



# Financial Disclosure

- Insmmed -

# Case presentation

- 66 year-old female with a history of prior pneumonia 15 years ago presents with productive cough.
- She has mild shortness of breath. No fevers, no hemoptysis. She has gained two pounds over the year.
- No other prior medical history, and currently not taking any medications
- Initial workup including autoimmune serologies and quantitative immunoglobulin levels were negative.
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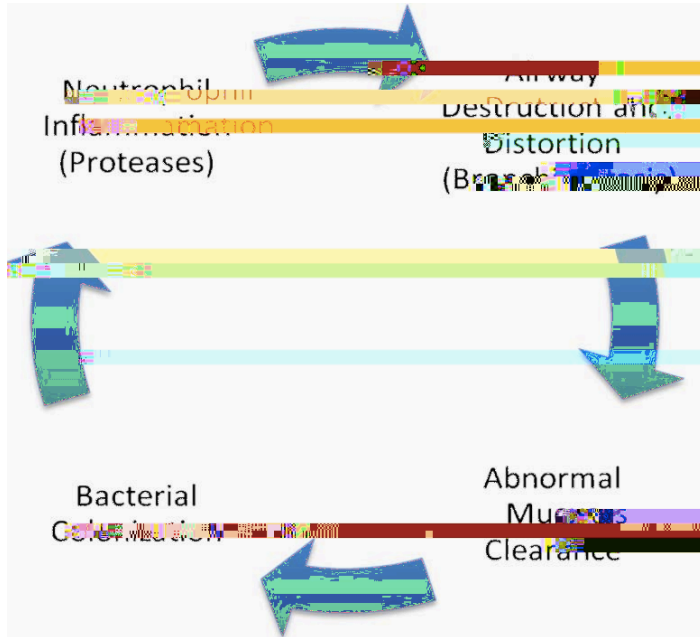




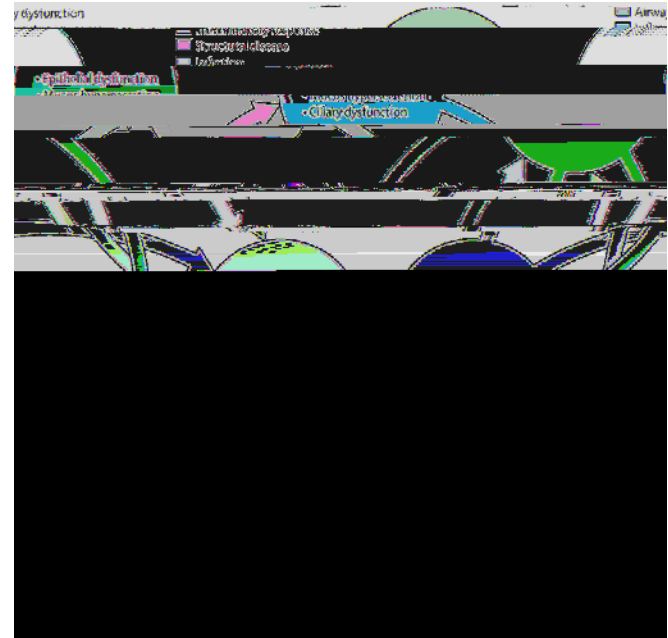
# CLEARANCE

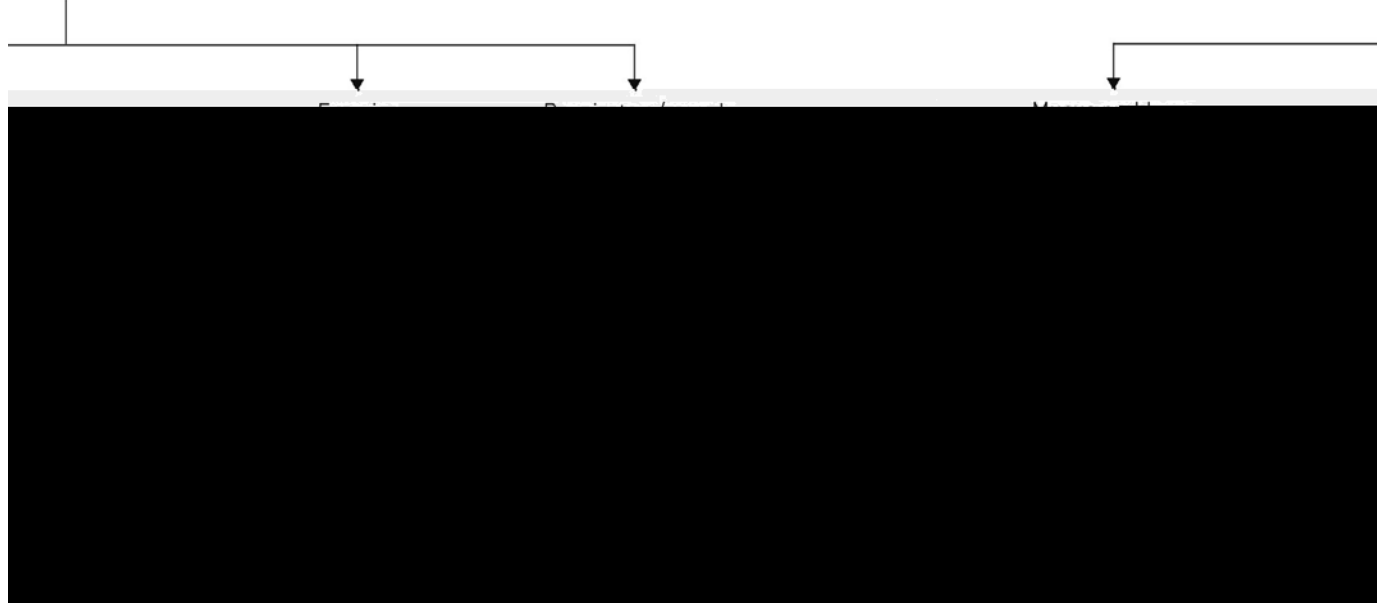
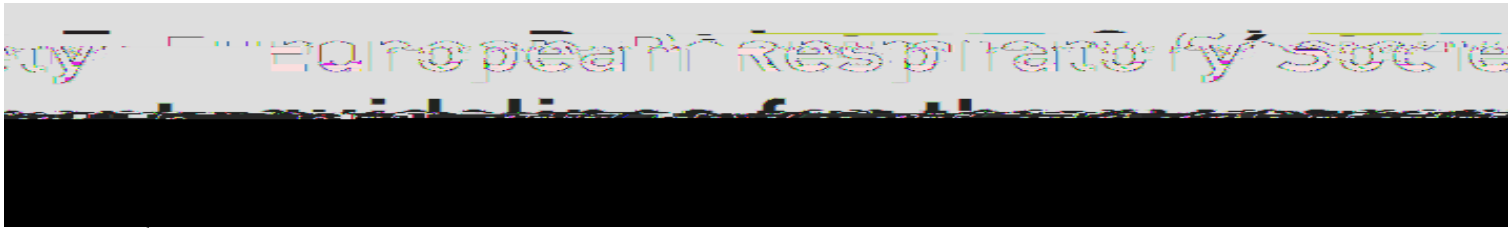
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# The vicious cycle and vortex



Cole, 1986





Polverino et al. Eur Respir J 2017





- Patients with chronic productive cough or difficulty to expectorate sputum should be taught an airway clearance technique (ACT) by a trained respiratory physiotherapist to perform once or twice daily.
- Adult patients with bronchiectasis and impaired exercise capacity should participate in a pulmonary rehabilitation programme and take regular exercise.
- Long-term mucoactive W U H D W P P H Q W L K Q G X S D W L Z L Q W K R Q F K L Z I F R D Y C H M I L F X O in expectorating sputum and poor quality of life and where standard ACTs have failed to control symptoms should be offered.
- We recommend not to offer recombinant human Dnase.

Polverino et al. Eur Respir J 2017

# Treating Cough Due to Nontuberculous Bronchiectasis With Nonpharmacological Airway Clearance

CHEST Expert Panel Report

- For children and adults with productive cough due to bronchiectasis related to any cause, we suggest that they be taught ACTs by professionals with advanced training in ACTs.
- We suggest that the frequency of ACTs should be determined by disease severity and amount of secretions.
- We suggest that ACTs are individualized as there are many different techniques.

## Adult Bronchiectasis Patients: A First Look at the United States

N. Olivier, MD, Kevin L. Eden, David Griffith, MD, Timothy R. Akasmit, MD, Anne E. O'Donnell, MD, Alan Barker, MD, Kenneth Winthrop, MD, M. Leigh Anne Daniels, MD, Margaret Johnson, MD, Edward M. Whittam, MD, Gerard Turino, MD, Betsy Carretta, MD, Charles L. Daley, MD, for the Bronchiectasis Registry Consortium

- 1826 patients
- Non-pharmacologic measures were used in 56% of patients.
- 48% used flutter or PEP device
- Chest percussion and postural drainage were utilized in 15% and 16% of patients, respectively.
- Mucoactive agents were used in 24% of patients; of these, 76% used hypertonic saline.
- Those with NTM were more likely to use non-pharmacologic measures.

Akasmit, et al, CHEST, 2017

# Airway Clearance in Non- Cystic Fibrosis Bronchiectasis: Analysis from the United States Bronchiectasis Research Registry

- Adult patients with productive cough and bronchiectasis, excluding CF and those on antibiotics for NTM
- 1320 patients
- 66.7% of subjects utilized airway clearance at baseline.
- Subjects were more likely to utilize airway clearance at baseline if they had experienced an exacerbation (75% vs 59%,  $p < 0.0001$ ) or hospitalization for pulmonary illness (28% vs 21%,  $p < 0.05$ ) in the prior two years.
- Of those with at least one-year follow-up data, 57% of subjects did not utilize airway clearance at follow-up.

Basavaraj, et al. ATS abstract, 2019

# Why is airway clearance not utilized more often?

- Providers may not be prescribing it.
- Patients may not perceive a benefit from it.
- May become a burden to the patient, limiting compliance.
- Research on the efficacy of airway clearance is limited.

# Airway clearance

- Improvement in exercise capacity and quality of life (QOL) in patients using an oscillatory device vs. management without chest therapy. (Murray, 2009)
- Improved symptoms, pulmonary function, and reduced CRP and sputum neutrophils in HFCWO vs. PEP device. (Nicolini, 2013)
- Improvements QOL and Leicester cough questionnaires, and fewer exacerbations, in those that performed ELTGOL (slow expiration with the glottis opened in the lateral position. (Munoz, 2018)











# Mucoactive agents

## 1. Expectorants

- Induce discharge or expulsion of mucus from the respiratory tract
- Examples include hypertonic saline and guaifenesin.

## 2. Mucoregulators

- Regulate mucous secretion or interfere with the DNA/F-actin network.
- Examples include carbocisteine and anticholinergic agents.

## 3. Mucolytics

- Decrease mucous viscosity
- Examples include N-acetylcysteine, erdosteine and DNase.

## 4. Mucokinetics

- Increase mucociliary clearance by acting on the cilia.
- Examples include bronchodilators and surfactants.

O'Neill, et al. *Respirology*, 2019



# 30 patients with non-CF bronchiectasis randomized to 7% hypertonic saline or placebo (0.9% normal saline) for 3 months

- 30 patients with non-CF bronchiectasis
- Randomized to 7% hypertonic saline or placebo (0.9% normal saline) for 3 months
- Excluded patients with pseudomonas
- Improvement in SGRQ scores in 7% hypertonic saline vs 0.9% normal saline

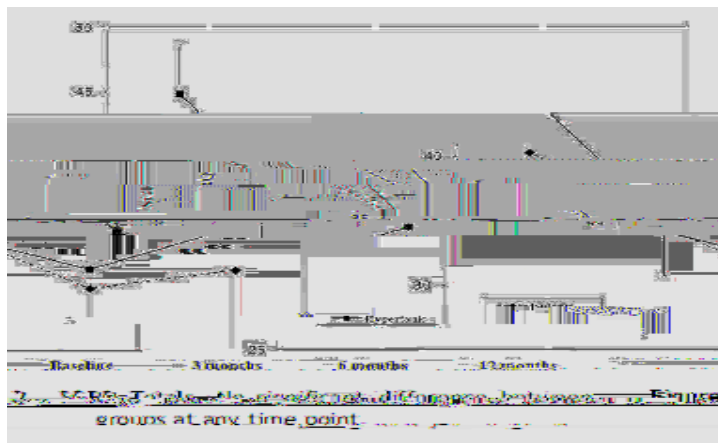
Table 2. Change in lung function over time (mean (SD))

Active (n)	Placebo (n)	P value	Phase
15.1 (8.2;22.0)	1.8 (-8.9;10.7)	<0.01	FEV <sub>1</sub> % change (95% C.I.)
11.2 (0.4;21.0)	0.7 (-7.1;8.0)	<0.01	FEV <sub>1</sub> % change (95% C.I.)

The long term effect of inhaled hypertonic saline 6% in cystic fibrosis bronchiectasis.

Caroline H.H. Nicolson<sup>a,\*</sup>, Robert G. Stirling<sup>b</sup>, Britte M. Borg<sup>c</sup>

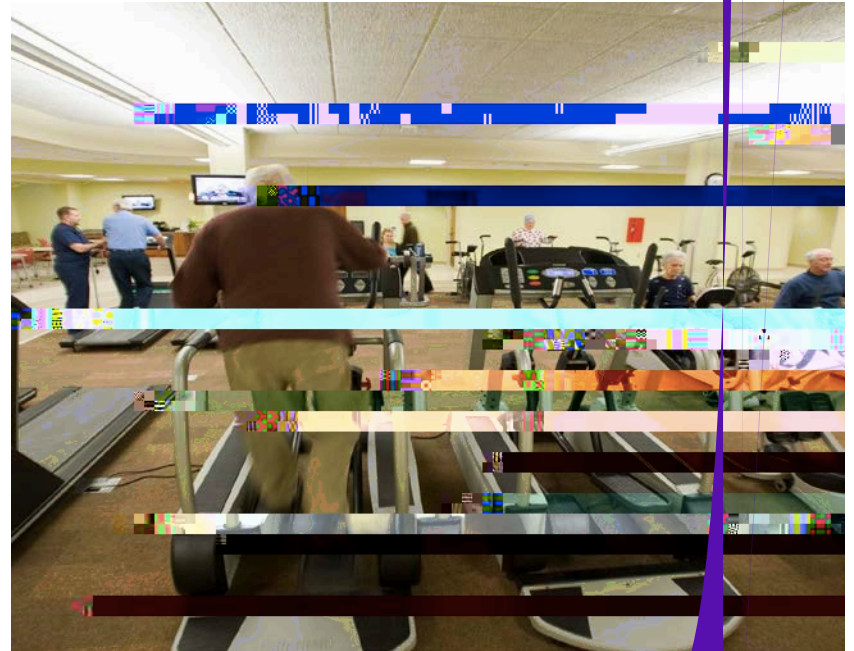
- 40 patients randomized to 6% hypertonic saline or 0.9% normal saline daily for 12 months
- Significant improvements in QoL, FEV<sub>1</sub>, and reduction in sputum colonization in both groups, no difference between the groups.

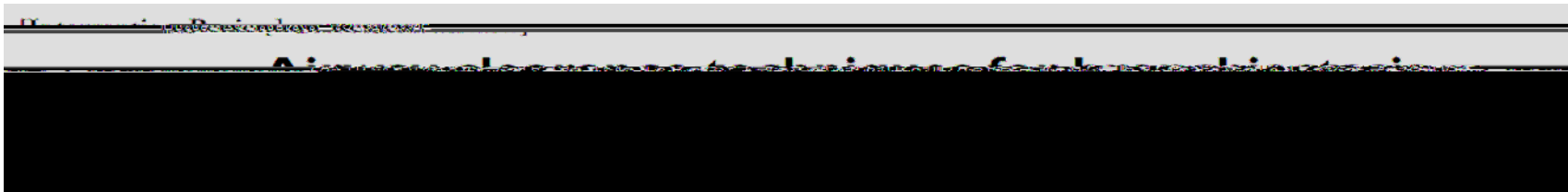


Nicolson, et al. Respiratory Medicine, 2012

# Pulmonary Rehabilitation

- Can help with mucociliary clearance.
- Short-term improvements in exercise capacity and QOL with a combination of endurance, strength and inspiratory muscle training (Newall, 2005).
- May increase time to first exacerbation (Lee, 2014).





- ACTs appear to be safe for individuals with stable bronchiectasis.
- There may be improvement in sputum expectoration, selected measures of lung function and health-related QOL.
- The role





# ENAC

- An epithelial sodium channel that regulates composition of airway surface liquid.
- It is downregulated in CF and its consequent upregulation in CF is a potential therapeutic strategy for reduction of mucus hypersecretion from the bronchus.
- It is a potential therapeutic strategy for reduction of mucus hypersecretion from the bronchus.

• It is being investigated in the primary ciliary dyskinesia (PCD) mouse model (18).

(18).



Physiotherapy

Principles of airway clearance



- Airway Clearance in the Normal Lung
- Hydration and Humidification
- Management Plan
- Choosing a technique
- Case Study



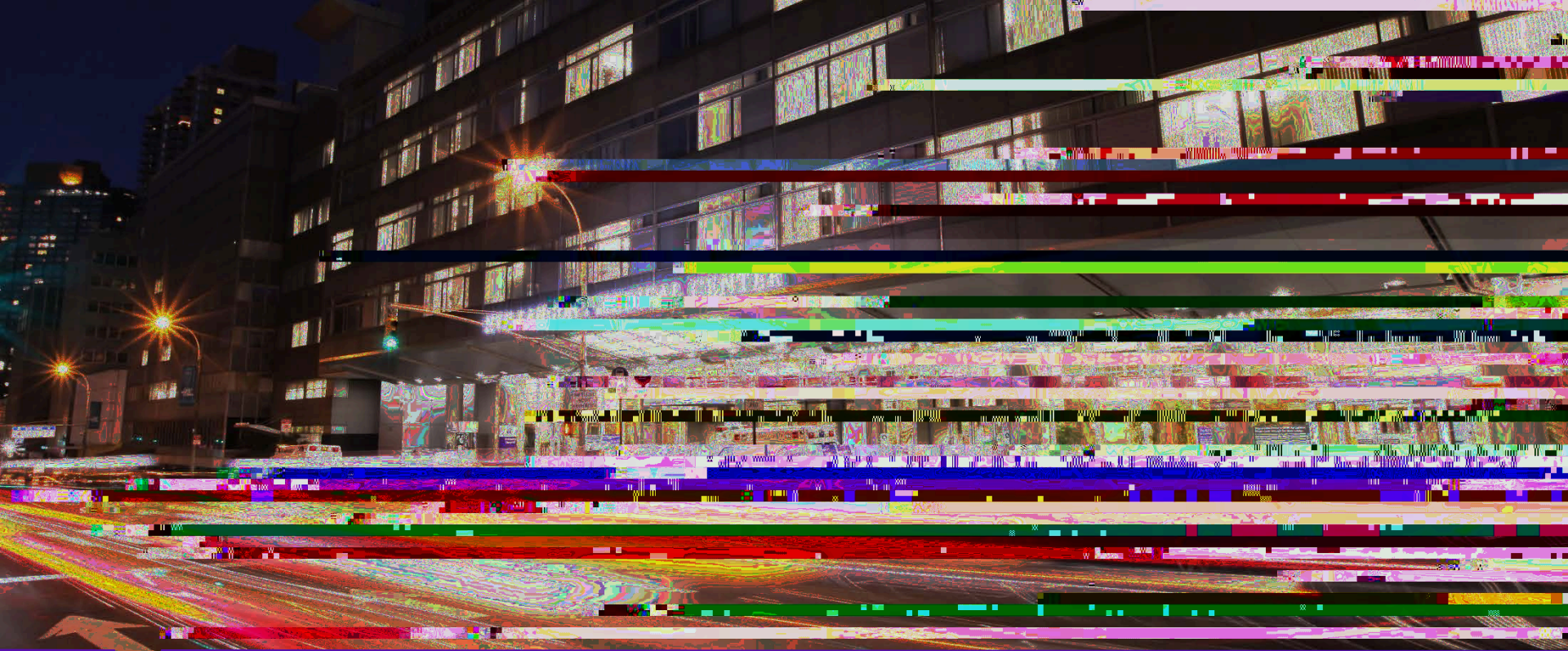
- Videos of physiotherapy techniques
- The active cycle of breathing technique
- Forced Expiration
- Positive Expiratory Pressure
- Percussion



- Wet Suction
- Exercise Prescription

# Summary

- Airway clearance is an important management strategy in bronchiectasis.
- Techniques include positive expiratory pressure devices, HFCWO, breathing techniques, manual chest therapy, mucoactive agents and pulmonary rehabilitation.
- Utilization is limited and patient adherence can be poor.
- Further research is needed.



THANK YOU

# References

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