Respiratory therapists (RTs) provide therapy to a wide variety of patients and are utilized in nearly every portion of healthcare. Many of the drugs and diagnostics used in cardiopulmonary support may be used in unconventional ways. This lecture is aimed at reviewing the literature and compiling the most common approaches concerning the use of Furosemide as an aerosolized treatment for dyspnea.

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# FUROSEMIDE AND DYSPNEA

## OBJECTIVES

- BREATHING AND DYSPNEA
- REVIEW FUROSEMIDE
- POSSIBLE INDICATION
- STARTING GUIDE
- CONCLUSION

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## COPD, CANCER, IPF, ETC.

Airflow limitation (in, out, or both)

Destruction of elastin

Dysfunction of the alveolus

Chemically mediated signals dull

Genetic alteration as the basal level

Impaired gas exchange

- Many, if not all, at some point experience dyspnea.
- As the diseases progress – this instance becomes more common
- One of the leading indicators to ER
- Separate the anatomical and the physiological and look at the subjective
- PRISm – Grade 4 may experience varying degrees of dyspnea that, like pain, cannot be truly quantified
- We a lot of the times look a select mechanisms: intra-extra thoracic, pulm vessels, heart problems, etc.

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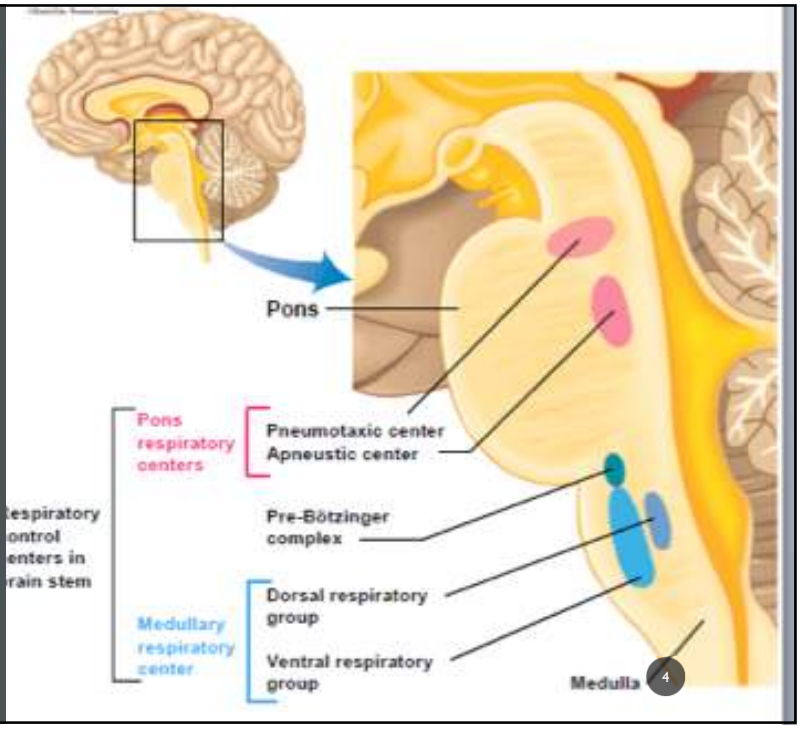
## BREATHING

- Pre-Botzinger Complex
- Medullary Control – rhymithicity – basic resp. generation
  - Ventral – exhale/inhale - prebot
  - Dorsal – inhale
- Pontine (pons) – intensity and frequency – fine tuning
  - Pneumotaxic – limits inhalation
  - Apneustic – encourage inhalation – depth and duration
- Central/Peripheral Chemoreceptors
- Mechanoreceptors* (hering-breuer)

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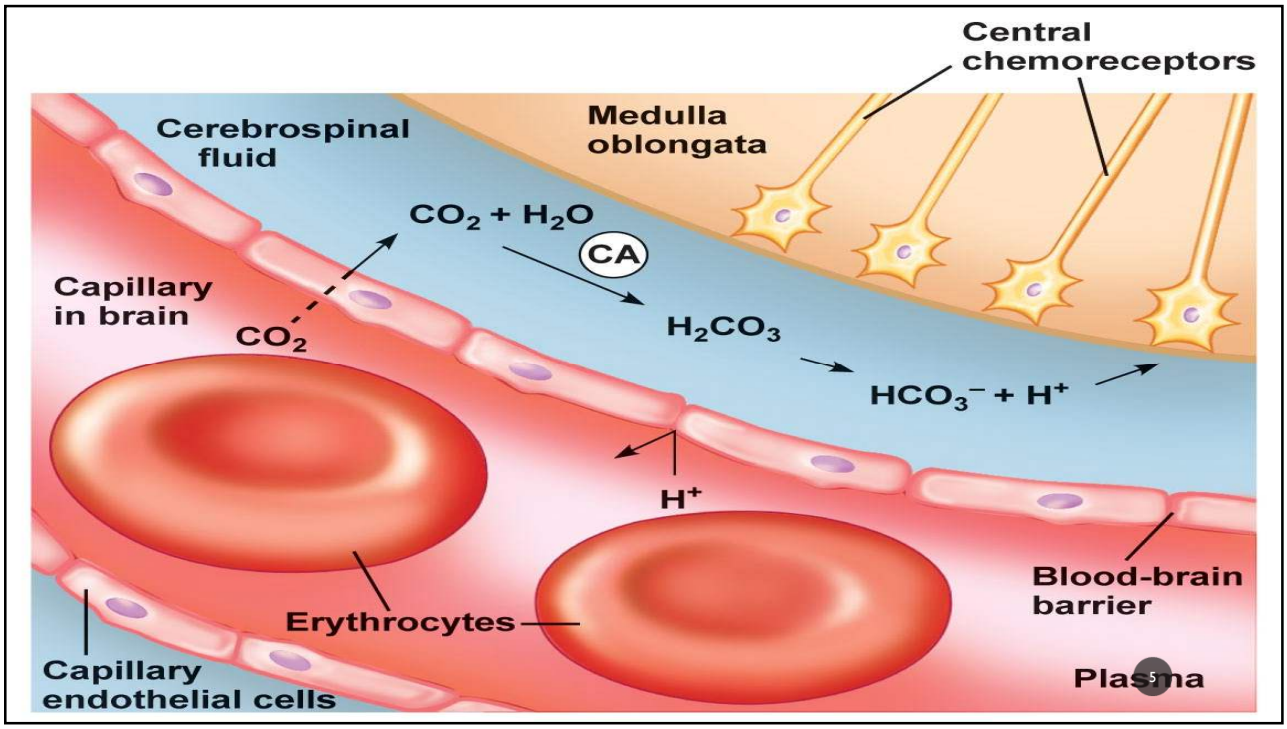
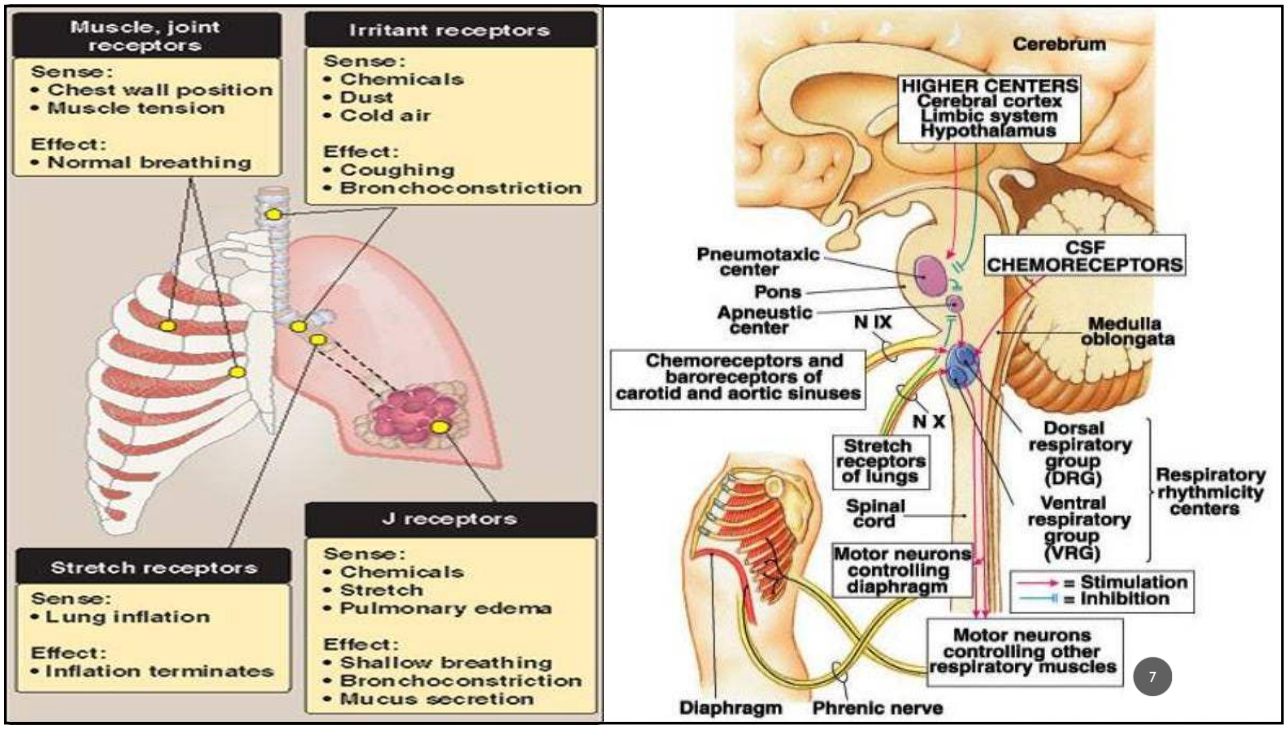



## STRETCH RECEPTORS

J-Receptors/C-Fibers - Stimulation of these sensory fibers is believed to be involved in evoking dyspneic sensations

- These vagal bronchopulmonary afferent C fibers are small, unmyelinated (C-Group Fibers) nerve fibers that provide sensory input from airway and lung structures.
- Stimulation by inhaled irritants elicits prominent reflex responses including apnea, smooth muscle contraction and mucus hypersecretion.


Muscle, joint receptors
Sense:
• Chest wall position
• Muscle tension
Effect:
• Normal breathing
Irritant receptors
Sense:
• Chemicals
• Dust
• Cold air
Effect:
• Coughing
• Bronchoconstriction
Stretch receptors
Sense:
• Lung inflation
Effect:
• Inflation terminates
J receptors
Sense:
• Chemicals
• Stretch
• Pulmonary edema
Effect:
• Shallow breathing
• Bronchoconstriction
• Mucus secretion
Cerebrum
HIGHER CENTERS
Cerebral cortex
Limbic system
Hypothalamus
Pneumotaxic center
Pons
Apneustic center
N IX
CSF CHEMORECEPTORS
Medulla oblongata
Chemoreceptors and baroreceptors of carotid and aortic sinuses
N X
Stretch receptors of lungs
Spinal cord
Dorsal respiratory group (DRG)
Ventral respiratory group (VRG)
Respiratory rhythmicity centers
Motor neurons controlling diaphragm
= Stimulation
= Inhibition
Motor neurons controlling other respiratory muscles
Diaphragm
Phrenic nerve
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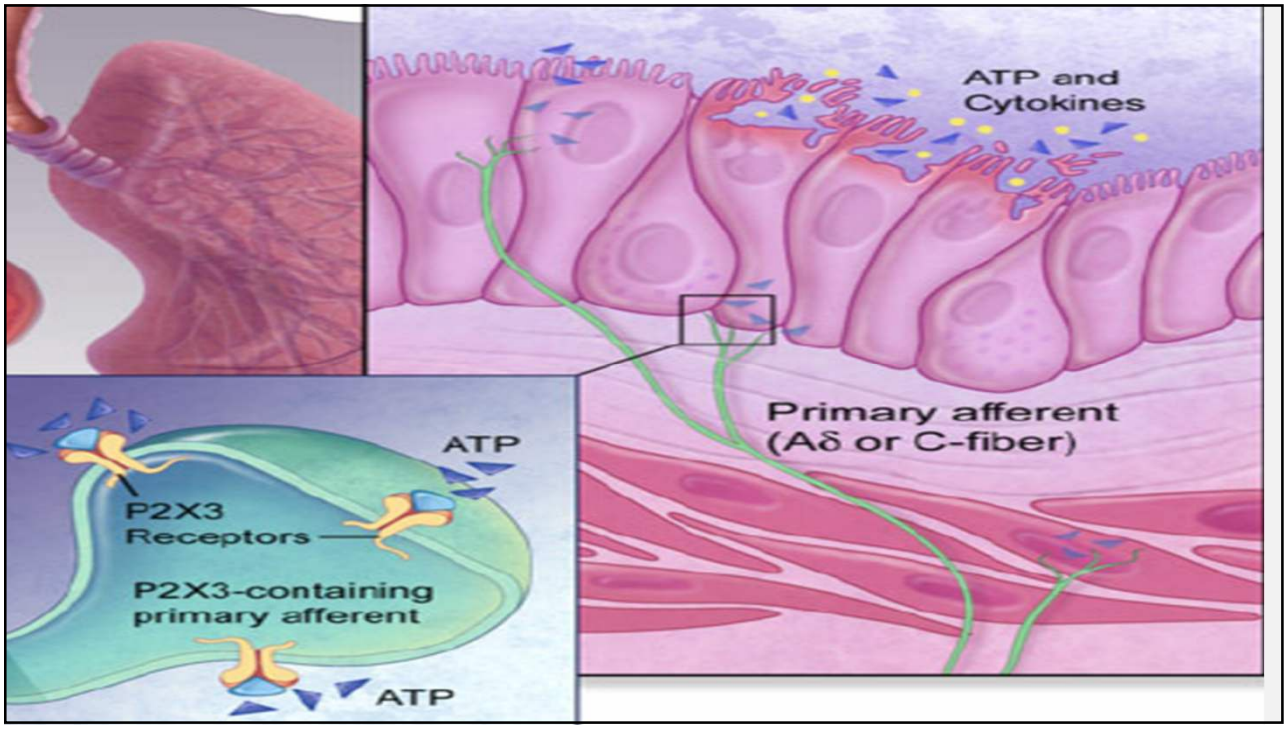
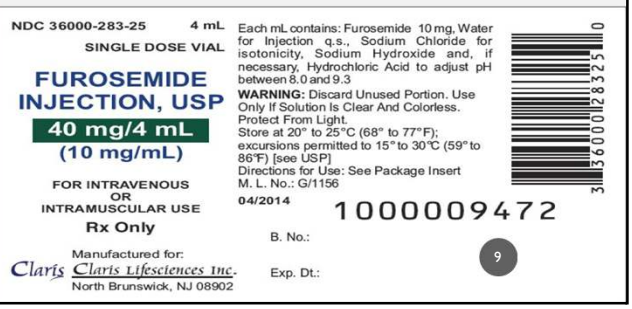
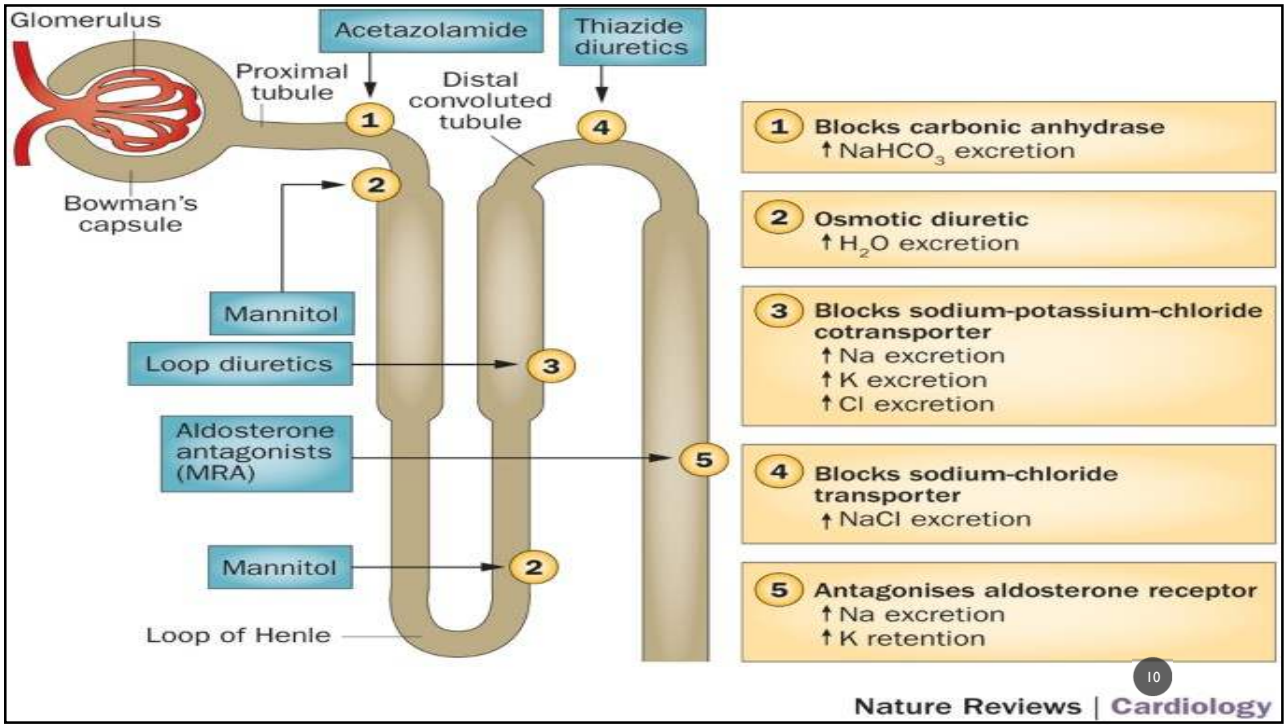

ATP and Cytokines
Primary afferent (Aδ or C-fiber)
ATP
P2X3 Receptors
P2X3-containing primary afferent
ATP

## FUROSEMIDE (LASIX) LASTS SIX HOURS (LOL)

- Lasix (furosemide), discovered in 1959 and later released in 1964
- Belongs to a group of medications known as loop diuretics.
- Works particularly on the thick ascending loop of Henle by preventing the re-absorption of water
- This type of medication is most commonly used to treat conditions such as systemic/pulmonary edema and hypertension.

- May cause dehydration or hypovolemia, hypokalemia, and other electrolyte imbalances.
- Muscle cramps, weakness, confusion, dizziness, nausea and vomiting, polydipsia, and arrythmia
- Can be given PO, IV, IM
- Number of contraindications and precautions as there is with any drug

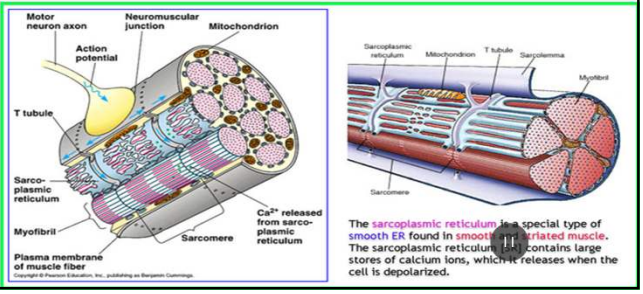


## HOW CAN IT HELP WITH DYSPNEA

- 50-70% of end stage pts experience dyspnea[5]
- J-Receptors/C-Fibers - Stimulation of these sensory fibers is believed to be involved in evoking dyspneic sensations – Lasix is to numb these
- Induces certain prostaglandin synthesis – made from arachidonic acid.
- Blocks certain pumps that can then also "waste" calcium – relaxes smooth muscle

- The vagal bronchopulmonary afferent C fibers are small, unmyelinated (C-Group Fibers) nerve fibers that provide sensory input from airway and lung structures. Stimulation by inhaled irritants elicits prominent reflex responses including apnea, smooth muscle contraction and mucus hypersecretion.
- Prostaglandin D2 (PGD2) is a potent bronchoconstrictor, and is thought to have a role in the pathogenesis of asthma. E1 and E2 are known for bronchodilation.
- Contraction occurs when an increase in the ionic calcium concentration **reduces troponin-tropomyosin inhibition and allows activation of the actomyosin-ATPase**.

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Aerosolized Lasix has also shown to improve pulmonary function testing

Motahar et al. (2013) states "The addition of inhaled furosemide to traditional therapy for COPD exacerbation reduced dyspnea and increased FEV1 up to 11%"

Dysregulation of these receptors has been noted – increasing sputum production and increased sensitivity to cough.

## PFTS

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## WHEN MIGHT WE USE IT

- Benefits and goals of palliative care
  - Physical
    - Relieve pain, manage symptoms and discomfort
  - Psychosocial
    - Provide goals of care discussions and provide emotional/mental support
  - Spiritual
    - Empower religiosity and aid in finding purpose and closure.

**Why can an approved drug be used for an unapproved use?** → FDA

From the **FDA's** perspective, once the FDA approves a drug, **health care** providers generally **can** prescribe the drug for an **off-label use if** they **believe** it is medically appropriate for their patient.

On February 11, 2022, the U.S. Court of Appeals for the 11th Circuit reversed a lower-court decision and found that Medicare must provide coverage for a beneficiary's off-label use of a medication in *Dobson v. Secretary of Health & Human Services*, No. 20-11996, 2022 WL 424813 (11th Cir. Feb. 11, 2022). → CoA

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## Guidelines [1,2,3,4,5,6]

**Indications**: Lasix could be considered in patients with severe dyspnea that is refractory to the standard treatments, including opioids.

- Advanced cancers and post-op patients
- Severe COPD including asthma
- Advanced congestive heart failure
- Advanced idiopathic pulmonary fibrosis

**Contraindications**: no contraindication for aerosolized Lasix as of late. Better practice is following the contraindications for PO and IV routes and use clinical judgement.

**Common Dosages**: 15mg – 120mg; 20 – 40mg diluted in 2 – 4cc NS is a common practice.

- Higher doses *have* shown to increase the urge to urinate and may aid in diuresis.

**Side Effects and Adverse Reactions**: transient nausea, sleeplessness and pharyngeal irritation. It was noted in one small study that patients actually suffered worsening of SOB that was not significant[5]. Diuresis and the urge to urinate increased in some patients, but was not significant. No other complications have been noted.

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## BENEFITS OF THIS

Improved quality of life

Improved functional capacity

Decreased lengths of stay

Decreased readmissions

Increase scope

- The pandemic we see with COPD is that of dyspnea
- More often is that which patients present to the emergency room or clinic
- Its not generally the cough, the sputum, the periodic increases in oxygen
- The idea of bronchodilation at its roots is that of quality of life – we know there is loss of lung function, and it is the job of the bronchodilator to keep the function as high as possible
- The less dyspnea a patient experiences the less likely they are to want to stay in facility
- For us? Another cog in or belt of tool – another research subject – another look at dyspnea

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## CONSENSUS

Nebulized Lasix has not been studied in depth enough to make recommendations at this time. Furthering the research and targeting the right patient population may yield a broader scope of practice for respiratory therapists and alleviate the feeling shortness of breath and increase patient comfort in those that suffer from end stage cardiopulmonary disease. More high-level evidence is needed.

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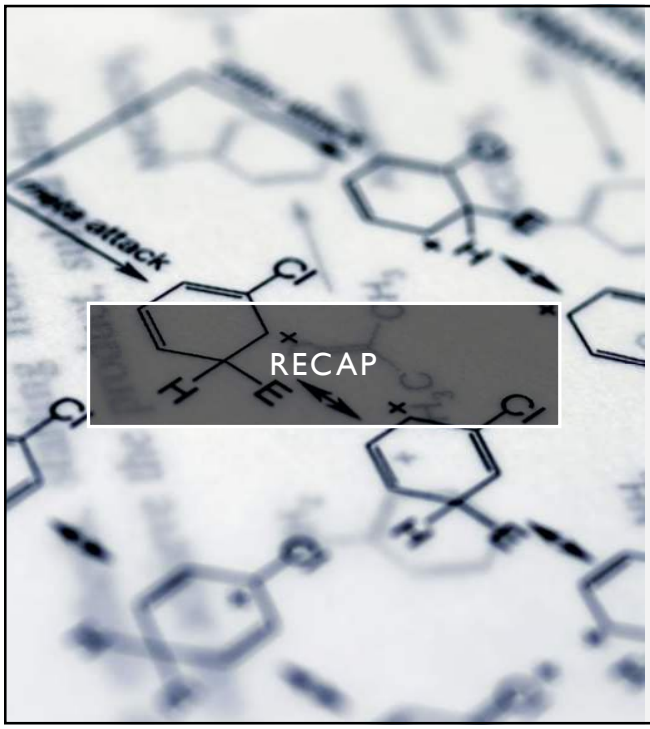


- Lung disease impairs QOL and presents with subjective dyspnea
- This dyspnea manifests via our chemical and electrochemical functions
- Neurologic control of ventilation is complex
- More attention may be needed to really focus on the root cause of dyspnea
- Lasix is a loop diuretic that is generally used to remove fluid from the body
- Theoretically, aerosolized Lasix impacts the stretch receptors in the lungs
- Intrigues me as to what other route can be used for dyspnea – how it can impact scope
- There is not a general consensus but a review of literature guideline
- It can increase PFT values which may further explain the alleviation of symptoms

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