Asthma Maintenance And Reliever Therapy

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Asthma

- Variable and reversible obstruction of the airways
- Inflammatory condition combined with bronchial hyper-responsiveness
- Not preventable

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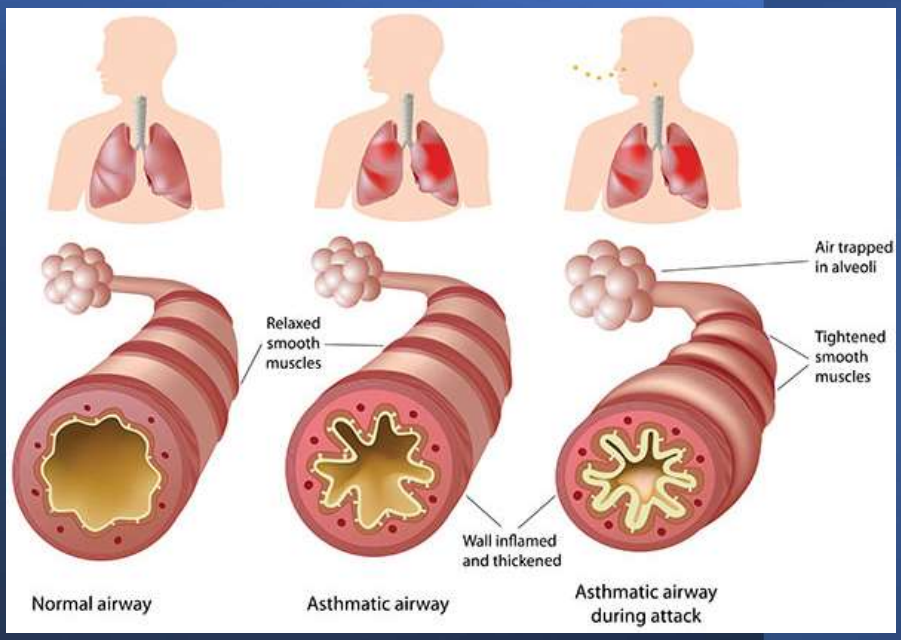

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Aim of management

- No daytime symptoms
- No night-time waking due to asthma
- No need for rescue medication
- No asthma attacks
- No limitations on activity including exercise
- Normal-near normal lung function (FEV_1 and/or PEF > 80% predicted or best)
- No or minimal side-effects from medication
- Adequate knowledge to manage disease

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When treating think about

- Take into account:

✓ Smoking

✓ **Lack of adherence**

✓ Suboptimal inhaler technique

✓ Alternative diagnosis

✓ Occupational exposures

✓ Seasonal factors

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- This dates from an era when asthma was thought to be a disease of broncho-constriction
- Patient satisfaction with, and reliance on, SABA treatment is reinforced by:
  - its rapid relief of symptoms
  - its prominence in A&E and hospital management of exacerbations
  - low cost
- *"My reliever gives me control over my asthma!"*
- When the reliever is SABA, poor adherence with maintenance controller exposes the patient to risks of SABA-only treatment

SABA as 1st line treatment for asthma

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Risks of regular SABA use

- Regular or frequent use of SABA is associated with adverse effects
  - β-receptor downregulation
  - decreased broncho-protection
  - rebound hyperresponsiveness
  - decreased bronchodilator response*(Hancox, Respir Med 2000)*
  - Increased allergic response
  - increased eosinophilic airway inflammation*(Aldridge, AJRCCM 2000)*
- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of ≥3 canisters per year (average 1.7 puffs/day) is associated with higher risk of emergency department presentations *(Stanford, AAAI 2012)*
  - Dispensing of ≥12 canisters per year is associated with higher risk of death *(Suissa, AJRCCM 1994)*

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Maintenance And Reliever Therapy

- Single inhaler
- Daily dosing, even when feeling well
- If symptoms get worse take an extra dose

- BTS/SIGN: Option at 'Initial add on therapy' step
- NICE: If asthma is uncontrolled in adults (aged 17 and over) on a low dose of ICS and a LABA, with or without an LTRA, as maintenance therapy, offer to change the person's ICS and LABA maintenance therapy to a MART regimen with a low maintenance ICS dose
- GINA: Step 3 and above

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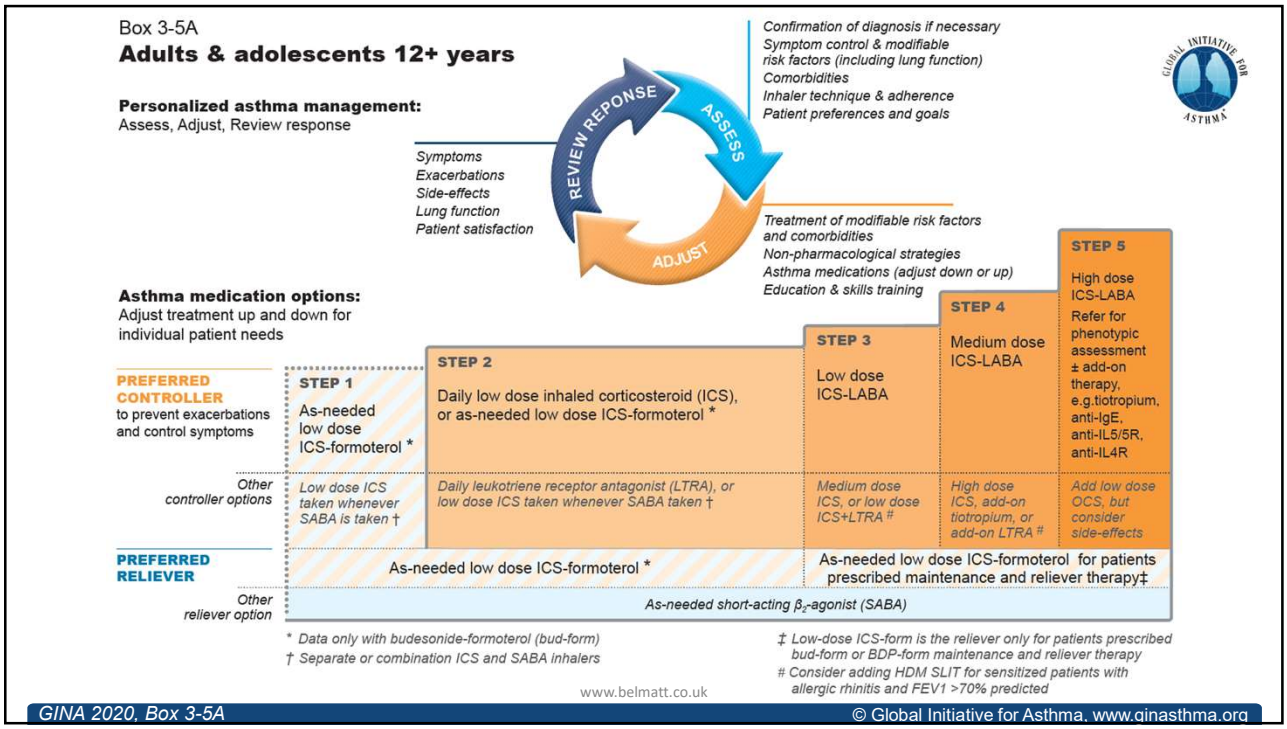

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Which inhalers?

- Contain budesonide and formoterol
  - DuoResp Spiromax 160/4.5
  - Fobumix Easyhaler 80/4.5 & 160/4.5
  - Symbicort 100/6 & 200/6
- Contain beclomethasone
  - Fostair 100/6pMDI & 100/6 NEXTHALER

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Special ingredient?

- Formoterol
  - potent selective beta2-adrenergic stimulant
  - rapid effect within 1-3 minutes (Salbutamol < 5minutes)
  - effect significant 12 hours after inhalation (Salbutamol = 4-6 hours)
  - effective daily dose range 12mcg – 48mcg per day (9mcg – 40mcg)
  - Maximum dose = 72mcg per day (54mcg)

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Care: special but not magical

- As with all beta2-adrenergic stimulants
  - Headache
  - Tremor
  - Palpitations
  - Aggression, psychomotor hyperactivity, anxiety, sleep disorders
  - Dizziness
  - Blurred vision
  - Tachycardia
  - Muscle cramps
  - Nausea
  - Bruising
  - Paradoxical bronchospasm
  - Cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia, extrasystoles

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The SYGMA studies

1 year and >3000 patients

SYGMA 1

- 3 groups:
  - Placebo BD + Terbutaline PRN
  - Placebo BD + Symbicort PRN
  - Budesonide BD + Terbutaline PRN

SYGMA 2

- 2 groups:
  - Placebo BD + Symbicort PRN
  - Budesonide BD + Terbutaline PRN

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Results

SYGMA 1

- PRN Symbicort > PRN terbutaline for asthma control and reduced exacerbations
- PRN Symbicort < Budesonide maintenance in asthma control achievement (study adherence = 79%)
- PRN Symbicort = Budesonide maintenance for asthma exacerbation

SYGMA 2

- PRN Symbicort < Budesonide maintenance for asthma exacerbation
- PRN Symbicort = Budesonide maintenance for exacerbations with less ICS
- Budesonide maintenance was better for asthma control achievement (study adherence = 63%)

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2 additional studies – PRN low dose Symbicort in mild asthma

12-month studies, open-label, no twice-daily placebo, i.e. the way it would be used in real life

- Novel START *(Beasley et al, NEJM 2019, n=668)*
- PRACTICAL *(Hardy et al, Lancet 2019, independent study, n=885)*
- ↓severe exacerbations vs SABA alone, and vs maintenance ICS, with small or no difference in symptom control, and lower average ICS dose

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Benefits of MART

- Better for concordance (easier to only have to use one inhaler)
- Reduced intake of inhaled steroids to control asthma symptoms and prevent asthma attacks
- Evidence of reduction in risk even if non-concordant and using only PRN
- Increase availability of ICS when needed is effective in aborting exacerbations
- Cheaper prescription costs
- Reduced carbon footprint
  - Fostair pMDI* – benefit is in needing 1 inhaler instead of 2
  - Fostair pMDI* is 'greener' than Ventolin
  - Rest of the available MART inhalers are DPIs

***Always use with a spacer device**

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Care needed

- Not for children under 18 – (although Symbicort is licensed in >12 years of age)
- Ensure patient is able to effectively use one of the inhalers licensed for MART
- Not appropriate when another ICS is needed
- Not appropriate with any other type of ICS/LABA combination
- Don't change those who are stable and concordant on current treatment.
- Careful education of patients about the specific issues around this management strategy is required

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