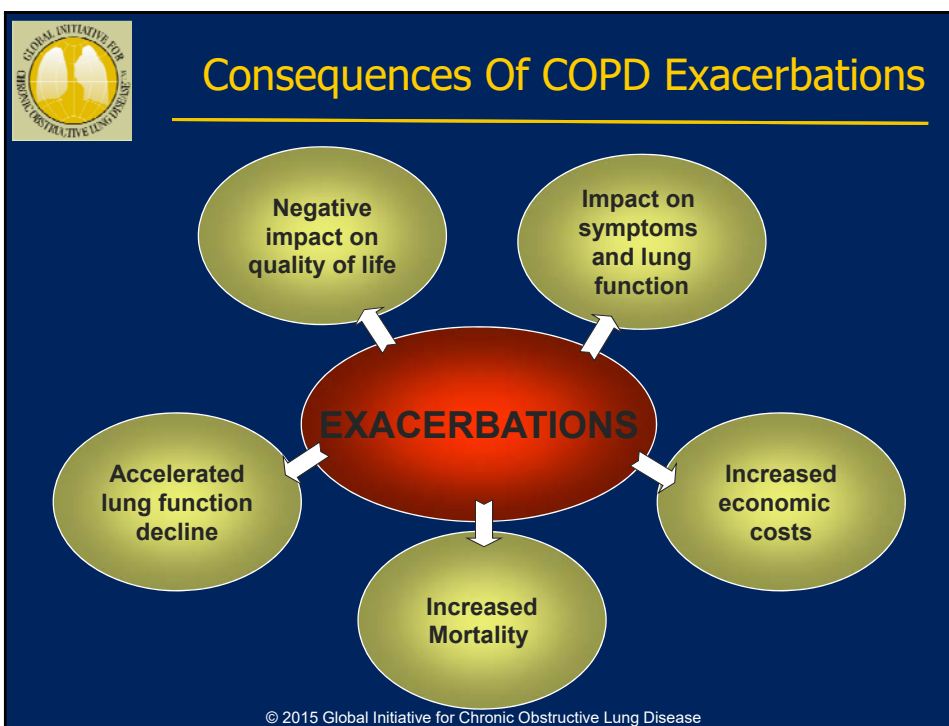
Symptoms and Signs	Differential Diagnoses ^a
Pulmonary	Pneumonia
Breathlessness	Congestive heart failure
Increased sputum volume	Pleural effusion
Increased sputum purulence	Pneumothorax
Expiratory wheeze	Pulmonary embolism
Cough	Cardiac ischemia
Increased work of breathing	Arrhythmia
Respiratory rate >20	
Cardiac	
Chest tightness	
Heart rate >110	
Psychiatric	
Confusion	
Sleepiness	
Insomnia	
Systemic	
Fatigue	
Malaise	

Pulmonary and extra-pulmonary manifestations of COPD exacerbation. Patients with COPD often have several comorbidities, hence alternative diagnoses may need to be ruled out.

^a Differential diagnoses listed are only some of the potential diseases that can present with symptoms and signs similar to COPD exacerbations.

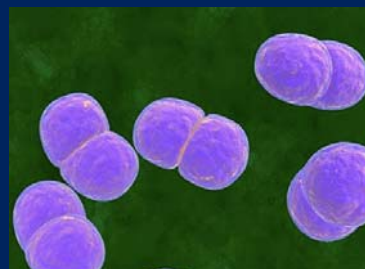
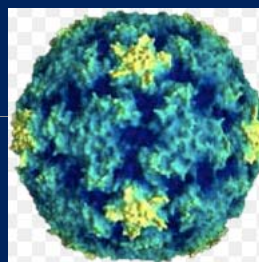
Med Clin N Am 101 (2017) 537–551

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Etiologies of AECOPD

- Respiratory viral infections → rhinovirus
 - More severe
 - Longer in duration
 - Precipitate more hospitalizations
- Bacterial infections
 - Moraxella
 - H. influenzae
 - S. pneumoniae
- Environmental factors
 - Pollution
 - Ambient temperature



Risk Factors for Exacerbations

- Frequent exacerbators: 2 or more / year
 - Worse health status
 - Increased morbidity
 - Strongest risk factor: number of exacerbations in the prior year
 - Changes in exacerbation frequency with worsening FEV1
- Increase in pulmonary artery: aorta cross section > 1
- Emphysema
- Airway wall thickness
- Chronic Bronchitis

SPIROMICS: Associations with AECOPD

- 1105 patients, 3 years
 - 538 (49%) at least one AECOPD
 - 567 (51%) had none
 - 82 (7%) at least one AECOPD each year
 - 23 (2%) had two or more acute exacerbations in each year.
 - In logistic regression, consistent AECOPD(≥ 1 event per year for 3 years) compared to no AECOPD
 - Higher baseline symptom burden
 - Previous exacerbations
 - Greater evidence of small airway abnormality on CT
 - Lower interleukin-15 concentrations
 - Higher interleukin-8 concentrations



Treatment of AECOPD

- Antibiotics-(when indicated) can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5-7 days.
- Bronchodilators
- Corticosteroids-improve lung function (FEV1), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5-7 days.
 - ERS/ATS 2017 guideline ≤ 14 days

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Table 5.4. Management of Severe but Not Life-Threatening Exacerbations*

- Assess severity of symptoms, blood gases, chest radiograph
- Administer supplemental oxygen therapy and obtain serial arterial blood gas measurement
- Bronchodilators:
 - Increase doses and/or frequency of short-acting bronchodilators
 - Combine short-acting β_2 -agonists and anticholinergics
 - Use spacers or air-driven nebulizers
- Add oral or intravenous corticosteroids
- Consider antibiotics (oral or occasionally intravenous) when signs of bacterial infection
- Consider noninvasive mechanical ventilation
- At all times:
 - Monitor fluid balance and nutrition
 - Consider subcutaneous heparin or low molecular weight heparin
 - Identify and treat associated conditions (e.g., heart failure, arrhythmias)
 - Closely monitor condition of the patient

*Local resources need to be considered.

2016 Global Initiative for Chronic Obstructive Lung Disease, Inc.



Antibiotics

- Reduce
 - Risk of short-term mortality by 77%
 - Treatment failure by 53%
 - Sputum purulence by 44%
- PRESCRIBE IF:
 - Increased cough, sputum purulence, and dyspnea
 - Increased cough and sputum purulence
 - Mechanical ventilation
 - Choice via local antibiogram
 - Tetracycline
 - Macrolide
 - Aminopenicillin with clavulanic acid
- Sputum cultures: Pseudomonas, resistant pathogens
 - Frequent exacerbators
 - Severe COPD
 - Mechanically ventilated



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Biomarkers to Guide Antibiotic Treatment

- CRP- controversial: elevated in viral and bacterial infections
- Procalcitonin
 - Reduces antibiotic exposure
 - Reduces side effects
 - Same clinical efficacy



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TABLE 1 Clinical effectiveness of procalcitonin-based protocols to initiate or discontinue antibiotics in patients presenting with acute exacerbations of chronic obstructive pulmonary disease

	Participants followed-up (studies)	Quality of the evidence (GRADE)	Relative effect* (95% CI)	Anticipated absolute effects	
				Risk with standard care	Risk difference with procalcitonin-guided protocols
Treatment failure for the index exacerbation	834 (5 RCTs)	Low ^{§,¶}	RR 0.81 [0.62–1.06]	206 per 1000	39 fewer failures per 1000 (78 fewer to 12 more)
Length of hospital stay for the index exacerbation	1042 (8 RCTs)	Moderate [§]	MD -0.76 [-1.95–0.43]	Mean length of hospital stay was 8.55 days	MD 0.76 fewer days (1.95 fewer to 0.43 more)
Proportion of patients who were prescribed antibiotics on admission	984 (7 RCTs)	Moderate [§]	RR 0.56 [0.43–0.73]	791 per 1000	348 fewer prescriptions per 1000 (451 fewer to 214 fewer)
Duration of the course of antibiotics	776 (6 RCTs)	Moderate [¶]	MD -3.83 [-4.32–3.35]	Mean duration of course of antibiotics was 8.27 days	MD 3.83 fewer days (4.32 fewer to 3.35 fewer)
Exacerbation recurrence rate at longest follow-up	496 (3 RCTs)	Low ^{§,¶}	RR 0.96 [0.69–1.35]	205 per 1000	8 fewer recurrences per 1000 (63 fewer to 72 more)
Re-hospitalisation rate at longest follow-up	398 (3 RCTs)	Low ^{§,¶}	RR 1.45 [0.92–2.29]	116 per 1000	52 more admissions per 1000 (9 fewer to 150 more)
Rate of re-hospitalisation due to an exacerbation at longest follow-up	298 (2 RCTs)	Low ^{§,¶}	RR 1.22 [0.71–2.09]	135 per 1000	30 more admissions per 1000 (39 fewer to 147 more)
Overall mortality at longest follow-up	1042 (8 RCTs)	Moderate [¶]	RR 0.99 [0.58–1.69]	41 per 1000	0 fewer deaths per 1000 (18 fewer to 29 more)

Data are presented as n, unless otherwise stated. GRADE (Grading of Recommendations Assessment, Development and Evaluation) working group quality of evidence assessments are as follows. High quality: further research is very unlikely to change the confidence in the estimate of effect; moderate quality: further research is likely to have an important impact on the confidence in the estimate effect and may change the estimate; low quality: further research is very likely to have an important impact on the confidence in the estimate effect and it is likely to change the estimate; very low quality: the estimate effect is very uncertain. RCT: randomised controlled trial; RR: risk ratio; MD: mean difference. [§]: The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI); [¶]: none of the included trials was blinded; [‡]: did not meet optimal information size criterion.

Eur Respir Rev 2017; 26: 160073

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Antibiotics or not? Use of Procalcitonin

- Cochrane Systematic Review
- 14 trials, total n= 4221
 - Not associated with increased treatment failure
 - Reduction in antibiotic exposure from 8→4 days



Schuetz P, Müller B, Christ-Crain M, Stolz D, Tamm M, Bouadma L, Luyt CE, Wolff M, Chastre J, Tubach F, Kristoffersen KB, Burkhardt O, Welte T, Schroeder S, Nobre V, Wei L, Bhatnagar N, Bucher HC, Briel M.

Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections.

Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD007498.

DOI: 10.1002/14651858.CD007498.pub2.

Predictors of Poor Outcomes

- Older age
- Lower BMI
- Comorbidities: cardiovascular disease, lung cancer
- Prior hospitalizations for AECOPD
- Severity of index AECOPD
- Need for long-term O₂ therapy at discharge

Indications for Noninvasive Mechanical Ventilation

- Preferred mode of ventilation
- pH less than or equal to 7.35 and/or PaCO₂ >45 mm Hg
- Clinical signs of respiratory muscle fatigue
- Persistent hypoxemia despite supplemental O₂



http://www.mayohealthcare.com.au/products/ventResp_images/Vision_image.jpg

Global Strategy for Diagnosis, Management and Prevention of COPD

Noninvasive Ventilation (NIV)

- Improves gas exchange
- Reduces work of breathing
- Reduces need for intubation
- Decreases hospitalization duration
- Decreases mortality

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GOLD Revision 2011

TABLE 11. CHECKLIST AT TIME OF DISCHARGE FROM HOSPITAL

- Reinforce smoking cessation measures
- Assure effective home maintenance of pharmacotherapy regimen
- Reassess inhaler technique
- Educate about maintenance regimen
- Give instruction regarding completion of steroid therapy and antibiotics, if prescribed
- Assess need for long-term oxygen therapy
- Assure follow-up visit in 4–6 wk
- Provide a management plan for comorbidities and their follow-up

Am J Respir Crit Care Med Vol 187, Iss. 4, pp 347–365, Feb 15, 2013

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Table 5.8. Interventions that reduce the frequency of COPD exacerbations	
Intervention class	Intervention
Bronchodilators	LABAs
	LAMAs
	LABA + LAMA
Corticosteroid-containing regimens	LABA + ICS
	LABA + LAMA + ICS
Anti-inflammatory (non-steroid)	Roflumilast
Anti-infectives	Vaccines
	Long term macrolides
Mucoregulators	N-acetylcysteine
	Carbocysteine
Various others	Smoking cessation
	Rehabilitation
	Lung volume reduction

FLAME Trial : LABA/LAMA v. ICS/LABA

- N= 3,362, 1 year
- Indacaterol/glycopyrronium v. fluticasone/salmeterol for reducing AECOPD
- 11% lower rate of AECOPD with LABA/LAMA ($p= 0.0003$)
- LABA/LAMA group- longer time to first exacerbation (71 vs. 51 days, $p < 0.001$)
- Lower annual rate of moderate or severe AECOPD ($p < 0.001$) (regardless of eosinophil count)
- Lower incidence of pneumonia 3.2% vs 4.8%, $p=0.02$

Wedzicha JA, et al. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. NEJM 2016; 374:2222-34.

FLAME Trial: Applicability to Clinical Practice

- Choose a LABA/LAMA over ICS/LABA for those with Group B disease
 - Regardless of blood eosinophil count



Wedzicha JA, et al. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. NEJM 2016; 374:2222-34.

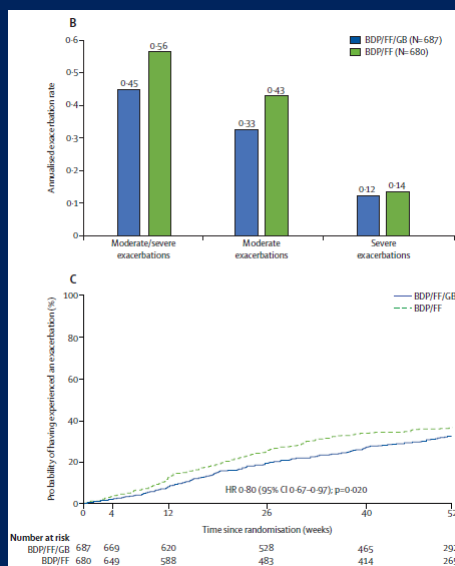
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TRILOGY: Single inhaler triple therapy vs. ICS/LABA for COPD

- 159 sites, 14 countries: 1368 received beclomethasone/formoterol or beclomethasone/formoterol/glycopyrronium
- LAMA/ICS/LABA
 - Improved FEV1 by 0.081L at week 26
 - 23% reduction in AECOPD

Singh D, et al. Single inhaler triple therapy versus ICS/LABA therapy for COPD (TRILOGY): a double-blind, parallel group, RCT. The Lancet 2016; 388.

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FULFIL Trial: Once-Daily Triple Therapy for COPD

- N = 1,810 Week 24
 - Triple therapy (n = 911), ICS/LABA therapy (n = 899)
 - Change from baseline in FEV1 was 142 mL (95% confidence interval [CI], 126,158) and -29 mL (95% CI, -46,-13); P < 0.001
 - Change SGRQ was -6.6 units (95% CI, -7.4,-5.7) and -4.3 units (95% CI, -5.2,-3.4); P < 0.001
 - Reduction in moderate/severe AECOPD rate with triple vs. ICS/LABA therapy (35% reduction, 95% CI, 14,51; P = 0.002).

Am J Respir Crit Care Med. 2017 Apr 4. doi: 10.1164/rccm.201703-0449OC. [Epub ahead of print]

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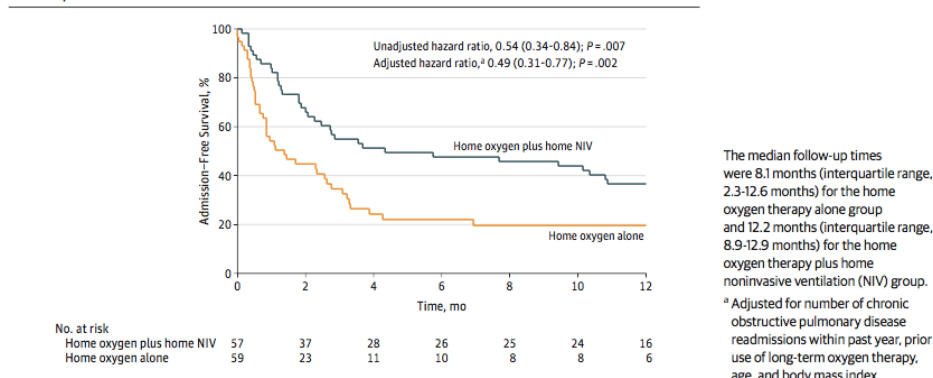
Home NIV post AECOPD

- Persistent hypercapnia ($\text{PaCO}_2 > 53$ mm Hg, 59) 2 weeks to 4 weeks after resolution of respiratory acidemia
- N= 28; home O₂ (~1 Lpm); N= 36; home O₂ + NIV (~1 Lpm)
- Home ventilator settings: IPAP of 24 (IQR, 22-26) cm H₂O, EPAP 4 (IQR, 4-5) cm H₂O, 14 (IQR, 14-16) breaths/minute, 1 year
- The median time to readmission or death was 4.3 months in the home O₂ plus NIV group vs 1.4 months (IQR, 0.5-3.9 months) in the home O₂ group, adjusted hazard ratio of 0.49 (95% CI, 0.31-0.77; $P = .002$).
- The 12-month risk of readmission or death was 63.4% home O₂ plus NIV group vs 80.4% in home O₂ group, absolute risk reduction of 17.0% (95% CI, 0.1%-34.0%).

JAMA. 2017;317(21):2177-2186.

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Figure 2. Kaplan-Meier Survival Plot of Time to Readmission or Death From Randomization to the End of Trial Follow-up at 1 Year



JAMA. 2017;317(21):2177-2186.

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Pulmonary Rehabilitation

- Improves dyspnea, health status, and exercise tolerance
- Reduces hospitalization in those who have had a recent exacerbation (< 4 weeks GOLD; <3 weeks ERS/ATS)



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Self-Management with Action Plans

- 22 studies, n= 3854
- Improvements in HRQoL
- Lower probability of respiratory-related hospital admissions
- No excess all-cause mortality risk was observed, but exploratory analysis showed a small, but significantly higher respiratory-related mortality rate for self-management compared to usual care.

Cochrane Database Syst Rev. 2017 Aug 4;8:CD011682. doi: 10.1002/14651858.CD011682.pub2. [Epub ahead of print]

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TASK FORCE REPORT
ERS/ATS GUIDELINE

Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline

Jadwiga A. Wedzicha [ERS co-chair]¹, Marc Miravittles², John R. Hurst³,
Peter M.A. Calverley⁴, Richard K. Albert⁵, Antonio Anzueto⁶, Gerard J. Criner⁷,
Alberto Papi⁸, Klaus F. Rabe⁹, David Rigau¹⁰, Pawel Sliwinski¹¹, Thomy Tonia¹²,
Jørgen Vestbo¹³, Kevin C. Wilson¹⁴ and Jerry A. Krishnan [ATS co-chair]¹⁵

ERJ 2017; 49:1600791

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TABLE 1 Recommendations for the treatment of chronic obstructive pulmonary disease (COPD) exacerbations

Recommendation	Strength	Quality of evidence
1 For ambulatory patients with an exacerbation of COPD, we suggest a short course (≤14 days) of oral corticosteroids	Conditional	Very low
2 For ambulatory patients with an exacerbation of COPD, we suggest the administration of antibiotics	Conditional	Moderate
3 For patients who are hospitalised with a COPD exacerbation, we suggest the administration of oral corticosteroids rather than intravenous corticosteroids if gastrointestinal access and function are intact	Conditional	Low
4 For patients who are hospitalised with a COPD exacerbation associated with acute or acute-on-chronic respiratory failure, we recommend the use of noninvasive mechanical ventilation	Strong	Low
5 For patients with a COPD exacerbation who present to the emergency department or hospital, we suggest a home-based management programme (hospital-at-home)	Conditional	Moderate
6 For patients who are hospitalised with a COPD exacerbation, we suggest the initiation of pulmonary rehabilitation within 3 weeks after hospital discharge	Conditional	Very low
7 For patients who are hospitalised with a COPD exacerbation, we suggest not initiating pulmonary rehabilitation during hospitalisation	Conditional	Very low

ERJ 2017; 49:1600791

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Early follow-up within 30 days after discharge

- 62,746 AECOPD admissions 1996-2006
- F/u within 30 days with PCP or pulmonologist
 - Reduced risk for ER visits ([HR], 0.86; 95% [CI], 0.83-0.90)
 - All-cause readmissions (HR, 0.91; 95% CI, 0.87-0.96).



Sharma G, et al. Outpatient follow-up visit and 30-day emergency department visit and readmission in patients hospitalized for COPD. *Arch Intern Med.* 2010; 170(18):1664-1670.

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What you can do...

- What are the practice patterns for treatment of AECOPD treatment inpatient/outpatient at your institution?
- Healthcare provider/patient/caregiver education
- COPD orderset
- Coordinator from inpatient to outpatient setting
- Prompt follow up post discharge (phone call/office visit)

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Thank you!

Questions?

My contact information:
Ni-Cheng Liang, MD
Office: 858-657-1869
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CLINICAL INSIGHTS TO TREATING THE PATIENT
WITH COPD AND ILD

Gordon Yung, MD
UCSD

Saturday September 30, 2017 – 3:30 p.m. – 4:10 p.m.

Gordon Yung, MD, received his medical degree from the University of Hong Kong. He is currently the Medical Director of the Lung Transplant Program at UCSD. His research interests are in COPD, interstitial lung disease and lung transplantation. Dr. Yung serves as a Clinical Professor of Medicine at UCSD.



Clinical Insights to Treating the Patient with COPD and ILD

California Thoracic Society
Fall Symposium & Educational Conference September 30, 2017

Gordon Yung, MD
Clinical Professor of Medicine

Where discoveries are delivered.™

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Overview

- Relationship between COPD and ILD
- Review of Combined Pulmonary Fibrosis and Emphysema (CPFE)
- Treatments
 - Specific treatment (e.g. pulmonary hypertension)
 - General treatment (if we have time...)

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COPD and ILD: Co-existng Conditions or Related Diseases?

COPD

- Chronic Bronchitis
- Emphysema
- > 300 million worldwide
- ?30 million US
- Smoking accounts for ~90%
- Increased risks of lung cancer

ILD

- > 200 conditions
- Prevalence?
- IPF > 100,00 in US
- Some smoking related conditions (IPF, RB-ILD, LCH)
- IPF: 2/3 smokers, 1-10% lung cancer

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Tea Vos. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015

COPD and ILD: Co-existng Conditions or Related Diseases?

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Tea Vos. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015

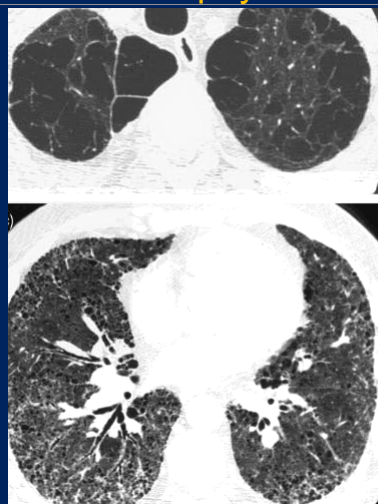
Combined Pulmonary Fibrosis and Emphysema

- First reported in 1974; first proposed as possibly a distinct entity in 2005
- Does Emphysema + Pulmonary Fibrosis = CPFE? Should CPFE only include those with UIP pattern? IPF only?
- Up to 30% of IPF patients may have evidence of emphysema on CT scan
- Problems of data:
 - Lack of/changing definitions:
 - Does Emphysema + Pulmonary Fibrosis = CPFE?
 - Should CPFE only include those with UIP pattern? IPF only?
 - What is IPF?
 - Lack of reliable means to quantify degree of PF and emphysema to determine outcome (e.g. mortality reported between 2.1 – 8.5 years)
- IPF and emphysema may share some immunologic pathways (TGF- β , oxidative stress etc.) and genetic mutations (telomere shortening): **synergy in smoking?**

Auerbach Chest 65 (1), 1974
Cottin Eur Respir J 26 (4), 2005
Mejia Chest 136 (1), 2009

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Combined Pulmonary Fibrosis and Emphysema

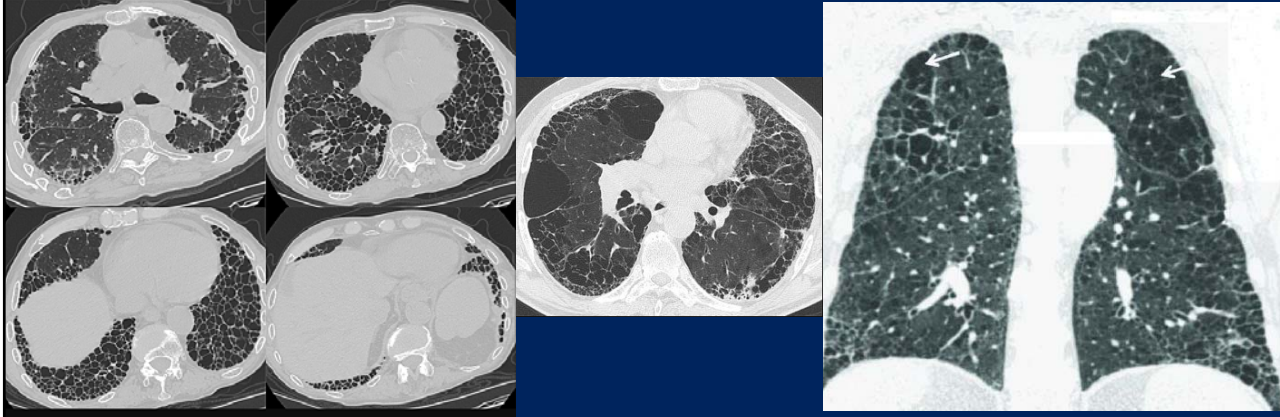


* Upper lobe centrilobular emphysema
** Lower lobe fibrosis

Cottin et al. Eur Respir J 2005

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Combined Pulmonary Fibrosis and Emphysema: Radiographic Dilemma



- * Separating emphysema from honeycombing
- ** Thick wall cysts
- *** Ground glass changes in 60%?

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Combined Pulmonary Fibrosis and Emphysema: General Observations

- Emphysema occurs before fibrosis
- Patients tend to male, older at presentation, and more heavy smokers (>40 pack year except with mutations)
- PFT's:
 - Lower DLCO
 - Relative preservation of lung volumes
 - Decline in PFTs mirrors more that of IPF and less of COPD
- Higher incidence of PAH
 - Correlates with DLCO
 - Can occur/progress rapidly

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Combined Pulmonary Fibrosis and Emphysema: Survival

- Earlier reports suggest worse overall survival
- However, recent study (*Jacob et al Eur Respir 2017*) suggest emphysema had no additional impact on survival, when corrected for age/gender/smoking status/baseline DLCO
- Multiple studies suggest CPFE patients who develop lung cancers have worse prognosis:
 - Implied more scrutiny on surgical resection as treatment
 - ?Use of pre-operative composite physiologic index (CPI) (Wells et al. Am J Respir Crit Care Med 2003):
 - Extent of fibrosis on CT scan – DLCO – FVC + FEV1
 - Seriously?

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What About Treatment For COPD + ILD? My Personal Bias!

- Big Picture: separate the 2 conditions
- **COPD treatment:**
 - Generally the same treatment as isolated COPD
 - In many cases, survival is limited by ILD rather than COPD
 - Many ILDs can have airway components that may respond to COPD treatments

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Treatment of ILD/COPD: The 'Interstitial Component'

- Decision to treat depends on etiology of ILD and its projected morbidity and mortality
- **Medications**
 - Anti-inflammatory and “immunosuppressants”
 - Underlying autoimmune diseases or those with “inflammation”
 - Antifibrotics
 - Lack of data except in IPF/mild COPD (may be...)

Collum et al. Pulmonary hypertension associated with idiopathic pulmonary fibrosis: current and future perspectives. Canadian Respir J 2017

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Treatment of ILD/COPD: PAH

- PAH therapy: None demonstrated efficacy in RCT on combined disease
 - When and why?
 - Presence of PAH ≠ Mortality/morbidity for many patients with isolated disease
 - ECHO?
 - Which one? ETRA/Prostinoids/NO or cGMP pathway
 - What route? Inhaled vs Oral / IV / SQ?

Collum et al. Pulmonary hypertension associated with idiopathic pulmonary fibrosis: current and future perspectives. Canadian Respir J 2017

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ILD and PAH Therapy: Endothelin Receptor Antagonists

- BUILD-1 (King: Am J Respir Crit Care Med 2011)
 - 616 IPF patients randomized to Bosentan vs placebo (2:1) x 1 year. No difference in change in FVC or DLCO or QOL
- ARTEMIS-IPF (Raghu: Ann Int Med 2013, Am J Respir Crit Care Med 2012)
 - Ambrisentan and IPF
 - ↑ risk of disease progression and resp hospitalization
- BPHIT (Corte: Am J Respir Crit Care Med 2014)
 - Bosentan for IPF or fibrotic NSIP + PAH
 - No change in PVR



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ILD and PAH Therapy: Prostanoids

- Saggar et al (Thorax 2014)
 - Prospective open label 12 week single center using iv/sq treprostinil
 - 15 patients with advanced PF and significant PAH (mPAP ≥ 35 mmHg)
 - Before and after treatment: 6MWT (171 ± 93 vs 230 ± 114 m), RAP (9.5 ± 3.4 vs 6.0 ± 3.7), CI (2.3 ± 0.5 vs 2.7 ± 0.6); mvO₂ (65 ± 7.2 vs 70.9 ± 7.4): no change in oxygenation

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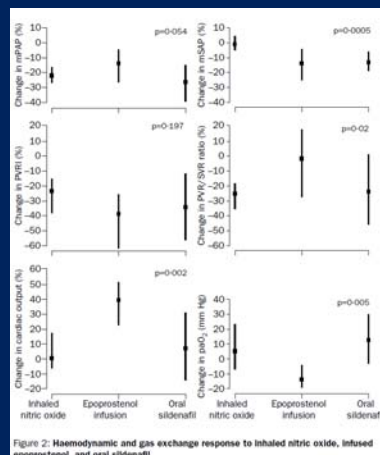
ILD and PAH Therapy: PDE5 Inhibitor Sildenafil

- Ghofrani et al: Sildenafil for treatment of lung fibrosis and pulmonary hypertension: a randomised controlled trial. Lancet 2002:
 - 16 patients with IPF, CREST, systemic sclerosis, silicosis, HP. All with NYHA functional class III/IV
 - Acute response to iNO then either single dose sildenafil or epoprostenol infusion till side effects

	Treatment group		
	Sildenafil (n=8)	Epoprostenol (n=8)	Total (n=16)
Age (years)	61.5 (38 to 79)	46.0 (27 to 75)	56.5 (27 to 79)
Heart rate (beats per min)	78.0 (60 to 108)	96.0 (61 to 123)	86.0 (60 to 123)
Mean pulmonary arterial pressure (mm Hg)	41.0 (25 to 62)	33.5 (25 to 59)	40.0 (25 to 62)
Mean systemic arterial pressure (mm Hg)	92.5 (65 to 104)	96.0 (61 to 123)	92.5 (61 to 123)
Cardiac index (L/min/m ²)	2.2 (1.4 to 3.2)	2.4 (1.4 to 4.3)	2.3 (1.4 to 4.3)
Systemic vascular resistance index (dyne/s/cm ⁵ /m ²)	2683.5 (2121 to 3820)	2692.8 (1536 to 5882)	2683.5 (1536 to 5882)
Pulmonary vascular resistance index (dyne/s/cm ⁵ /m ²)	1186.1 (515 to 3296)	961.8 (448 to 3057)	1108.7 (448 to 3296)
Mixed venous oxygen saturation (%)	70.4 (57 to 76)	66.5 (38 to 75)	69.5 (38 to 76)
Partial pressure of arterial oxygen (mm Hg)	77.0 (72 to 104)	63.0 (50 to 102)	73.5 (50 to 104)
Partial pressure of carbon dioxide (mm Hg)	41.0 (32 to 49)	36.3 (27 to 57)	37.3 (27 to 57)
Vital capacity (%)*	65.8 (25 to 87)	49.0 (23 to 75)	55.0 (23 to 87)
Diffusion capacity for carbon monoxide gas*	23.0 (13 to 72)	27.5 (14 to 63)	24.5 (13 to 72)
Pulmonary shunt flow	4.0 (0 to 17)	4.8 (3 to 28)	4.8 (0 to 28)

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Ghofrani et al: Sildenafil for treatment of lung fibrosis and pulmonary hypertension: a randomised controlled trial. Lancet 2002: **Acute Response**



- iNO: ↓ PVR, ↑ CI, ?mild ↑ PaO₂
- PGI₂: ↓ PVR, ↑↑ CI, ↓ SVR and increase in pulm shunt flow (16.8 (10.8-35.9) → decrease PaO₂
- Sildenafil: within 15 min, peak 45-60 min. ↓ PVR, variable CI, ↑ PaO₂

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ILD/COPD and PAH Therapy: Sildenafil

- STEP-IPF: 180 patients: 12 + 12 (cross-over) week sildenafil in advanced IPF (no assessment of PAH)
 - Did not meet primary endpoint of $\geq 20\%$ increase in 6MWT
 - +ve secondary endpoints (QOL, gas exchange)
 - Subanalysis: those with RV dysfunction better preserved 6MWT
 - (Zisman et al. N Eng J Med 2010)
- 10 COPD patients without PH: 4 + 4 weeks (cross-over) sildenafil
 - No effect on 6MWT or VO₂ max
 - Sildenafil increased A-a gradient at rest (25.9 vs 23.0 mmHg, P=0.02) + worsening symptoms by SGRQ)
 - (Opposite changes in healthy subjects in altitude related hypoxia)

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ILD/COPD and PAH Therapy: Sildenafil

- Holverda et al (Pulm Pharmacol Ther 2008)
 - 18 COPD patients given single dose of sildenafil
 - Sildenafil attenuated mPAP during exercise without increase in SV or CO, or PO₂ (Baseline PAH: 68% -> 51% increase in mPAP). No change in exercise capacity
- Vitulo et al (J Heart Lung Transplant 2017)
 - RTC using sildenafil in COPD + PAH (mPAP 39, PVR 7) x 16 weeks on 28 patients (18 treatment)
 - ↓ PVR (-1.67 vs 0.13)
 - ↑BODE, DLCO and QOL
 - - No change in gas exchange

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Bottomline: ILD/COPD and PAH Therapy

- **ETRA:** No!
- **Prostanoid:**
 - Reserve for severe PAH (mPAP >35 mmHg)
- **PDE5 inhibitor/Sildenafil:**
 - Consider use with severe PAH
 - May worsen or improve PO₂

Long Term iNO in Combined Pulmonary Fibrosis and Emphysema

TABLE 1 Short-term effects of inhaled nitric oxide on hemodynamic measurements and arterial blood gas

	Pre-operative	Post-operative Day 1 (on ventilator)		Post-operative Day 2 (after extubation)	
		Baseline	On INO	On INO	Off INO
Supplemental oxygen	4 l/min	45%	45%	4 l/min	4 l/min
pH	7.45	7.42	7.42	n/a	n/a
PaO ₂ (mm Hg)	76	68	112	n/a	n/a
PaCO ₂ (mm Hg)	40	40	38	n/a	n/a
Blood pressure (mm Hg)	115/75	103/64	98/61	105/54	88/47
Heart rate (beats/min)	80	112	107	99	107
PAP (mean) (mm Hg)	88/45 (55)	99/49 (66)	80/42 (55)	76/32 (47)	90/40 (57)
PCWP (mm Hg)	18	15	11	5	7
Cardiac output (l/min)	3.45	4.47	4.56	5.87	3.81
PVR (Wood units)	12	11.3	9.58	7.1	13

Yung et al. Outpatient inhaled nitric oxide in a patient with idiopathic pulmonary fibrosis: a bridge to lung transplantation. J Heart Lung Transplant 2001)

Long Term iNO in Combined Pulmonary Fibrosis and Emphysema

TABLE II Exercise study after 3 months of inhaled nitric oxide

	On iNO + 4 l/min O ₂		Off iNO + 4 l/min O ₂	
	Rest	End of exercise*	Rest	End of exercise†
pH	7.43	7.41	7.42	7.47
PaO ₂ (mm Hg)	98	76	63	52
PaCO ₂ (mm Hg)	38	37	35	29
Blood pressure (mm Hg)	135/75	130/70	104/70	90/70
Heart rate (beats/min)	84	97	107	119

*After 4 minutes of steady-state exercise at 1 mile per hour.

†After 2 minutes 30 seconds of steady-state exercise at 1 mile per hour.

Yung et al. Outpatient inhaled nitric oxide in a patient with idiopathic pulmonary fibrosis: a bridge to lung transplantation. J Heart Lung Transplant 2001)

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General Treatment: ILD/COPD

- Oxygen
- Pulmonary rehabilitation
- Transplant: implication of oxygen/PH/recurrent COPD exacerbations
- Treatment of associated conditions
 - Bronchiectasis and infections
 - OSA
 - GERD, aspirations and esophageal diseases

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PANEL – Q & A

Ni-Cheng Liang, George Su, Stephanie Tsao,
Trina Limberg, Gordon Yung

Saturday September 30, 2017 – 4:10 p.m. – 4:30 p.m.

CLOSING REMARKS

Saturday September 30, 2017 – 4:30 p.m.