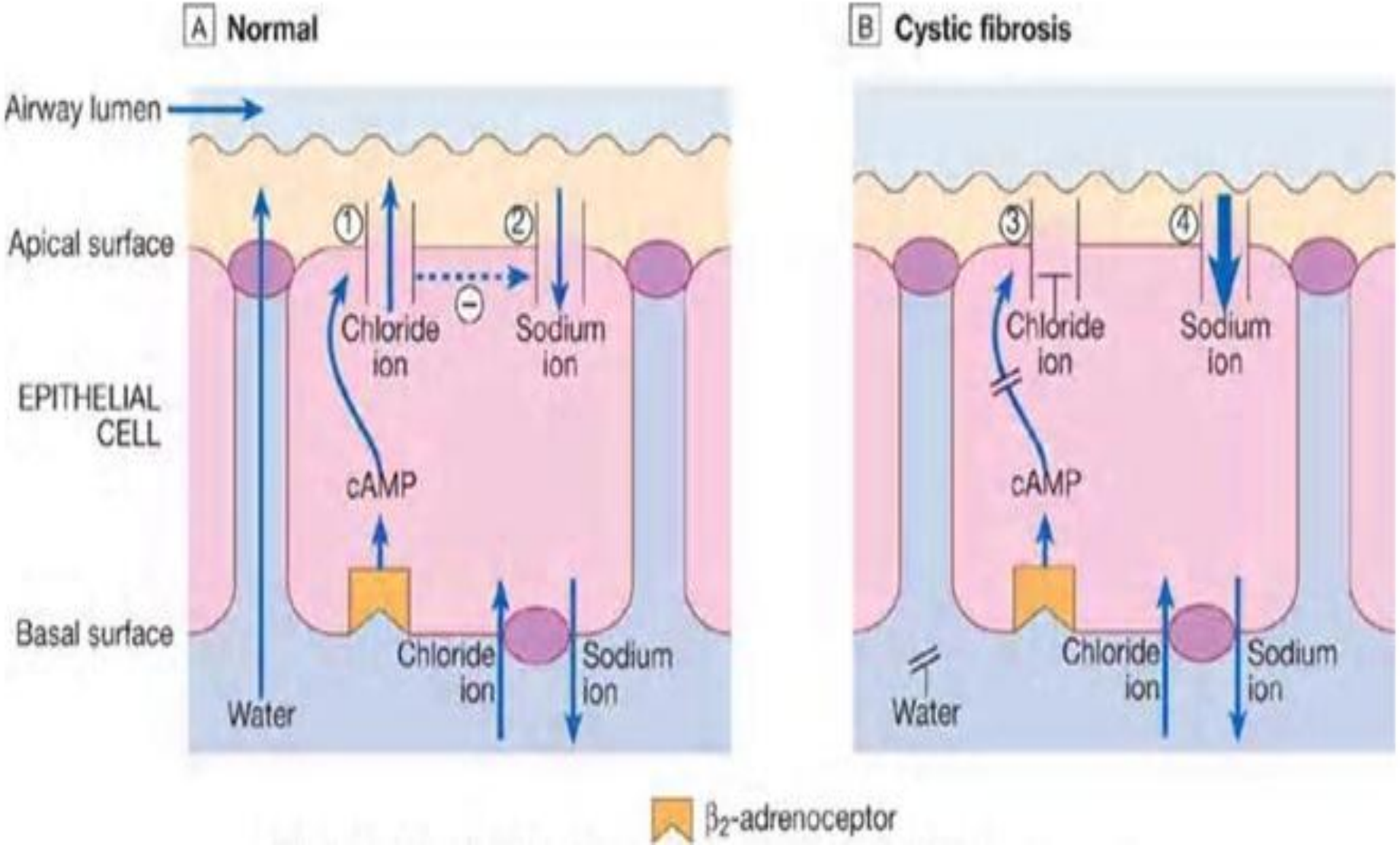
CYSTIC FIBROSIS (CF)

Genetics and pathogenesis

- mutations affecting a gene on the long arm of chromosome *7*
- the gene codes for a chloride channel known as cystic fibrosis transmembrane conductance regulator (*CFTR*)
- (*CFTR*) influences salt and water movement across epithelial cell membranes.
- increased sodium and chloride content in sweat
- increased resorption of sodium and water from respiratory epithelium
- dehydration of the airway epithelium predisposes to chronic bacterial infection and ciliary dysfunction, leading to bronchiectasis.

Cystic fibrosis: basic defect in the pulmonary epithelium



Clinical findings

- **transport dysfunction:**
  - **thick secretions from exocrine glands**
    (lung, pancreas, skin, gonads)
  - **blockage of secretory ducts**
- **results in :**
  - **severe lung disease**
  - **pancreatic insufficiency**
  - **azoospermia**
    (Most men with CF are infertile due to failure of development of the vas deferens)
- **presents in childhood with recurrent lung infections that become persistent and chronic lead to bronchiectasis in childhood**
- **chronic lung infections**
  - **S. *Aureus: early***
  - **P. *aeruginosa: most common***
  - ***Burkholderia cepacia : worse prognosis but less common***
  - **aspergillosis (benign 'colonisers' do not require specific therapy).**

Clinical findings

- allergic bronchopulmonary aspergillosis
- coexistent asthma

Complications of cystic fibrosis

Respiratory

- Infective exacerbations of bronchiectasis
- Spontaneous pneumothorax
- Haemoptysis
- Nasal polyps
- Respiratory failure
- Cor pulmonale
- Lobar collapse due to secretions

Gastrointestinal

- Malabsorption and steatorrhoea
- Distal intestinal obstruction syndrome
- Biliary cirrhosis and portal hypertension
- Gallstones

Others

- Diabetes (25% of adults)
- Delayed puberty
- Male infertility
- Stress incontinence due to repeated forced cough
- Psychosocial problems
- Osteoporosis
- Arthropathy
- Cutaneous vasculitis

Investigations

- **sweat chloride test**
  - increased concentrations of sodium, chloride, and potassium > 60 mmol/L is diagnostic in children
  - heterozygotes have normal sweat tests (and no symptoms)

- **PFTs**
  - characteristic of obstructive airway disease
  - early: only small airways will be affected
  - later: characteristics of obstructive disease with airflow limitation, hyperinflation, decreased Dco

- **ABGs**
  - hypoxemia, hypercapnia later in disease with eventual respiratory failure and cor pulmonale

Investigations

- CXR
  - hyperinflation
  - increased pulmonary markings
  - bronchiectasis

Treatment

- chest physio and postural drainage
- bronchodilators (ventolin +/– atrovent)
- inhaled DNase (reduces mucus viscosity)
- antibiotics (e.g. ciprofloxacin)
- Regular nebulised antibiotic therapy (colomycin or tobramycin) is used between exacerbations in an attempt to suppress chronic *Pseudomonas* infection.
- lung transplant

Treatments that may reduce chest exacerbations and/or improve lung function in CF

Therapy	Patients treated
Nebulised recombinant human DNase 2.5 mg daily	Age ≥ 5, FVC > 40% predicted
Nebulised tobramycin 300 mg 12-hourly, given in alternate months	Patients colonised with *Pseudomonas aeruginosa*
Regular oral azithromycin 500 mg three times/week	Patients colonised with *Pseudomonas aeruginosa*

- **DNA ase** البشري إرذاذاً لحل الحمض النووي للخلايا الالتهابية المخربة المسؤولة عن لزوجة المفرزات

Treatment of non-respiratory manifestations of CF

- Malabsorption :
  oral pancreatic enzyme supplements and vitamins.

- Diabetes (25% of patients)often requires insulin therapy

Prognosis

- median survival age is 31 years for males and 30.5 for females

- death usually due to lung disease
  (pneumonia, respiratory failure, cor pulmonale)