

# Salt inhalation in pulmonary diseases, especially for Cystic Fibrosis (CF)

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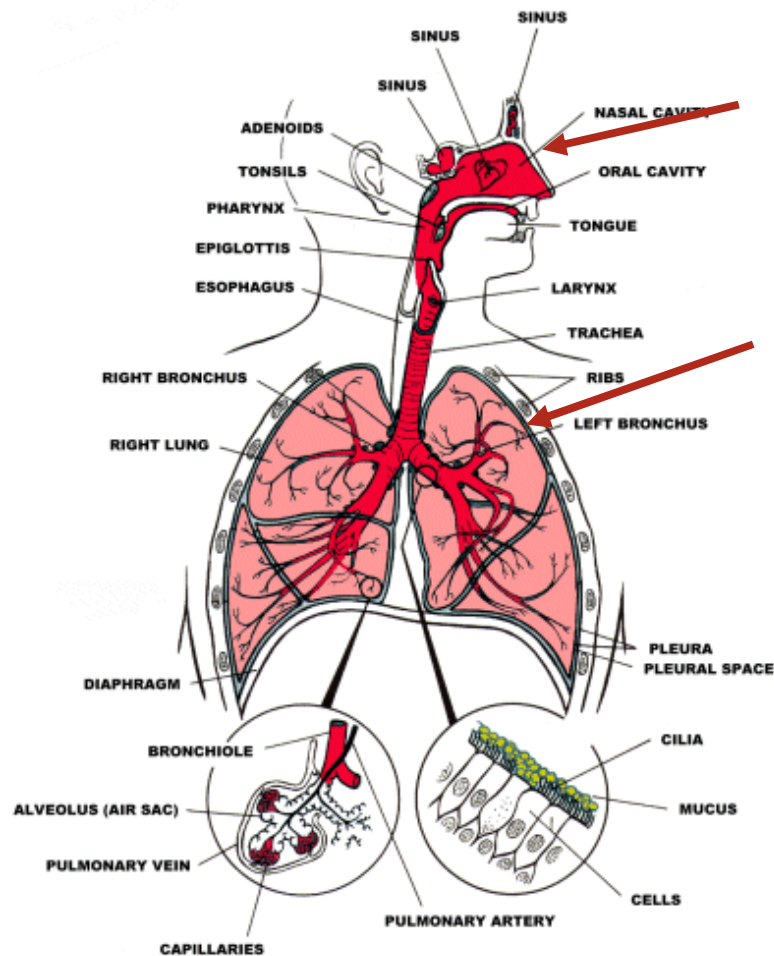


# Content

- Physiology
- Salt inhalation – Indications
- Salt inhalation – how?
- Pulmonary diseases
  - Asthma
  - COPD
  - Cystic Fibrosis**
- Saline inhalation
- Dry salt aerosol inhalation

# Protection mechanisms of the respiratory tract

## THE RESPIRATORY SYSTEM



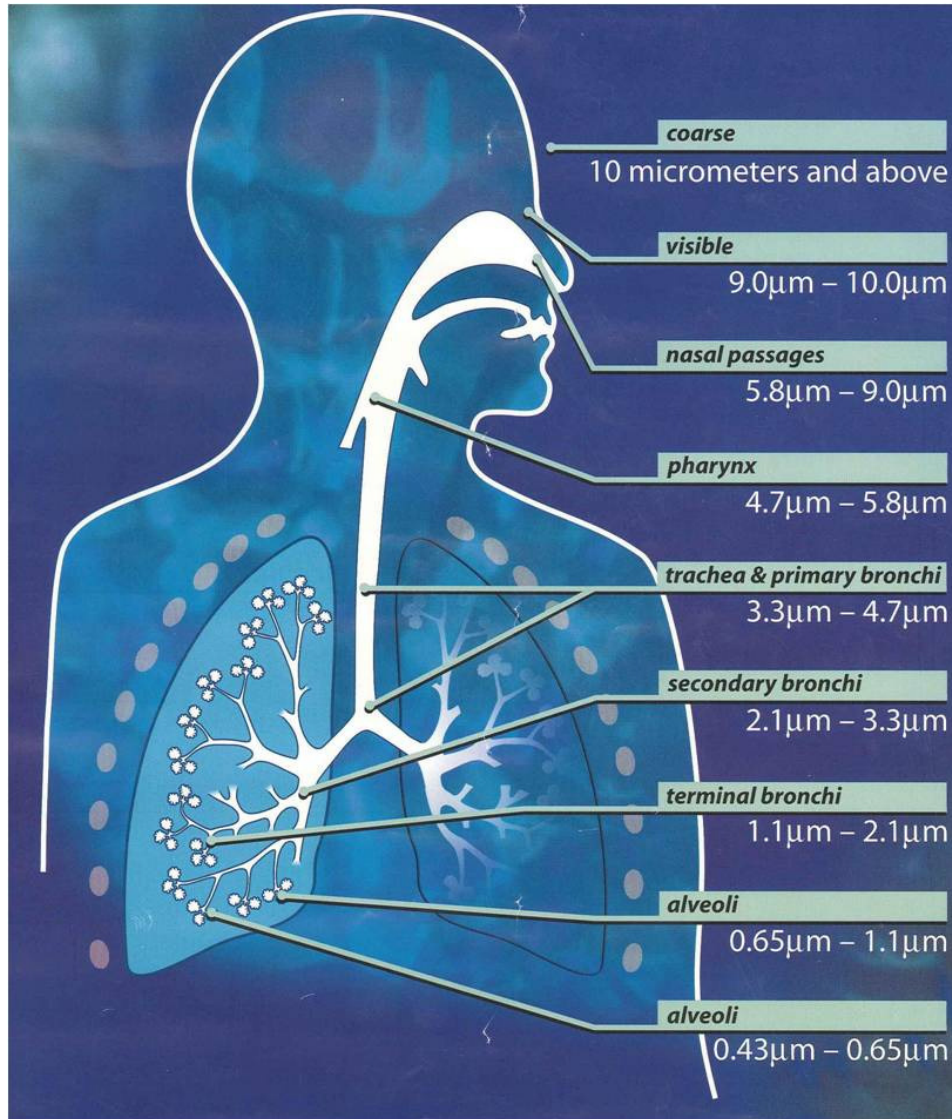
Filtering of inhaled air through the nose

Mobilisation and expectoration of mucus

- mucociliary clearance
- ciliary flow (cough, harrumph)



# Therapeutical particle sizes



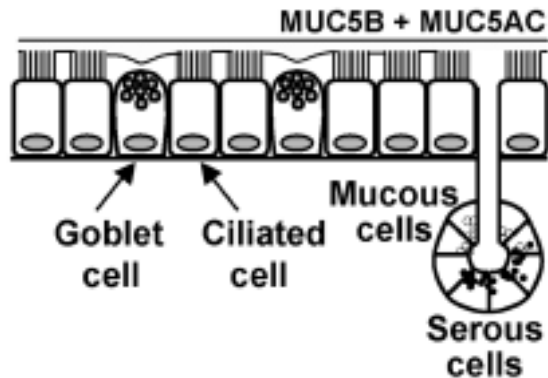
Solutions, nasal drainage

Saline inhalers,  
aerosol spray

Aerosol spray,  
dry salt aerosol

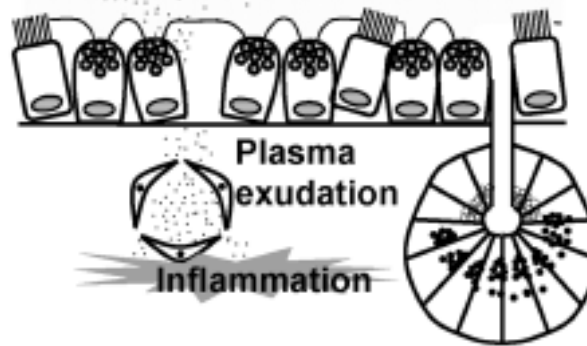
# Pulmonary diseases

## Normal



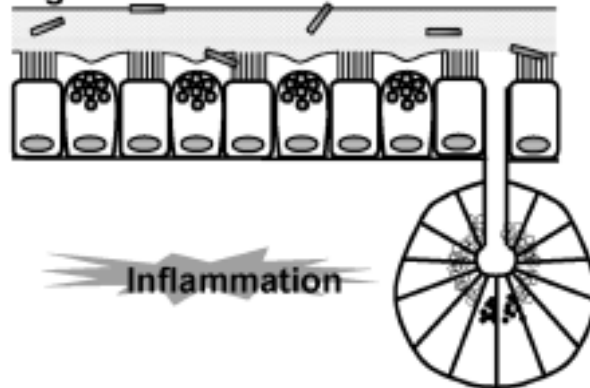
## Asthma

Icgf MUC5B  $\gg$  MUC5AC  $\gg$  MUC2



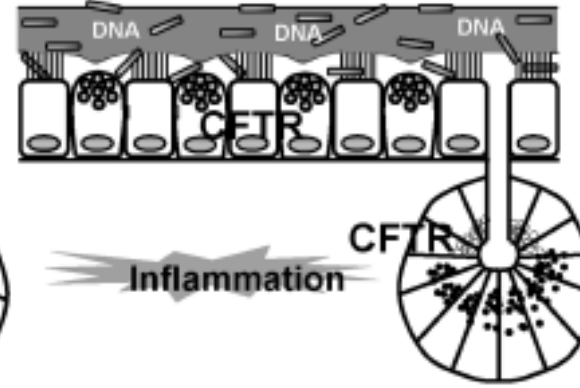
## COPD

Icgf MUC5B  $<$  MUC5AC  $\ll$  MUC2



## CF

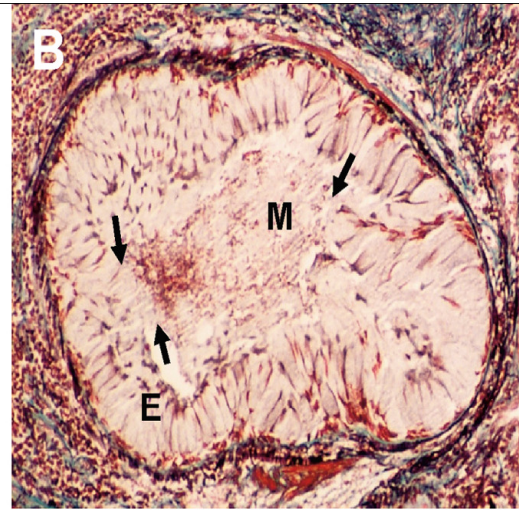
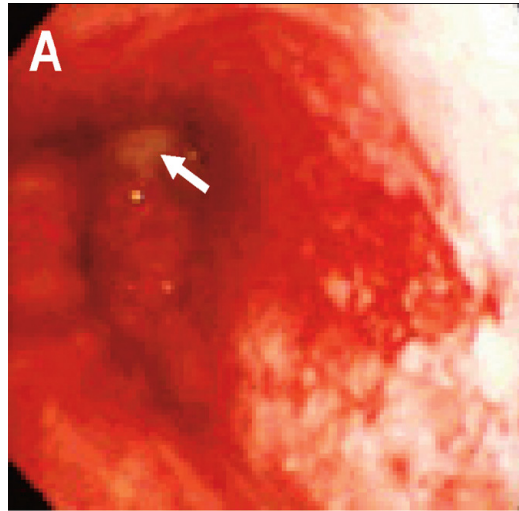
MUC5AC + MUC5B  $\gg$  MUC2





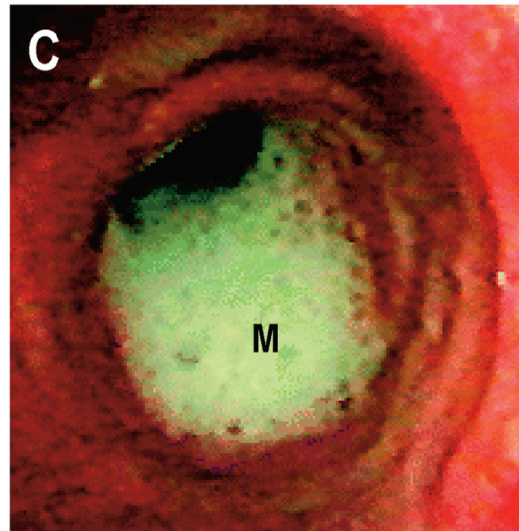
# Pulmonary diseases

Asthma



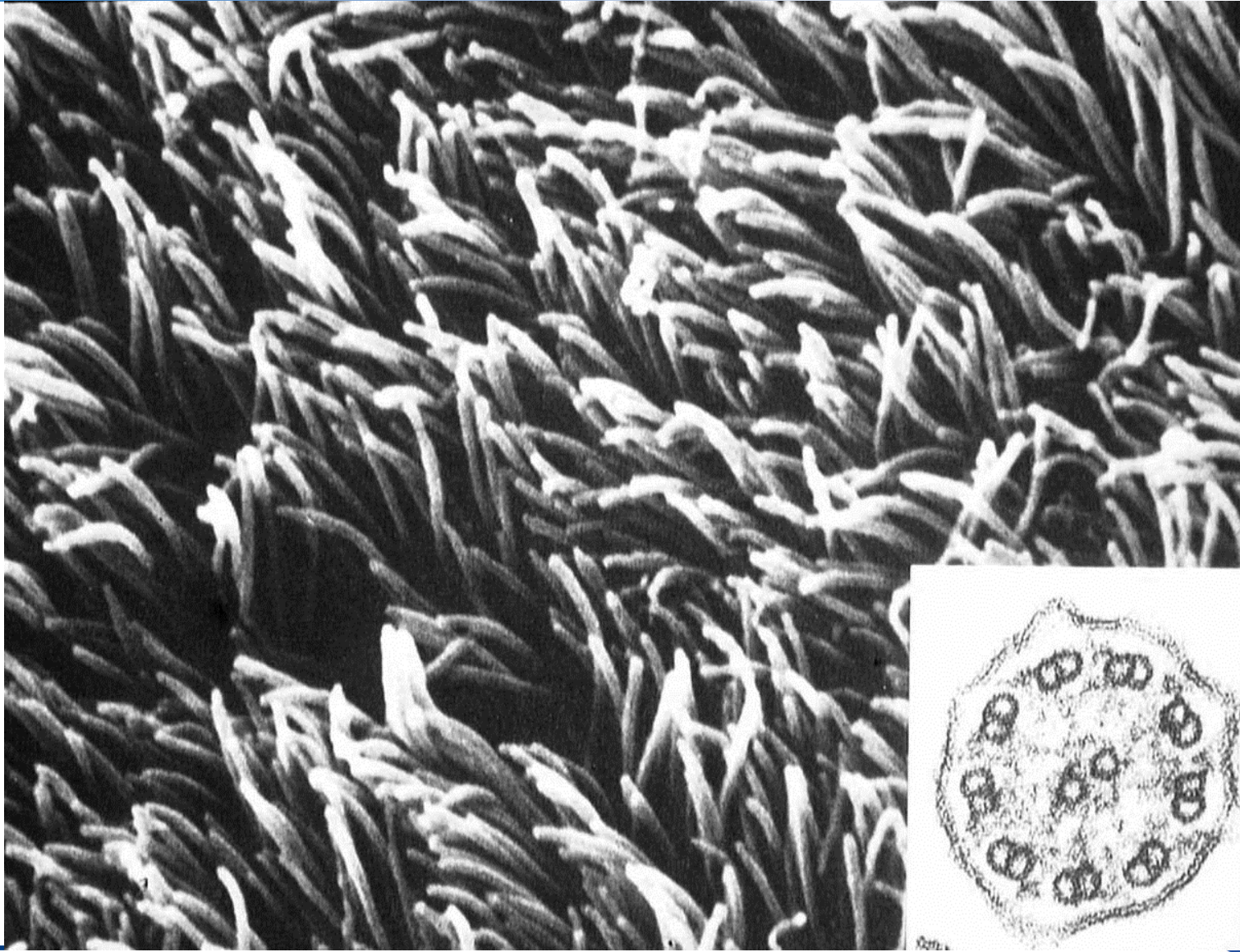
Asthma

COPD



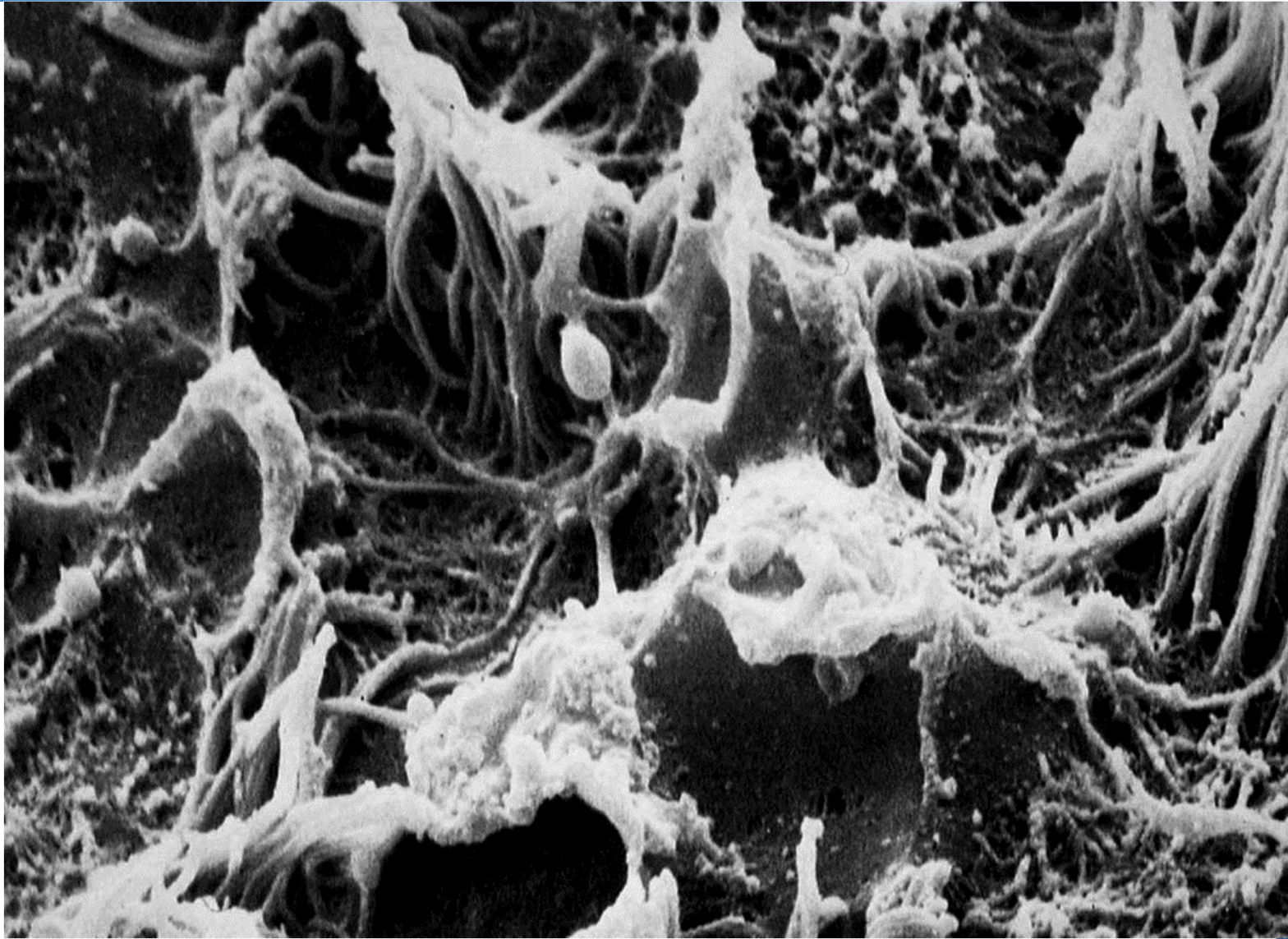
CF

# Ciliary epithelia - normal





# Bacteria - Pseudomonas



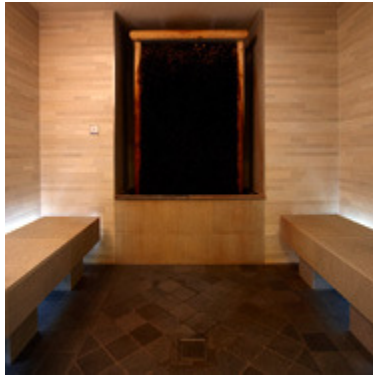


# Available therapies

- Physiotherapy
- Sports
- Autogeneous drainage
- Medical drugs
  - anti-obstructive – bronchial dilatation
  - anti-inflammatory – e.g. inhalative antibiotics
- **secretolysis**

# Saline versus dry salt aerosol

## Saline evaporation



- Saline is immediately recognised
- Cleansing activity at skin significantly
- Secretolysis beneficial
- Saline medically indicated:
  - short term obstruction, similar to asthma attack
  - only under medical observation !
  - cross infections possible

## Dry salt micronisation



- Dry salt difficult to notice
- Secretolysis beneficial
- Dry salt causes:
  - no bronchial obstruction !
  - instant secretolysis !
  - no need for medical observation !
  - no cross infections !

# Saline versus dry salt aerosol

salt caves

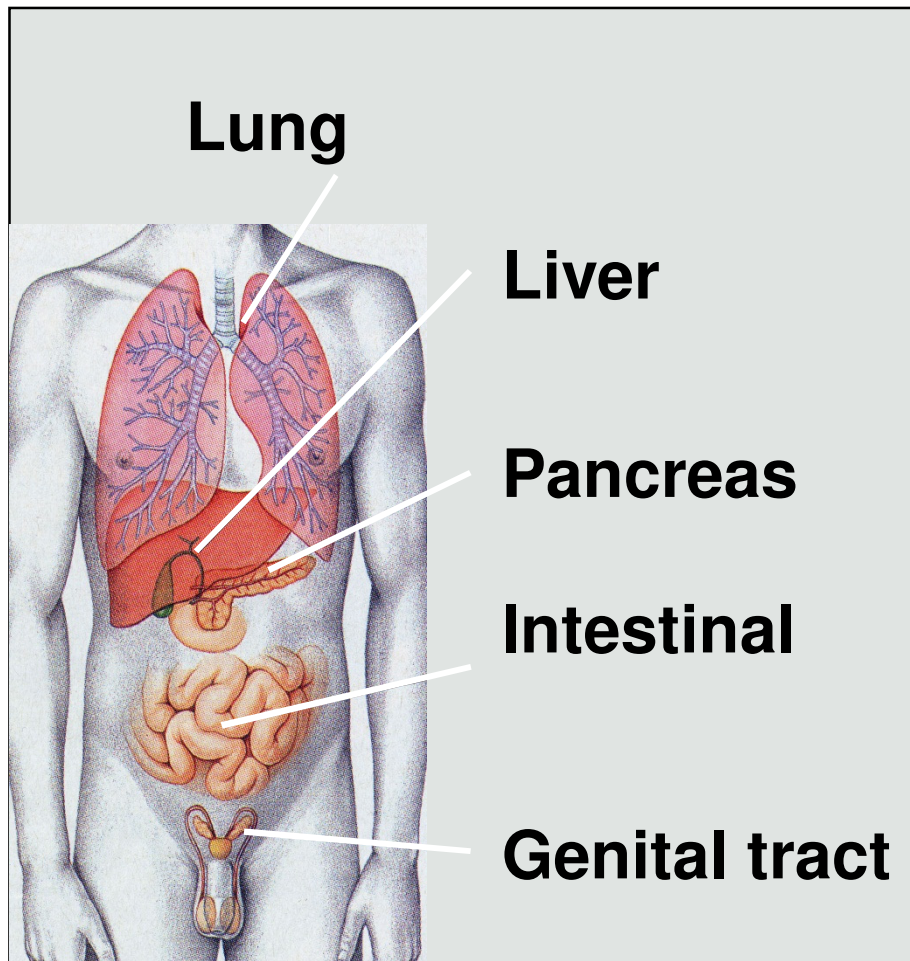




# Pulmonary diseases

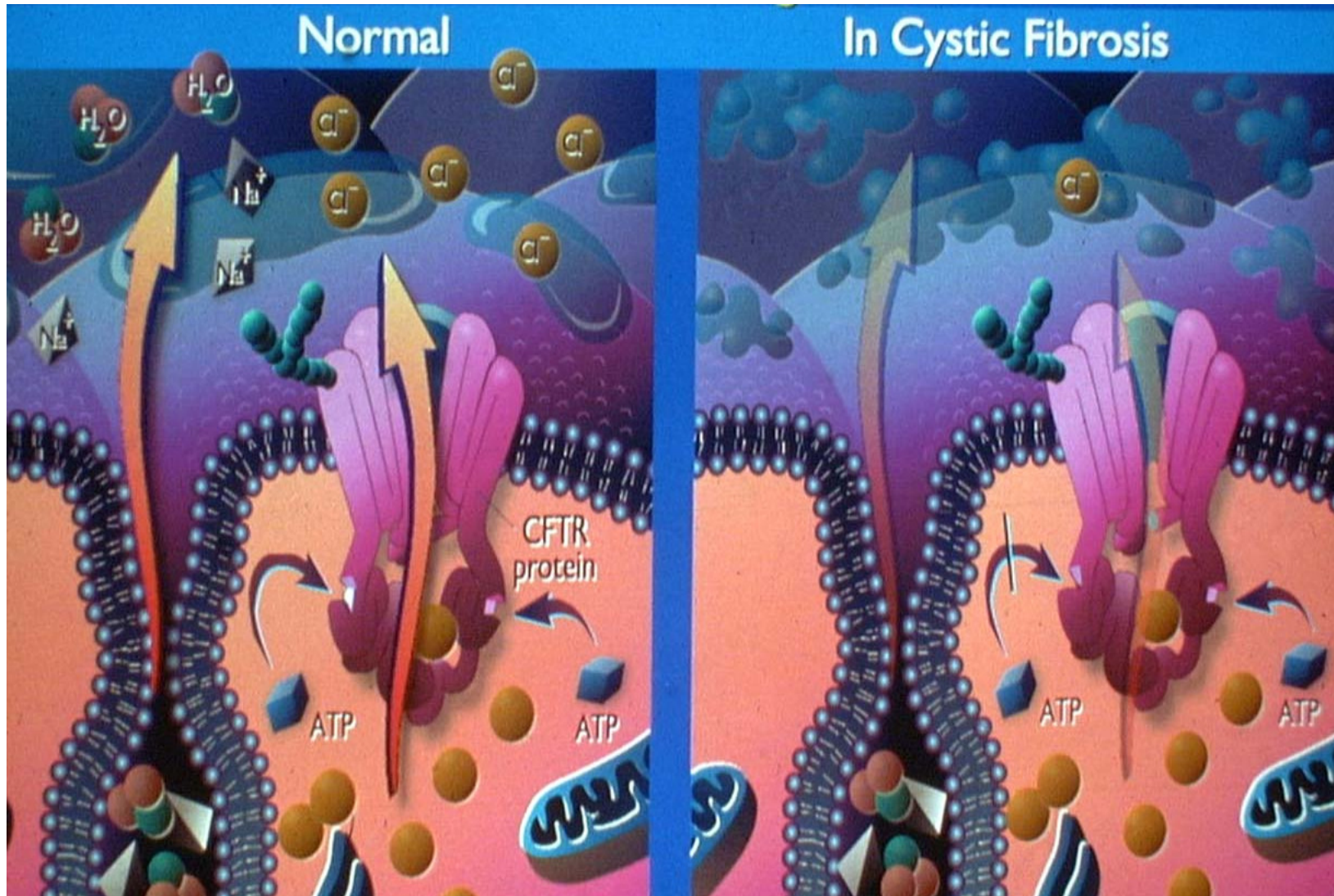
- Viral infections (Influenza-, RS-, Adenoviruses)
  - sinusitis, laryngitis and otitis media
- Cystic fibrosis, Asthma as well as acute and chronic bronchitis
- Pollen-, housemite allergies

# Cystic fibrosis



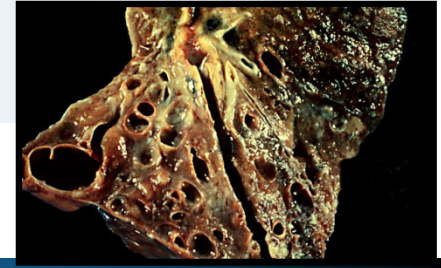
- 100.000 patients world wide
- Gene defect 1989, *CFTR*
- No gene therapy available
- Life expectancy  
1980: 18 y  
2010: 40 y
- Bacterial lung infections determines the illness

# CFTR defect





# CFTR defect

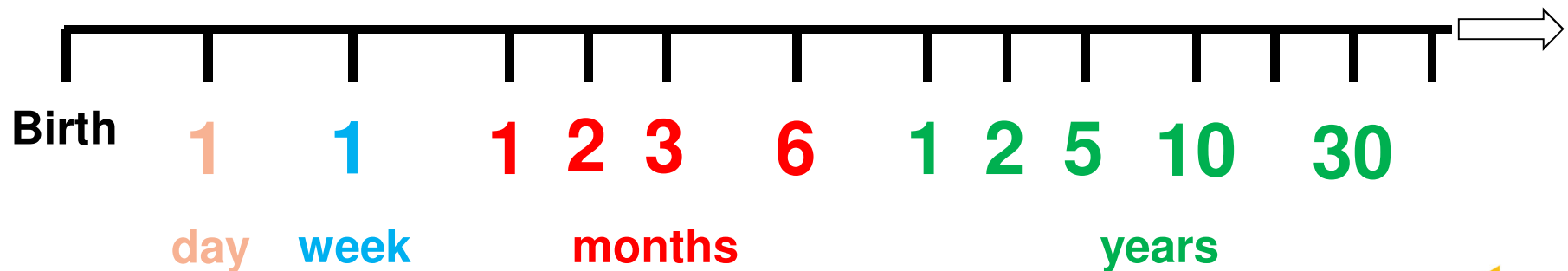


Lung disease

Liver and Gall bladder

Pancreas insufficiency

Meconium ileus



# Airway manifestation

- Chronic Sinusitis, nasal polyposis
  - **Chronic bronchitis, pneumonia**
  - Allergic Aspergillosis (ABPA)
  - **Ventilation disorders: atelectases, trapped air**
  - Oxygen shortage, drumstick fingers
- ➔ global pulmonary insufficiency, pneumothorax, hemorrhage
- ➔ right heart insufficiency, edema

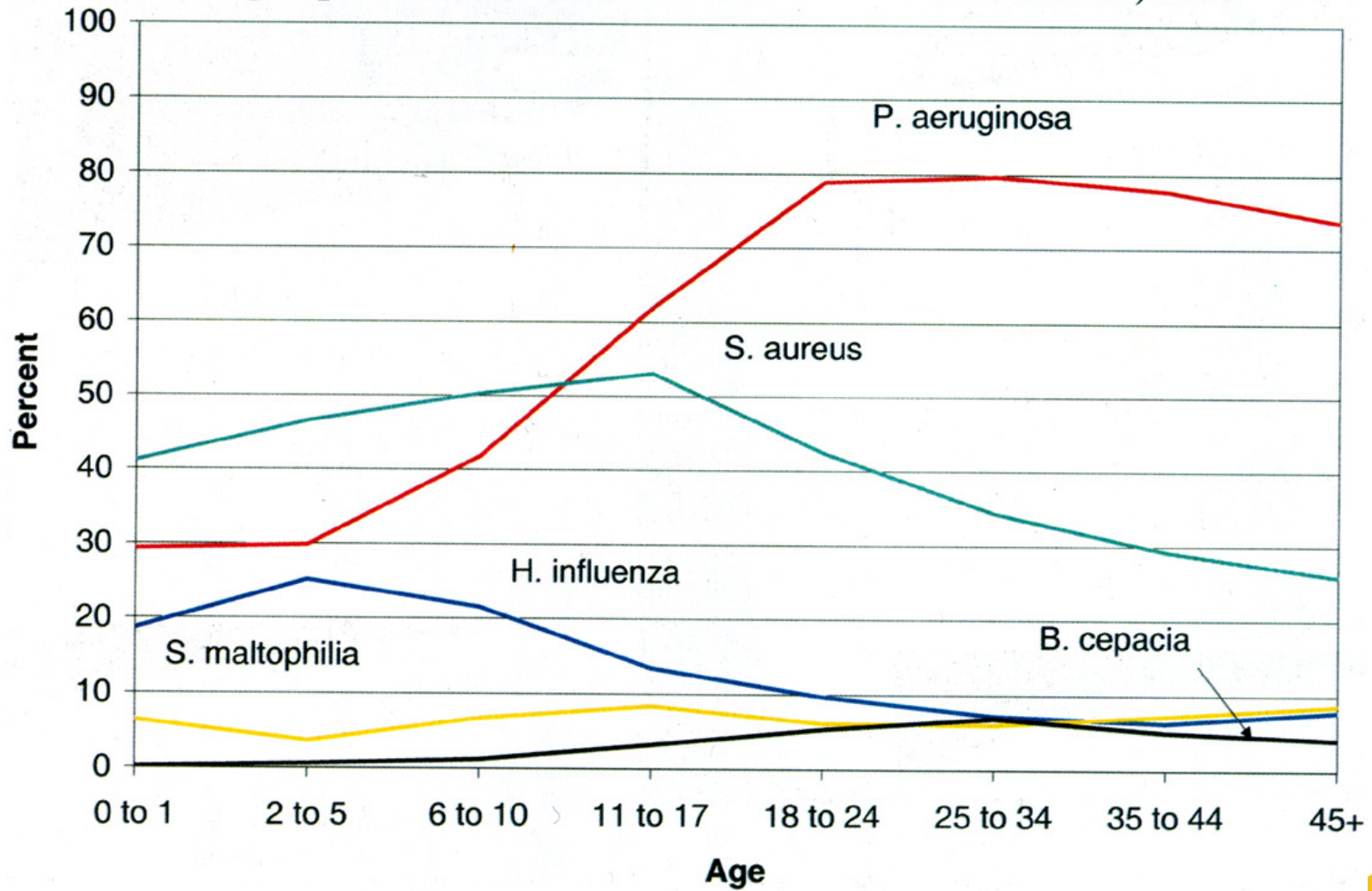
# Circulus vitiosus





# Pulmonary infections

Age Specific Prevalence of Infections in CF Patients, 2000



# Pulmonary - secretolysis

Established:

- **rhDNase (Pulmozyme):** Splitting DNA ➤ fluidized sputum

disadvantages:

- expensive
- saline inhalation
- inhalation device/ immobility
- effektive only at high inflammation/ WBC

- **Mannitol (Bronchitol):** high molecular, non absorbable sugar alcohol, dry inhalation via capsules

advantages:

- rapid
- less bronchial obstruction
- improved mobility
- very effective

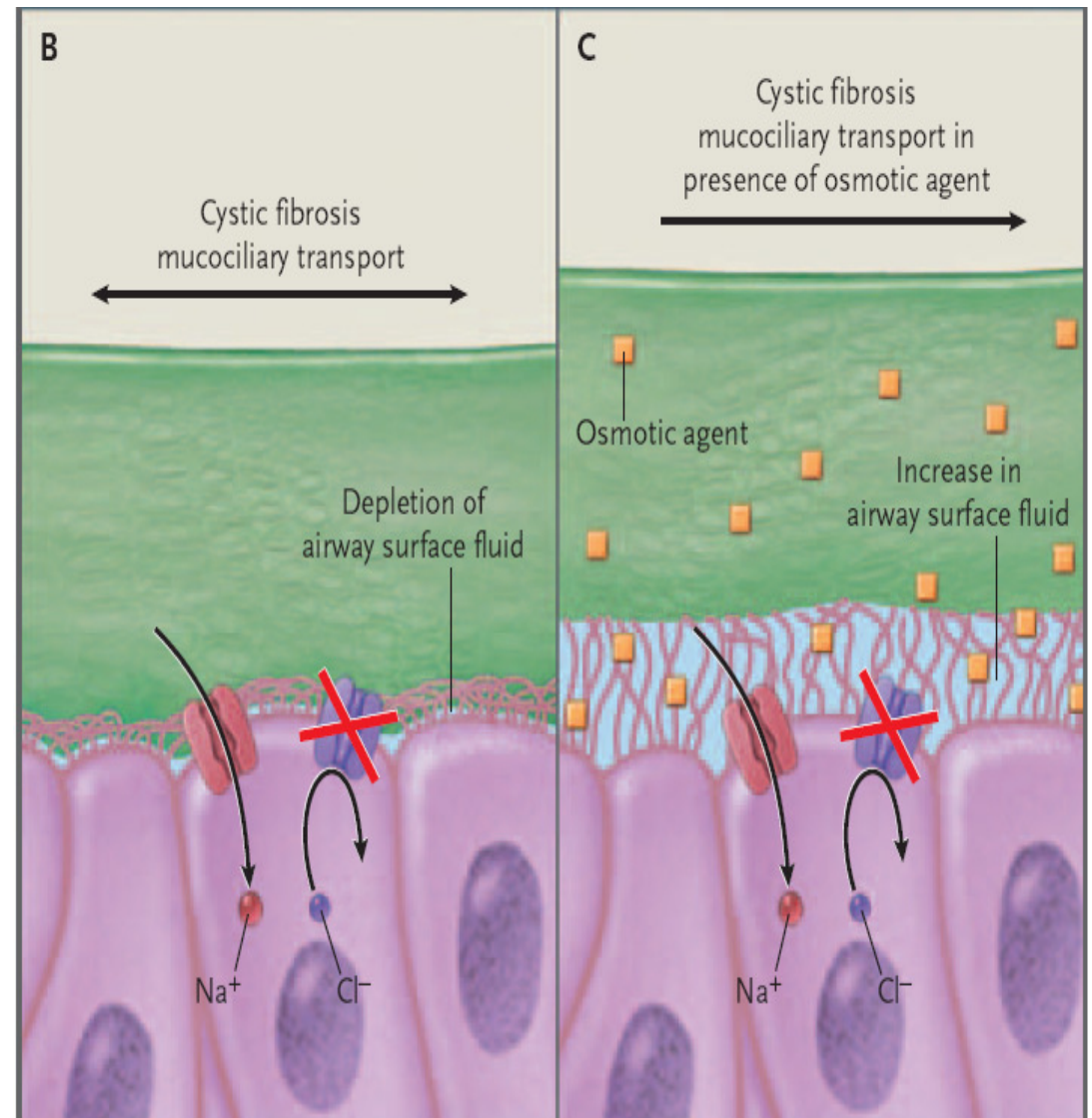
# Secretolysis

## Hypertonic saline: 3% vs 6% vs 7%

- minimizes viscosity
- increases surface fluid
- improves mucoclearance
- increases lung function in CF

### Disadvantages:

- spasmolysis necessary
- coughing
- bronchial obstruction
- saline inhalation
- decreased mobility
- requires inhalation device



# Secretolysis – hypertonic saline

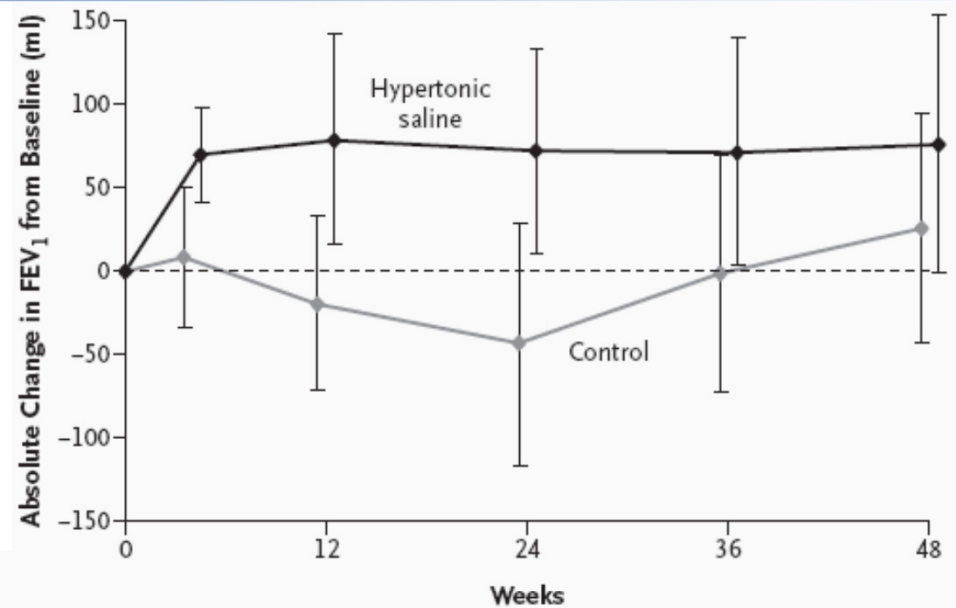
<b>FEV1</b>	<b>NaCl 0,9%</b>	<b>NaCl 7%</b>
<b>Cardinale, 2003:</b> (n=25/25)	=	=
<b>Elkins, 2006:</b> (n=78/75)	<b>-0,91%</b>	<b>4,41 %</b>

Wark, McDonald. Hypertonic saline for cystic fibrosis. Cochrane Review, 2010

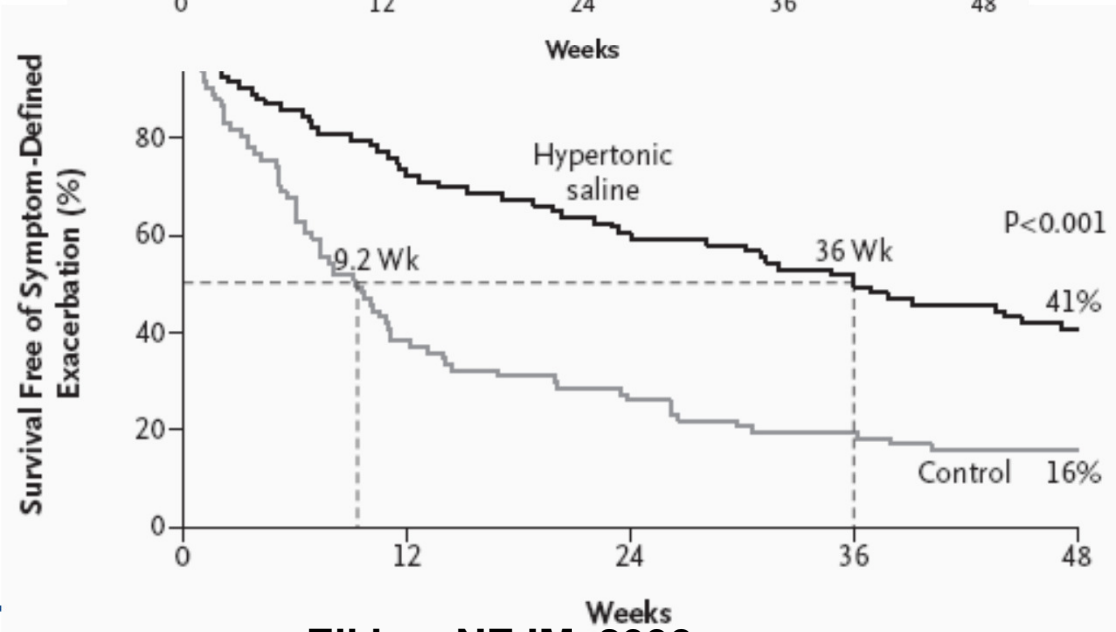


# Secretolysis – hypertonic saline

FEV<sub>1</sub>



Exacerbations



# Secretolysis – dry salt aerosol

Asthma – COPD – Bronchiectases – CF (n= 127)

Change of flow-volume loop parameters at various terms of halotherapy ( Mean±SE)

Parameter, % baseline	Treatment		
	7 days	14 days	End of course
Number of cas	115	98	124
VC	0 ± 0.9	2 ± 1.3	2 ± 0.9*
FVC	2 ± 0.9*	3 ± 1.3*	2 ± 1.0*
FEV <sub>1</sub>	3 ± 1.2*	3 ± 1.6	2 ± 1.3
PEF	4 ± 1.4*	3 ± 1.9	3 ± 1.2*
FEF <sub>50</sub>	7 ± 1.5*	7 ± 2.9*	2 ± 2.0

\* significant ( $p < 0.05$ , here and further) changes vs initial values (paired t-test)

# Secretolysis - dry salt aerosol

## Dry salt aerosol - Inhalation, pilot study I 2009/2010:

- n = 6 adult CF patients
- objectives: Secretolysis  $\uparrow$  ?,  
FEV1  $\uparrow$  ?,  
Obstruction ?,  
Symptomimetics ?



	<b>Sputum amount [g]</b>	<b>Leukocytes [/<math>\mu</math>l]</b>	<b>log Pseudom.</b>	<b>FVC [%]</b>	<b>FEV1 [%]</b>	<b>MMEF [%]</b>
mean	<b>+ 7,1</b>	<b>+ 38,5</b>	<b>+ 0,31</b>	<b>+ 6,4</b>	<b>+ 3,8</b>	<b>+ 6,6</b>
SD	$\pm 4,4$	$\pm 77,9$	$\pm 0,52$	$\pm 11,5$	$\pm 2,5$	$\pm 6,1$
T-test	0,008	0,049	0,017	0,19	0,019	0,05

# Secretolysis - dry salt aerosol

## Planned phase II trial:

<b>Studiencode</b>	<b>CF-TroSa II</b>	
<b>Protokolltitel</b>	<b>Die Therapie von Mukoviszidose-Patienten mit Trockensalz-Inhalation über einen Zeitraum von 5 Tagen</b>	
<b>Studiendesign</b>	<b>Klinische Studie der Phase II, randomisiert, einfach verblindete Kohortenstudie</b>	
<b>Stichprobenumfang</b>	<b>n = 2 x 10 jugendliche und erwachsene Patienten ohne Geschlechtsdiskriminierung</b>	
<b>Studiendauer</b>	<b>Geplanter Studienbeginn:</b> <b>Geplante Dauer der Studie:</b> <b>Studiendauer / Patient:</b>	<b>04/2013</b> <b>12 Monate</b> <b>1 Woche</b>
<b>Hypothese</b>	<b>Die Anwendung von zwei unterschiedlichen Trockensalz-Inhalationen, 2mg/m<sup>3</sup> und 20mg/m<sup>3</sup>, hat einen signifikanten Effekt auf die Sekretolyse und die Lungenfunktion.</b>	



# Secretolysis - dry salt aerosol

**planned: dry salt aerosol inhalation**

**in Asthma ?**

**in COPD ?**

- curative use in respiratory diseases
- preventive use in respiratory cleansing and allergic and asthmatic disorders

# Summary

	Hypertonic saline	Dry salt aerosol
• Spasmolysis	√	- (!)
• Secretolysis	√	√
• Obstruction	++	- (!)
• Lung function	√	√
• Mobility	-	√
• Preventive use	-	√
• phase II and III studies in CF needed		
• in Asthma ?		
• in COPD first trial finished		
• in skin diseases ?		

Herzlichen Dank !

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