COPD[1]

BTS guidelines
- Full: Thorax 1997; **52** (Suppl 5)
- Summary from BTS website www.brit-thoracic.org.uk

NICE guidelines, endorsed by BTS
- Full: Thorax 2004; **59** (Suppl 1)
- From NICE website www.nice.org.uk

ABC of COPD, serialised in *BMJ* from **332**:1142

A chronic disorder characterised by airway obstruction (FEV_1<80% and FEV_1/FVC<70%)
- Does not change appreciably over several months
- Not fully reversible (cf. asthma)
- Usually progressive

Aetiology

Mostly smoking; also
- Genetic: α_1-antitrypsin deficiency (1-2% only)
- Environmental: maternal smoking, low birth weight, occupation (cadmium, coal, cotton, grain, cement), respiratory infections

Diagnosis

Combination of clinical and spirometric features.

Clinical
Patients over 35 with risk factor (usually smoking) and one or more out of
- Exertional SOB
    - MRC dyspnoea scale
        - 1 – not troubled by SOB except on strenuous exercise
        - 2 – SOB when hurrying or walking up a slight hill
        - 3 – walks slower than contemporaries on level ground because of SOB, or has to stop for breath when walking at own pace
        - 4 – stops for breath after walking about 100m or after a few minutes on level ground
        - 5 – too SOB to leave the house, or SOB when dressing/undressing
- Chronic cough
- Regular sputum
- Wheeze
- Frequent winter 'bronchitis'

Systemic features (10 point scale[2])
- B – BMI
- O – (airflow) obstruction
- D – dyspnoea (MRC scale)
- E – exercise (6 min walk)

- Better correlation with survival than FEV_1

[1] Comprises
- Chronic bronchitis (defined *clinically* as productive cough on most days for 3m of 2 successive years)
- Emphysema (defined *histologically* as enlargement of air spaced distal to terminal bronchiole with destruction of alveolar walls)

[2] CELLI, B.R. ET AL. (2004): The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *NEJM* **350**:1005-1012.

Note: frequent PVCs are a known feature

Spirometry

- FEV_1<80% and FEV_1/FVC<70%

Category	FEV_1	Features
Mild	50-80% (BTS) ≥80% (GOLD)	Little/no SOB Smoker's cough No abnormal signs
Moderate	30-49% (BTS) 30-79% (GOLD)	SOB ± wheeze on moderate exertion Cough ± sputum Variable abnormal signs
Severe	<30% (both)	SOB on any exertion/at rest Prominent cough/wheeze Signs: overinflation, hypoxic and hypercapnic features esp. during exacerbations

PEFR (no need unless asthma suspected)

- Serial records over 1w to demonstrate lack of variability

Other lung function tests (no need unless clinical severity out of proportion to spirometric findings)

- Helium dilution
  - RV/TLC>35% indicating air trapping
- ↓DLCO in emphysema

Reversibility testing (>200ml and 15% increase in FEV_1)

- Not always necessary, but should be performed if asthma is thought likely or if the response to treatment is surprisingly good
- Bronchodilators: may be markedly positive in misdiagnosed chronic asthma
- Oral steroids (30mg prednisolone for 2w, in moderate or severe disease)

CXR

- Excludes other pathology but cannot diagnose COPD

ECG, echo

- To assess cardiac status if features of cor pulmonale

FBC

- Check for secondary polycythaemia, or anaemia as an alternative cause of breathlessness
- Raised eosinophils suggest asthma

α1-antitrypsin

- If FH
- See lists

Differentiation from asthma

	COPD	Asthma
Age	>35	Any
Smoker or ex-smoker	Nearly all	Possibly
Cough	Chronic and productive	Intermittent and non-productive
Breathlessness	Persistent and progressive	Intermittent and variable
Night time waking with breathlessness and/or wheeze	Uncommon	Common
Significant diurnal or day to day variability of symptoms	Uncommon	Common
FH	Uncommon unless family members also smoke	Common
Concomitant eczema or allergic rhinitis	Possible	Common
Ix		>400ml response to bronchodilators >400ml response to 30mg oral prednisolone daily for 2w

		Serial PEFR measurements showing ≥20% diurnal or day-to-day variability FEV_1 and FEV_1/FVC ratio return to normal with drug therapy

Treatment of stable COPD

Pharmacological

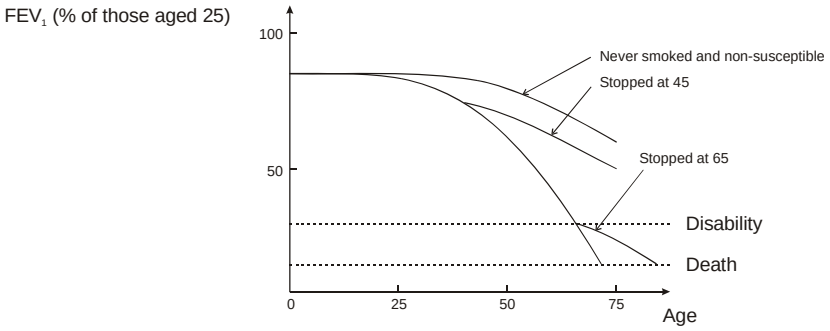
SOB and exercise limitation

- Bronchodilators prn (short-acting β_2-agonist or anticholinergic)
  - Two effects
    - Reduce high bronchomotor tone
    - Reduce dynamic hyperinflation (worsened hyperinflation with exercise), thus reducing work of breathing
- Bronchodilators regularly (combination therapy)
- Add long-acting bronchodilator (LABA or anticholinergic (tiotropium, also more $mAChR_{1/3}$-selective than short-acting anticholinergics – $M_{1/3}$ mediate bronchodilatation, M_2 bronchoconstriction))
- Consider further long-acting bronchodilator
- Consider adding inhaled steroid
  - Also if $FEV_1 \leq 50\%$ and ≥2 exacerbations in 12m
- Consider adding theophylline

- Mucolytics (carbocisteine, mecysteine) if high sputum production (endorsed by NICE)
- Future developments
  - Oral PDE_4-inhibitors (e.g. roflumilast, cilomilast) on the horizon – fewer adverse effects cf. non-selective PDE inhibitors (e.g. theophylline) but still cause nausea and diarrhoea, hence PDE_{4B}-inhibitors being considered
  - Ultra-long acting (once daily) β_2-agonists

Non-pharmacological

- Smoking cessation is essential*
  - Higher quit rates with
    - Active cessation programme
    - Nicotine replacement
  - Does not restore lung function, but prevents accelerated decline seen in COPD[3]
    - Non-smokers <35ml/y
    - Non-smokers homozygous for α_1-antitrypsin deficiency 80ml/y
    - Smokers 50ml/y
    - Susceptible smokers >100ml/y



  - Pharmacological adjuncts
    - NRT is the treatment of choice, but non-nicotine drugs are an alternative
    - NRT
      - Mode of action
        - Central: stimulates receptors in ventral tegmental area
        - Peripheral

[3] FLETCHER C. & PETO R. (1977): The natural history of chronic airflow obstruction. *BMJ* **1**:1645-8.

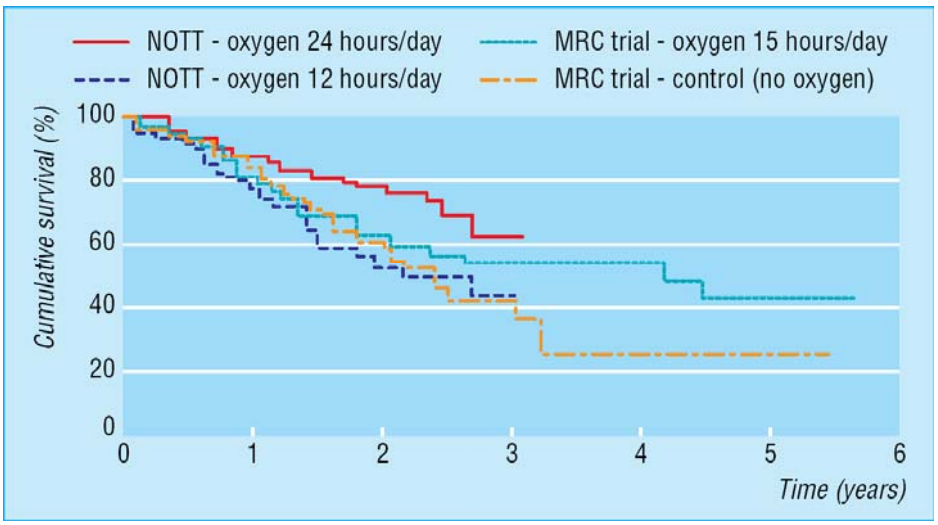
        - Cannot parallel rapid rise in arterial concentrations produced by a cigarette
        - Doubles quit rate
        - Decision pathway
            - Willing to quit in next 30 days? – if no, give clear advice to quit
            - Dependency? – if no, can stop without NRT
        - Stop after 6-8 weeks
    - Bupropion (Zyban®)[4]
        - Atypical antidepressant
            - Non-competitive nicotine antagonist
            - Dopamine, serotonin and noradrenaline reuptake inhibitor
        - Unknown which of the above mechanisms mediates its effect. Structurally similar to an appetite suppressant, so partially prevents the weight gain associated with quitting.
        - Like NRT, doubles quit rate
        - Start one week before intended quit date.
        - Adverse effects
            - Seizures, hence CI in epileptics and those on medication that lower the seizure threshold (e.g. antipsychotics, antidepressants, steroids), as well as in pregnancy
            - Rashes, Stevens-Johnsons
        - Inhibits P_{450}
    - Varenicline
        - Partial agonist at $\alpha_4\beta_2$ nicotine receptor
        - More effective than nicotine replacement and bupropion
    - Nortriptyline
        - Effective but not licensed for smoking cessation
    - Future developments
        - Agents acting on 'reward' systems: e.g. rimonabant (cannabioid CB_1 antagonist)
        - Nicotine vaccine, causes production of antibodies that stop nicotine from entering the brain
- NICE recommends: 'If a smoker's attempt to quit is unsuccessful with treatment using either NRT or bupropion, the NHS should normally fund no further attempts within 6 months. However, if external factors interfere with a person's initial attempt to stop smoking, it may be reasonable to try again sooner.'

- Exercise
- Weight loss
- Influenza and pneumococcal vaccination

In advanced disease

- Pulmonary rehabilitation
    - Better effect than medical Rx, but expensive and underused
    - Comprises exercise training, education (re smoking cessation, breathing control, exercise) and nutritional advice
- LTOT*
    - DoH guidelines
        - Two assessments >3w apart
            - PO_2<7.3, FEV_1<1.5l, FVC<2l
            - *Or* pH=7.3-8.0 with PHT
        - *Must* stop smoking!
    - MRC trial shows ↑3y survival by 50% if PO_2 maintained at ≥8.0kPa for ≥15h/day
    - NOTT (Nocturnal Oxygen Therapy Trial, American) compared 12 and 24h of continuous oxygen; terminated prematurely due to better survival in 24h group

[4] RODDY, E. (2004): Bupropion and other non-nicotine pharmacotherapies. *BMJ* **328**:509-11.



Source: *BMJ* **333**:34

- PRN oxygen
  - Symptomatic benefit only
  - May be useful in reducing dynamic hyperinflation and exercise desaturation
  - Thus, should be considered in patients with episodes of severe SOB not relieved by other treatments
- Non-invasive ventilation
  - Probably beneficial even on a domiciliary basis, but no funds
- Surgery
  - For complications (bullae, pneumothoraces)
  - For disease
    - Lung volume reduction*
      - Reduces pathological hyperinflation
      - Esp. if heterogeneous disease with upper lobe bullae – need CT, and V/Q to judge differential ventilation
      - CI if $FEV_1/TF<20\%$ predicted
      - Mortality 5%; no improvement in 25% (no good method of identifying non-responders pre-OP)
    - Transplantation (single or double)
      - Usually not an option due to shortage of donor organs and mortality (15% at 1y, 50% at 5y)
- Air travel
  - Commercial aircraft are pressurised to a cabin pressure of 8000 feet, at which the PO_2 is roughly equivalent to that of 15% O_2 at sea level
  - Need for in-flight oxygen

Sats on air	Recommendation
>95%	Oxygen not required
92-95% (without risk factors)	Oxygen not required
92-95% (with risk factor)	Hypoxic challenge test
<92%	In-flight oxygen required (2-4 l/min)
Already on LTOT	Increase flow rate

    - Risk factors: $FEV_1<50\%$ predicted, lung Ca, respiratory muscle weakness and other restrictive ventilatory disorders, within 6 weeks of hospital discharge
    - Hypoxic challenge test: breathing 15% oxygen at sea level to mimic reduced in-flight PO_2
      - $PO_2>7.4$: no oxygen required
      - $6.6<PO_2<7.4$: borderline
      - $PO_2<6.6$: oxygen required
  - Inform airline and check availability of O_2 on flight

* Proven to ↑survival

Complications

- Acute exacerbations
    - Infection
    - Pneumothorax
    - PE
    - Heart failure
    - Ca
    - Disease progression
- Respiratory failure
- Polycythaemia
- Cor pulmonale

Treatment of acute exacerbations

Presentation: ↑SOB/wheeze/chest tightness/sputum volume or purulence/fluid retention

Treat at home or in hospital?

- Mild SOB?
- Good general condition?
- Not on LTOT?
- Absence of cyanosis?
- Normal level of consciousness?
- Good level of activity?
- Able to cope at home?
- Good social circumstances?

Home treatment

- Bronchodilators: add or increase
- Antibiotics: if 2 or more out of ↑SOB, ↑sputum volume, purulent sputum
- Oral steroids: not unless already on steroids, steroids known to be beneficial, no response to bronchodilators alone, first presentation

- Arrange follow-up

Hospital treatment

As for home treatment, except

- Bronchodilators
    - Moderate exacerbation: nebulised β_2-agonist *or* ipratropium bromide; if no response, consider IV aminophylline
    - Severe exacerbation: nebulised ipratropium bromide *and* β_2-agonist; if no response, consider IV aminophylline
- Oxygen
    - 24-28%, check ABG within 60min

- If pH<7.26 and rising PCO_2, consider ventilatory support (NIPPV, IPPV or intubation) or doxapram
    - IPPV appropriate if
        - Clear basis for current deterioration
        - First episode of respiratory failure
        - Acceptable QOL
        - No previous full medical assessment
        - Few/no co-morbidities
- Xanthines: controversial – meta-analysis of four trials suggests no added benefit

- Arrange follow-up