

# Identifying and Managing Respiratory Diseases and Symptoms after Transplant

## Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023



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University of Kansas Medical Center

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## Objectives

- Lung Basics
- Monitoring lung function
- Pulmonary conditions after transplant
- Management of those conditions
- What can you do?

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# Lungs

## Respiratory system

The diagram illustrates the human respiratory system. On the left side, labels include: Nasal Cavity, Nostril, Soft palate, Hard Palate, Oral Cavity, Larynx, Trachea, Carina of Trachea, Right Main Bronchus, and Right Lung. On the right side, labels include: Pharyngeal Tonsil, Nasopharynx, Oropharynx, Tongue, Epiglottis, Esophagus, Left Main Bronchus, Bronchi, Left Lung, and Diaphragm. A bracket on the right side groups the Pharyngeal Tonsil, Nasopharynx, and Oropharynx under the label 'Pharynx'.

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# Lungs

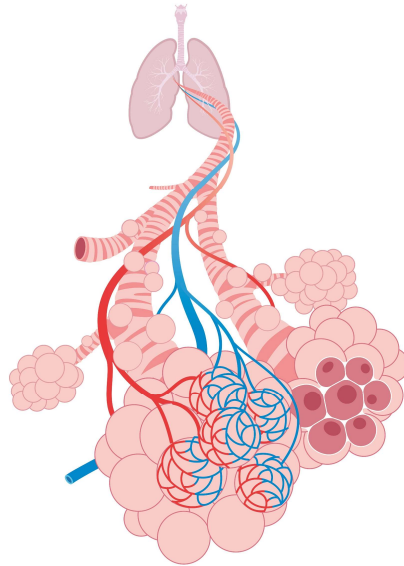
This anatomical illustration shows a frontal view of the human respiratory system. The trachea is centrally located, branching into the left and right main bronchi. The lungs are shown in a reddish-pink color, with the diaphragm visible at the bottom. The surrounding thoracic cavity and rib cage are also depicted.

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## Lungs



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## Spirometry

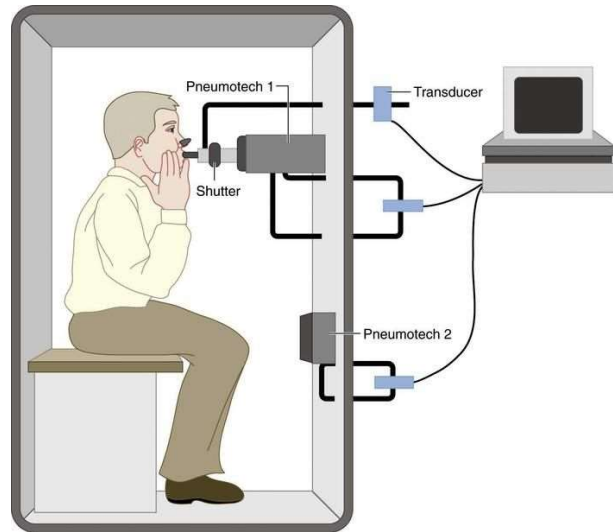
- Forced exhalation maneuver
- Calculates
  - Forced Vital Capacity (FVC)
  - Forced Expiratory Volume in 1 second (FEV1)
  - FEV1/FVC



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# Plethysmography

- Allow calculation of residual volume and total lung capacity
- Combined with assessment of diffusion capacity



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# Pulmonary Function Testing

-The University of Kansas Health System-  
PULMONARY FUNCTION LAB  
Kansas City, KS, 66160

Name: [REDACTED] BME: 29.4  
 Tech: [REDACTED] Height: 73.00 Age: 86  
 Doctor: [REDACTED] Weight: 223.00 Sex: Male [REDACTED]

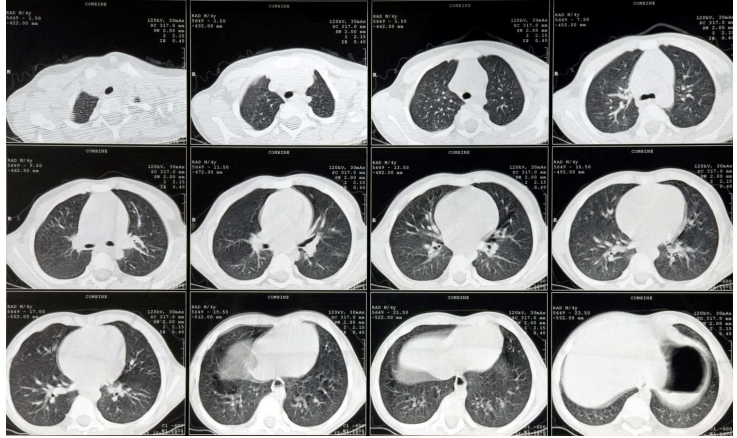
	Pre-Bronch			Post-Bronch		
	Actual	Pred	LLN% Pred	Actual	% Pred	% Chng
---- SPIROMETRY ----						
FVC (L)	3.05	4.28	3.26	71		
FEV1 (L)	2.17	3.01	2.15	72		
FEV1/FVC (%)	71	70	60	101		
FEV1/SVC (%)	66	70		94		
FEF 25-75% (L/sec)	1.42	1.96	0.21	72		
FEF Max (L/sec)	6.17	7.12	4.60	86		
Gaw (L/s/cmH2O)		1.03				
Raw (cmH2O/L/s)		1.45	0.66			
---- LUNG VOLUMES ----						
SVC (L)	3.26	4.28	3.26	76		
IC (L)	2.79	3.99		70		
TGV (L)	3.80	4.24	2.80	89		
RV (Pleth) (L)	3.33	2.95	2.21	112		
TLC (Pleth) (L)	6.60	7.68	6.10	85		
RV/TLC (Pleth) (%)	51	41	33	123		
---- DIFFUSION ----						
DLC <sub>0.05</sub> (ml/min/mmHg)	24.03	23.72	11.64	101		
DLC <sub>0.05</sub> (ml/min/mmHg)		23.72	11.64			
DLVA (ml/min/mmHg/L)	3.68	3.27	1.81	112		
VA (L)	6.53	7.40	6.03	88		

Spirometry demonstrates a mild reduction in vital capacity.  
 Residual volume is normal.  
 Total lung capacity is normal.  
 Transport factor (Diffusion Capacity) not corrected for hemoglobin is normal.  
 RV/TLC is increased.

IMPRESSION:  
 Normal pulmonary function studies.

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# CT Scan



# Bronchoscopy



## Pulmonary Conditions after Transplant

- Pre-existing lung conditions
- Infection
- Drug Toxicity
- GVHD

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## Pre-Existing Lung Conditions

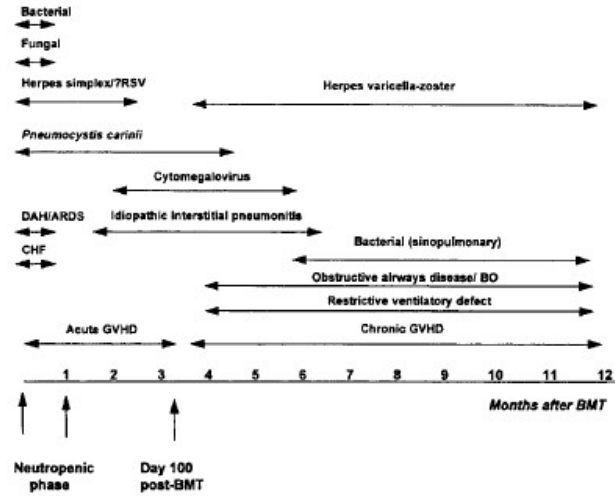
- Asthma
- COPD
- Interstitial Lung Diseases (Scarring)
- Pulmonary Embolism (Blood Clot)
- Long-COVID



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# Infections

- Bacterial
- Viral
- Fungal
- Pneumocystis



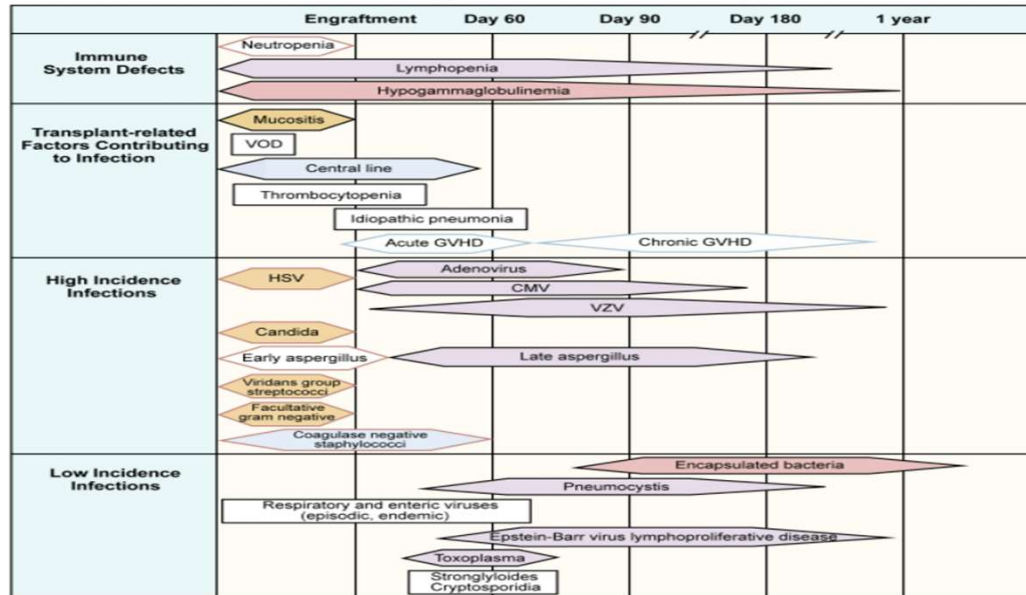
Folz RJ and Cirino-Marcano M. Murray and Nadel's Textbook of Respiratory Medicine. Chicago: Saunders, 2010. Print.



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Phases of Predictable Immune Suppression and Associated Opportunistic Infections



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# Drug Toxicity

- Medications used to treat malignancies may cause inflammation and toxicity in the lungs
- May present with:
  - Cough (bronchitis)
  - Shortness of breath
  - Pleurisy
- May increase risk of infection
- Can cause pneumonitis, fibrosis and inflammation

**TABLE 72-2. Classification of Drug-Induced and Related Pulmonary Diseases by Type of Medication**

<b>CHEMOTHERAPEUTIC</b>	Nitrofurantoin	Dipyridamole
<i>Cytotoxic</i>	*Acute	Flecainide
Azathioprine	Chronic	*Protamine
*Bleomycin	Sulfasalazine	Tocainide
Busulfan	<b>ANTI-INFLAMMATORY</b>	<b>INHALANT</b>
Chlorambucil	*Acetylsalicylic acid	Aspirated oil
Cyclophosphamide	Gold	*Oxygen
Etoposide	Interferons	<b>INTRAVENOUS</b>
Interleukin-2	Leukotriene antagonists	*Blood products
Melphalan	Methotrexate	*Ethanolamide maolate (sodium morrhuate)
*Mitomycin C	Nonsteroidal anti-inflammatory agents	Ethiodized oil (lymphangiogram)
Nitrosoureas	*Penicillamine	Talc
Procarbazine	<b>ANALGESIC</b>	<b>MISCELLANEOUS</b>
Tumor necrosis factor	*Heroin	Appetite suppressants
Vinblastine	*Methadone	Bromocriptine
Zinostatin	*Naloxone	*Complement-mediated leukostasis
<i>Noncytotoxic</i>	*Placidyl	Dantrolene
*Bleomycin	*Propoxyphene	*Hydrochlorothiazide
*Cytosine arabinoside	*Salicylates	Methysergide
*Gemcitabine	<b>CARDIOVASCULAR</b>	Radiation
*Methotrexate	*Amiodarone	Systemic lupus erythematosus (drug-induced)
*Procarbazine	Angiotensin-converting enzyme inhibitors	*Tocolytic agents
<b>ANTIBIOTIC</b>	Anticoagulants	*Tricyclics
*Amphotericin B	*β-Blockers	L-Tryptophan

\*Typically present as acute or subacute respiratory insufficiency.

Folz RJ and Cirino-Marciano M. *Murray and Nadel's Textbook of Respiratory Medicine*. Chicago: Saunders, 2010. Print.

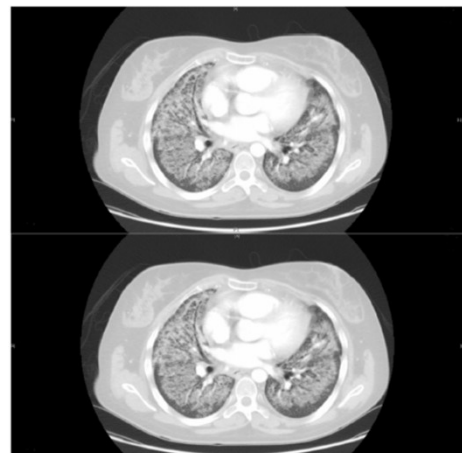
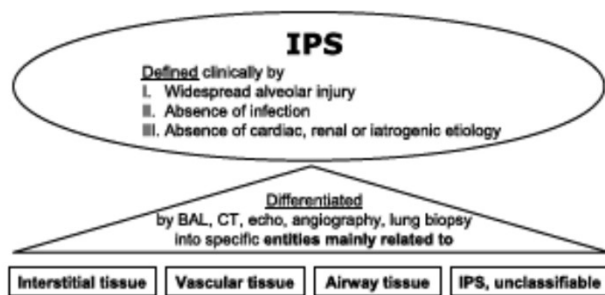


## Graft-versus-Host Disease (GVHD)

- Idiopathic Pneumonia Syndrome
  - Occurs first 90 days after transplant
- Organizing Pneumonia
  - Can occur anytime after transplant
  - Typically follows an infection
- Bronchiolitis Obliterans Syndrome
  - Most common manifestation
  - Typically occurs 3 months to 3 years after transplant

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## Idiopathic Pneumonia Syndrome

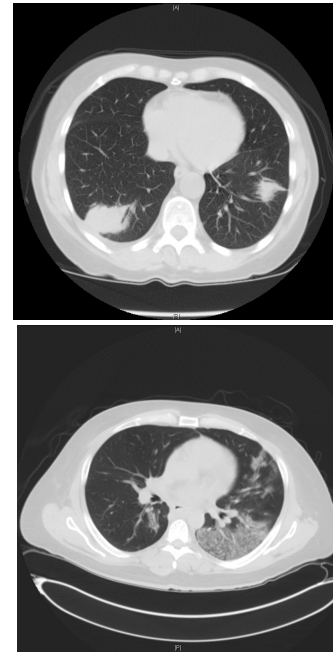


- Develops in 3-15% of post-HSCT patients
- Within 4 months of transplant

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## Organizing Pneumonia

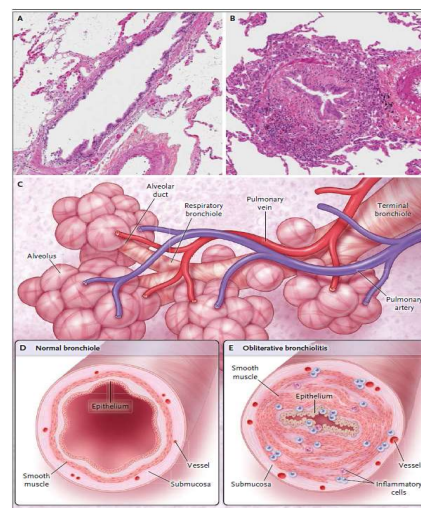
- Symptoms typically include cough, shortness of breath and pleurisy
- Pattern on CT is highly suggestive
- Usually requires bronchoscopy to exclude infection
- Responds well to steroids



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## Bronchiolitis Obliterans Syndrome

- Inflammation in the bronchioles (middle airways)
- If not treated promptly can cause scarring
- May be asymptomatic
  - Occasionally presents with cough and shortness of breath



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## Bronchiolitis Obliterans – Risk Factors

- Busulfan-based regimens
- 14 months or longer duration from leukemia diagnosis to transplant
- Peripheral blood stem cell source
- Female donor to male recipient
- Grade II-IV acute GVHD
- Previous interstitial pneumonitis
- Presence of airflow obstruction prior to transplant
- Age
- History of viral respiratory tract infections

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## Bronchiolitis Obliterans Syndrome

**Table 2—Suggested Diagnostic Criteria for BO**

Suggested Criteria

1. Allogeneic HSCT
2. Chronic GVHD
3. Evidence of airflow obstruction with  $FEV_1/FVC < 0.7$  and  $FEV_1 < 75%$  predicted
4. Air trapping or small airway thickening or bronchiectasis on HRCT of the chest with inspiratory and expiratory cuts, residual volume of PFT  $> 120%$  predicted
5. Absence of infection based on clinical symptoms, radiographs, microbiologic cultures, sputum culture, or BAL
6. Pathologic confirmation of constrictive bronchiolitis (biopsy not required for clinical diagnosis if all above criteria met)

BO = bronchiolitis obliterans; GVHD = graft-vs-host disease; HRCT = high-resolution CT scan; PFT = pulmonary function test. See Table 1 legend for expansion of other abbreviations. (Adapted with permission from Soubani and Pandya.<sup>57</sup>)

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## How Do We Treat?

- Management of systemic GVHD
  - Corticosteroids
  - Ruxolitinib (Jakafi )
  - Belumosudil (Rezurock)
  - Ibrutinib (Imbruvica)
  - Extracorporeal photopheresis
  - Rituximab

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## How Do We Treat?

- Pulmonary GVHD
  - Inhaled steroids
    - Reduce inflammation at site of medication deposition
    - Both fluticasone (Flovent) and budesonide/formoterol (Symbicort) have been studied
  - Montelukast (Singulair)
    - Blocks allergic pathway signaling
  - Short-acting bronchodilators (albuterol)
    - Immediately improve bronchial relaxation



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## How Do We Treat?

- Assess for need of supplemental oxygen
- Pulmonary rehabilitation
- Assess for other conditions
  - Sleep apnea
  - Pulmonary hypertension
  - Asthma
  - Chronic infections

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## What Can I Do?

- Optimize Medications
  - Treat underlying asthma and COPD
  - Assessed prior to transplant with PFT
- Smoking/vaping cessation
- Environmental stimuli
  - Air pollution
  - Air purifiers?



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## What Can I Do?

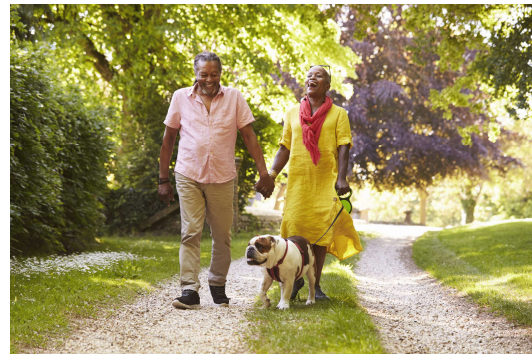
- Infection avoidance
  - Many/Most respiratory conditions after transplant follow a viral illness
  - Best way to prevent these conditions is by avoiding illness
    - Masks
    - Hand hygiene
    - Sick contact avoidance
    - Vaccination



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## What Can I Do?

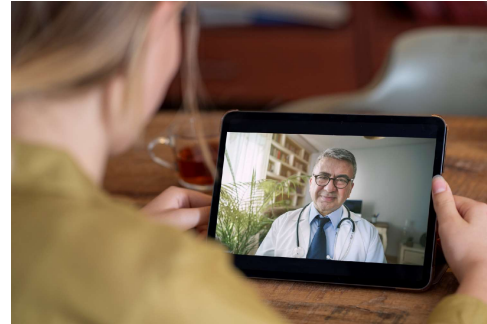
- Physical activity
  - Improves/maintains functional status
  - Prevents complications of debilitation
  - Earlier recognition of symptoms
  - Innumerable positive benefits



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## What Can I Do?

- Symptom detection
  - Notify transplant teams with new symptoms
    - Cough +/- sputum production
    - Chest pain
    - Shortness of breath
    - Abnormal breathing sounds/patterns (wheezing)
  - Leads to earlier evaluation
    - PFT/CT chest
  - Earlier detection of new conditions often leads to more effective treatments
- Home spirometry?



## Conclusion

- Lungs are susceptible to a myriad of conditions after transplant
- Regular PFT monitoring after transplant is standard of care
- New respiratory symptoms after transplant require further investigation
  - Typically with PFT and CT chest
- Promote lung health in yourself
  - Exercise
  - Infection avoidance
  - Avoiding noxious Stimuli

# Thank You

- Dr. Sunil Abhyankar, MD
- Dr. Joseph McGuirk, MD
- Dr. Leyla Shune, MD
- Dr. Anuraj Singh, MD
- Lung GVHD Consortium Group



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# QUESTIONS?



**Kyle Brownback, MD, FCCP**  
 University of Kansas Medical Center

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## LET US KNOW HOW WE CAN HELP YOU



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