


# CYSTIC FIBROSIS

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***“Wehe dem Kind, das beim Kuss auf die Stirn salzig schmeckt, er ist verhext und muss bald sterben”***

*“Woe is the child who tastes salty from a kiss on the brow, for he is cursed, and soon must die”*


## What is Cystic Fibrosis?

Chronic, progressive and life limiting autosomal recessive genetic disease characterized by chronic respiratory disease, pancreatic insufficiency, elevation of sweat electrolytes and male infertility

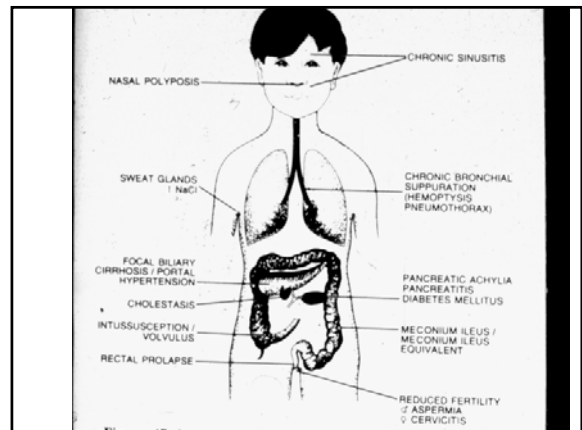


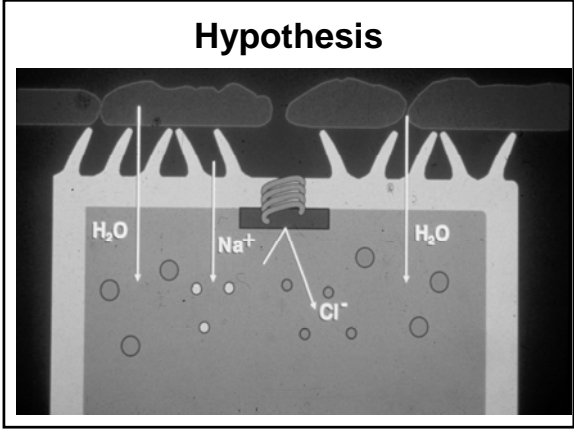
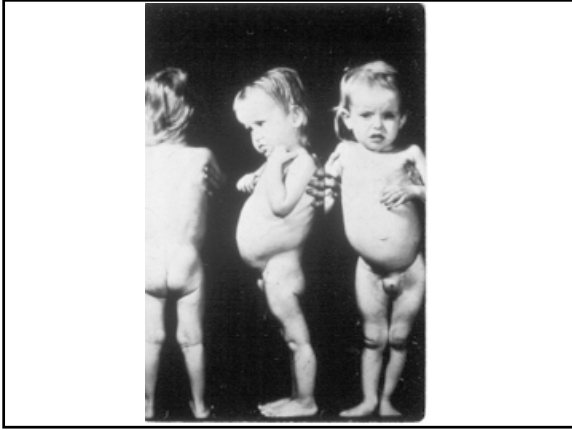
- ## Presentation (CF PANCREAS)
- C** Chronic respiratory disease
  - F** Failure to thrive
  - P** Polyps
  - A** Alkalosis, metabolic
  - N** Neonatal intestinal obstruction
  - C** Clubbing of fingers
  - R** Rectal prolapse
  - E** Electrolyte ↑ in sweat
  - A** Aspermia / absent vas deferens
  - S** Sputum – S.aureus/P.aeruginosa

## Genetics of CF



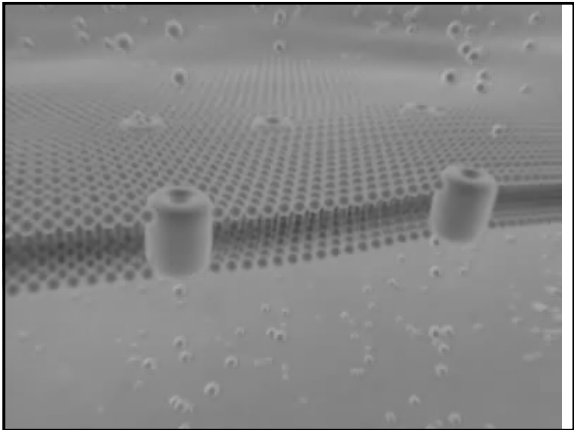
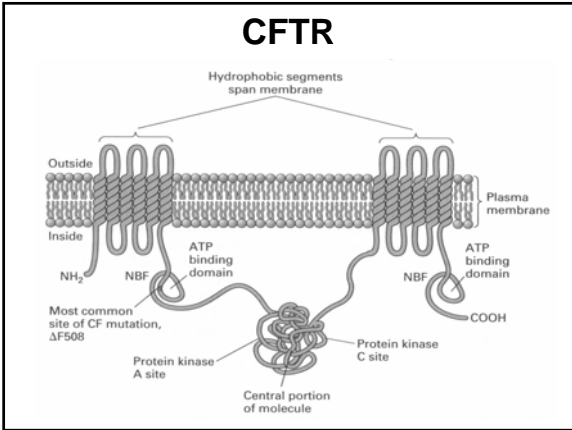
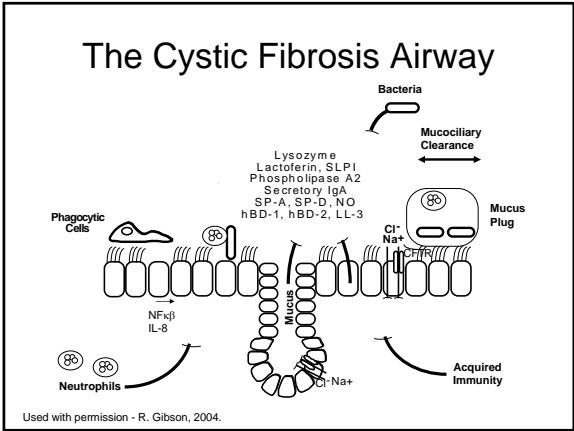
- Most common lethal genetic disease in Caucasians
  - 30,000 affected individuals in US
  - 27,000 in Europe
- CFTR - cAMP regulated chloride channel located in apical membrane of glandular epithelium
  - Long arm of chromosome #7
    - D508 most common mutation
    - 1000 identified mutations
  - Encodes for a protein of 1480 amino acids
  - Defective ion transport

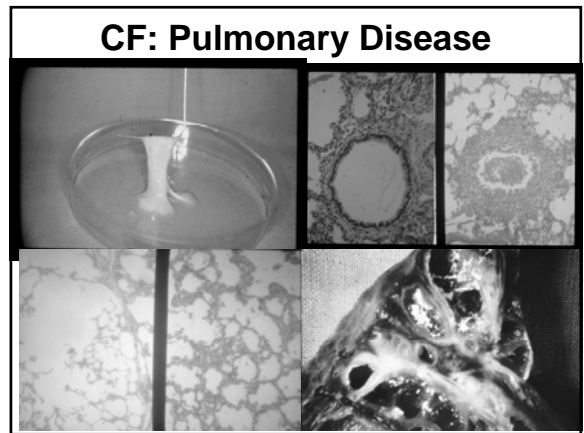
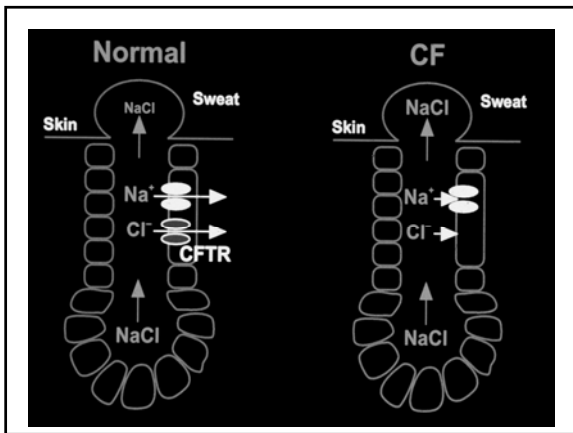
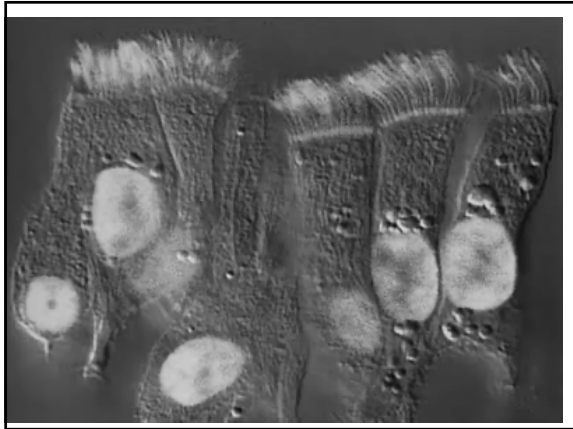




### CFTR

- Abnormalities in the CFTR protein change the constituents of mucous and result in abnormal reabsorption of water, creating thickened mucus and inadequate mucociliary function.
- The CF airway has many changes leading to mucous plugging, chronic infection, and inflammation.



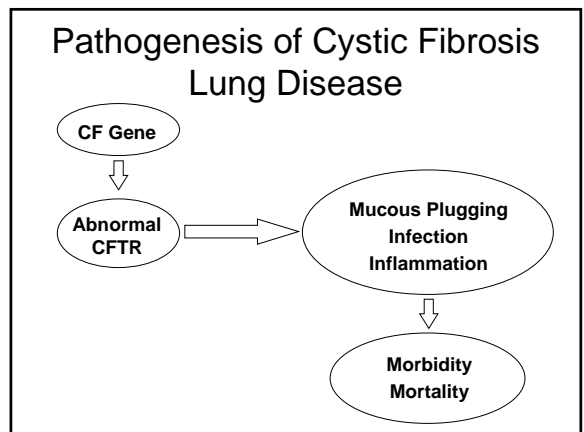


### The sweat test ( Chloride)

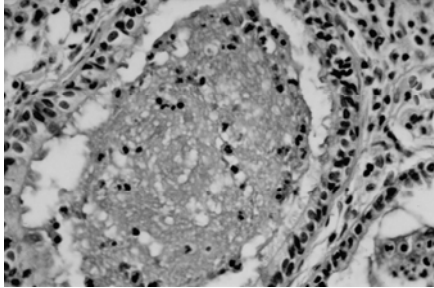
**Normal**  
Under 40 mEq/L

**Borderline**  
40-60 mEq/L

**Positive**  
Over 60 mEq/L

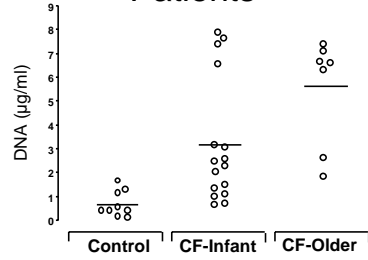


### Airway Mucous Plugging, Infection, and Inflammation in Cystic Fibrosis



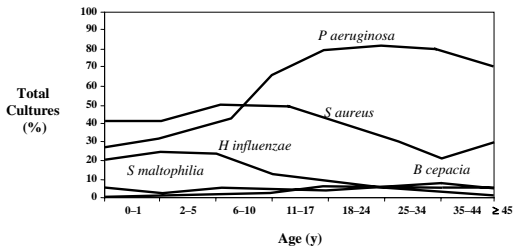
Used with permission – J. Wagener, 2004.

### DNA in Bronchoalveolar Lavage Fluid from Cystic Fibrosis Patients

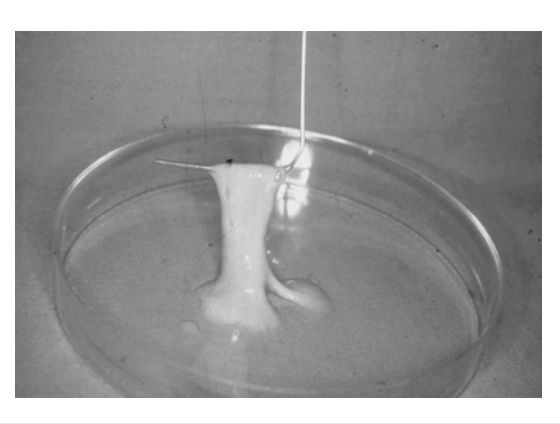


Kirchner et al. *Am J Respir Crit Care Med* 1996; 154: 1426-1429.

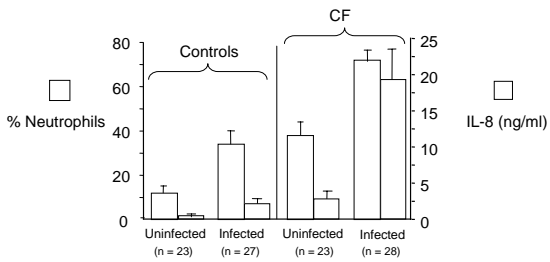
### Major Airway Pathogens by Patient Age, 1999



Patient Registry 1999 Annual Data Report. Bethesda, Md: Cystic Fibrosis Foundation; 2000.

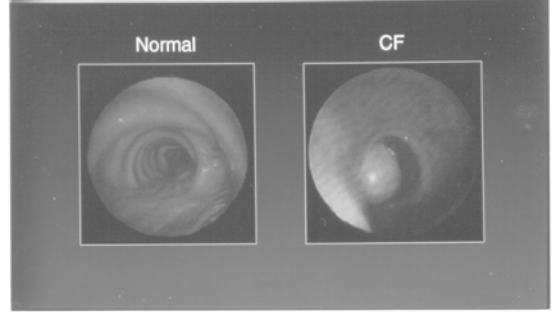


### Evidence of increased inflammation in BALF of infants with CF

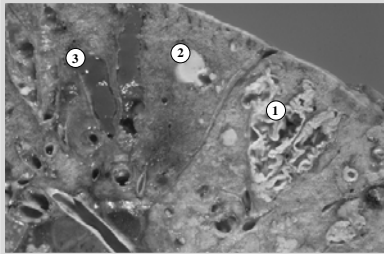


Adapted from Muhlebach et al. *Am J Respir Crit Care Med* 1999; 160: 186-191.

### Bronchoscopic Views of Normal and CF Airways



## CF Lung: End-Stage Bronchiectasis



## Signs and Symptoms of Pulmonary Exacerbation

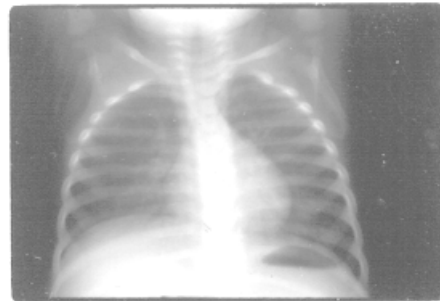
- Increased cough
- Increased sputum
- Weight loss
- School/work absenteeism
- Increased dyspnea
- New chest findings
  - rales, wheezes
- Decreased exercise tolerance
- Decreased FEV1
  - down 10%
- New radiographic findings

## CF Lung Function

### PULMONARY FUNCTION TESTS:

	NORMAL	MILD	MODERATE	SEVERE
FEV <sub>1</sub>	NL	NL	↓ (70%)	↓↓ (40%)
FEF <sub>25-75</sub>	NL	↓ (70%)	↓↓ (40%)	↓↓↓ (20%)
MEFV				
VC	NL	NL	↓	↓↓
TLC	NL	NL or ↑	NL or ↑	↓
RV/TLC	25%	↑ (35%)	↑↑ (50%)	↑↑↑ (70%)
PaO <sub>2</sub>	NL	↓ (94)	↓↓ (85)	↓↓↓ (60)
PaCO <sub>2</sub>	NL	NL	NL	↑↑

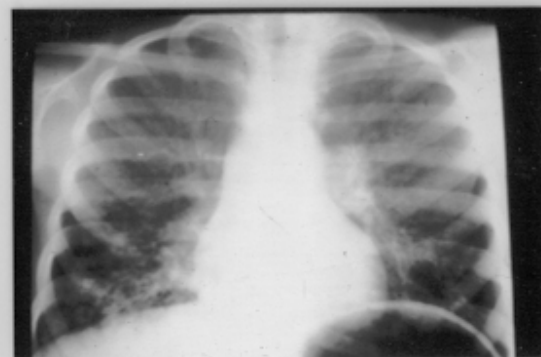
## CF mild disease



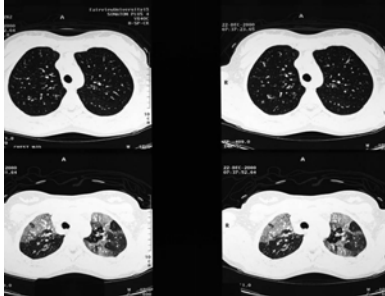
## Lung function in CF

- ↑ A-a gradient
- ↓ compliance
- ↓ flow rates at low lung volumes
- ↑ slope of phase III nitrogen washout
- ↑ physiologic dead space
- ↓ exercise tolerance

### Bronchiectasis



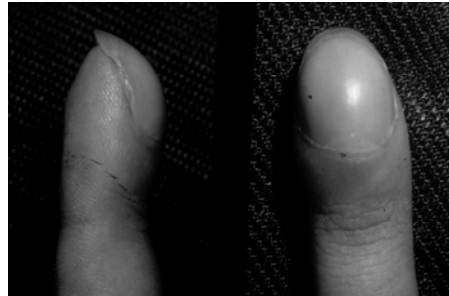
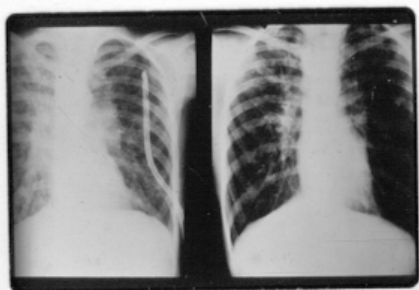
### High-Resolution Inspiratory and Expiratory CT Scan in 12 year old



Used with permission - C. Milla, 2004.



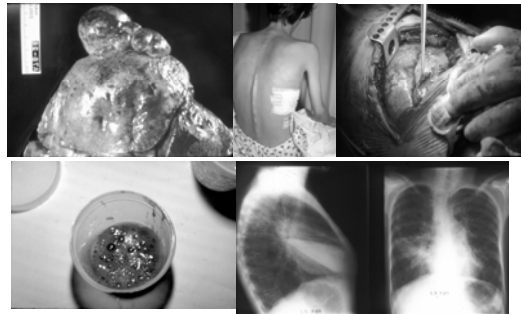
### CF Pneumothorax



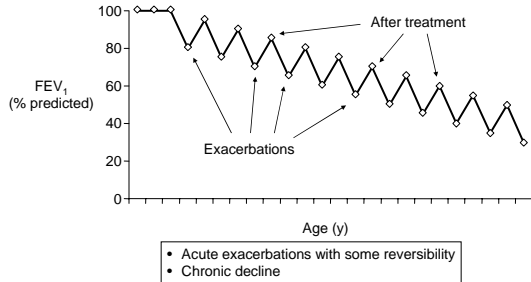
BLEBS



### CF: Pulmonary Complications

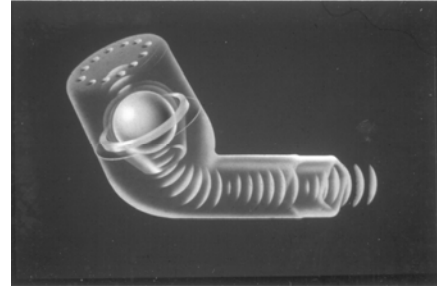


## Exacerbations Contribute to the Deterioration of Lung Function



Used with permission from P. Flume.

## CF Flutter



## CF: Respiratory management

- Regular visits to CF Center
- Airway clearance
- Mucus thinners (DNase, hypertonic saline)
- Antibiotics( PO-IV-Aerosol)
- Anti inflammatory drugs



## Anti-inflammatory Rx

- **Steroids**
    - inhaled v oral
  - **Ibuprofen**
  - **Macrolides**
- ISSUES**
- Safety
  - Adherence
  - ? Delay in progression of the disease

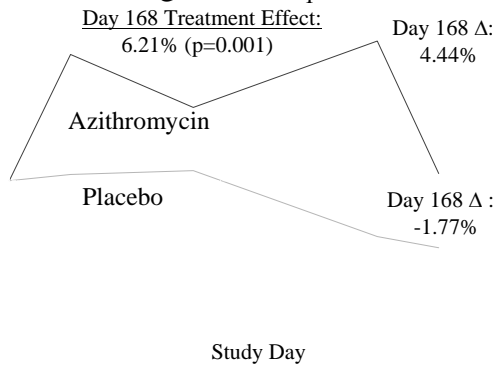
## Airway Clearance

- CPT
  - Vest
  - Flutter
  - ACB
- ISSUES**
- Reflux
  - Risk factor for *Pa*
  - Adherence

## Diffuse Pan-bronchiolitis (DPB)

- DPB clinically resembles CF
  - More common in Japan than in Western countries
  - Age of onset between 30 and 60 years of age
- Chronic lower respiratory tract infection
  - Neutrophils predominant inflammatory cell
  - *H. influenzae* and *S. pneumonia* early in disease
  - *P. aeruginosa* major pathogen later
    - 70% of patients have mucoid strains
  - Progress to bronchiectasis and respiratory failure
- Pancreatic insufficiency *not* a clinical feature

## Relative Change in FEV<sub>1</sub> % Predicted



## Treating Airway infections

- Prophylactic treatment
  - prevent colonization
- Exacerbations
  - improves lung function
  - reduces inflammation
  - decreases bacterial density
- First isolates
  - may delay colonization

## DNase

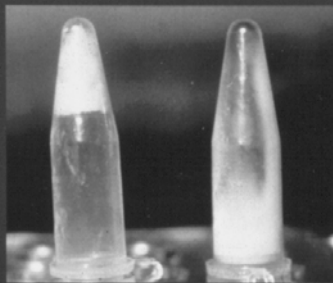
- Recombinant DNase
- Hydrolyzes DNA
- Aerosolized

## Antibiotics

- Oral
- IV
- Aerosolized
- Special Considerations:
  - Volume of distribution
  - Sensitivities
  - Drug Interactions
  - Side effects

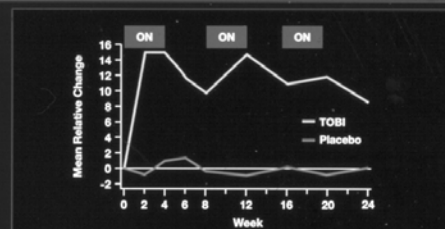


## Pulmozyme Increases the Pourability of Cystic Fibrosis Sputum



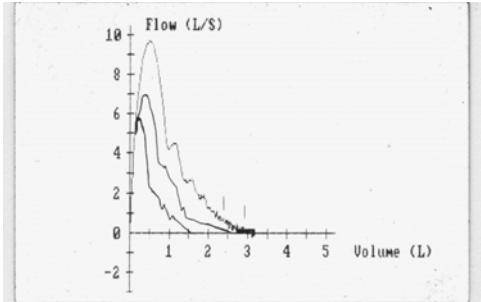
Shek S, et al. *Proc Natl Acad Sci USA* 1990;87:9188-92

## Mean Relative Change in FEV<sub>1</sub> % Predicted (002 Study)



Bonny BW. Presented at the Eleventh Annual North American Cystic Fibrosis Conference, October 25-31, 1997, Honolulu, Hawaii.

## CF PFT's



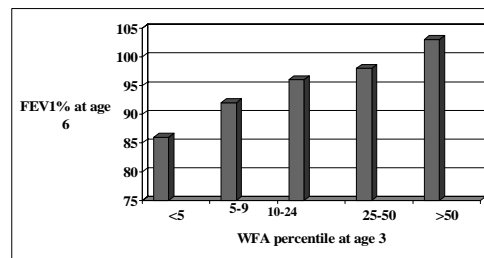
## CF: Pancreas-malabsorption



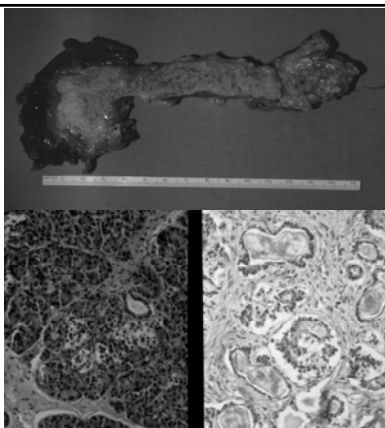
## CF: Gastrointestinal Disease

- Pancreatic insufficiency/malabsorption
- Lipo-soluble vitamin deficiency
- Failure to thrive
- Neonatal intestinal obstruction (15%)
- Recurrent distal intestinal obstruction
- Biliary stasis

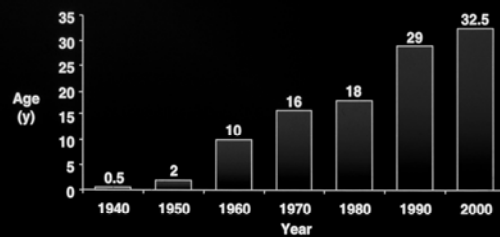
## Nutrition and CF



Konstan et. Al. Pediatr Pulmonol 2000



## Median CF Survival Age, 1940-2000



Data from Cystic Fibrosis Foundation, Bethesda, Md. Available at [http://www.cff.org/infodepresentation\\_files/frame.htm#fsd0015.htm](http://www.cff.org/infodepresentation_files/frame.htm#fsd0015.htm).

