# Cystic fibrosis by Dr Amel Alameeri & Prof McKone

## OVERVIEW OF CYSTIC FIBROSIS

Cystic fibrosis (CF) is the commonest autosomal recessive genetic disease that primarily affects the respiratory system. CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The most common mutation, the F508del, is found in 90% of CF patients in Ireland. Over 1,000 additional mutations have been identified that cause CF, but only a small number account for most cases of CF in Ireland.

## Pathophysiology:

CFTR is a membrane protein that regulates salt transport across the cell. Deficiency in CFTR leads to the build up of thick tenacious secretions in organs expressing CFTR including the respiratory tract, hepatobiliary tree/pancreas, sweat glands and reproductive organs.

## COMMON COMPLICATIONS OF CYSTIC FIBROSIS

1. Bronchiectasis with chronic bacterial infection.
2. Pancreatic Insufficiency.
3. CF Related Diabetes Mellitus (CFRD).
4. CF Related Liver Disease (CFLD)
5. Osteopenia/Osteoporosis.
6. Chronic sinusitis.
7. Gastro-oesophageal reflux
8. Distal intestinal obstruction syndrome (DIOS)
9. Obstructive azoospermia in males

**Approach to I.V. Antibiotic selection for exacerbations due to *P. aeruginosa* infection.**

***CHECK PATIENT ALLERGIES FIRST***

1. Ceftazidime and Tobramycin if sensitive and previous clinical response.
2. Choose combination antibiotics that have worked during the previous exacerbation. (Beta-lactam combined with an aminoglycoside if possible)
3. Choose combination antibiotics based on most recent sputum culture and sensitivity. (Beta-lactam combined with an aminoglycoside if possible)

## Clinical features

### Sinopulmonary

The most serious complication of CF is progressive lung disease with most patients eventually dying as a result of respiratory failure. Patients with CF develop recurrent pulmonary infections that lead to progressive scarring of the airways and bronchiectasis. Early in the course of the disease, these infections are predominantly caused by bacteria such as *Haemophilus influenza* and *Staphylococcus aureus*. Over time as lung damage progresses, most CF patients become colonized with *Pseudomonas aeruginosa* which is associated with a more rapid decline in lung function. Rarer infections that occur in the CF lung like *Burkholderia cenocepacia* , which has been associated with rapidly progressive and often fatal lung infection known as “cepacia syndrome”. Other pulmonary complications of CF (ABPA) and infections (NTM) .Chronic sinusitis is common in patients with CF. The microbiology of CF sinusitis is similar to that seen in the lungs.

### Gastrointestinal

Pancreatic insufficiency is observed in 95% of patients with CF and presents soon after birth in the majority of cases. Certain mutations in the CFTR gene are associated with preserved pancreatic function (R117H, A455E). CF can also lead to obstruction of the GI tract : meconium ileus where obstruction occurs due to meconium impaction soon after birth. In older patients with CF, sub-acute bowel obstruction frequently occurs as a result of pancreatic insufficiency leading to poorly digested food blocking the bowel (DIOS) .Liver disease is relatively common in CF occurring in 17-24% of patients and is the second most common cause of death. The mechanism of CF liver disease is similar to that of lung and pancreatic disease with bile duct obstruction leading to chronic obstructive hepatopathy and eventually cirrhosis.

**CRITERIA FOR THE DIAGNOSIS OF**
CF Related Liver Disease (CFLD)

i) LFTs > 1.5 U.L.N. for > 6 months
or
ii) LFTs > 3 U.L.N. on two occasions
or
iii) Abnormal liver ultrasound.
and
iv) Other chronic liver diseases excluded.

### Endocrine

Up to 30% of CF patients will develop clinical diabetes mellitus (known as CF related diabetes mellitus (CFRD)). CFRD tends to present predominantly during adolescence and adulthood and should be screened for in all CF patients. Osteopenia and osteoporosis are increasingly common in CF and patients should be screened for at regular intervals.

**CRITERIA FOR THE DIAGNOSIS OF COMMON CF COMPLICATIONS CF Related Diabetes (CFRD)**

i) Fasting blood sugar > 7mmol/L
or
ii) Random blood sugar > 11.1mmol/L
or
iii) 2 h postprandial blood sugar > 11.1mmol/L
Should be documented on at least 2 occasions - OGTT should be carried out annually

### Fertility/Sweat glands

Infertility is common in males due to obstruction and eventual destruction of the vasa deferens. Fertility is usually preserved in female patients with CF. Sweat gland dysfunction increases the risk of heat stroke in warm climates.

**Nutritional Management of Cystic Fibrosis**

Impaired growth and malnutrition have been associated with poorer survival and quality of life in patients with CF .The aetiology of malnutrition is threefold:

1.Pancreatic insufficiency leading to malabsorption of nutrients.
2.Increased energy requirements due to chronic infection and inflammation.
3.Decreased energy intake due to chronic infection and illness.

Adequate nutrition to sustain ideal weight (BMI 22-23 kg/m2).

-Doses should not generally exceed 10,000 units of lipase/ kg body weight / day.

Common agents used include the following
- Creon 10,000 (10,000 IU lipase)
- Creon 25,000 (25,000 IU lipase)

## CF maintenance medications :

1. Pulmonary Maintenance Therapy
a) Pulmozyme (Dornase alpha) 2.5mg once a day via Neb
b) Hypertonic Saline (3-7%) twice a day via Neb
c) Azithromycin 500mg once a day Mon/Wed/Fri (250mg if weight < 40kg)
Monthly inhaled antibiotics for Pseudomonas (two rotating or one with a month off between cycles)
Tobramycin podhaler or nebulizer twice a day
Colomycin inhaler or nebulised. twice a day
Aztreonam nebulized three times
Levofloxacin nebulized twice a day

2. CFTR Modulation
a) Elexacaftor/Tezacaftor/Ivacaftor – CF patient with at least one copy of F508del
b) Tezacaftor/ivacaftor – F508del/residual function mutation or F508del/F508del
c) Lumacaftor/ivacaftor – F508del/F508del
d) Ivacaftor – Gating mutation (R117H/G551D)

3. Sinusitis
a) Saline irrigation three times a day.
b) Fluticasone one puff nasal once a day.

4. Liver Disease
a) Ursodeoxycholic acid 20mg/kg/day in two divided doses.

5. Vitamin Supplementation
a) DEKA supplements one tablets daily.

6. Bone Disease
a) Osteopenia - Calcichew D3 forte (500mg Ca, 400u VitD) one tablet twice a day.
b) Osteoporosis - Alendronate 70mg po once a week.

7. Asthma/ABPA
a) Symbicort 200/6 two puffs twice a day.
b) Prednisolone 40mg tapered to IgE.
c) Itraconazole/Voriconazole

**Physiotherapy roles**

1. Airway clearance (techniques such as autogenic drainage, and adjuncts such as PEP, Acapella and NIV) 2. Set up and maintenance of NIV 3. Exercise prescription and supervision 4. Musculoskeletal assessment and treatment 5. Incontinence assessment and treatment 6. Sinus health.

**Symptoms and Signs of Acute Exacerbation:**

**Symptoms:**
1. Increased frequency and duration of cough
2. Increase or change in sputum volume/appearance.
3. Increased shortness of breath, chest congestion
4. Decreased exercise tolerance.
5. Decreased appetite

**Signs:**
1. Increased respiratory rate
2. Use of accessory breathing muscles
3. Change in auscultatory chest findings
4. Decline in FEV1 (>10% drop from baseline (relative))
5. Fever / leukocytosis / weight loss
6. New infiltrate of chest radiograph



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