CYSTIC FIBROSIS

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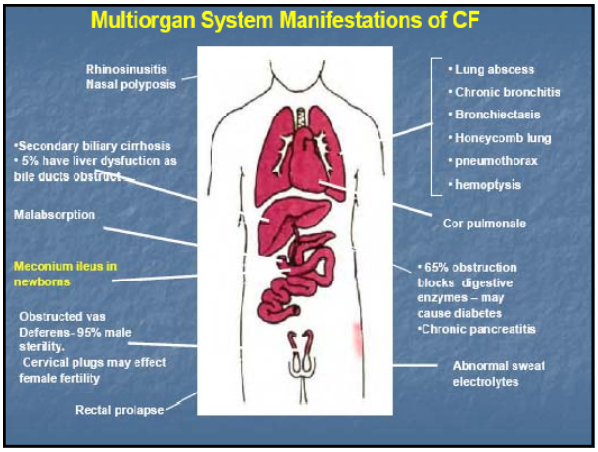
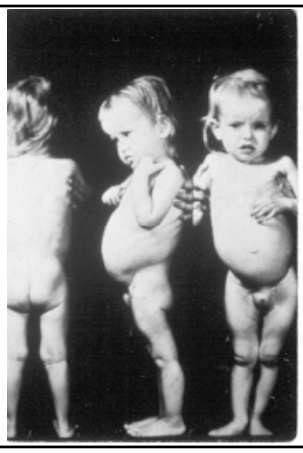
What is Cystic Fibrosis?

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

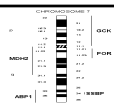
"Wehe dem Kind, das beim Kuss auf die Stirn salzig schmekt, er ist verhext und muss bald sterben"

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



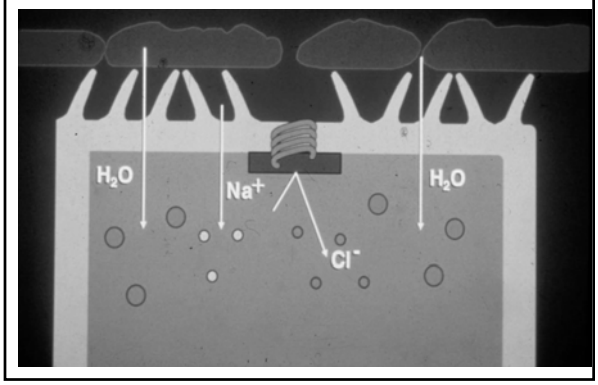


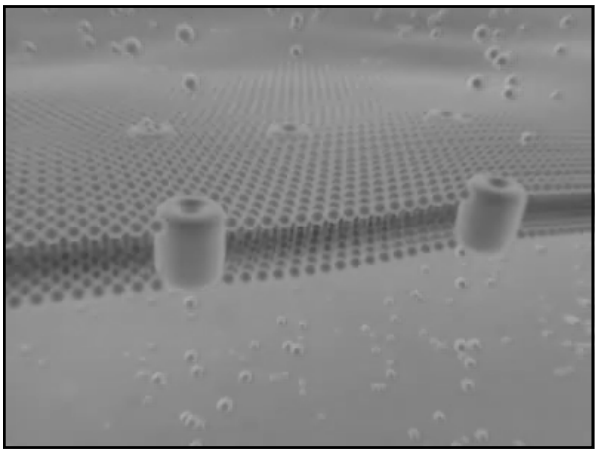
Genetics of CF



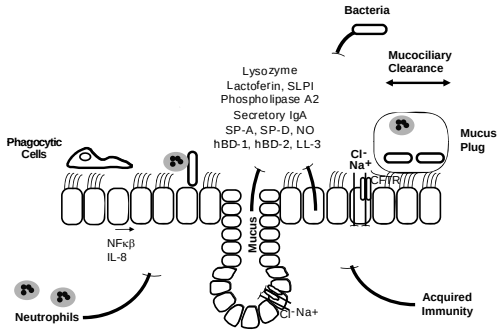
- **Most common lethal genetic disease in Causasians**
  - **30,000 affected individuals in US**
  - **27,000 in Europe**
- **CFTR - cAMP regulated chloride channel located in apical membrane of glandular epithelium**
  - **Encodes for a protein of 1480 amino acids**
  - **Defective ion transport**
  - **Long arm of chromosome #7**
    - **D508 most common mutation**
    - **> 1500 identified mutations**

Ion Transport





The Cystic Fibrosis Airway



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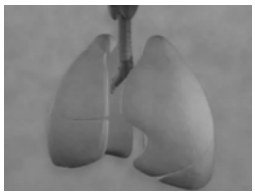
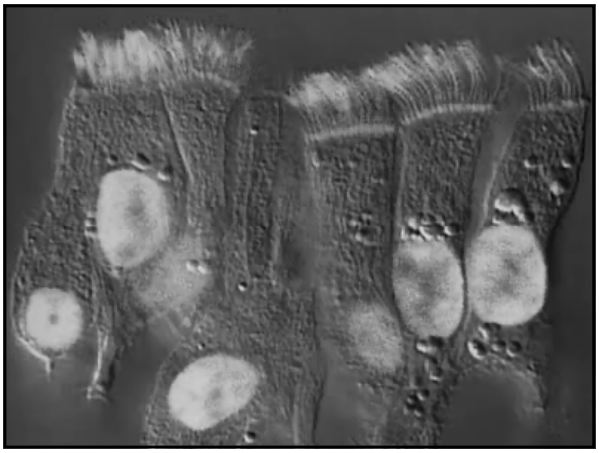
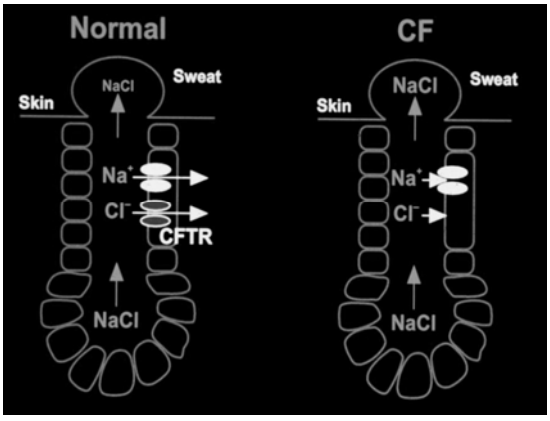
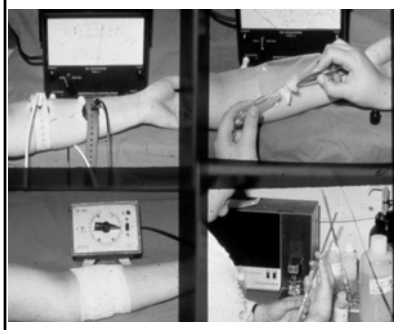






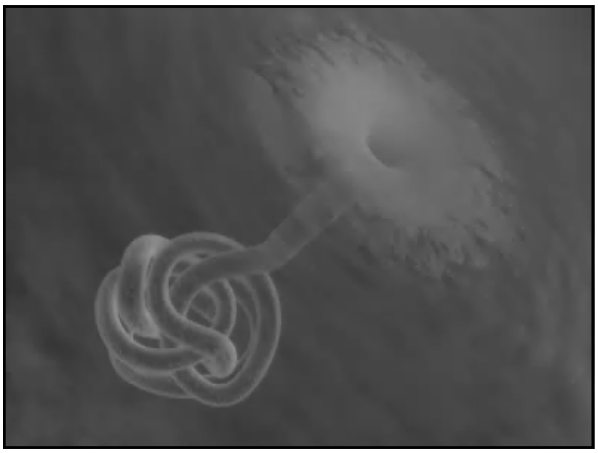
The sweat test (Chloride)



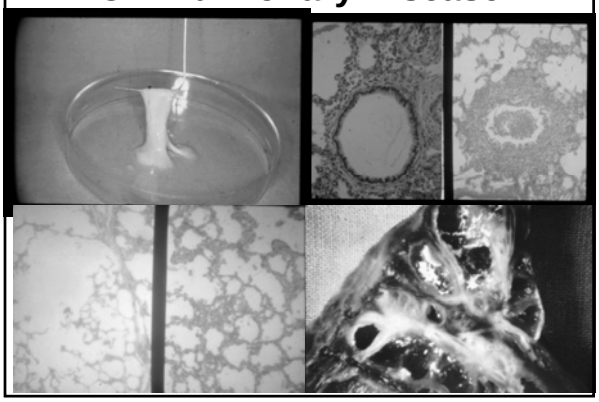
Normal
Under 40 mEq/L

Borderline
40-60 mEq/L

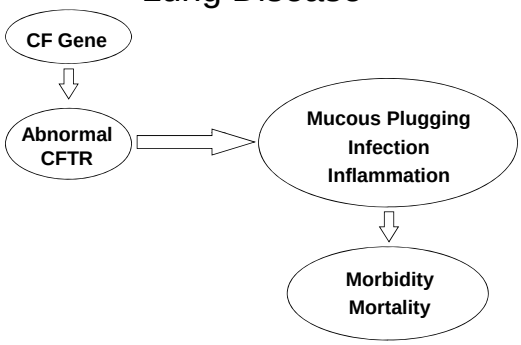
Positive
Over 60 mEq/L



CF: Pulmonary Disease



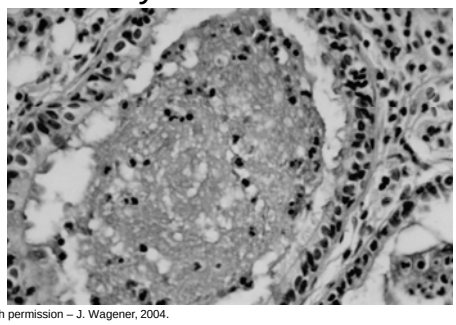
Pathogenesis of Cystic Fibrosis Lung Disease



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

Airway Mucous Plugging, Infection, and Inflammation in Cystic Fibrosis



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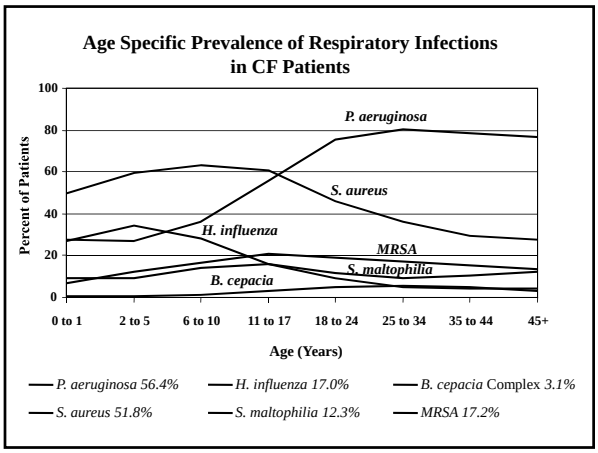
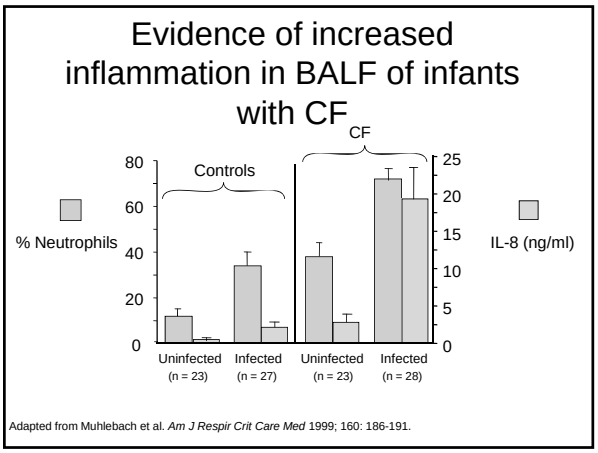
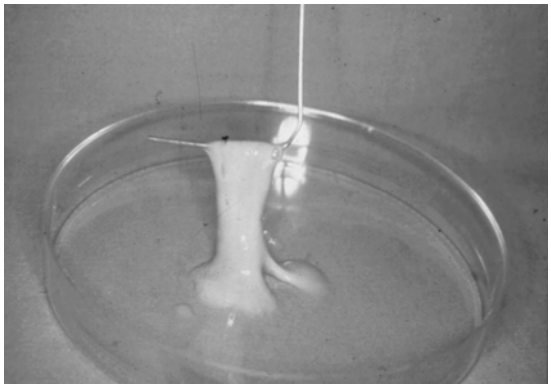
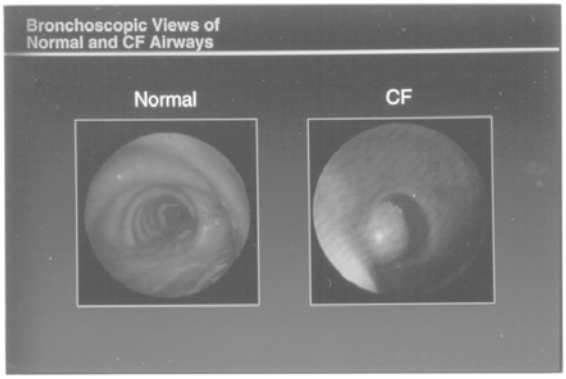


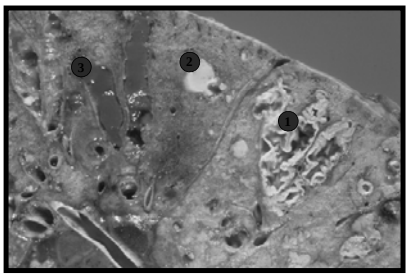


Adapted from Muhlebach et al. *Am J Respir Crit Care Med* 1999; 160: 186-191.





CF Lung: End-Stage Bronchiectasis



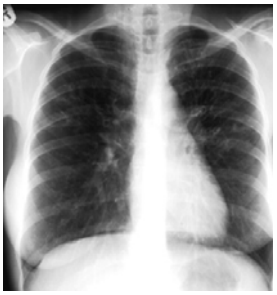
CF Lung Function

PULMONARY FUNCTION TESTS:

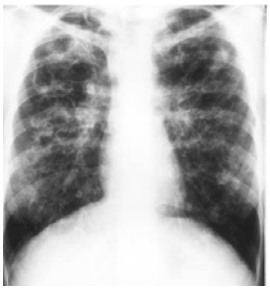
	NORMAL	MILD	MODERATE	SEVERE
FEV_1	NL	NL	↓ (70%)	↓↓ (40%)
FEF_{25-75}	NL	↓(70%)	↓↓ (40%)	↓↓↓ (20%)
MEFV				
VC	NL	NL	↓	↓↓
TLC	NL	NL or ↑	NL or ↑	↓
RV/TLC	25%	↑ (35%)	↑↑ (50%)	↑↑↑ (70%)
PaO_2	NL	↓ (94)	↓↓ (85)	↓↓↓ (60)
$PaCO_2$	NL	NL	NL	↑↑

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

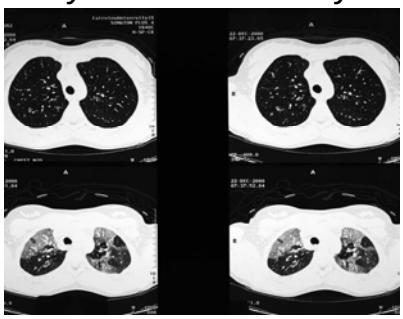


CF mild disease: hyperinflation, increased markings



CF advanced disease: with bronchiectasis

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



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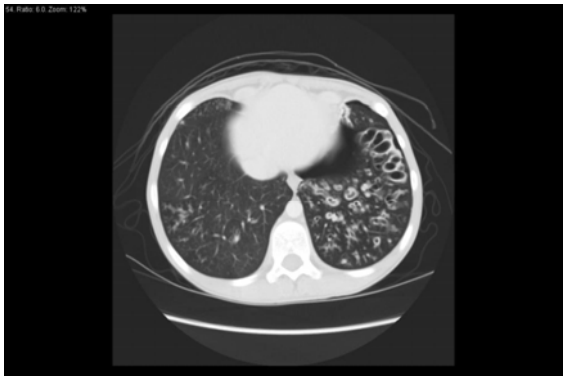
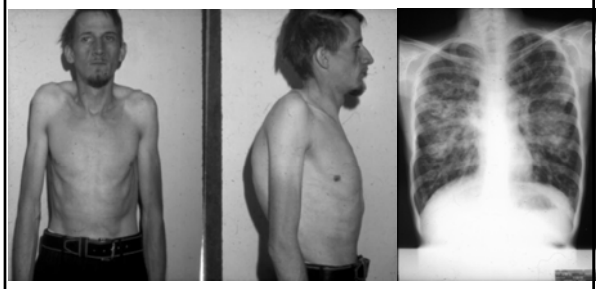
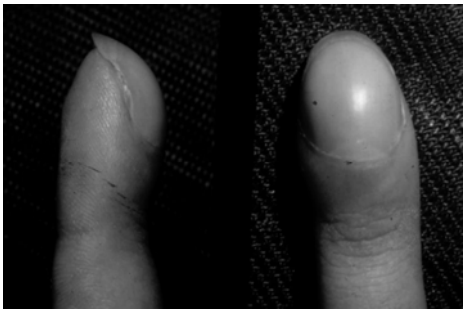
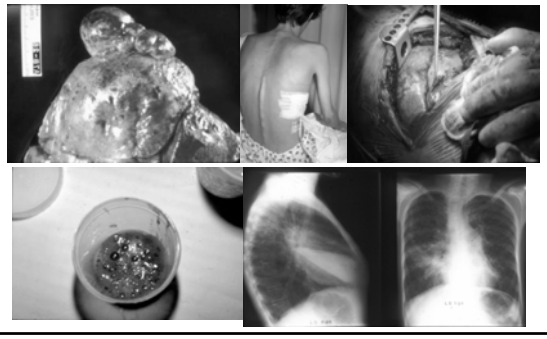






CF: Pulmonary Complications



CF: Respiratory management

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

Airway Clearance

- CPT
- Vest
- Flutter
- ACB

ISSUES

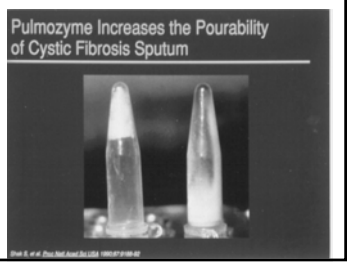
- Reflux
- Adherence

Airway Clearance

- Chest Physical therapy
- Vest – mechanical percussion
- Flutter, Acapella
- Breathing techniques : ACB
- Exercise

Mucolytic agents

- Recombinant DNase
- Hypertonic saline

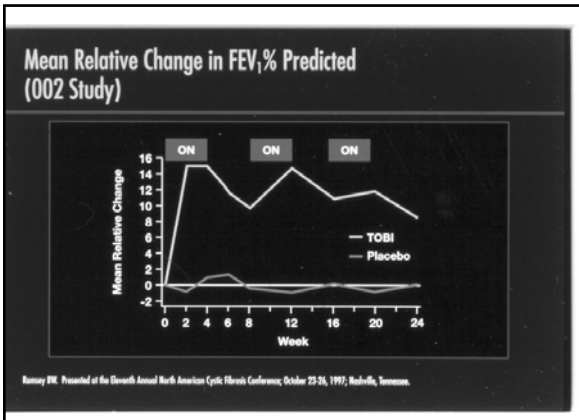


Treating Airway infections

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

Antibiotics

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

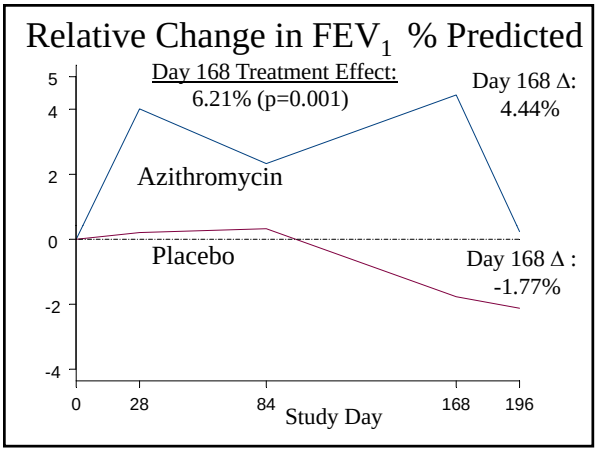


Anti-inflammatory Rx

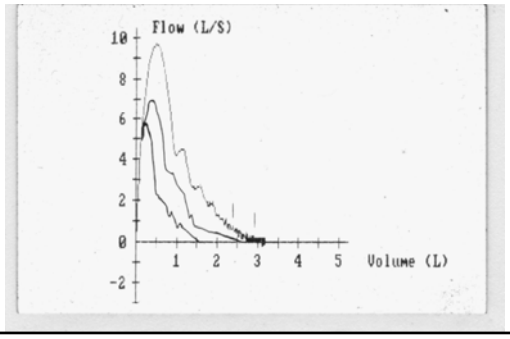
- **Steroids**
  - **inhaled v oral**
- **Ibuprofen**
- **Macrolides**

ISSUES

- Safety
- Adherence
- ? Delay in progression of the disease

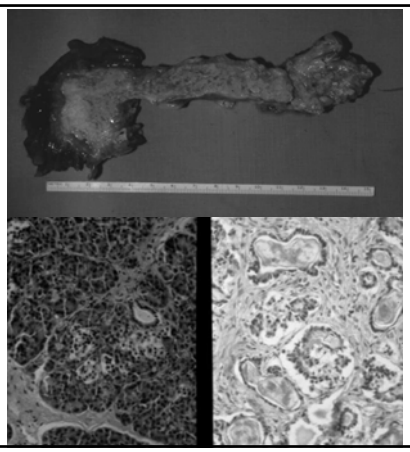


CF PFT's

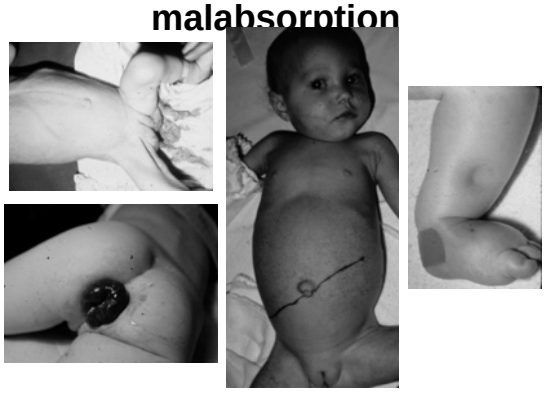


CF: Gastrointestinal Disease

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

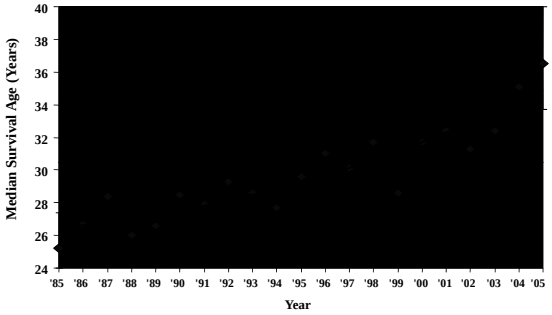


CF: Pancreas-malabsorption



Median Predicted Survival Age, 1985-2005

(with 95 percent confidence bounds)



As of August 2006, the median predicted survival is 36.5 years for 2005.