Cystic Fibrosis

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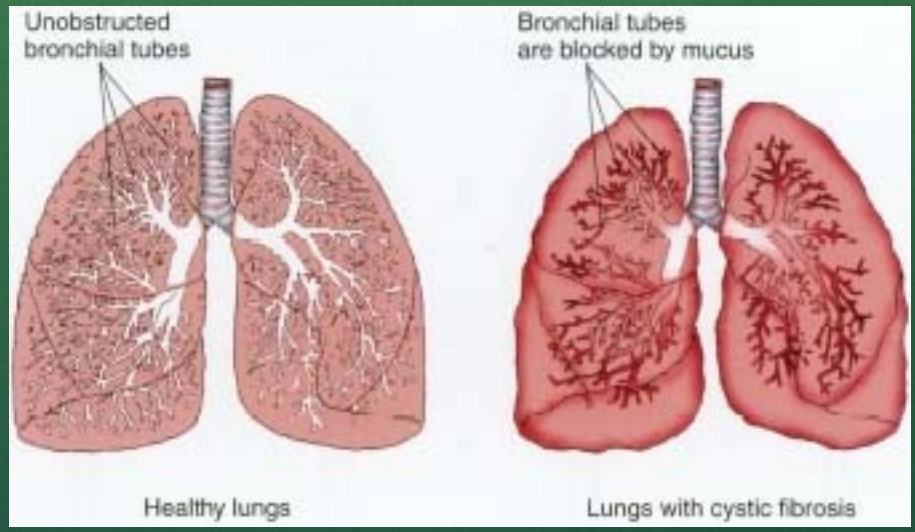
Statistics

- Affects about 30,000 children and adults in the US (70,000 worldwide)
- About 1000 new cases diagnosed each year
- More than 70% of the patients are diagnosed by age 2.
- Predicted mean age of survival is in late 30s
- 45% of the population is age 18 or older.

Overview of the Disease

- Body produces thick, sticky mucus that clogs lungs
  - Sweat
  - Digestive juices.
- Abnormal transport of chloride and sodium ions across an epithelium.
  - Infection
  - Blocks pancreas
    - Scarring and cyst formation → name
  - Stops digestive enzymes from reaching intestines
  - Infertility/Delayed puberty
- Occurs commonly in people of African-American, Northern European, and Hispanic heritage.



Classical Diagnostics

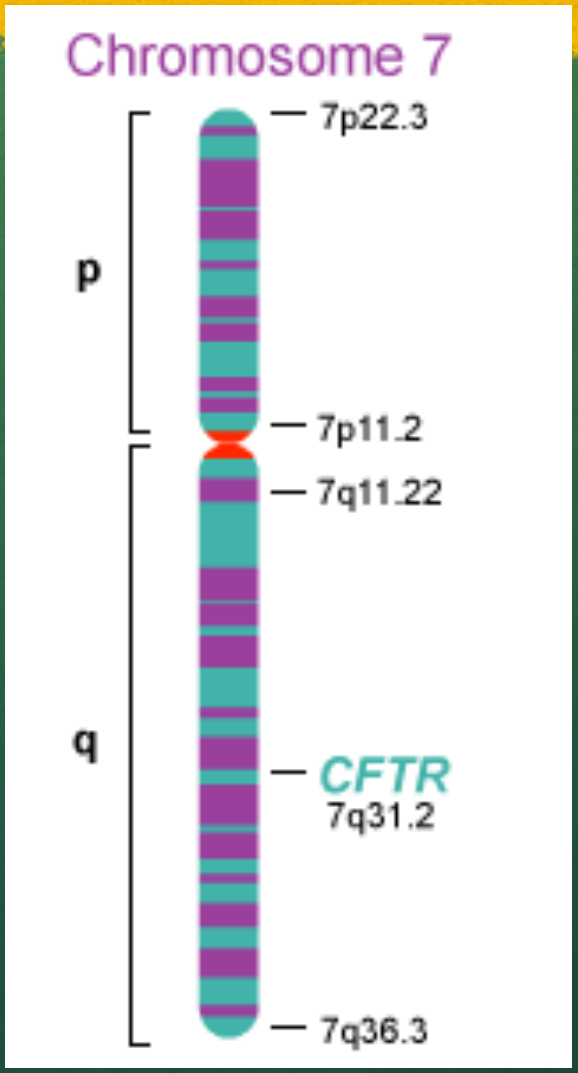
- Misdiagnosed with whooping cough, chronic bronchitis, or pneumonia.
- Since 1700s German, “salt” test
  - “A child whose forehead tastes like salt when kissed will soon die.”
- 1930s: illness first described by Dr. Paconi.
  - Celiac syndrome → changes in pancreas in children.
- Term coined by Dr. Dorothy Andersen
  - Vitamin A deficiency
- Sweat test
  - Concentration of chloride in sweat.
  - More chloride = increasing likely of CF.

Classical Treatments

- 1955: Dr. Shwachman's work
  - Early diagnosis
  - Active treatment
  - Proper nutrition (high fat diets)
- Antibiotics (penicillin) commonplace
- Initially thought to be Vitamin A deficiency, then challenged.

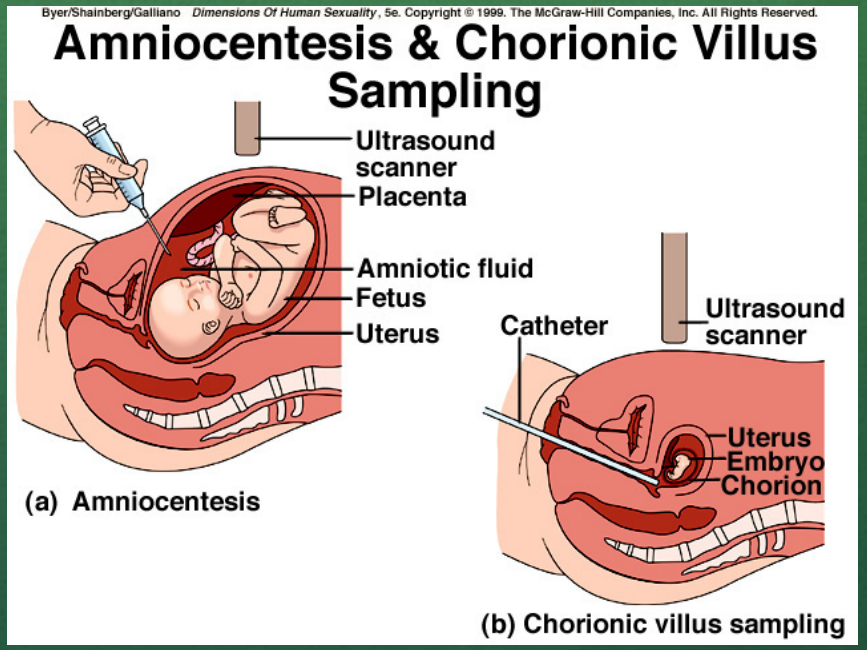
Genetic Overview

- Caused by defect in CFTR
  - Cystic Fibrosis Transmembrance Conductance Regulator
- Autosomal recessive
- Locus: 7q31.2.
- 1480 AA normal protein size.
- Delta 508 mutation
  - Most common
  - 1st nucleotide-binding domain (NBD1)
- Responsible for producing chloride channel protein found in membranes of cells that line passageways.
  - Organs affected:
    - Lungs
    - Liver
    - Pancreas
    - Intestines
    - Reproductive tract
    - Skin



Novel Diagnostics

- Immunoreactive trypsinogen (IRT) test; high levels = more chance of having CF.
  - Tests for pancreatic function
- Genetic testing
  - CFTR gene with delta 508 mutation
  - Pre-birth screening methods:
    - CVS
    - Amniocentesis
- Sweat chloride test
- Chest X-Ray/CT Scan
- Fecal fat test (increased fat = increased risk of CF)
  - Test for enzymes like trypsin in stool.
- Lung function test



Modern Treatment

- Antibiotics
- Mucus-thinning drugs
  - Pulmozyme: enzyme breaks DNA apart
    - Mucus viscosity.
- Physiotherapy
  - Chest clapping to loosen mucus.
- Brachiodilators (help expand lungs).
- Nebulizers.

Novel Gene Therapy

- 1993: gene therapy with promising results
  - Used virus as vector to transplant correct gene.
  - Fat capsules, synthetic vectors, nose drops, drizzling cells → other vectors.
  - Need to figure out best vector.
  - March 16, 2012 → Largest CF trial at Oxford
    - Breath in gene via nebulizer.
- *Pseudomonas aeruginosa* gene mapping
  - Most common cause of chronic and fatal lung infections
  - Design better drugs
- CFFT (CF Foundation Therapeutics) sponsors genetic database to speed up research.

Real Life Struggles…

- http://www.youtube.com/watch?v=Twjg7v-pTO4
  - 2:00- 3:30

Works Cited

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- http://www.ncbi.nlm.nih.gov/books/NBK22202/ (Genes and Disease book)
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