Meconium Ileus in Cystic Fibrosis

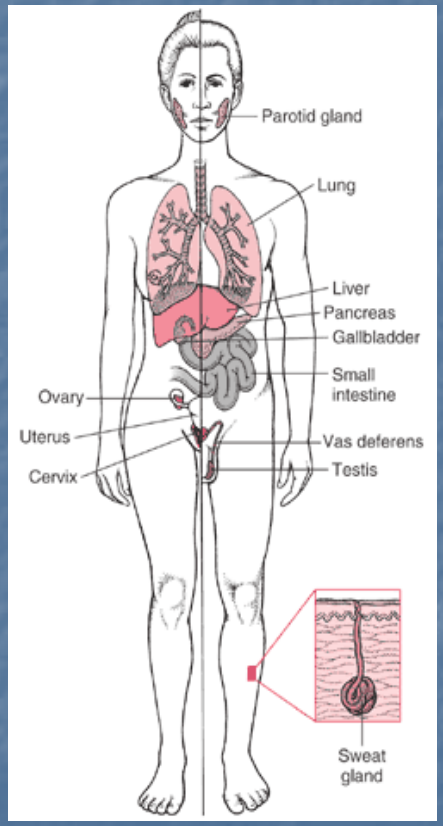
Valery Dronsky MD
Kings County Hospital Center
Department of Surgery
July 21, 2006

Case Presentation- HPI

- An xx hour old xx male was transferred form Lutheran Medical Center with diagnosis of intestinal obstruction, possible jejuenal atresia to Kings County Hospital
- CC: abdominal distension, vomiting and failure to pass meconium
- Family Hx: maternal and paternal, Native American Indians with cystic fibrosis trait

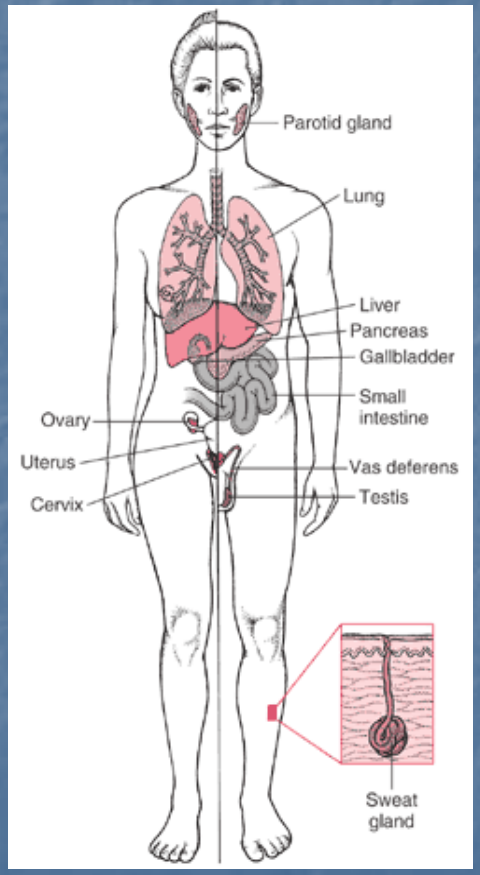
Case Presentation

- Vitals:
  - Temperature: 99
  - HR: 176
  - BP: 76/40
  - Resp: 57
  - Pulse Oximetry: 99%



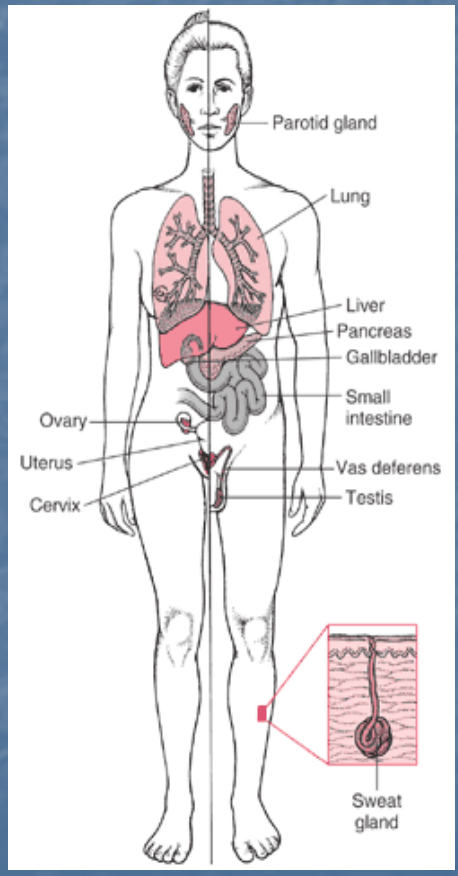
Case Presentation-CBC

- WBC 3.76
- Hgb 14.8
- Hct 45.5
- Platelets 248
- Neut 7%
- Bands 13%
- Lymph 71%



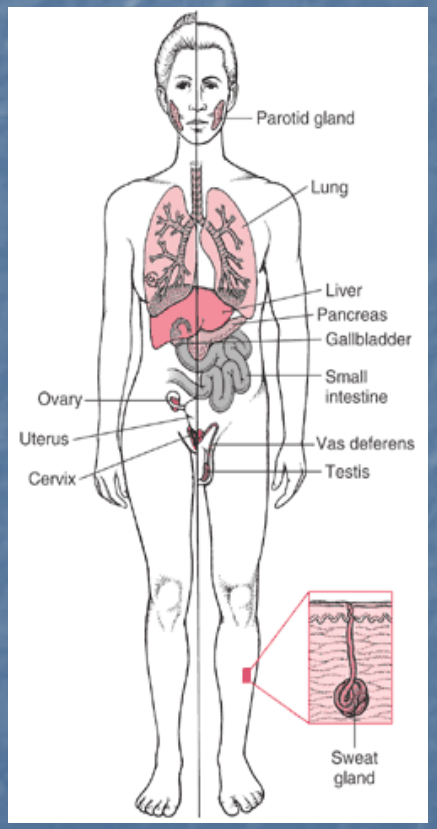
Case Presentation-Chemistry

- Na 133
- K 3.8
- Cl 107
- CO_2 14
- BUN 8
- Cr 0.8
- Glucose 334
- Calcium 7.9



Case Presentation-ABG

- pH 7.31
- pCO2 31.9
- pO2 112
- sO2 99.1%
- HCO 17.4
- BE -9.3

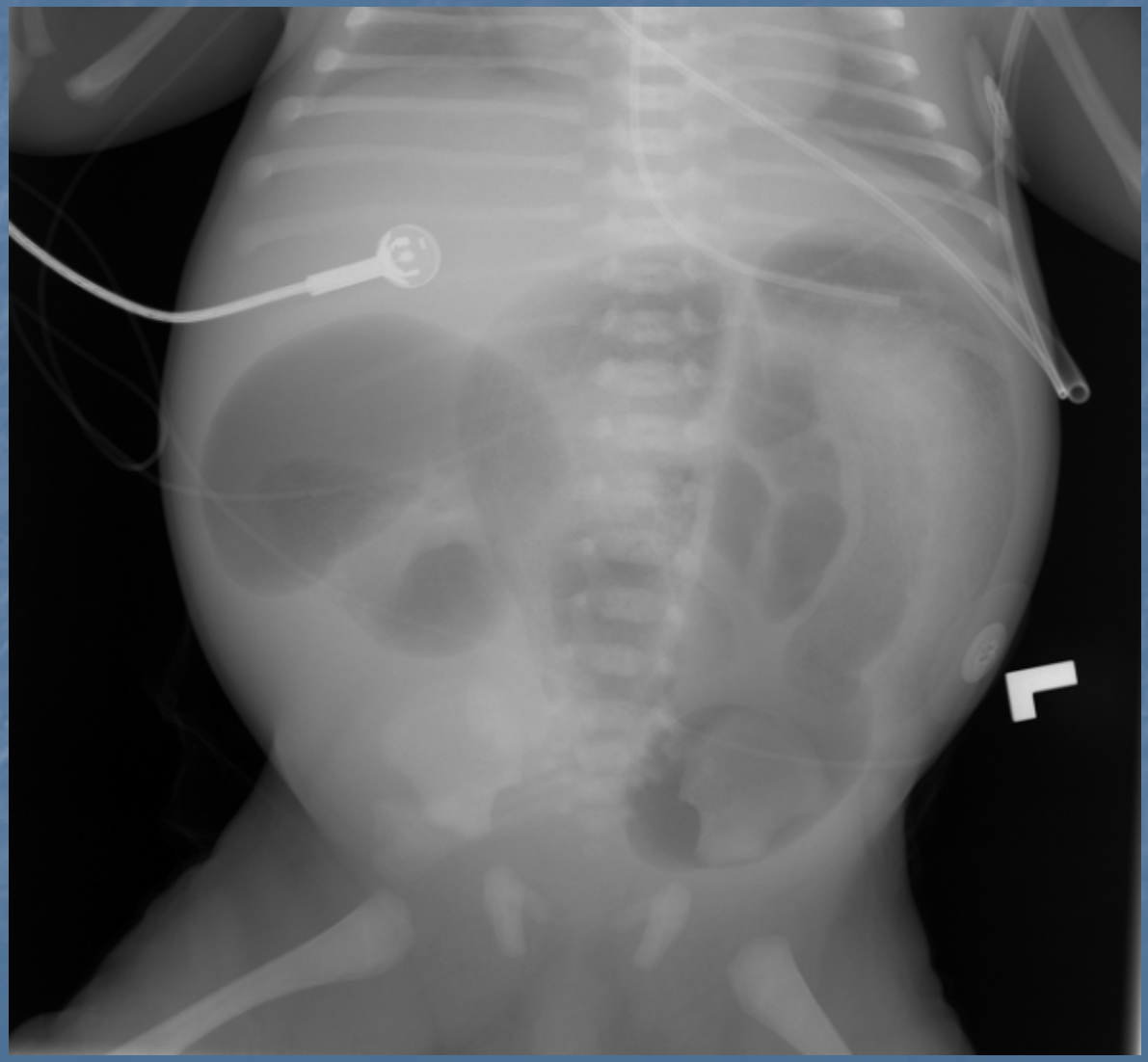


Meconium Ileus

Case Presentation- Abdominal XR

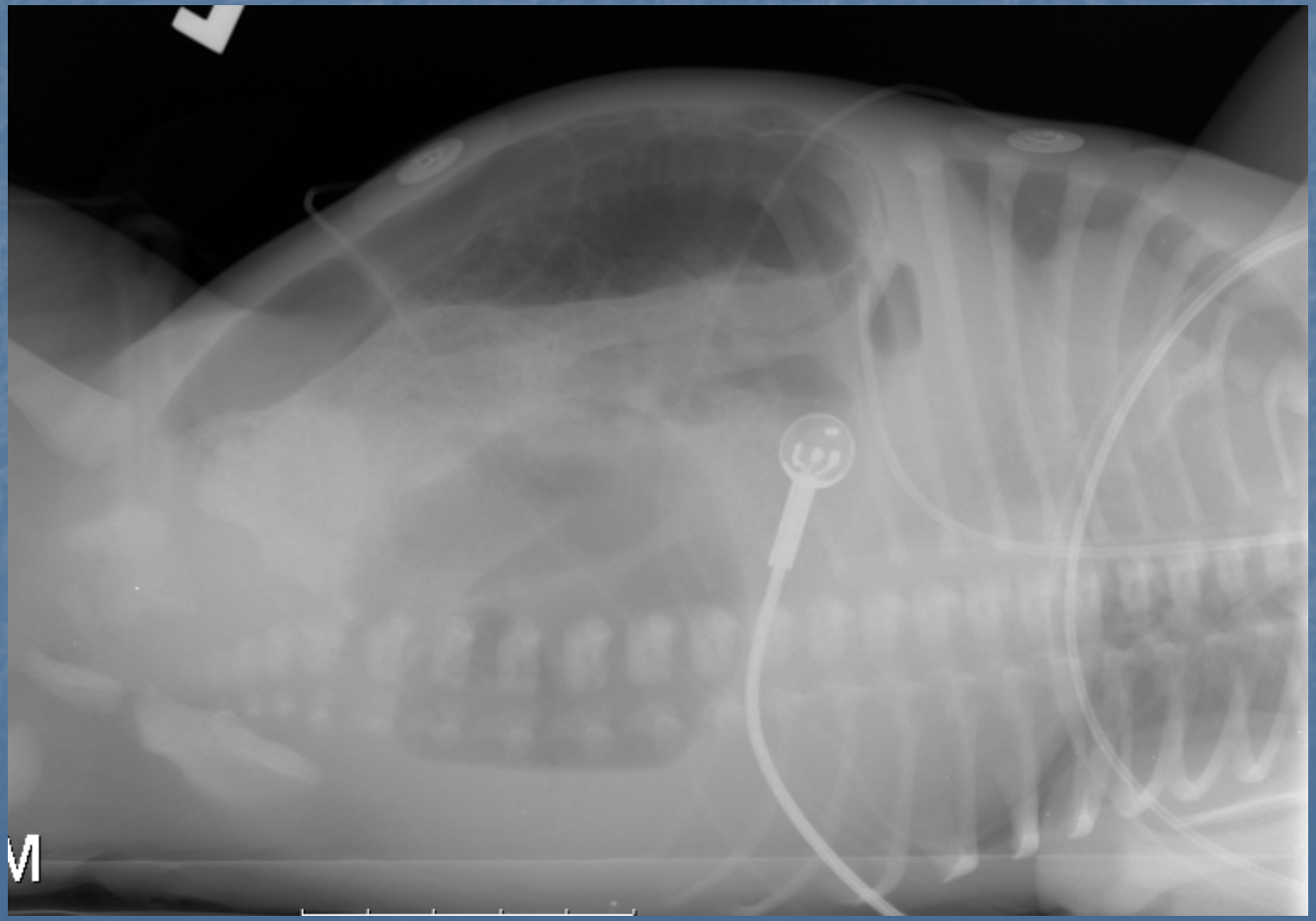
High intestinal obstruction, possible pneumatosis and intraperitonial free air.

Worrisome for NEC



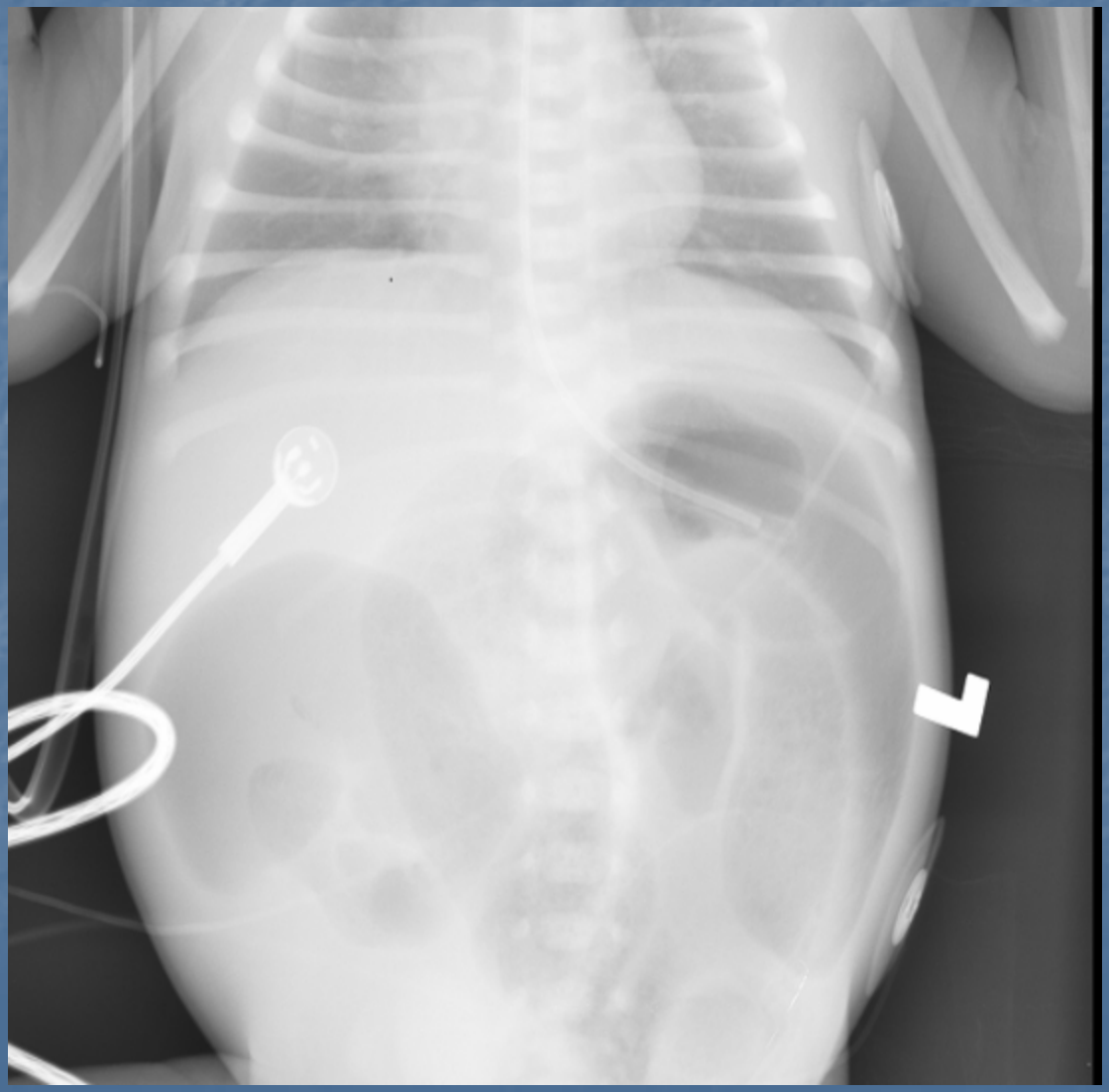
Meconium Ileus

Case Presentation-Abdominal XR



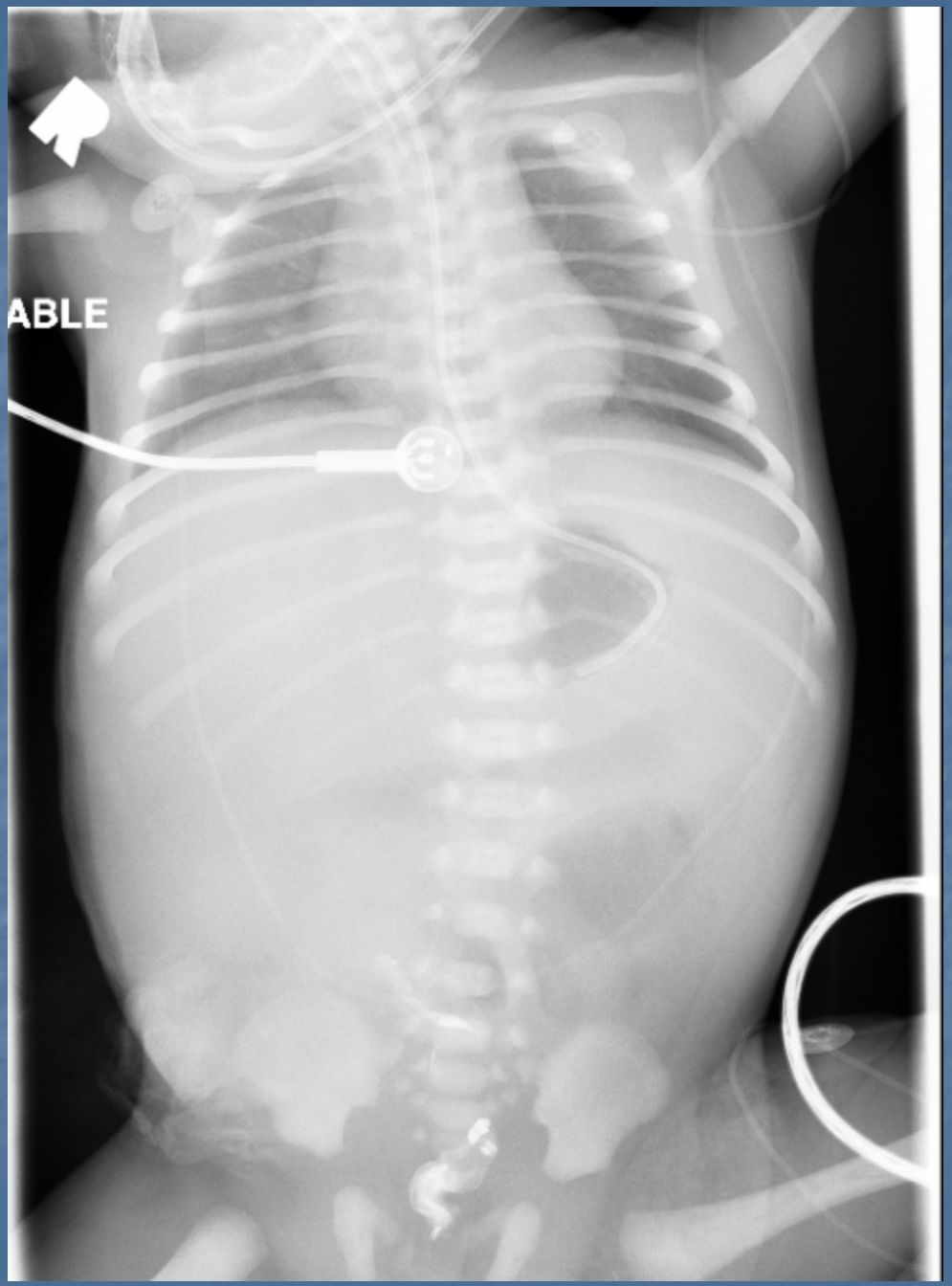
Case Presentation-Barium Enema

- High intestinal obstruction
- Barium could only reached level of distal sigmoid colon
- May represent obstruction due to plugs or atretic or stenotic segment



Case Presentation- Barium Enema

- High intestinal obstruction
- Barium could only reached level of distal sigmoid colon
- May represent obstruction due to plugs or atretic or stenotic segment



Case Presentation- OR

- Procedure: laparotomy with lysis of adhesion, resection of segments of jejunum and ileum, jejeunostomy, with mucous fistula of ileum
- Findings Jejeunal atresia, inspissated meconium in the distal ileum with in utero volvulus of ileum with perforation

Case Presentation

- Postoperative diagnosis
  - Jejeunal atresia and meconium ileus with volvulus and perforation
  - Etiology: cystic fibrosis
- Intra-operative cultures:
  - E.Coli, heavy growth

Case Presentation- Post op Course

- Course complicated by
  - enterococcus fecalis sepsis
  - Broviac catheter sepsis
- Appropriate antibiotic therapy instituted
- Nutritional support: TPN

Case Presentation – Post op Course

- Blood Culture 7/12/06: negative
- Clinical status improved; pt is pre-op to restore bowel continuity

Meconium Ileus in Cystic Fibrosis

Valery Dronsky MD
Kings County Hospital Center
Department of Surgery

Meconium Ileus

Cystic Fibrosis Habitus

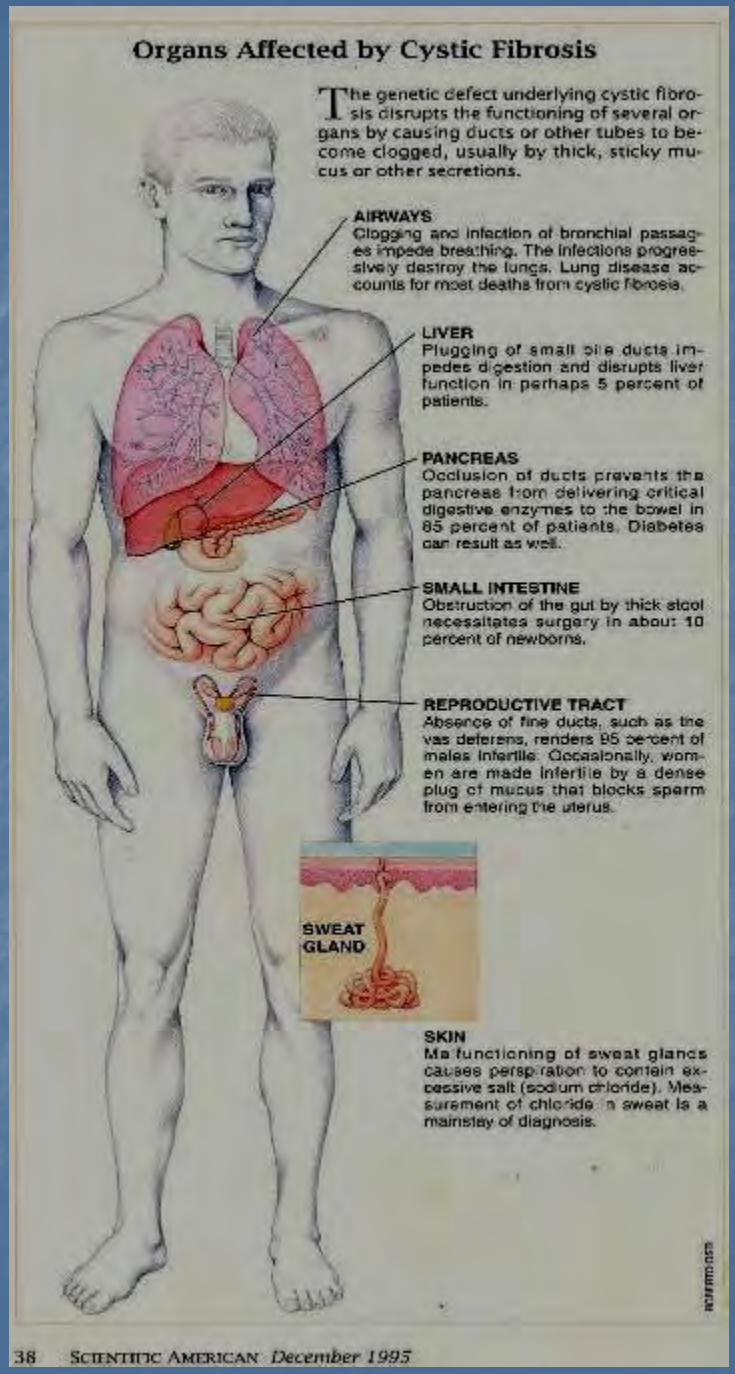
Cystic Fibrosis - Introduction

- Inherited monogenic disorder presenting as a multisystem disease.
- Typically presents in childhood
  - only 7% of CF patients diagnosed as adults
- Most common life limiting recessive trait among whites

Meconium Ileus

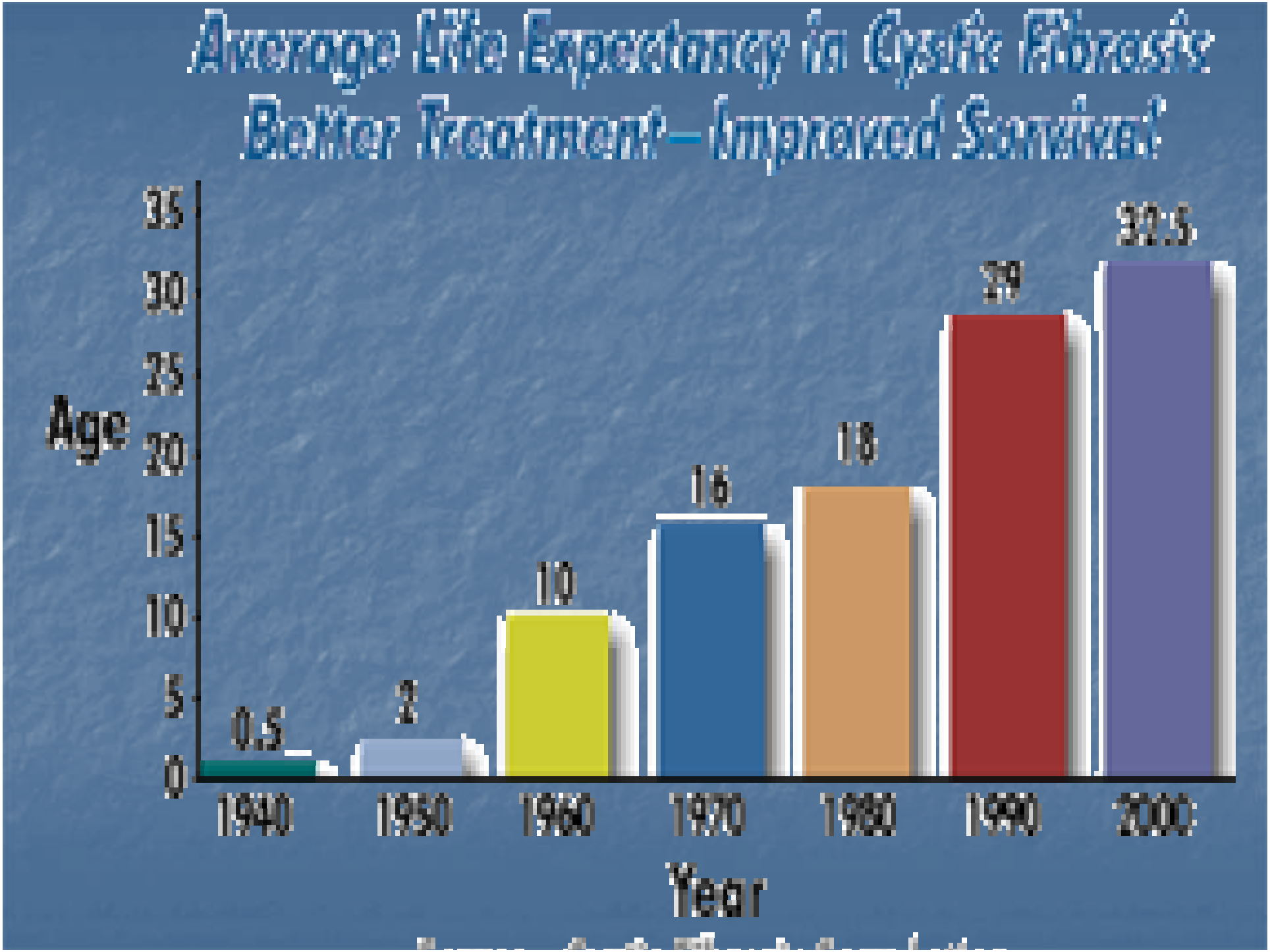
CF-Introduction

- Term coined 1938- “cystic fibrosis of the pancreas”
- Symptoms of classical CF:
  - Meconium ileus - obstruction of bowel in newborn 20%
  - Chronic lung infections and inflammation 90% of patients
  - Pancreatic insufficiency 85% of patients
  - Increased electrolyte level in sweat
  - Diabetes Mellitus
  - Liver cirrhosis
  - CBAVD-congenital bilateral aplasia of the vas deferens in 95% of males

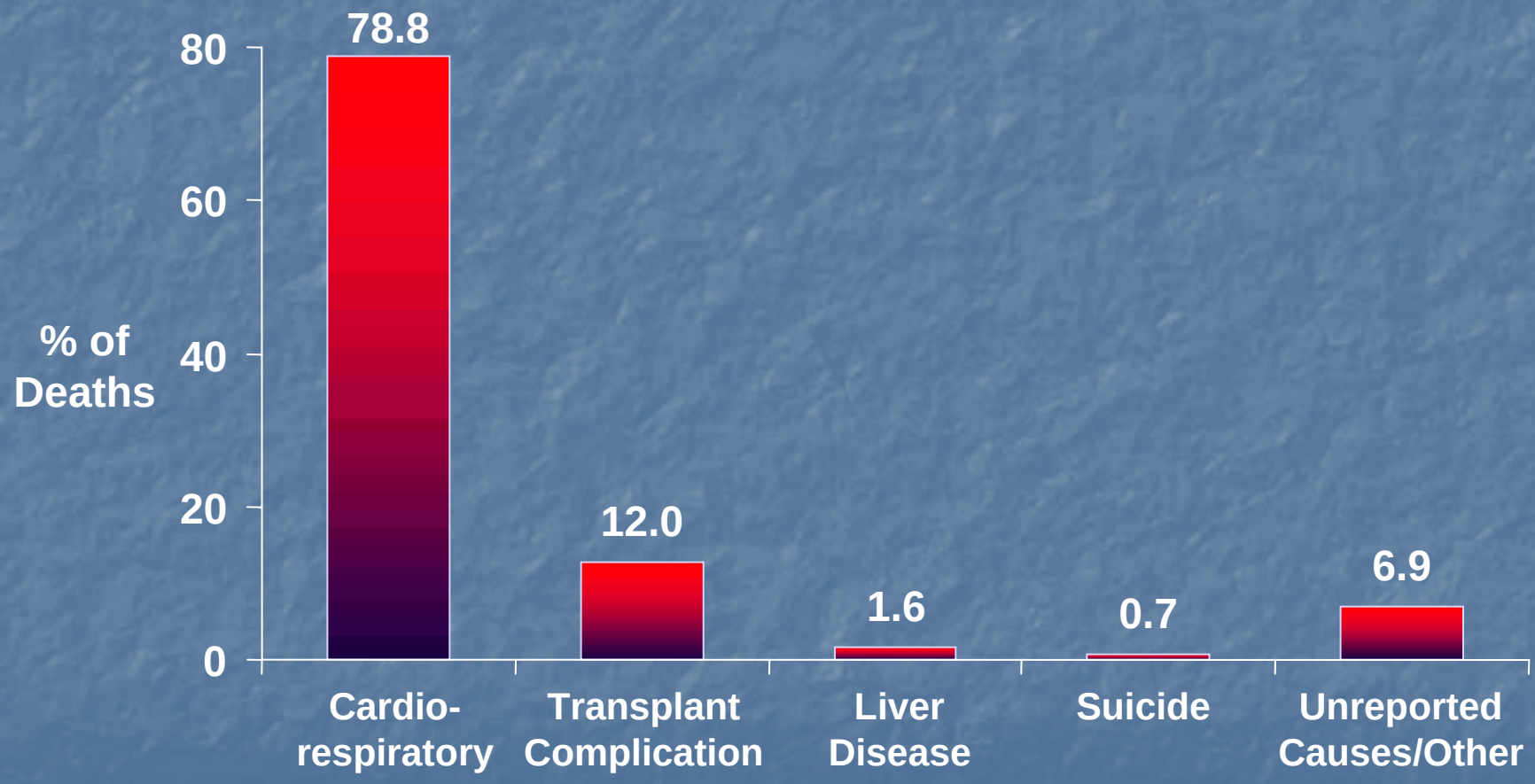


Cystic Fibrosis - Prognosis

- Prognosis improving
  - >38% of CF patients are older than 18
  - 13% of CF patients are older than 30
- Median survival
  - Males: 32 years
  - Females: 29 years



CF-Primary Causes of Death



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

Genetics of CF

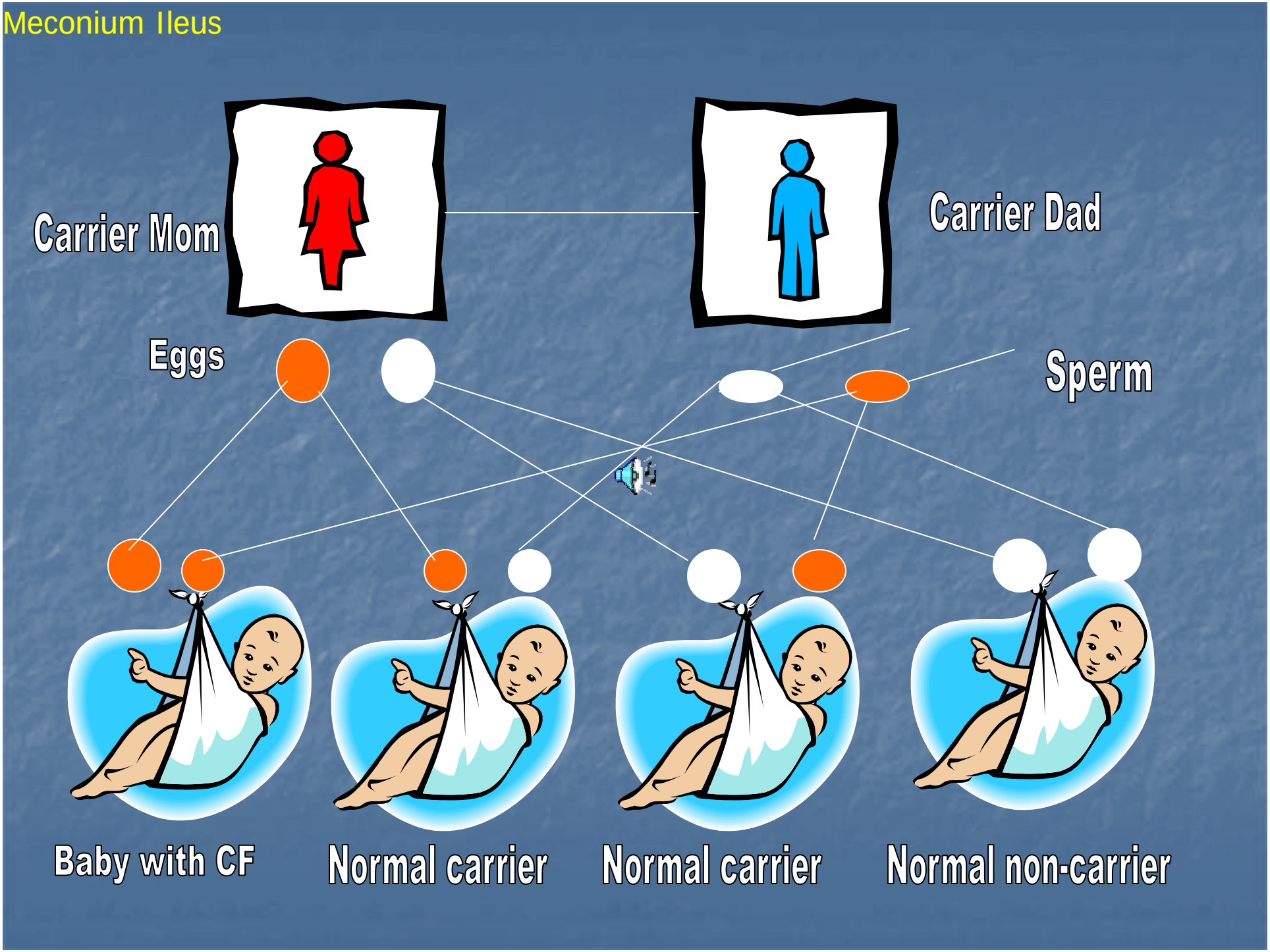
- Autosomal recessive
- Gene located on chromosome 7
- Prevalence- varies with ethnic origin
  - 1 in 3000 live births in Caucasians in North America and Northern Europe
  - 1 in 17,000 live births of African Americans
  - 1 in 90,000 live births in Hawaiian Asians

Cystic Fibrosis Foundation. Facts about Cystic Fibrosis. 2003 May

Chance of Being a CF Carrier by Ethnic Background

Ethnic group	Affected child	Carrier rate	**Ability to Detect mutation**
Europ. Cauc	1/3000	1/29	80%
Ash. Jewish	1/3000	1/29	97%
Hispanic Am	1/9200	1/46	57%
African Am	1/15,000	1/65	69%
Asian Am	No data	1/90	unknown

Meconium Ileus



Genetics of CF

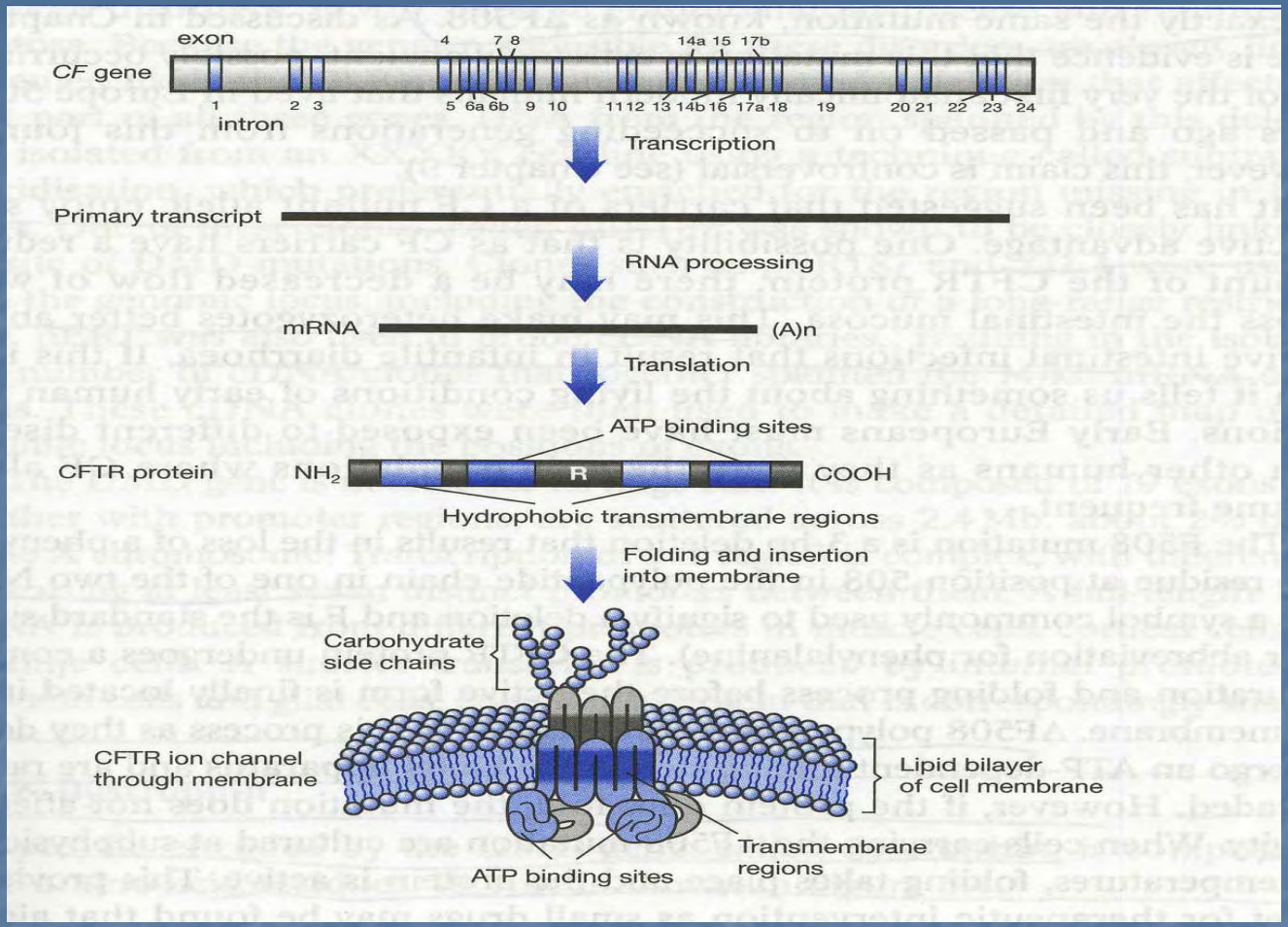
- Most common mutation
  - Occurs in 70% of CF chromosomes
  - 3 base pair deletion leading to absence of phenylalanine at position 508 ΔF_{508} of the CF Transmembrane conductance Regulator-CFTR
- Large number >1000 of relatively uncommon mutations ~2%

Genetics of CF

- Native Americans have the second highest incidence rates of cystic fibrosis
- One in 10,500 Native Americans has cystic fibrosis
- Compared with one in 3,200 Whites
- The delta-F508 mutation has not been found in any American Indian cystic fibrosis patient.
- According to the American Society of Human Genetics, genetic tests can detect about 94 percent of those mutations found in American Indians
- Recent surveys conducted on specific American Indian populations found even higher incidences: one in 3,970 in the Pueblo Indian people and one in 1,580 among the Zuni Indians.

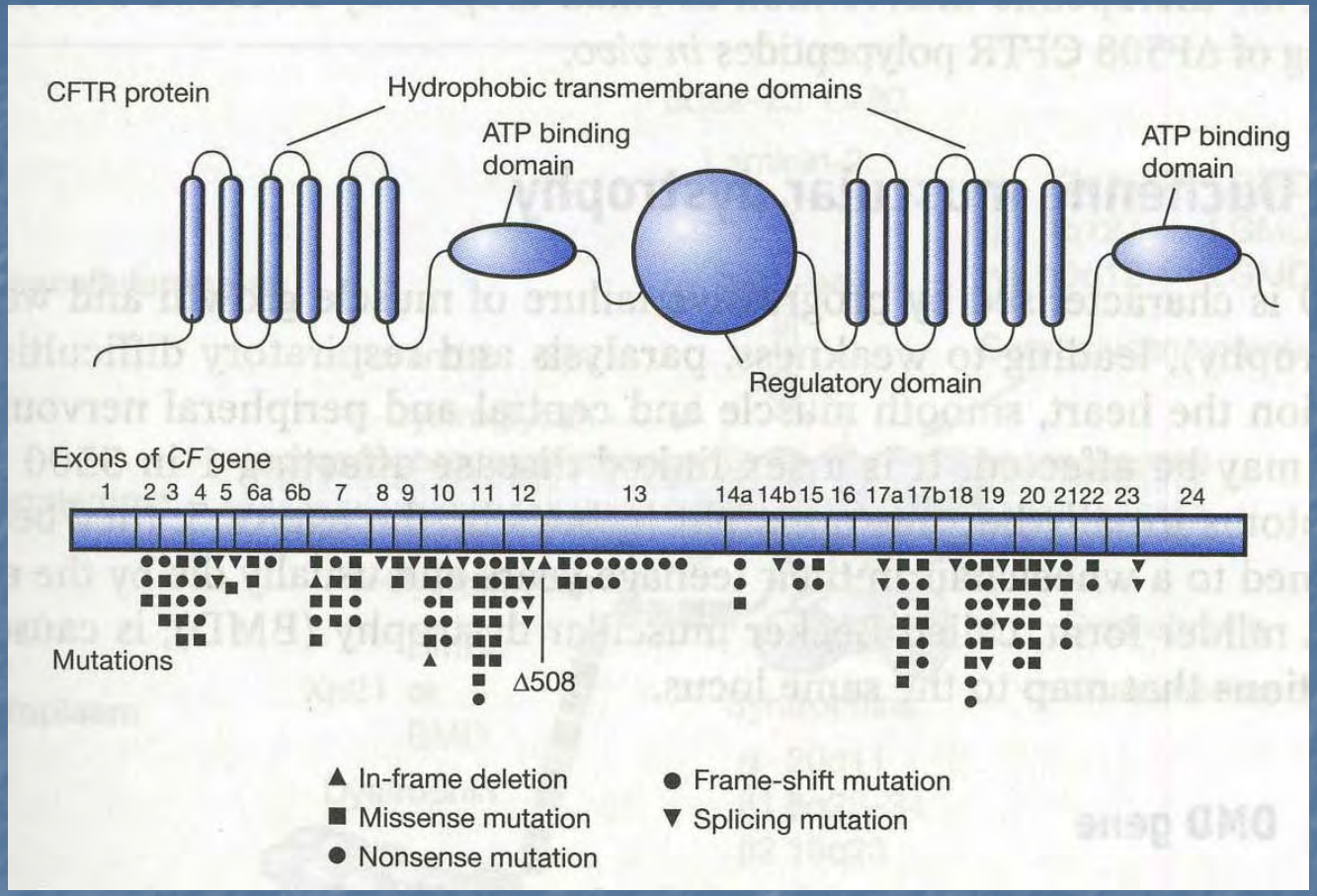
Cystic Fibrosis Foundation. Facts about Cystic Fibrosis. 2003 May

Genetics of CF



- The CFTR protein- Cystic fibrosis Transmembrane conductance Regulator
  - Single polypeptide chain, 1480 amino acids
  - Cyclic AMP regulated chloride channel
  - Regulator of other ion channels
  - Found in the plasma membrane of normal epithelial cells

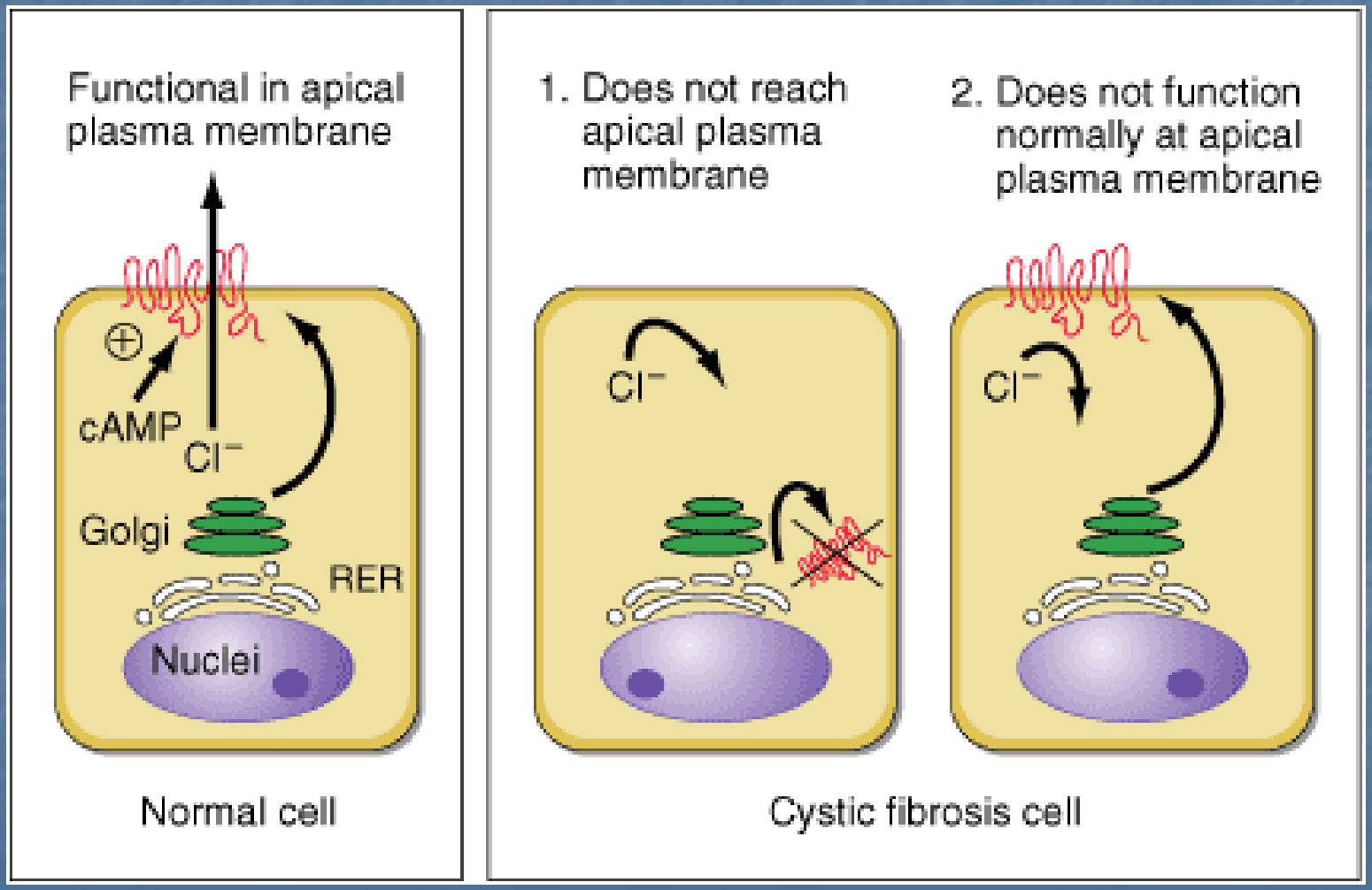
CF Genetics



- Mutations in *CFTR*- Cystic Fibrosis Transmembrane conductance Regulator, located on chromosome 7p31.2
- CFTR is a chloride ion transporter that binds ATP and hydrolyzes it for energy to transport Cl-

Meconium Ileus

CF-Mutation of CFTR



Meconium Ileus

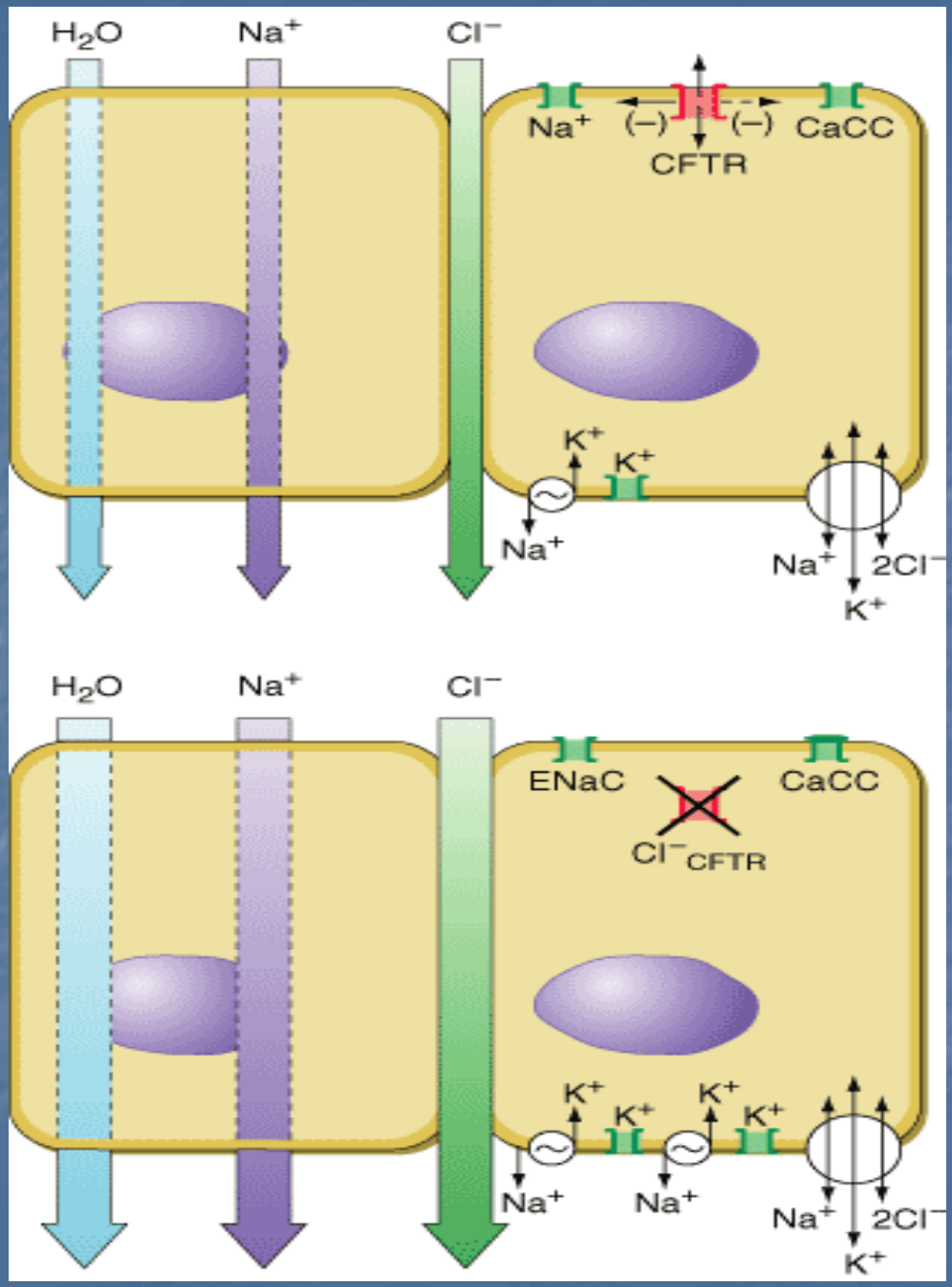
CF-Pathophysiology - Primary defect

Decreased chloride ion export

- Absence of cAMP-dependent kinase and PKC-regulated chloride transport
- Increased sodium ion absorbance
- Insufficient hydration of epithelial surfaces: lungs, pancreas, sweat glands, etc; sticky mucus on epithelium that can't be cleared by cilia
- Bacteria such as *S. aureus* and *Pseudomonas aeruginosa* colonize the lungs

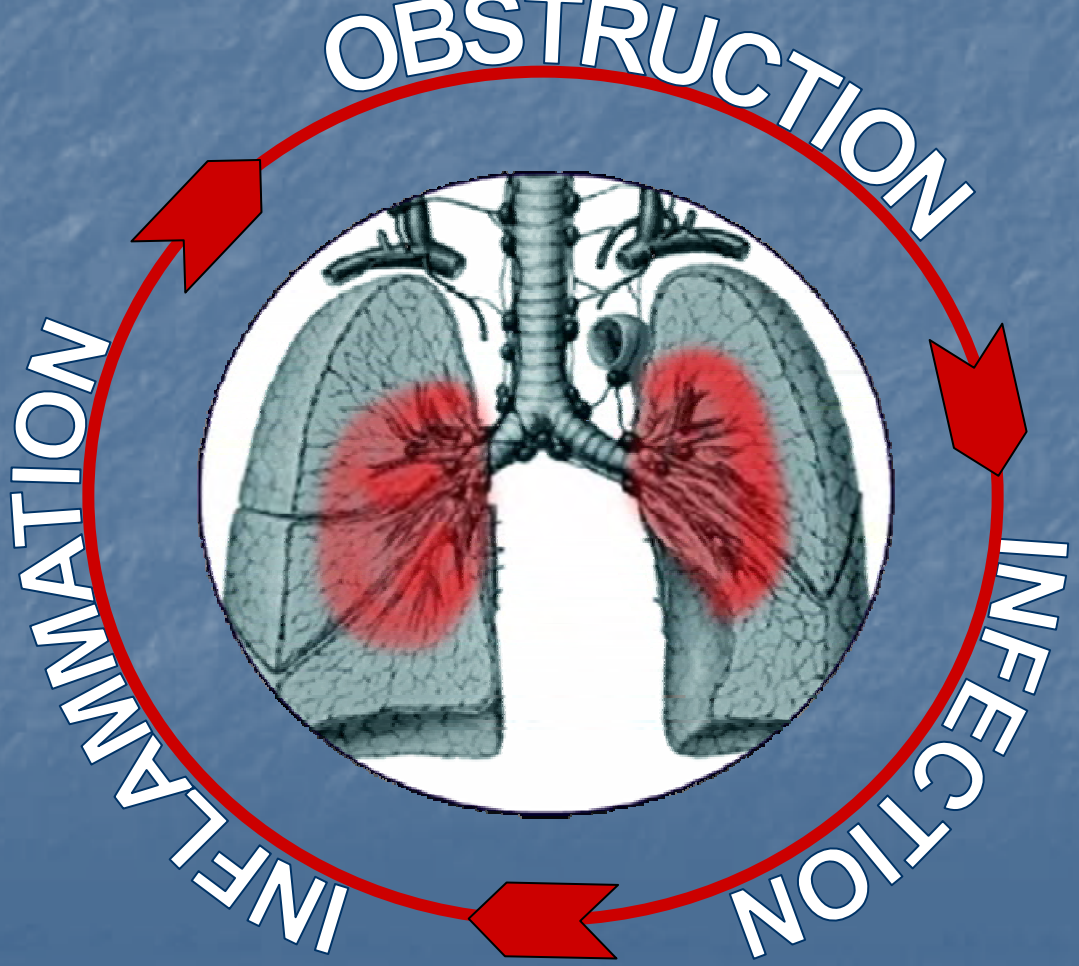
Meconium Ileus

- Normal airway epithelia
- CF altered airway epithelia



Meconium Ileus

CF-Vicious Cycle: Obstruction, Infection, and Inflammation



Multiorgan System Manifestations of CF

Rhinosinusitis
Nasal polyposis

•Secondary biliary cirrhosis
• 5% have liver dysfuction as bile ducts obstruct

Malabsorption

Meconium ileus in newborns

Obstructed vas Deferens- 95% male sterility.
Cervical plugs may effect female fertility

Rectal prolapse

- Lung abscess
- Chronic bronchitis
- Bronchiectasis
- Honeycomb lung
- pneumothorax
- hemoptysis

Cor pulmonale

• 65% obstruction blocks digestive enzymes – may cause diabetes
•Chronic pancreatitis

Abnormal sweat electrolytes

CF-Manifestations

- Common presentations
  - Meconium ileus
  - Failure to thrive
  - Chronic cough
  - Recurrent pulmonary infiltrates

CF-Manifestations

- Respiratory tract
  - Chronic sinusitis
    - Nasal obstruction
    - Rhinorrhea
    - Nasal polyps in 25%; often requires surgery
  - Chronic cough
    - Persistent
    - Viscous, purulent, green sputum

CF-Manifestations

- Respiratory tract
  - Lung function
    - Small airway disease is first functional lung abnormality
    - Progresses to reversible as well as irreversible changes in FEV1
    - Chest x-ray may show hyperinflation, mucus impaction, bronchial cuffing, bronchiectasis

CF-Manifestations

- Respiratory tract
  - Complications
    - Pneumothorax
      ~10% of CF patients
    - Hemoptysis
    - Digital clubbing
    - Cor pulmonale
    - Respiratory failure

CF-Manifestations

- Genitourinary
  - Late onset puberty
    - Due to chronic lung disease and inadequate nutrition
  - >95% of male patients with CF have azospermia due to obliteration of the vas deferens
  - 20% of female patients with CF are infertile
  - nevertheless >90% of completed pregnancies produce viable infants

CF-Manifestations

- Gastrointestinal
  - Exocrine pancreatic insufficiency
    - Found in >90% of CF patients
    - Protein and fat malabsorption
    - Frequent bulky, foul-smelling stools
    - Vitamin A, D, E, K malabsorption
    - Sparing of pancreatic beta cells
      - Beta cell function decreases with age
  - Increased incidence of GI malignancy

Meconium Ileus

CF-Diagnosis

Hx. Family CF

Genetic testing

Meconium ileus

IRT test for trypsinogen

Sweat chloride

Hx. Resp infection

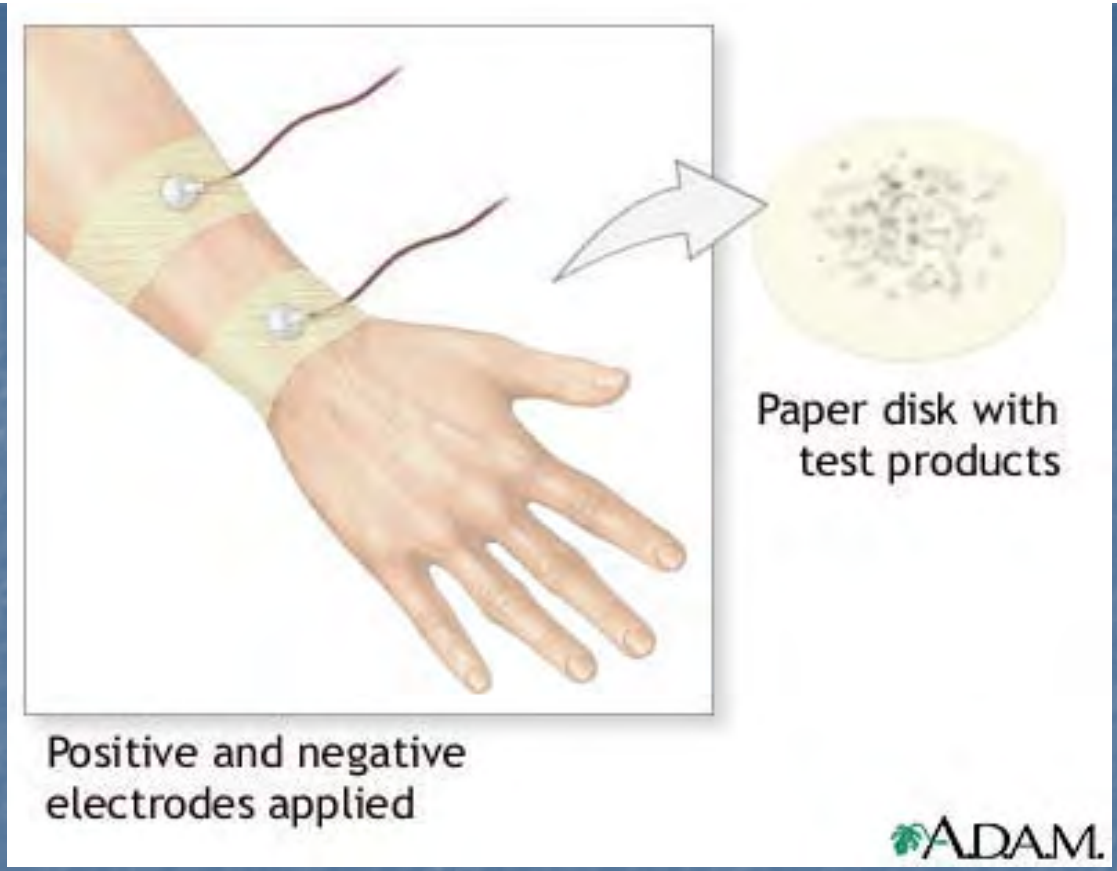
Hx. Pancreatic insufficiency

CF-Diagnosis

- Criteria
  - One of the following
    - Presence of typical clinical features
    - History of CF in a sibling
    - Positive newborn screening test
  - Plus laboratory evidence for CFTR dysfunction
    - Two elevated sweat chloride concentrations on two separate days
    - Identification of two CF mutations
    - Abnormal nasal potential difference measurement

Meconium Ileus

Sweat Test



The sweat test measures the level of chloride in the sweat using a small electric current.
Pilocarpine increases sweating+ Mild electric current.
The sweat is collected on a gauze for 30 minutes, then weighed in a weighing jar
Chloride >60 mEq/L- Cystic Fibrosis

Surgical considerations in CF

- Jejunoileal atresia
- Meconium ileus
- Intussusception
- Fibrosing colonopathy
- Inguinal hernias
- Bronchiectasis
- Pneumothorax
- Hepatobiliary and pancreatic disease
- Rectal prolapse

M.M. Olsen, M.W.L. Gauderer, M.K. Girz and R.J. Izant Jr., Surgery in patients with cystic fibrosis, *J Pediatr Surg* **22** (1987), pp. 613–618

Meconium Ileus

- MI is a unique form of congenital intestinal obstruction in which the meconium of the fetus forms concretions in the distal ileum that completely occlude the bowel lumen
- MI is the first clinical manifestation of CF
- Only 6% to 20% show the obstructive syndrome
- MI is considered pathognomonic for CF
- Although MI may occur with pancreatic aplasia and total colonic aganglionosis

M.D. Stringer, R.J. Brereton, D.P. Drake, E.M. Kiely, M. Agrwal and P.D.E. Mouriquand *et al.*, Meconium ileus due to extensive intestinal aganglionosis, *J Pediatr Surg* **23** (1994), pp. 501–503.

Meconium Ileus

-The meconium is extremely viscid, leading to an intraluminal obturator-type obstruction of the terminal ileum.

-50% neonates present with a simple uncomplicated obturation obstruction.

-The remaining 50% present with complications

.M. Caresky, J.L. Grosfeld, T.R. Weber and M.A. Malangoni, Giant cystic meconium peritonitis (GCMP): improved management based on clinical and laboratory observations, *J Pediatr Surg* **17** (1982), pp. 482–489.

Meconium Ileus- Uncomplicated

- Terminal ileum is filled with firm concretions
- Bowel in this area is small in diameter and molded around the inspissated lumps of meconium
- Proximally, the ileum becomes dilated and filled with thick sticky meconium with gas and fluid found within the small bowel above this area.

J.M. Caresky, J.L. Grosfeld, T.R. Weber and M.A. Malangoni, Giant cystic meconium peritonitis (GCMP): improved management based on clinical and laboratory observations, *J Pediatr Surg* **17** (1982), pp. 482–489.

Meconium Ileus

Meconium Plug

Meconium Ileus- Complications

- Volvulus
- Gangrene
- Atresia
- Perforation
- GCMP- Giant Cystic Meconium Peritonitis

M.M. Olsen, M.W.L. Gauderer, M.K. Girz and R.J. Izant Jr., Surgery in patients with cystic fibrosis, *J Pediatr Surg* **22** (1987), pp. 613–618

Meconium Ileus

Meconium Ileus-Presentation

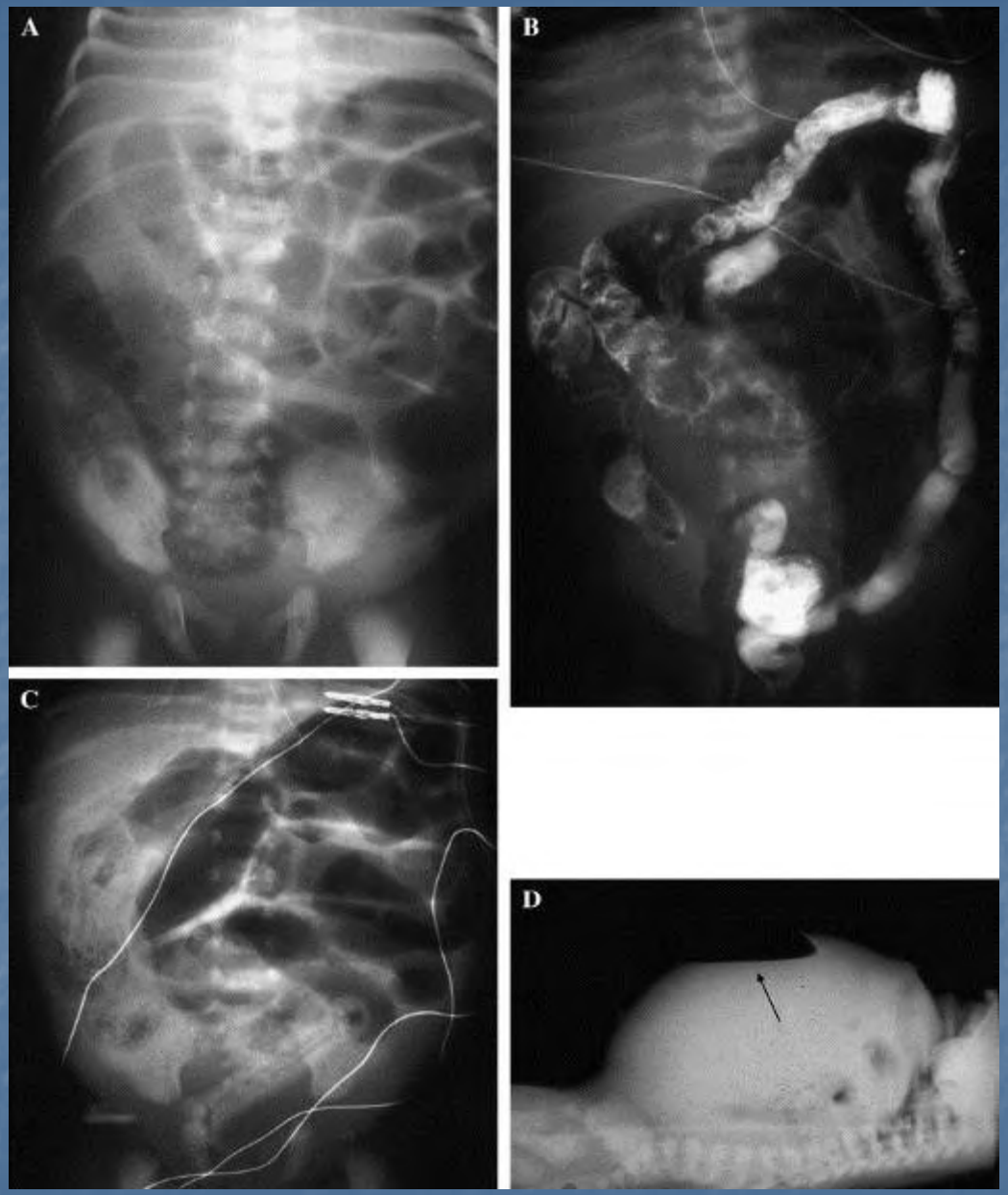
- Meconium ileus and peritonitis may be detected on prenatal ultrasound in up to 19%

- More commonly presented in the neonatal period with:
  - -abdominal distension
  - -bilious vomiting
  - -failure to pass meconium

R.B. Goldstein, R.A. Filly and P.W. Callen, Sonographic diagnosis of meconium ileus in utero, *J Ultrasound Med* **6** (1987), p. 663

Abdominal radiographs in simple MI

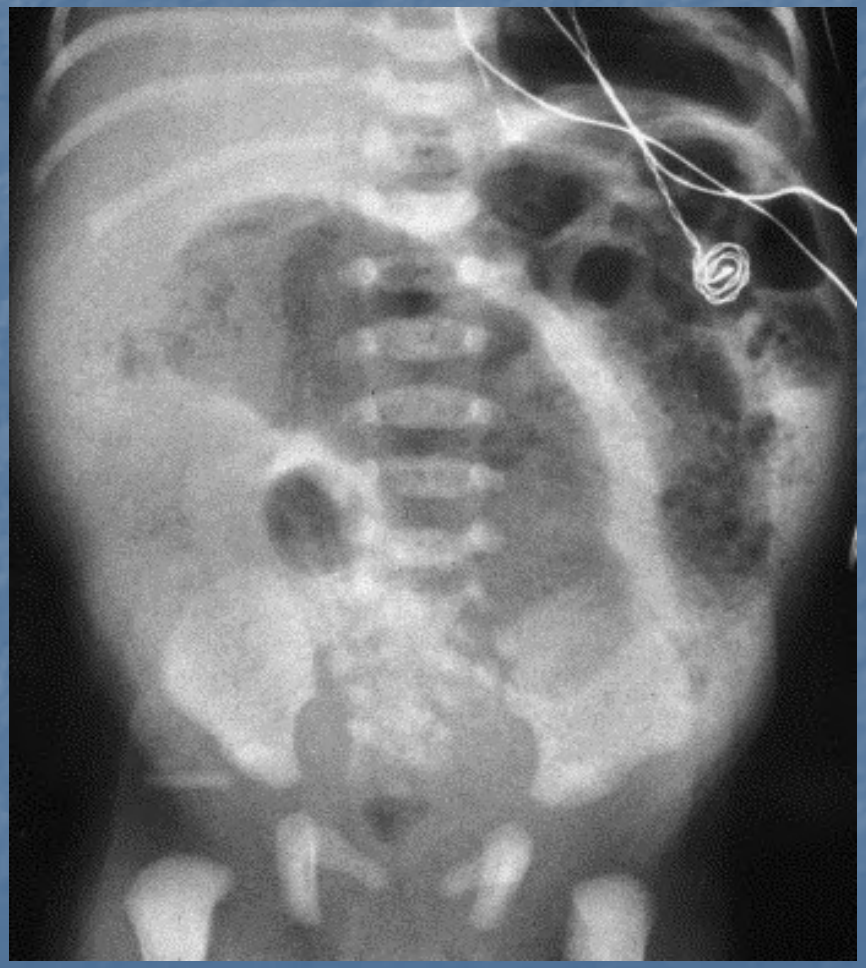
- Dilated small bowel often without air-fluid levels
- Viscosity of the meconium does not allow an air interface with the fluid.



E.B.D. Neuhauser, Roentgen changes associated with pancreatic insufficiency in early life, *Radiology* **46** (1946), pp. 319–328.

Abdominal Radiographs in Simple Meconium Ileus

- Soap-bubble appearance- Neuhauser's sign as a result of meconium mixing with swallowed air.
- Highly suggestive but not pathognomonic of CF



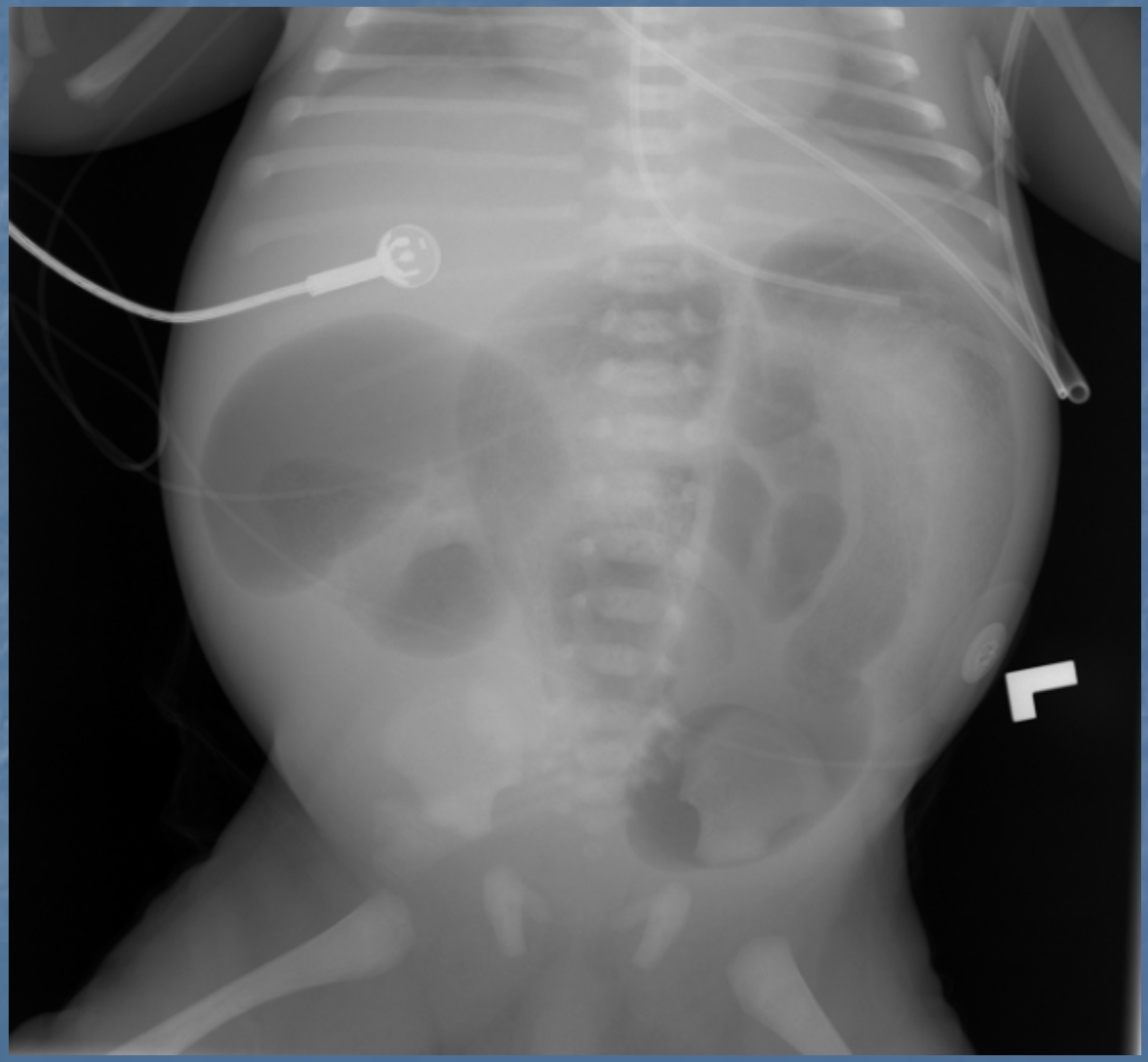
E.B.D. Neuhauser, Roentgen changes associated with pancreatic insufficiency in early life, *Radiology* **46** (1946), pp. 319–328.

Meconium Ileus

Abdominal XR

High intestinal obstruction, possible pneumatosis and intraperitonial free air.

Worrisome for NEC



Meconium Ileus

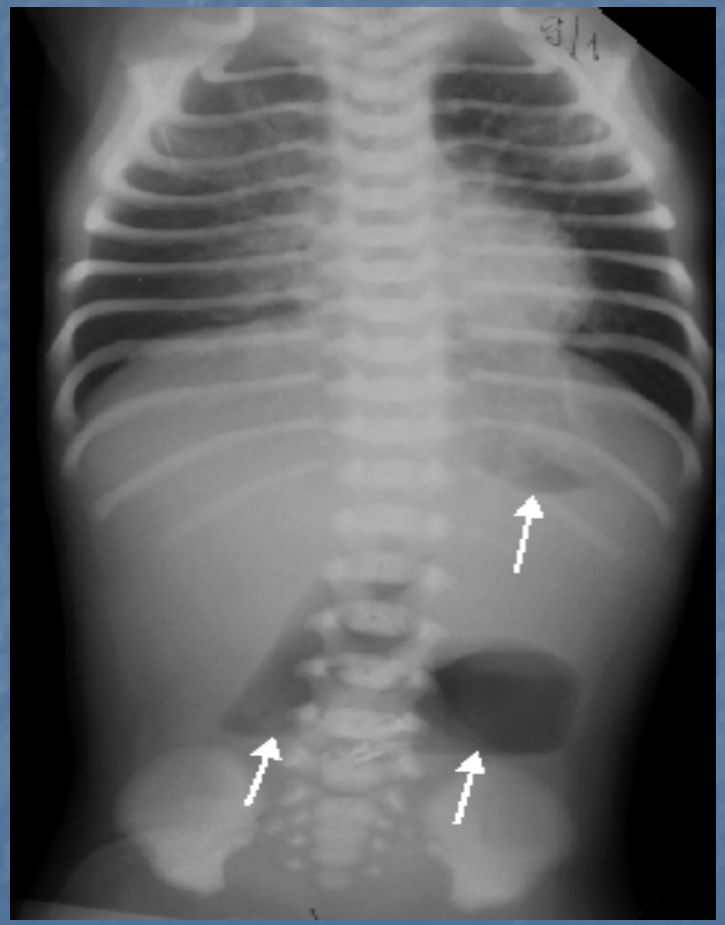
Barium Enema:

1. shows an unused colon; microcolon
2. inspissated meconium pellets within the terminal ileum
3. locates the cecal position indicating whether malrotation is present

The last part of the small intestine has dried out “pebbles” of meconium (stool surrounded by contrast dye, arrow) in the newborn with meconium ileus.

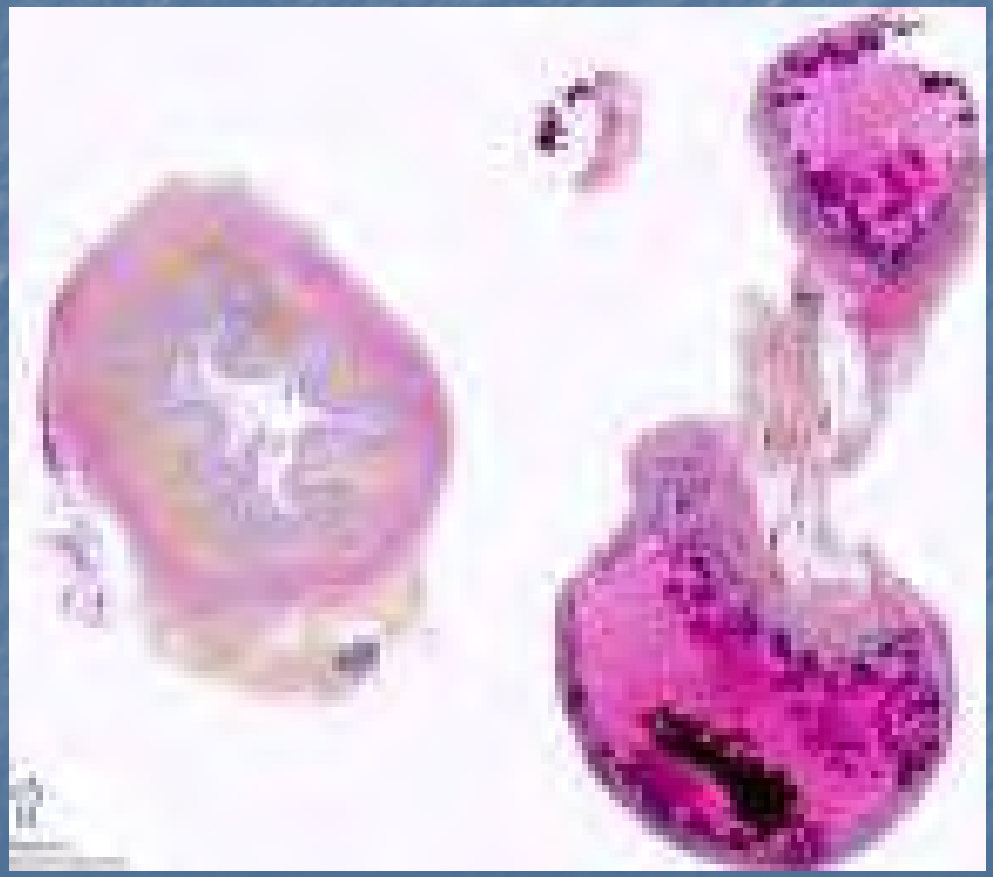
Findings in Complicated MI

- Peritoneal calcifications
- Mass effect
- Air-fluid levels related to atresia



E.B.D. Neuhauser, Roentgen changes associated with pancreatic insufficiency in early life, *Radiology* **46** (1946), pp. 319–328.

CF-Pathology



Treatment of MI

- A hypertonic enema-Gastrografin was introduced by Noblett in 1956
- Hypertonic enema washout is now the procedure of choice for simple MI.
- Gastrografin 25%-50% dilution is infused into the rectum under fluoroscopic control
- Passage of meconium pellets followed by semiliquid meconium occurs over the next 24 to 48 hours

H.R. Noblett, Treatment of uncomplicated meconium ileus by Gastrografin enema: a preliminary report, *J Pediatr Surg* **4** (1969), pp. 190–197.

Meconium Ileus

Treatment of MI

Treatment of MI

- On occasion, a repeat hypertonic enema- Gastrografin may be required.
- After 2 failed attempts at nonoperative hyperosmolar washout, operative intervention is indicated
- Complications:

  -bowel perforation

  -hypotension

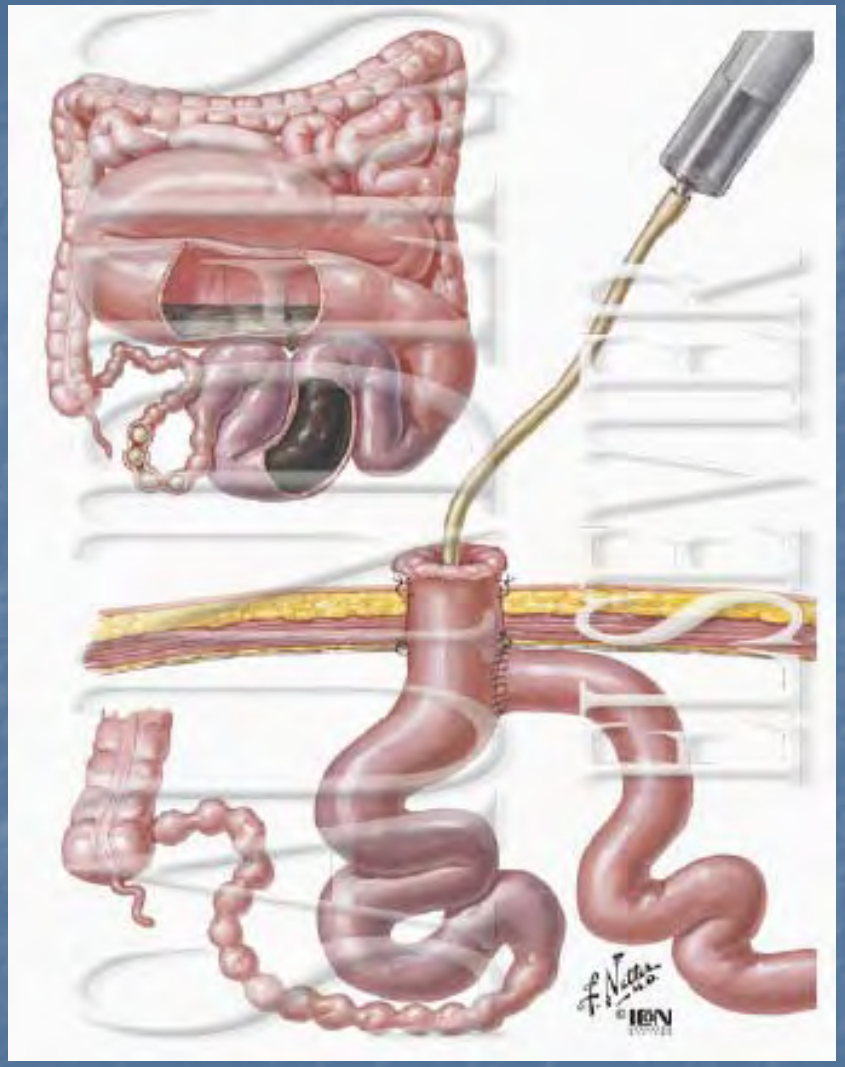
  -necrotizing enterocolitis

F.J. Rescorla, J.L. Grosfeld, K.W. West and D.W. Vane, Changing patterns of treatment and survival in neonates with meconium ileus, *Arch Surg* **124** (1989), pp. 837–840.

Meconium Ileus

Operative Intervention

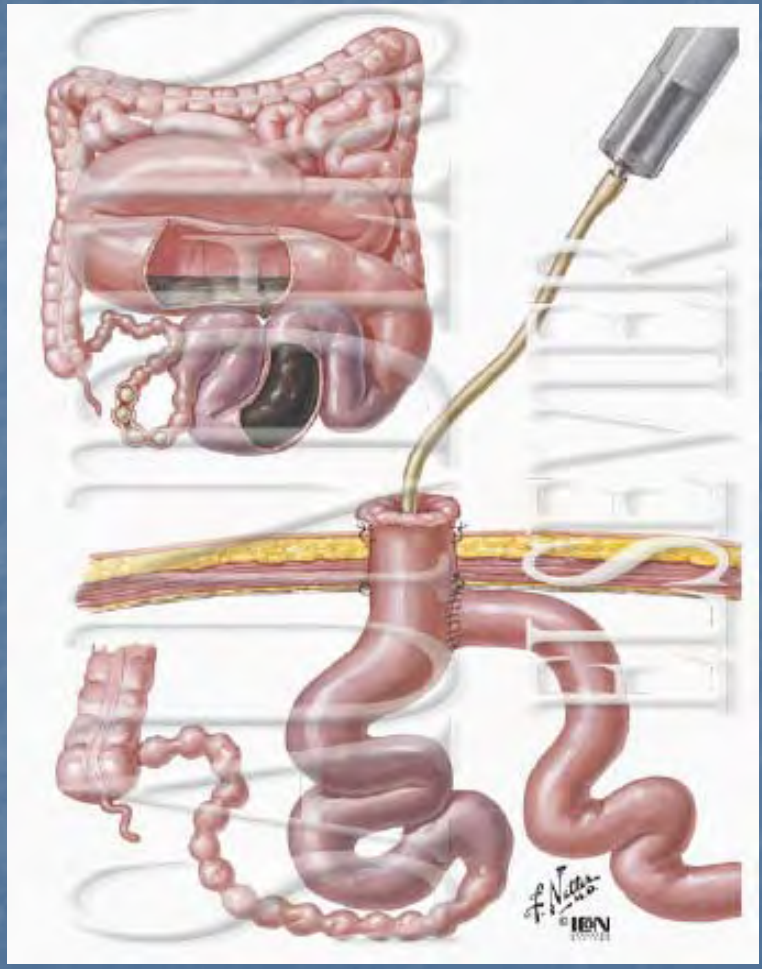
- Enterotomy and intraoperative saline irrigation initially for mechanical separation of the pellets from the bowel wall and evacuation of the meconium
- Purse-string suture is placed in the antimesenteric wall of the bowel and a red rubber catheter is inserted through a small incision within the purse-string



F.J. Rescorla and J.L. Grosfeld, Contemporary management of meconium ileus, *World J Surg* **17** (1993), pp. 318–325

Operative Intervention

- Gentle instillation of diluted hypertonic enema Gastrografin into the proximal bowel and terminal ileum to avoid bowel perforation.
- Meconium is removed through the enterotomy, and the pellets either are removed or flushed distally into the colon.
- At the conclusion of the procedure the enterotomy is closed.



F.J. Rescorla and J.L. Grosfeld, Contemporary management of meconium ileus, *World J Surg* **17** (1993), pp. 318–325

Operative Intervention

- Hypertonic enema - Gastrografin is contraindicated in complicated MI, which always managed operatively
- In cases of atresia without compromised bowel procedure of choice is resection of the dilated atretic segment, distal irrigation, and primary anastomosis

J.L. Grosfeld, T.V.N. Ballantine and R. Shoemaker, Operative management of intestinal atresia and stenosis based on pathologic findings, *J Pediatr Surg* **14** (1979), pp. 368–375

Operative Intervention

- In cases of perforation, volvulus or GCMP-Giant Cystic Meconium Peritonitis
  - Resection and temporary enterostomy are preferred

F.J. Rescorla and J.L. Grosfeld, Contemporary management of meconium ileus, *World J Surg* **17** (1993), pp. 318–325.

The operative mortality/survival rate

- The mortality rate for MI and peritonitis was approximately 55% in the 1960s and 1970s
- The survival rate for patients with simple MI is 93%
- Complicated MI is 89%
- A multidisciplinary approach to the management of the operative patient with CF including respiratory care, nutrition support, and pancreatic enzyme therapy allows for a low operative morbidity and mortality

D.A. Caniano and B.L. Beaver, Meconium ileus: a fifteen year experience in forty-two neonates, *Surgery* **102** (1987), pp. 699–703.

Summary

- CF is an inherited, monogenic disorder presenting as a multisystem disease
- Pathophysiology is related to abnormal ion transportation across epithelia
- Respiratory, GI and GU manifestations
- Treatment is currently preventative and supportive

Question#1

- Abdominal XR in newborn reveals “double-bubble” sign, which of the following conditions it can be seen?
- A-Meconium ileus
- B-Duodenal atresia
- C-Normal newborn right after delivery
- D-Malrotation of the midgut
- E-Annular pancreas

Answer:B,C,D,E

Question#2

- A newborn develop progressive abdominal distention and bilious vomiting. Abdominal XR reveals distended bowel loops of varying size with air-fluid levels and “soap suds” appearance in the right lower quadrant. Which of the following procedures should be performed next?
- A-Gastrografin enema
- B-Gastrografin upper GI radiography
- C-Sweat chloride test
- D-Paracentesis
- E-Laparotomy

Answer:A

Question#3

- Which of the following is/are Meconium Ileus complications?
- A-Volvulus
- B-Gangrene
- C-Atresia
- D-Perforation
- E-GCMP

Answer:A,B,C,D,E

Question#4

- What percentage of patients with Meconium ileus show the obstructive syndrome
- A-95-100%
- B-50-60%
- C-6-20%
- D-12-35%
- E-35-65%

Answer:C