Paediatric Respiratory Updates

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Cough in healthy children

- Definition of chronic cough in kids [1]
  - Acute cough can last up to 4 weeks.
  - Chronic cough is daily cough of at least 4 weeks in duration.

- The 2017 CHEST Guideline and American College of Chest Physicians (ACCP) showed that the use of cough management protocols or algorithms improves clinical outcomes in children aged ≤ 14 years [1].

- A multicentre, single-blind RCT nested within a prospective cohort study of children (<15 years) with chronic cough in Australia showed that applying an evidence-based cough management algorithm in non-specialist settings improves cough resolution [2].

Differential diagnosis of chronic cough

- **Neonatal**
  - Congenital malformations
  - Aspiration syndromes
  - Primary Immunodeficiency
  - Cystic fibrosis
  - Ciliopathy like Primary Ciliary Dyskinesia
  - Congenital Infections : CMV, Chlamydia
  - Anatomical : Subglottic cysts or tracheomalacia, laryngeal cleft, tracheal stenosis
- **Very acute onset**
  - Inhaled foreign body
- **Older age**
  - Asthma
  - GORD
  - Congenital airway anomalies – Tracheomalacia, cleft,
  - Primary or secondary Immunodeficiency
  - Cystic fibrosis
  - Ciliopathy like Primary Ciliary Dyskinesia
  - GORD, aspiration
  - Post-infection

Nature of cough

- **Associated with wheezing or breathlessness**
  - Asthma
  - Inhaled FB
  - Recurrent pulmonary aspiration
  - Cardiac disease
  - Airway compression (vascular, cysts)
  - Tracheobronchomalacia, bronchiolitis
- **Associated SOB and restrictive lung defect**
  - Interstitial lung disease
- **Wet or productive cough**
  - Bronchiectasis, suppurative lung disease
  - Protracted Bacterial Bronchitis (PBB)
  - Pertussis, Viral LRTI
  - Immunodeficiency
- **Relentlessly progressive cough**
  - Inhaled foreign body, lobar collapse, TB
  - Rapidly expanding intra-thoracic lesion
- **True haemoptysis**
  - Pneumonia, lung abscess, bronchiectasis, retained inhaled foreign body, TB, pulmonary hypertension

What Triggers the cough?

- Exercise, cold air, nocturnal cough, change in environments: Asthma
- Feeding: Recurrent aspiration, GORD, Tracheo-oesophageal fistula
- Lying down: Postnasal drip, GORD, PBB
- Attention: Psychogenic
- Medication: ACE inhibitor-induced cough

Cough pointers for early referral [1]

Pulmonary

- Daily moist or productive cough
- Chest pain
- Haemoptysis
- Abnormal cough characteristics (brassy, plastic bronchitis, paroxysmal with/without post tussive vomiting, staccato, cough from birth)
- Recurrent pneumonia
- Hypoxia/cyanosis
- History of previous lung disease or predisposing causes (neonatal lung disease, foreign body aspiration)
- Exertional dyspnoea
- Dyspnoea at rest or tachypnoea
- Chest wall deformity
- Auscultatory findings (stridor, wheeze, crackles)
- Chest radiography abnormalities
- Pulmonary function test abnormalities
- Cough with feeding, dysphagia, severe vomiting
- Night sweats/weight loss
- Environment – Damp, mould, ETS, crowded home

Systemic

- Cardiac abnormalities
- Digital clubbing
- Failure to thrive
- Medications or drugs associated with chronic cough
- (ACEI, illicit drugs use)
- Neurodevelopmental abnormalities
- Fever
- Immune deficiency (primary or secondary
- History of contacts (Tuberculosis)
- Family History of lung disease

Investigations of Chronic Cough

Haematological:

- FBC and differentials, ESR, CRP
- Ig G,A,M,E, T and B lymphocyte, Vaccine antibodies, Complements
- Blood film

Infective

- TB (Gastric lavage x3, Mantoux, Elispot)
- Sputum for microbiology assessment (culture and sensitivity, mycology, mycobacterium, cytopathology)
- Mycoplasma IgM or Pertussis PCR

Radiological

- CXR

Children with chronic productive cough should be referred to tertiary respiratory paediatrician for investigations and treatment [1].

Investigations at Tertiary care

- **Lung function tests**
  - Spirometry ± bronchodilator response
  - Methacholine challenge tests
  - Allergy testing (Skin prick or RAST)
  - FeNO, NNO

- **Radiological**
  - CT chest with contrast to evaluate airway structures and parenchymal lung disease
  - Barium study, Impedance Study
  - Tubo-oesophragm

- **Sweat test (exclude Cystic Fibrosis)**
- **Ciliary biopsy (excludes ciliopathy)**
- **Bronchoscopy (Flexible/MLB) – to assess for structural airway anomaly and obtaining sample for micro**
- **Referral to SLT to exclude swallow abnormality, VFSS**
- **Referral to chest physio/ dietician**
- **Referral to other subspecialities (ENT, Neurology etc)**

ACCP Chronic Cough Guidelines: What is new?

- Chronic cough and gastroesophageal reflux in children (GORD).
  - Treatment for GORD should not be used in the absence of gastro-intestinal clinical features of reflux.
  - If GORD is present, treatment should be as per evidence-based GORD-specific guidelines and acid suppressive therapy should not be used solely for their chronic cough.
  - After treatment for 4-8-weeks, response should be re-evaluated[3]
- Asthma medications should not be used for cough unless other evidence of asthma is present.
- Rhinosinus condition should be managed adequately.

ACCP Chronic Cough Guidelines: What is new?

- Psychogenic cough, habit cough, or tic cough is explained as cough occurring in the absence of identified medical disease and that does not respond to medical treatment.
- The diagnosis of somatic cough can be made only after extensive evaluation has been performed that includes ruling out tic disorders and uncommon causes and the patient meets the DSM-5 criteria for a somatic symptom disorder.
- Non-pharmacological trials of hypnosis or suggestion therapy or combinations of reassurance, counselling, or referral to a psychologist and/or psychiatrist is recommended [4].

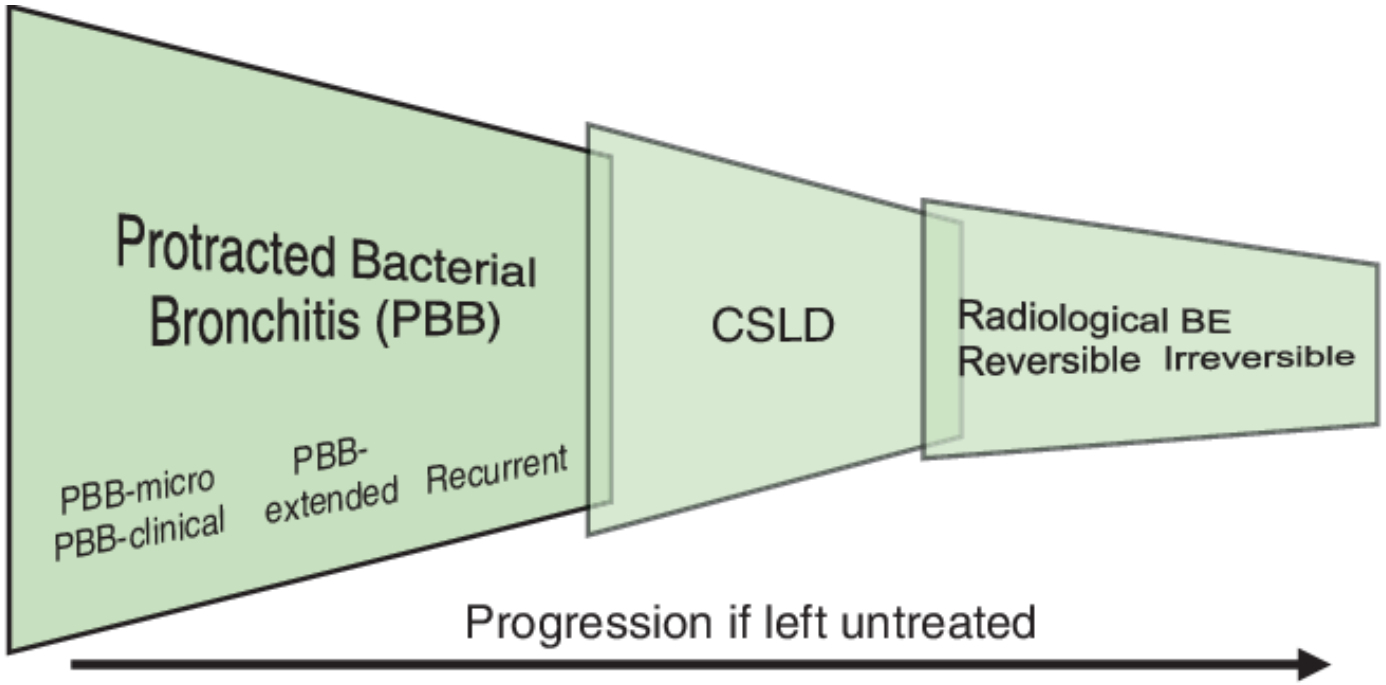
Protracted Bacterial Bronchitis & Bronchiectasis Paradigm

- Protracted Bacterial Bronchitis (PBB)
  - presence of chronic wet cough in <5yr with absence of specific pointers other than **disturbed sleep** [5].
- **Worsening** of symptoms during URTI's
- **Does not respond** to brochodilators
- Does not have wheeze but has a "**rattle"** i.e. *airway secretions in the airway*
- **Retrospective** diagnosis

- 40% of children have endobronchial infections
  - Haemophilus influenza, Streptococcus pneumonia , Moraxella catarrhalis
- Under-recognition and under-treatment PBB can lead to the development of chronic suppurative lung disease (CSLD) and bronchiectasis [6].
- Recurrent PBB (≥ 3 episodes/yr): Must rule out bronchiectasis

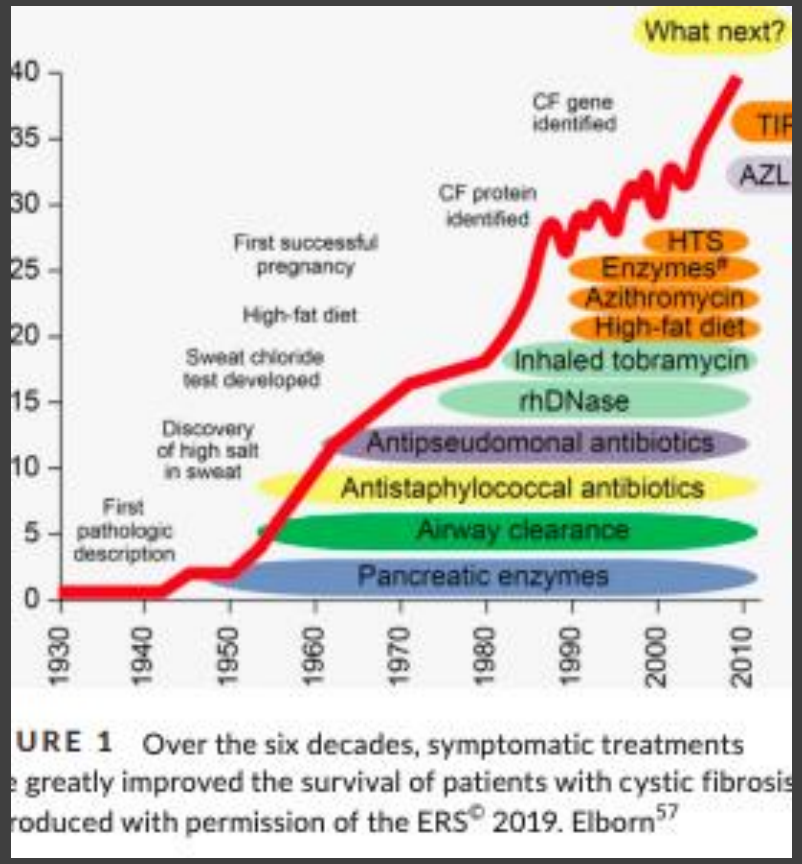
Clinical spectrum of PBB, CSLD & Bronchiectasis

- Chest radiographs show only peripheral changes and spirometry is normal.
- Digital clubbing and abnormal spirometry is seen with severe bronchiectasis[7].
- 2-4 weeks Co-Amoxiclav

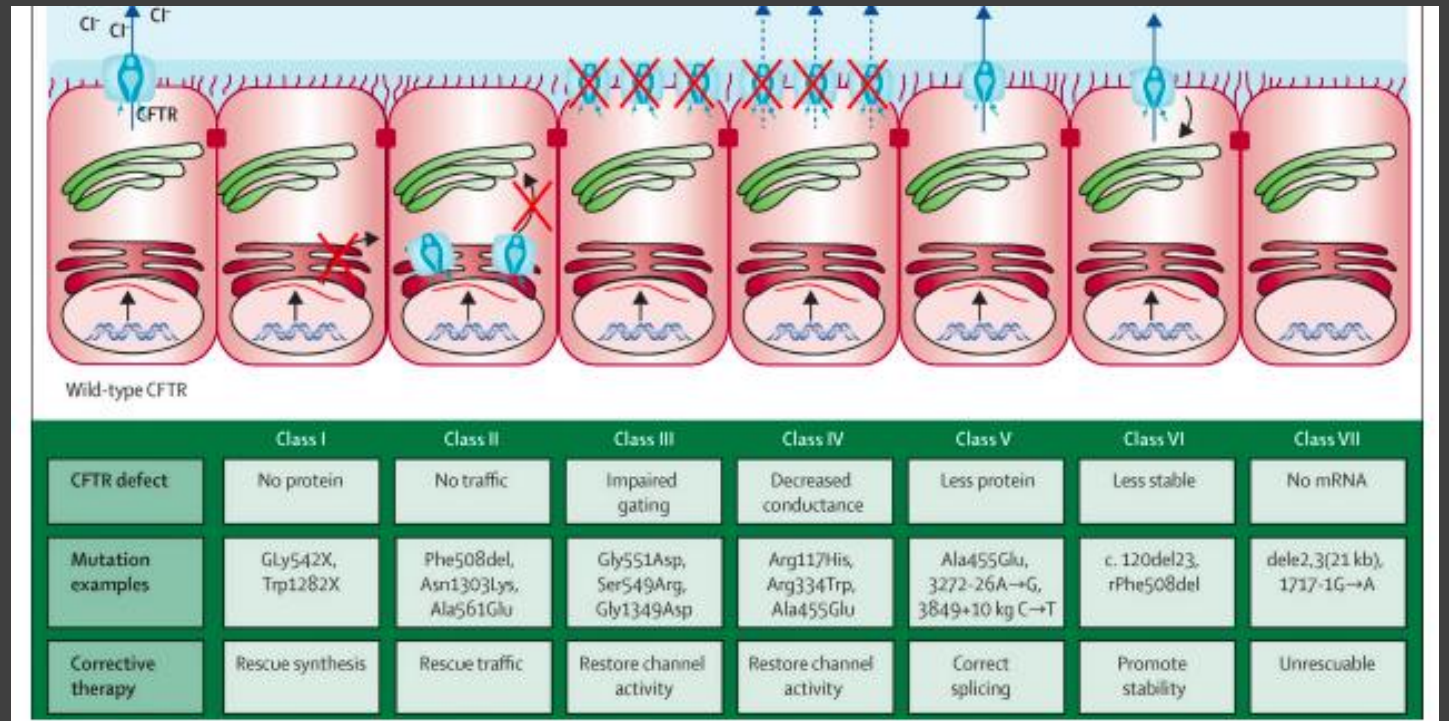


Lancet 2018;392:866-79

Chang AB, Marchant JM. Breathe 2019



URE 1 Over the six decades, symptomatic treatments greatly improved the survival of patients with cystic fibrosis roduced with permission of the ERS© 2019. Elborn[57]



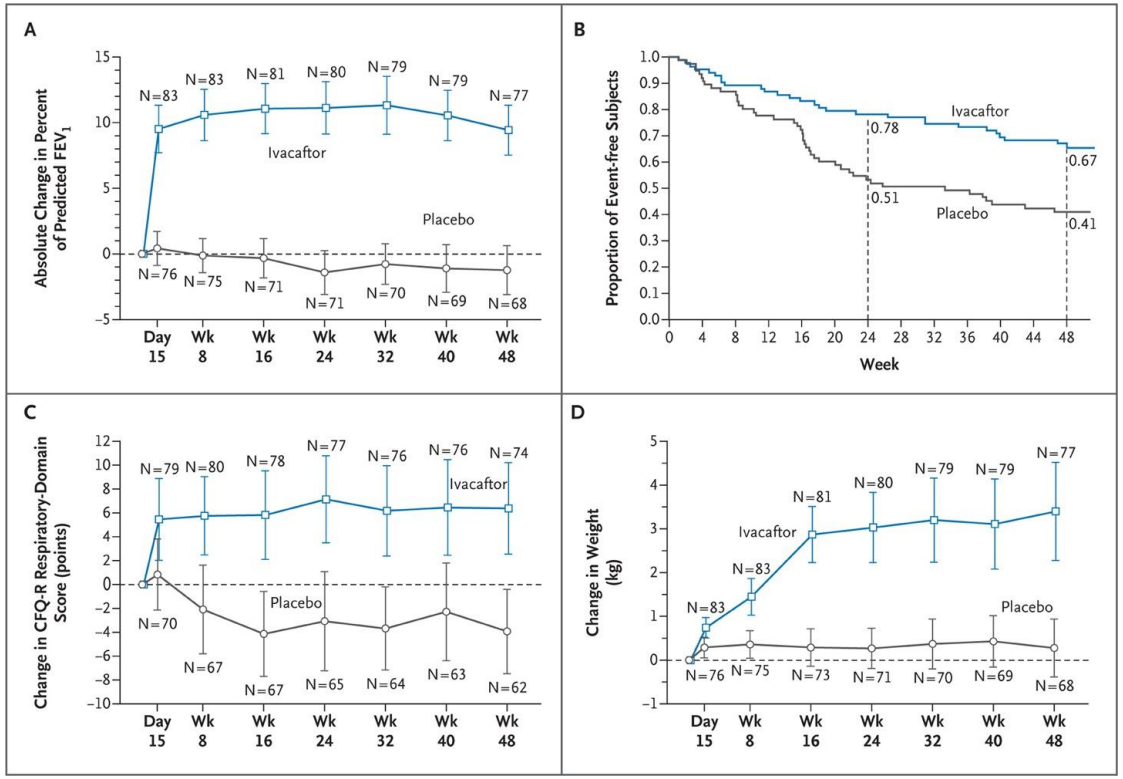
	Class I	Class II	Class III	Class IV	Class V	Class VI	Class VII
CFTR defect	No protein	No traffic	Impaired gating	Decreased conductance	Less protein	Less stable	No mRNA
Mutation examples	GLy542X, Trp1282X	Phe508del, Asn1303Lys, Ala561Glu	Gly551Asp, Ser549Arg, Gly1349Asp	Arg117His, Arg334Trp, Ala455Glu	Ala455Glu, 3272-26A→G, 3849+10 kg C→T	c. 120del23, rPhe508del	dele2,3(21 kb), 1717-1G→A
Corrective therapy	Rescue synthesis	Rescue traffic	Restore channel activity	Restore channel activity	Correct splicing	Promote stability	Unrescuable

FIGURE 2 Classes of *CFTR* mutations and their respective therapeutic strategies. CFTR mutations are grouped into seven functional classes, with the expectation that the same type of modulator will be applicable to all the defects in one class. Class VII mutations are not expected to be rescuable by a modulator. A therapeutic strategy for Class VII mutations could be stimulation of alternative chloride channels, gene therapy, gene editing or the addition of messenger ribonucleic acid. rPhe508del = rescued Phe508del.

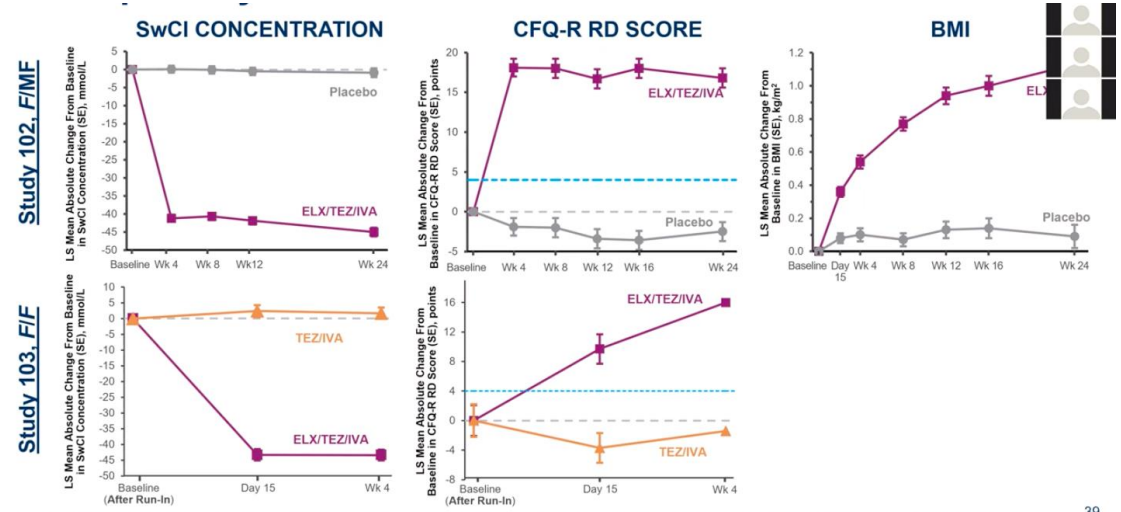
Cystic Fibrosis

- Potentiator (Ivacaftor) – allows opening of CFTR ion channels present at the cell surface i.e. G551d mutations
- Correctors (Lumacaftor) – improves function of class II mutations i.e. F508del
- Next Generation Modulators:
- Orkambi (Ivacaftor & Lumacaftor) – 2 copies of F508del
- Symdeko (Tezacaftor and Ivacaftor) – 2 copies of F508del or 1 other mutation
- Trikafta (Ivacaftor, Tezacaftor and Elexacaftor) – 1 F508del or atleast 1 other mutation

Ivacaftor



Symdeko vs Trikaftor



BMI, body mass index; LS, least squares; CFQ-R RD, cystic fibrosis questionnaire-revised respiratory domain; MF, minimal function; MMRM, mixed-effects model for repeated measures; SwCl, sweat chloride.
Data are LS means based on an MMRM; dotted blue line indicates a change in 4 points, which is the minimal clinically important difference for pwCF with stable disease.[1] 1. Quittner AL, et al. *Chest* 2009; 135: 1610-1618.

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QUESTIONS?