

Introduction

Chr 7q autosomal recessive. Mutations in the CF transmembrane conductance regulator (CFTR) gene. Commonest $\Delta F508$. Primarily an ATP-responsive Cl^- channel but also affects Na^+ transport across the resp epithelium, composition of cell surface glycoprotein and antibacterial defences.

Epidemiology

Prevalence is 1 in 2,000 with calculated carrier frequency of 1 in 25.

Pathology

High sodium sweat. Normal primary secretion of sweat duct, but CFTR does not absorb Cl^- , which remain in the lumen and prevent Na^+ absorption.

Pancreatic insufficiency. Normal pancreatic enzymes production, but defects in ion transport & so water movement produce dehydration of secretions and stagnation in the pancreatic ducts.

Biliary disease. Similarly the bile becomes concentrated & plugging occurs in the biliary tract.

GI disease. Low volume secretions of \uparrow viscosity, changes in fluid movement across SB & LB.

Respiratory disease.

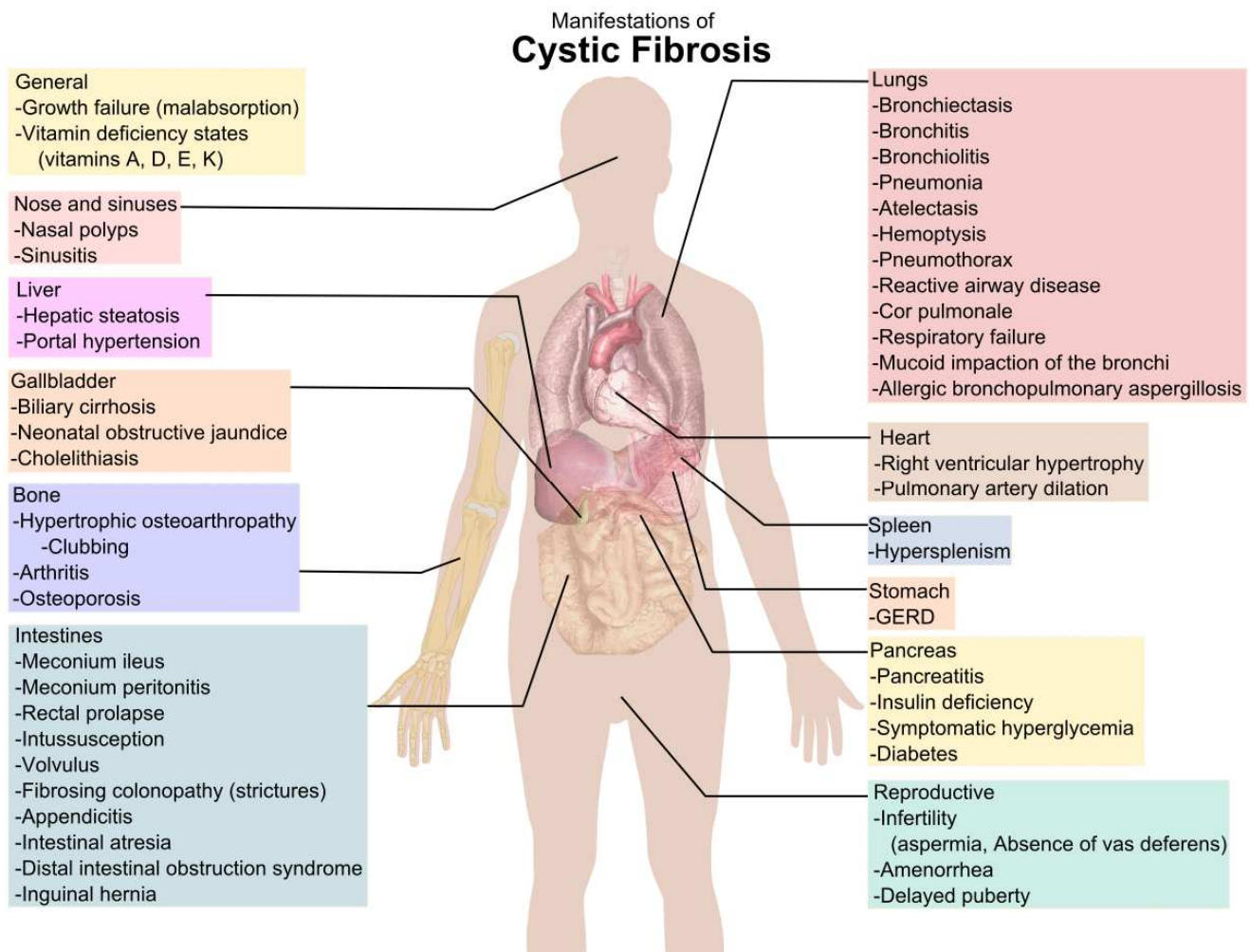
- Dehydration of the airway surfaces \rightarrow \downarrow mucociliary clearance and \uparrow bacterial colonisation.
- $[NaCl]$ \rightarrow \downarrow local bacterial defences.
- Cell surface glycoprotein changes \rightarrow \uparrow bacterial adherence.

All \rightarrow inflammatory lung damage from $\uparrow\uparrow$ neutrophilic response (IL8 and neutrophil elastase).

Presentation

As normal digestive fn possible with $<5\%$ pancreatic fn, can present at any age.

Commonest presentation is recurrent LRTI with chronic sputum production.



Investigations

Screening - DNA analysis or blood immunoreactive trypsinogen (IRT)

Sweat test: $[Cl^-] > 60 \text{ mmol/l}$ with $[Na^+] < [Cl^-]$.

Stool elastase/faecal fats for pancreatic insufficiency.

Management

Disease:

- Bronchodilators for wheezing, inhaled or oral steroids if persistent.
- Chest physiotherapy twice daily and increased with infective exacerbations.
- Mucolytics: recombinant human **DNAase** or hypertonic **saline**
- Non-invasive ventilatory support (BIPAP) may bridge to transplant.
- Lung transplantation.
- CFTR potentiators: **Ivacaftor** for G551D mutation (doesn't work for homozygous $\Delta F508$).
- Gene therapy is currently undergoing investigation.

Complications:

Respiratory infection/colonisation:

- Usual resp bacteria plus *S. aureus*, *H. influenzae*, *P. aeruginosa* +/- *Burkholderia cepacia* which may repeatedly or colonise lungs. Fungi may also colonise incl *Aspergillus* & *Candida* spp.
- Antibiotics
 - Often prolonged IV courses so PICC or PortaCath may be inserted.
 - Rx often includes **gentamicin** and **piperacillin** or **ceftazidime** or **ciprofloxacin** to cover *Pseudomonas*. **Flucloxacillin** for staph
 - Long courses of nebulised high dose **tobramycin** may impede colonisation
 - Long term **prednisolone** on alternate days for up to 2 years.

Nasal Polyps: steroids initially, if this fails polypectomy (50% require repeat within 2 years).

Pneumothorax: ICC, pleruodesis if recurrent, but may be a CI to transplant.

Pancreatic insufficiency:

- Enteric-coated enzyme preparations e.g. **Creon**, **Pancreaze**, etc.
- Vitamin supplements (A, D and E), calcium, occ biphosphonates
- High calorie intake (130% normal), if insufficient: enteral feeding with via gastrostomy.
- Constipation common: high fluid/fibre intake \pm **lactulose**

Diabetes: **insulin**

Liver disease:

- **Ursodeoxycholic acid** improves bile flow
- Liver transplantation if mild pulmonary involvement, to support long-term survival.

Reproduction: early counselling about male infertility and genetic counselling.

Prognosis

Median survival in 1999 was 30 years. Estimated survival for child born now is 40-50 years.

