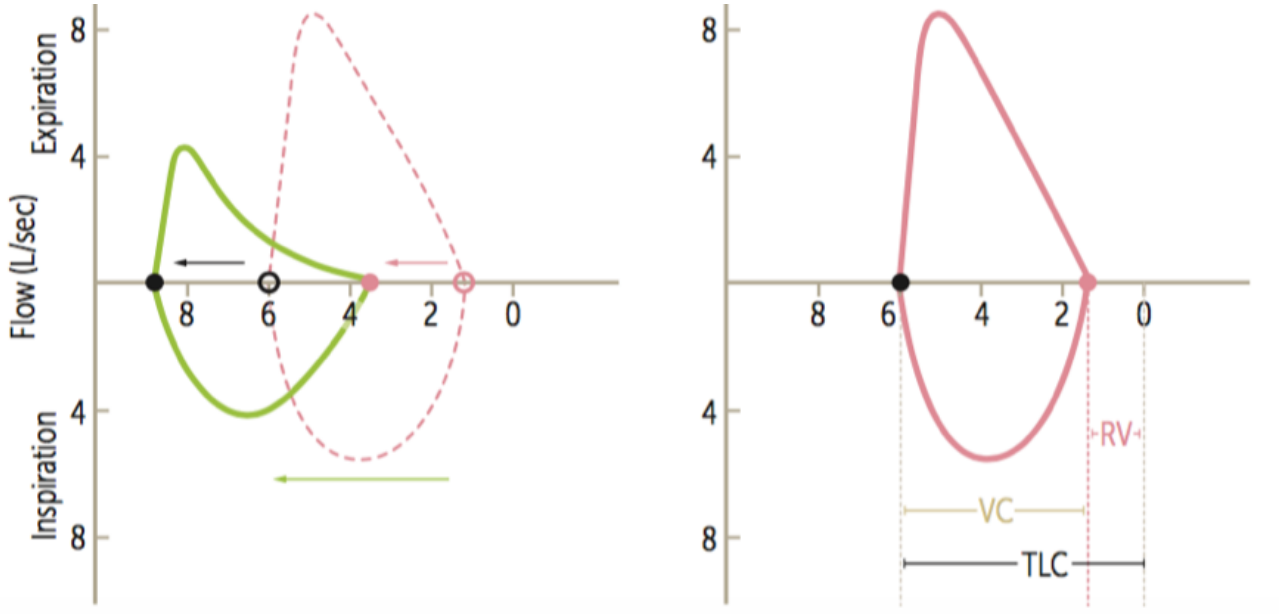
Griffith University Medicine Society
Gold Coast, Australia

Year 1 Peer Based Learning 2020
Systems - Respiratory System

Please note – this learning resource has been produced by the GUMS Academic Team. It is possible that there are some minor errors in the questions/answers, and other possible answers that are not included below. Make sure to check with other resources.

Case 1:

Toby Acco is a 70 year old male. He has a 20 pack year history of smoking. His flow volume loop is shown below; normal is shown for reference.



1. **Define what is meant by pack year**
   - A pack year is a term used to express the amount of smoking exposure a person has had over time.
   - The calculation used is:
     - Number of cigarettes per day / 20 x number of years of smoking = number of pack years

2. **What is the difference between a lung 'capacity' and 'volume'**
   - Air in the lungs is measured in terms of lung volumes and lung capacities.
   - Volume measures the amount of air for one function (such as inhalation or exhalation)
   - Lung capacity is any two or more volumes (for example, how much can be inhaled from the end of a maximal exhalation).

3. **Define the lung volumes/capacity shown on the graph at the right**
   - **TLC: total lung capacity -** measures the total amount of air that the lung can hold. It is the sum of the residual volume, expiratory reserve volume, tidal volume, and inspiratory reserve volume.

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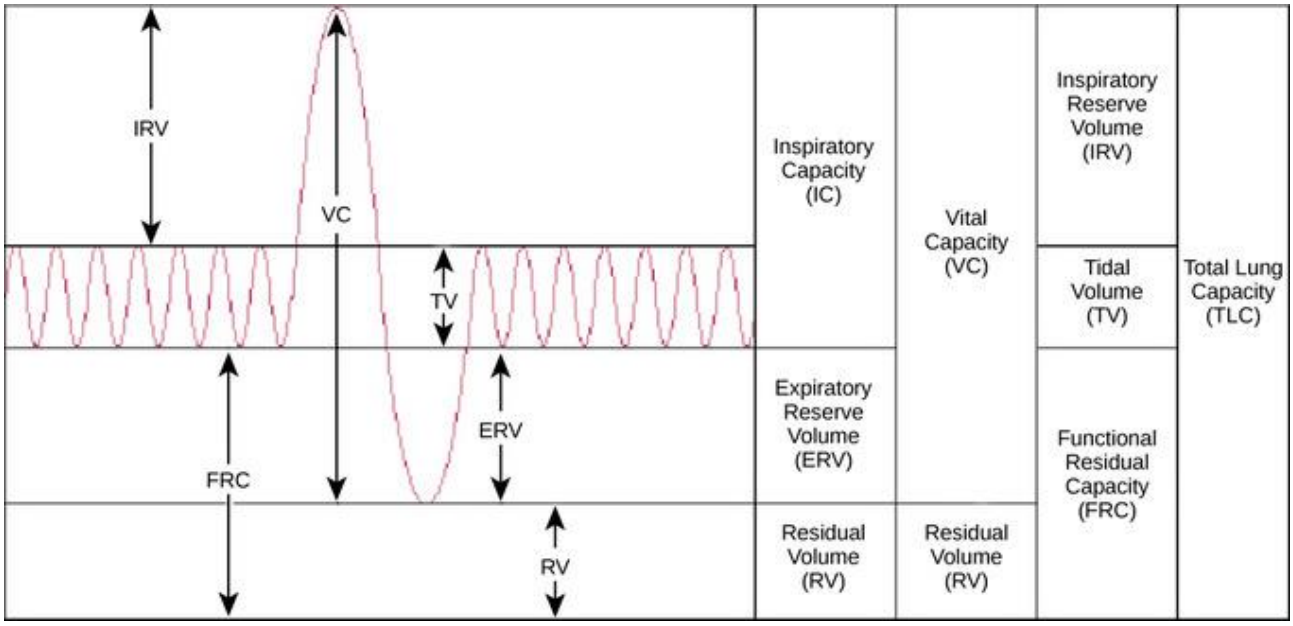
- **VC: vital capacity** - measures the maximum amount of air that can be inhaled or exhaled during a respiratory cycle. It is the sum of the expiratory reserve volume, tidal volume, and inspiratory reserve volume.
- **RV: residual volume -** the volume of unexpended air that remains in the lungs following maximum expiration



4. **State the pattern of lung disease Toby has and how RV and TLC from question 3 have changed. State the underlying mechanism for this.**
   - Obstructive pattern
   - RV and TLC increase compared to normal
   - Air trapping occurs because of reduced elasticity of alveoli and mucous plugging of bronchi/ioles → less air able to be breathed out in 1 second

5. **Summarise the differences between obstructive and restrictive lung diseases by completing the table below:**

Type	**Obstructive**	**Restrictive**
Description	Increased resistance to air flow caused by narrowing of airways	Impaired ability of the lungs to expand (as a result of reduced lung compliance)
Causes	COPD (chronic bronchitis, emphysema) Bronchial asthma Bronchiectasis, cystic fibrosis	**Intrinsic causes (parenchymal diseases)** **Interstitial lung disease** (e.g., sarcoidosis, pneumoconioses, idiopathic pulmonary fibrosis) **Alveolar** (e.g., pneumonia, pulmonary edema or hemorrhage) **Extrinsic causes (extrapulmonary causes)** **Diseases of the pleura and pleural cavity** (e.g., chronic pleural effusion, pleural adhesions, pneumothorax) **Deformities of the thorax/mechanical limitation** (e.g., kyphoscoliosis, ankylosing spondylitis, obesity, ascites, pregnancy) **Respiratory muscle weakness** (e.g., phrenic nerve palsy,

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			myasthenia gravis, ALS, myopathies)
Spirometric findings	**FEV_1**	↓	Normal or ↓
	FEV_1/FVC	↓	Normal or ↑
	Vital capacity	↓	↓
	Residual volume	↑	Normal or ↓
	Total Lung capacity	Normal or ↑	↓
	resistance to air flow	↑	Normal
	Lung compliance	Normal	Normal (extrinsic causes) or ↓ (intrinsic causes)

table adapted from Amboss - pulmonary function testing

6. **What is the most likely diagnosis? Define this disease**
    - **Chronic obstructive pulmonary disease(COPD)**
    - is characterised by persistent airflow limitation due to varying combinations of small airways disease and alveolar destruction.
    - It is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, most commonly tobacco smoke, and is generally progressive
    - COPD – broad term for emphysema and chronic bronchitis, used because they share the same risk factor of smoking and commonly occur together.
        - **Chronic bronchitis:** productive cough for at least 3 months each year for 2 consecutive years
        - **Emphysema:** permanent dilatation of pulmonary air spaces distal to the terminal bronchioles, caused by the destruction of the alveolar walls and the pulmonary capillaries required for gas exchange.

7. **Outline the pathophysiology of chronic inflammation and tissue destruction in the above diagnosed condition**
    - **Chronic inflammation:** results from significant exposure to noxious stimuli
        - Increased number of neutrophils, macrophages, and CD8+ T lymphocytes
        - Promotes goblet cell proliferation, mucus hypersecretion, and impaired ciliary function → chronic productive cough
        - Smooth muscle hyperplasia of the small airways and pulmonary vasculature (mainly due to hypoxic vasoconstriction) → pulmonary hypertension → cor pulmonale
    - **Tissue destruction**

- Bronchopulmonary inflammation ↑ proteases, and nicotine use (or other noxious stimuli) inactivates protease inhibitors (especially α1-antitrypsin) → imbalance of protease and antiprotease → ↑ elastase activity → loss of elastic tissue and lung parenchyma (via destruction of the alveolar walls), which causes:
  - Enlargement of airspaces → ↓ elastic recoil and ↑ compliance of the lung → ↓ tethering of small airways → expiratory airway collapse and obstruction → air trapping and hyperinflation → ↓ ventilation (due to air-trapping) and ↑ dead space → ↓ DL_{CO} and ↑ ventilation-perfusion mismatch (Va/Q) → hypoxemia and hypercapnia
  - ↓ Blood volume in pulmonary capillaries → ↑ dead space → ↓ DL_{CO} and ↑ Va/Q → hypoxemia and hypercapnia
- overabundance of free radicals → contributes to chronic inflammation and inactivation of anti-elastase → exacerbates breakdown of elastic tissue

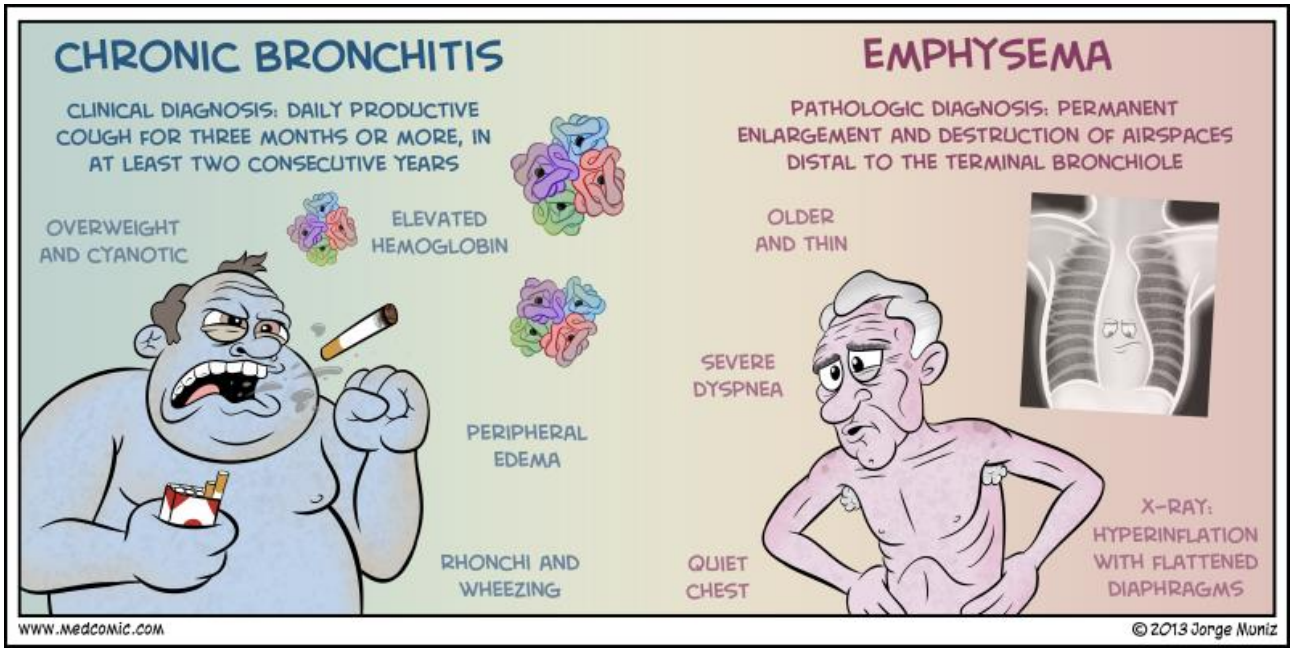
8. **For the following signs/symptoms, state which is more characteristic of chronic bronchitis vs emphysema and explain why:**
   - **Cyanosis**
     - chronic bronchitis because of hypoxaemia and polycythaemia.
     - Insensitivity in CO_2 results in loss of respiratory drive → relies on hypoxia
     - Mucus plugging causes a low V/Q ratio (decreased ventilation across the entire lungs) → hypercapnia and hypoxaemia
     - This is not as much of an issue in emphysema because the V/Q ratio is more normal or even high (increased ventilation because of increased lung compliance and decreased blood flow due to reduced SA in the alveoli
   - **Prolonged expiration with pursed lips**
     - Emphysema - because pursed lips helps maintain alveolar pressure to prevent collapse at the end of expiration
   - **Productive cough**
     - chronic bronchitis. Mucous hypersecretion
   - **Wheezing**
     - chronic bronchitis. Mucous hypersecretion causes obstruction of conducting airways

9. **What is meant by pink puffer and blue bloater**
   - **Pink Puffer - emphysema**
     - Features

- noncyanotic
- cachetic
- pursed lip breathing
- mild cough

- PaO_2 - slightly reduced
- $PaCO_2$ - normal (possibly in later hypercapnia)

- **Blue Bloater - Chronic bronchitis**
  - Features
    - Productive cough
    - overweight
    - peripheral oedema
  - PaO_2 - markedly reduced
  - $PaCO_2$ - increased(early hypercapnia)



10. **What if a patient also presented with liver cirrhosis? Which one of the diseases (chronic bronchitis or emphysema) is more likely to also occur concurrently? State what protein is defective and the mechanism for developing the disease it causes**
    - **Panacinar emphysema.**
    - characterized by destruction of the entire acinus of the lung.
    - Macroscopically panlobular emphysema affects the lower lobes more severely
    - Associated with alpha-1-antitrypsin deficiency
      - results in imbalance of protease-antiprotease and allows proteases/elastases from neutrophils to cause damage to lung and liver

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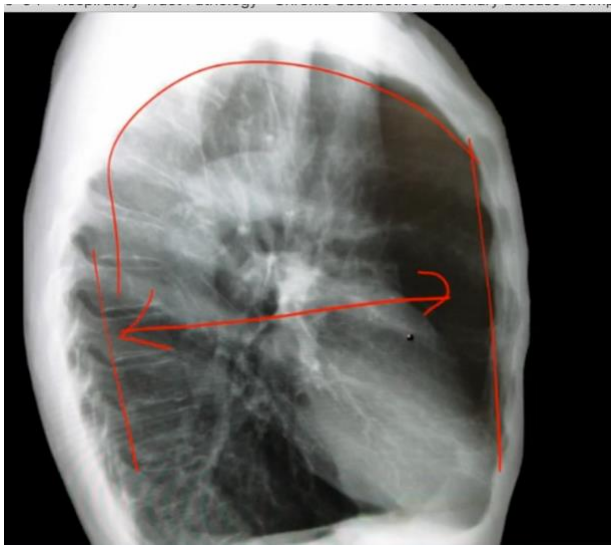
11. **Which disease is more likely to have the following x-ray? Explain**



- Increased AP diameter – barrel chest seen in emphysema.
- Lung recoil has a tendency to collapse inwards and the chest wall has a tendency to pull outwards.
- Loss of elastic recoil means the chest wall wins → barrel chest.
- Other features seen on xray: increased lung field lucency and flattened diaphragm, both due to hyperinflation

12. **Which disease is more likely to cause infection as a complication? Explain**
    - Chronic bronchitis – mucous hypersecretion and impaired clearance of mucous create a breeding ground for infections

13. **What is the effect of hypoxia on the pulmonary vasculature? Explain in ONE sentence the impact of long-term COPD on the heart and name this condition**
    - Hypoxia causes vasoconstriction of pulmonary vasculature.
    - When vasoconstriction is widespread, this causes pulmonary hypertension and right heart failure – **cor pulmonale**.

14. **You administer ipratropium. State the MOA**
    - Muscarinic antagonist – blocks the vagal tone on the smooth muscle of bronchi and reduces vasoconstriction and mucous secretion

15. **Would you administer supplemental oxygen? Discuss**
    - For emphysema, hyperventilation means that blood is well oxygenated until late stage.
    - For chronic bronchitis – too much oxygen can cause loss of respiratory drive
    - May lead to hypercapnic respiratory failure in some COPD patients. COPD patients are able to optimize their gas exchange by hypoxic vasoconstriction. By administering excess oxygen, this overcomes hypoxic vasoconstriction, increasing blood supply to areas which are poorly ventilated, creating a V/Q mismatch

10 years later, Toby Acco presents with distended neck veins, ipsilateral partial ptosis, miosis and anhidrosis.

16. **What disease (don't need to be specific) has he most likely developed now? What lobe of the lung is most likely affected? What other structures could also be compressed here and what should you look for?**
    - Pancoast tumour compressing T1 root of brachial plexus
    - Superior lobe of lung
    - Other structures
        - Bbrachial plexus – muscle wasting

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- Subclavian artery – pallor,
- Subclavian vein – oedema in upper limb
- Recurrent laryngeal nerve – hoarseness of voice

Toby Acco then goes on to complain about an altered mental state

17. **If these were caused by his lung cancer, elucidate TWO possible mechanisms for this**
    - **Small cell lung cancer** → releases ADH, causing SIADH → hyponatraemia → altered mental state
    - **Squamous cell lung cancer** → released PTHrP (parathyroid hormone-related protein) → hypercalcaemia → altered mental state

18. **Complete the following table, comparing the main features of lung cancers:**

	location in lung	risk factors	paraneoplastic syndromes	histological features	treatment
small cell lung cancer	Central	Smoking Male	ADH hypersecretion, Lambert eaton, ACTH	Neuroendocrine tumour, poorly differentiated	chemo
adenocarcinoma	peripheral	Female Non-smokers	nil	Back to back glands mucin	resection
squamous cell	Central	Smoking male	Hypercalcaemia	Keratin pearls Intercellular bridges	Resection

****Hint in remembering - "Squamous and small cell carcinomas are 's'entral and caused by smoking, have paraneoplastic syndromes, are more common in males. Adenocarcinoma mostly the opposite"**

Toby Acco goes onto develop a fever and the following x-ray whilst in hospital:

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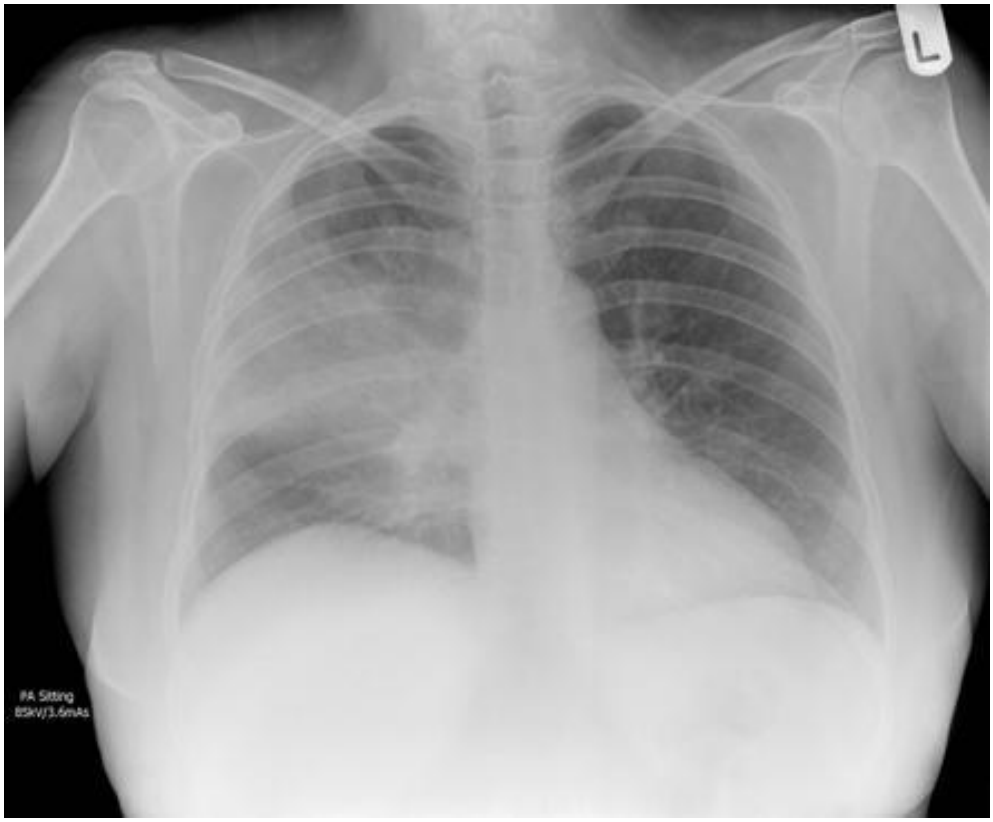

19. **State the diagnosis. What predisposed him to this infection? What are the most common causative organisms? What is the treatment for this?**
    - Middle lobar pneumonia
    - Predisposed to infection by COPD
    - Most common organisms include - Haemophilus influenzae, Moraxella catarrhalis or Streptococcus pneumoniae
    - Treat with amoxicillin (penicillin) or doxycycline (tetracycline)

Case 2

11 year old James Mcdonald comes to your clinic with his mum. James complains of a persistent dry cough for the past couple of months that is triggered by exercise and can become worse at night. He also gets SOB quickly when exercising and in the past few weeks, he says he feels a tightness in his chest.

20. **What is the most likely diagnosis**
    - Asthma

21. **What are some predisposing risk factors**
    - Family history of asthma
    - History of allergies
    - Atopic dermatitis, allergic rhinitis (i.e. eczema and hay fever)
    - Childhood exposure to secondhand smoke

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22. What is the pathophysiology of this condition

- Chronic inflammatory disorder of the airways
- It consists of the following three pathophysiologic processes:
    - **Bronchial hyperresponsiveness**
    - **Bronchial inflammation**
        - Symptoms are primarily caused by inflammation of the terminal bronchioles, which are lined with smooth muscle but lack the cartilage found in larger airways.
        - Overexpression of Th2-cells → inhalation of antigen results in production of cytokines (IL-3, IL-4, IL-5, IL-13) → activation of eosinophils and induction of cellular response (B-cell IgE production) → bronchial submucosal edema and smooth muscle contraction → bronchioles collapse
    - **Endobronchial obstruction caused by:**
        - Bronchospasm
        - Hypertrophy of smooth muscle cells
        - Increased mucus production
- **Allergic asthma - IgE-mediated type 1 hypersensitivity**
    - exposure to antigen → B-lymphocytes produce **IgE antibodies** against antigen → bind to **IgE receptors on mast cells** in the airways - causes **mast cell sensitization** → on **re-exposure** antigens bind to preformed IgE antibodies on IgE receptors on mast cells → **mast cell degranulation**
    - Mast cell degranulation causes release of:
        - histamine - vasodilation;bronchoconstriction, mucus, secretion
        - spasmogens - airway smooth muscle contractions
        - prostaglandins (PGD_2)
        - Cysteinyl Leukotrienes
        - other inflammatory markers - interleukins, tumour necrosis factor (TNF_α)
        - chemotaxins - eosinophils, helper T lymphocytes monocytes, neutrophils, mast cells
- pathophysiologic changes include
    - increased number of blood vessels
    - subepithelial fibrosis (collagen deposition)
    - goblet cell hyperplasia
    - smooth muscle hyperplasia and hypertrophy
    - increased volume of submucosal glands

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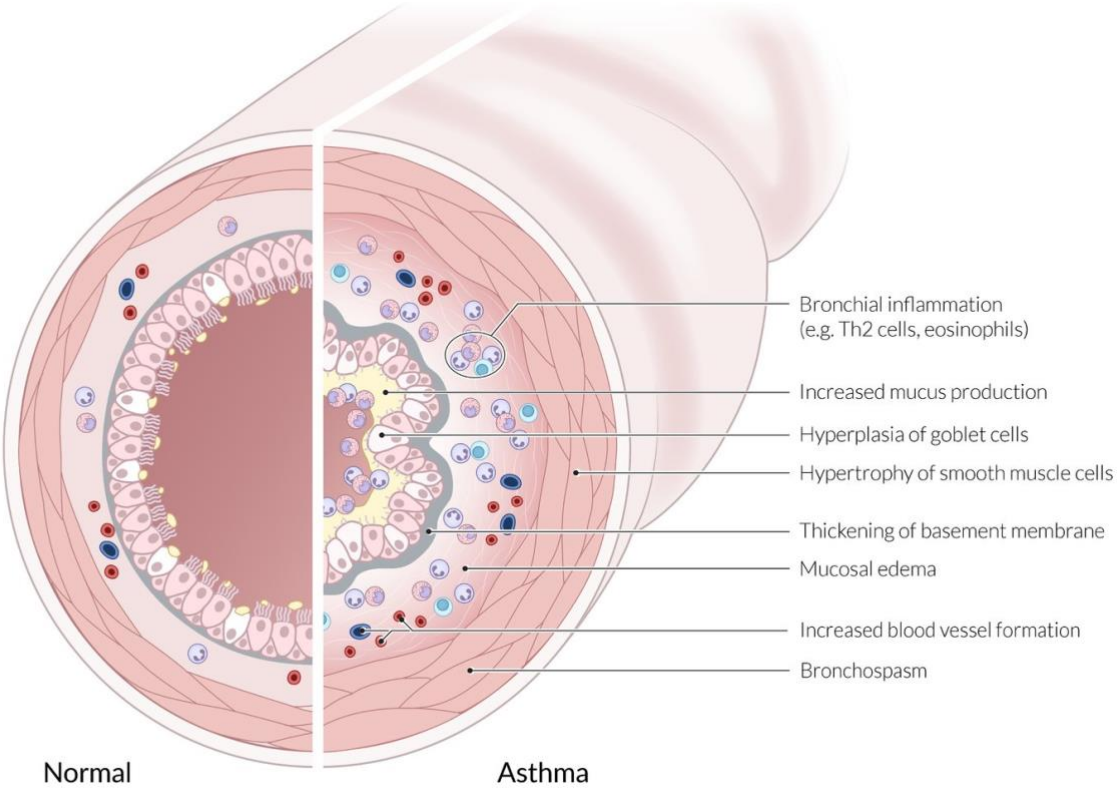

23. Compare COPD and Asthma using the table below

	Asthma	**COPD**
Age at diagnosis	Often childhood or adolescence, although nonallergic asthma can manifest after the age of 40	Typically > 40 years old
Etiology	allergic stimuli, usually have a family history	exposure to cigarette smoking (majority of cases)
Clinical presentation	Episodic: symptom-free phases, sudden attacks wheeze, chest tightness, dyspnoea, cough	Insidious onset and chronic progression over years chronic cough/sputum, persistent or worsening dyspnoea
Airflow limitation	reversible	partially reversible/persistent airflow limitation
Inflammatory mediator	eosinophils	neutrophils

24. What is meant by the terms “relievers” and “preventers” and provide some examples

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- **Relievers**
  - Are bronchodilators
  - Used in the acute treatment of asthma
  - Produce bronchodilation
  - examples
    - B2-adrenoceptor agonists
    - Muscarinic receptor antagonists
    - Methylxanthines
    - Cysteinyl leukotriene receptor antagonists
- **Preventers**
  - Are anti-inflammatory agents used to prevent asthmatic attacks
  - Reduce inflammatory response
  - Relieve airway obstruction
  - Limit long term damage to respiratory tract
  - Examples
    - Glucocorticoids - inhaled and systemic
    - Cromoglicate and nedocromil
    - Monoclonal antibody against human IgE

25. Summarise the medications used in asthma management in the table below

Drug Class	Examples	Mechanism of Action	Primary use	Side effects
Beta-2 agonists	**short acting - (SABA) -3-5 hours** salbutamol terbutaline **Long acting (LABA) - 8-12 hours** salmeterol indacaterol formoterol	**direct action on beta-2 adrenergic receptors to induce bronchodilation** **stabilise ast cell membrane - inhibiting mast cell inflammatory mediator release** inhibit release of TNF_{α} from monocytes prevent microvascular leakage reduce airway oedema enhance mucus clearance by increasing ciliary action	**SABA:** acute exacerbations **LABA:** long-term maintenance treatment	generally mild and tolerable **common**: tremor,s palpitations, headache **infrequent:** peripheral vasodilation, hyperglycemia (high dose), tachycardia, muscle cramps, agitation, insomnia
Muscarinic antagonists	**Short-acting (SAMA):** ipratropium bromide	Competitively inhibit postganglionic muscarinic	adjunct therapy when B2 agonists are inadequate	rare with inhaled preparations but include dry mouth, urinary retention

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	(non-selective block) **Long-acting (LAMA):** tiotropium bromide (more selective for M3)	receptors in bronchial smooth muscle → bronchodilation		antimuscarinic (anticholinergic toxicity - vasodilation, decreased sweating, dilation of pupils, blurry vision, hallucinogenic ****remember them as**** hotas a hare, blind as a bat, dry as a bone, red as a beet, mad as a hatter**
Methylxanthines	Theophylline Aminophylline	Inhibits phosphodiesterase (PDE) → ↑ cAMP levels → anti-inflammatory and mild bronchodilatory effect relaxes bronchial smooth muscle inhibits histamine release from mast cells some antiinflammatory action increases mucus clearance	not used that often anymore due to **LOW THERAPEUTIC INDEX** Severe airways obstruction, including acute asthma (aminophylline, rarely used) Maintenance treatment in severe asthma and COPD **(rarely used)**	nausea, vomiting, diarrhoea, gastro-oesophageal reflux, headache, insomnia, irritability, anxiety, tremor, palpitation, tachycardia, seizures ****NOTE**** theophylline is metabolised by liver P450 enzymes → drug interaction → monitor serum concentrations caffeine or chocolate can increase side effects whereas smoking increases metabolism of theophylline and reduces it plasma concentration
Glucocorticoids - **inhaled** - **systemic**	**inhaled** Beclomethasone Fluticasone Budesonide Ciclesonide **systemic** Methylprednisolone Prednisone	**Inhibits phospholipase A2 -** a key enzyme in the synthesis of leukotrienes and prostaglandins Reduces mucosal inflammation Blocks production of cytokines e.g. interleukins, involved in the inflammatory response Reduces leukotriene-induced bronchoconstriction Blocks synthesis of IgE receptors on mast cells Blocks synthesis of histamine in mast cells	**Clinical uses** Prophylactic use for preventive treatment of asthma for acute exacerbations of asthma and COPD, a short course of oral prednisolone is prescribed Used parenterally in acute severe asthma **inhaled** Long-term maintenance treatment (first line) **systemic** Used in severe and refractory cases	**Inhaled** Inhaled corticosteroids produce negligible systemic reactions **Oropharyngeal candidiasis - rinse mouth out after use of steroid inhaler** **systemic** Fluid retention Immune suppression Growth retardation in children Suppression of adrenal cortisol secretion
Mast cell stabilisers	Cromoglicate nedocromil	prevents release of mast cell activators (currently disputed role) Weak anti-inflammatory action	Prophylactic use, effective in children Preventive treatment prior to exercise or unavoidable exposure to known allergens in patients ≥ 5	**Common:** cough, throat irritation, bitter taste, transient bronchospasm **Rare:** allergic reaction including severe bronchospasm

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			years old	
leukotriene receptor antagonists	Montelukast Zafirlukast	Act as competitive antagonists of leukotrienes at the cysteinyl leukotriene receptor (CysLT1) ↓ Bronchoconstriction and inflammation	Long-term maintenance treatment (particularly in children) Exercise-induced and aspirin-induced asthma steroid sparing properties Similar efficacy to low dose corticosteroids but lack adverse effects of corticosteroids Not a substitute for bronchodilators or corticosteroids Effective as add-on therapy in mild persistent asthma and in combination with other medications in more severe conditions	headache, abdominal pain, diarrhoea ****NOTE** from TGA** - *"There is a known association between montelukast and neuropsychiatric events (such as agitation, sleep disturbance and depression) including, in rare cases, suicidal thinking and behaviour"* - although these are rare, beware now a lot of parents can be reluctant to start montelukast- they need good counselling**
Monoclonal Antibody against human IgE	Omalizumab	Binds to immunoglobulin E (IgE), reducing the immune system's response to allergen exposure.	for moderate to severe, persistent and proven (by skin test) allergic asthma not controlled by inhaled steroids	injection site reactions, rash

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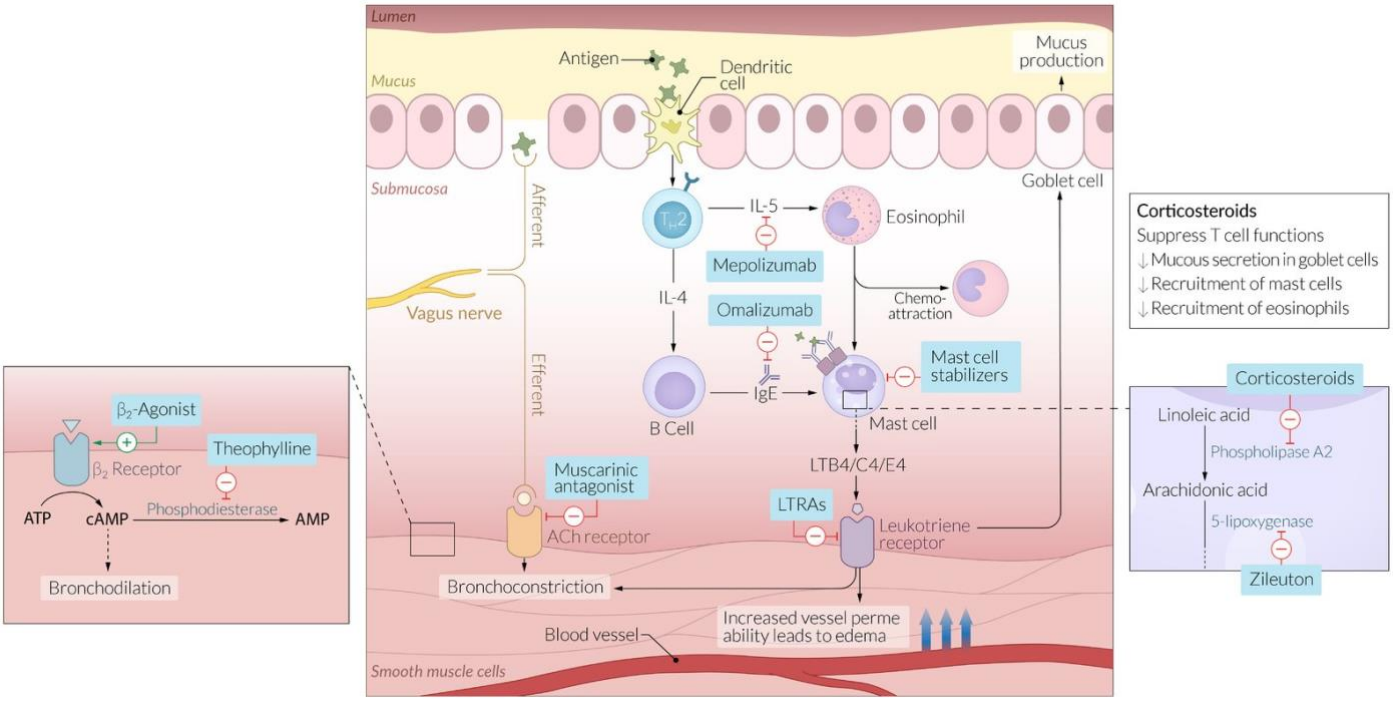

image from Amboss - Asthma

SEE STEPWISE APPROACH TO MANAGEMENT - PICTURE NEXT PAGE

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Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

National Asthma Council | Australian Asthma Handbook

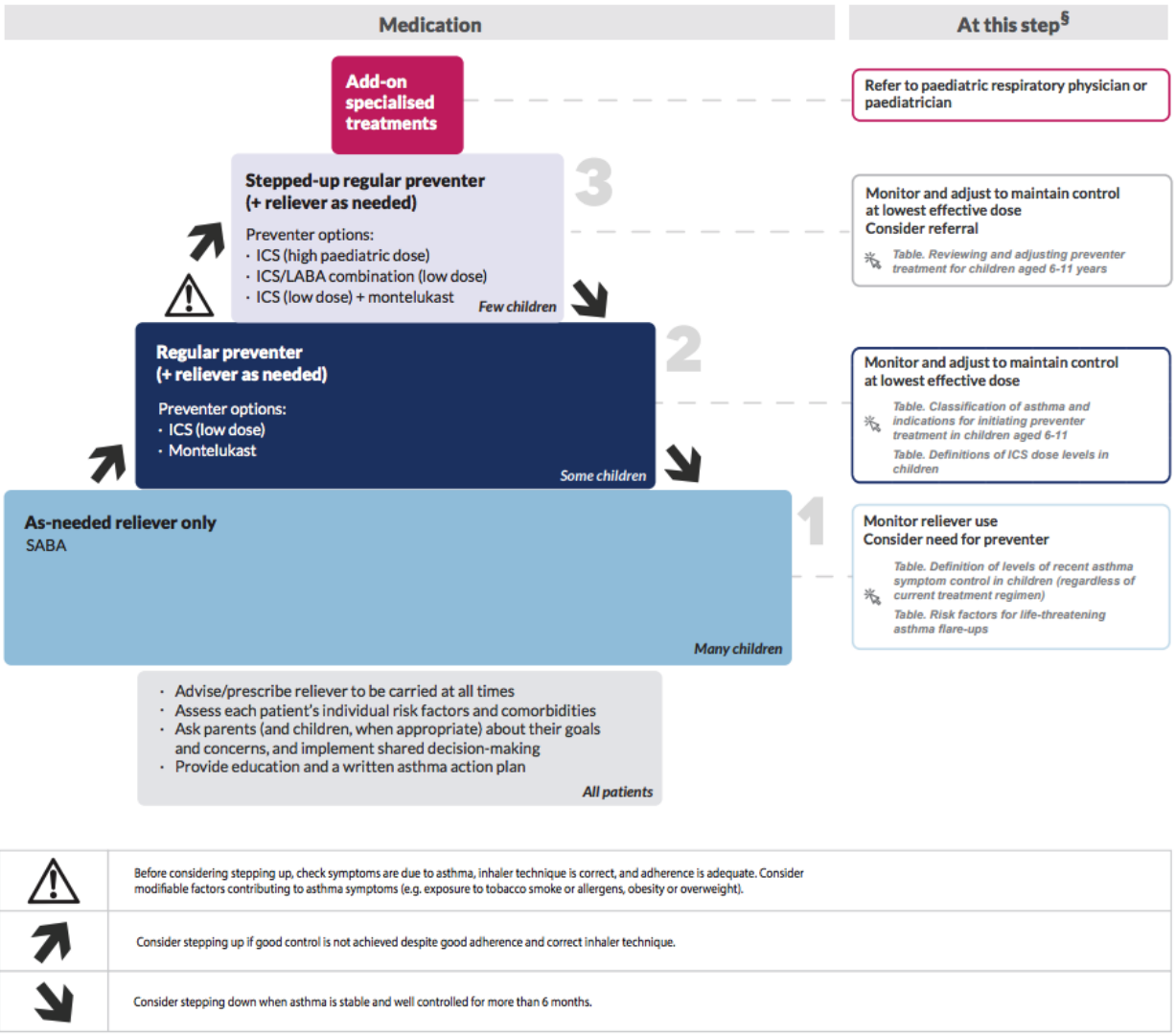

Image from National Asthma Council - Australian Asthma Handbook

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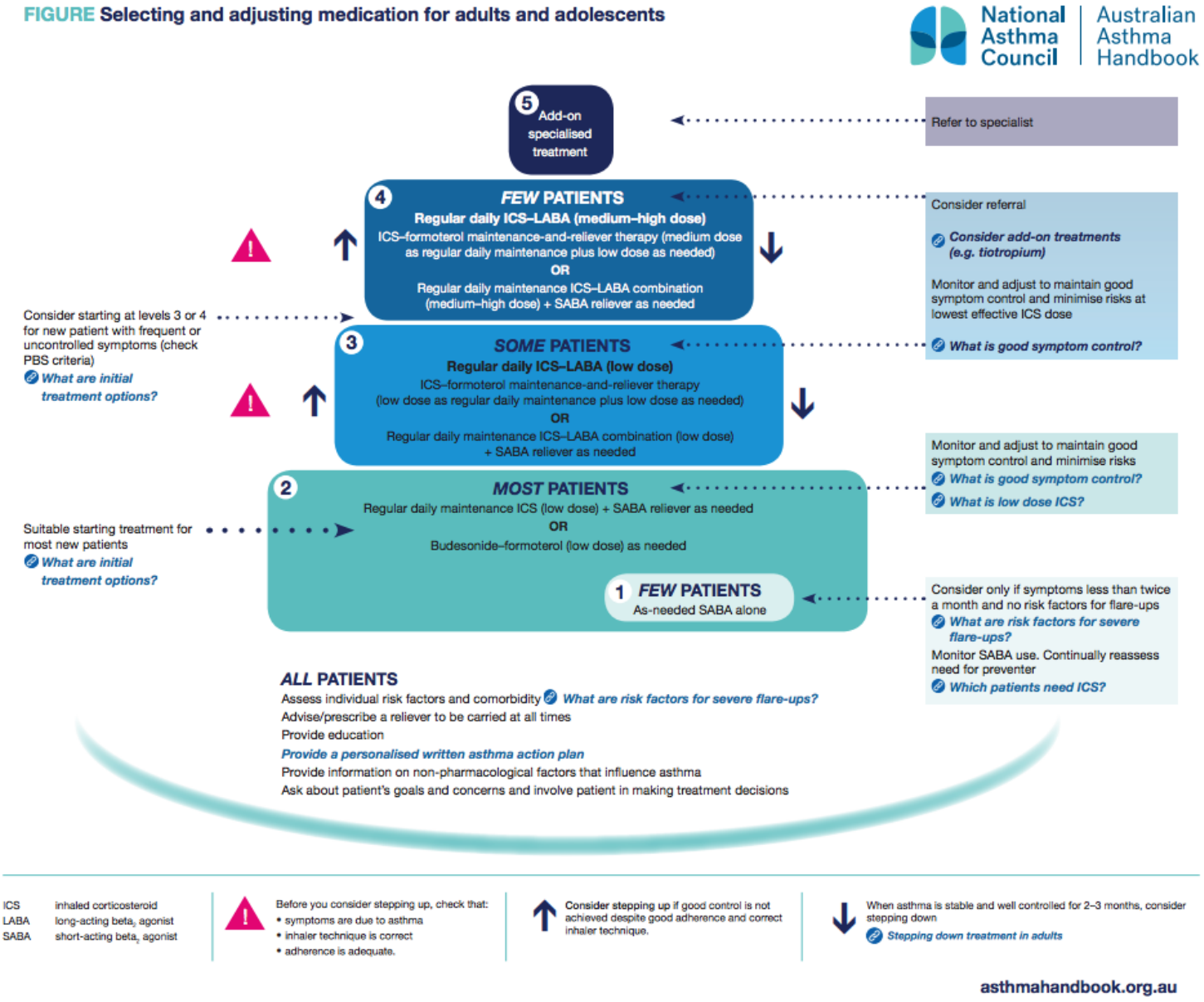

Image from National Asthma Council - Australian Asthma Handbook

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https://gums2020.typeform.com/to/e0h7US

References

- Amboss
- eTG
- UpToDate
- AMH
- Niru lectures

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- https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Book%3A_General_Biology_(Boundless)/39%3A_The_Respiratory_System/39.2%3A_Gas_Exchange_across_Respiratory_Surfaces/39.2C%3A_Lung_Volumes_and_Capacities#:~:text=Air%20in%20the%20lungs%20is,end%20of%20a%20maximal%20exhalation).
- Australian Asthma Handbook