THE UNIVERSITY OF WESTERN AUSTRALIA

DENT 3005:Introduction to Pharmacology

Respiratory Drugs

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Acknowledgement: Sheetal Maria Rajan

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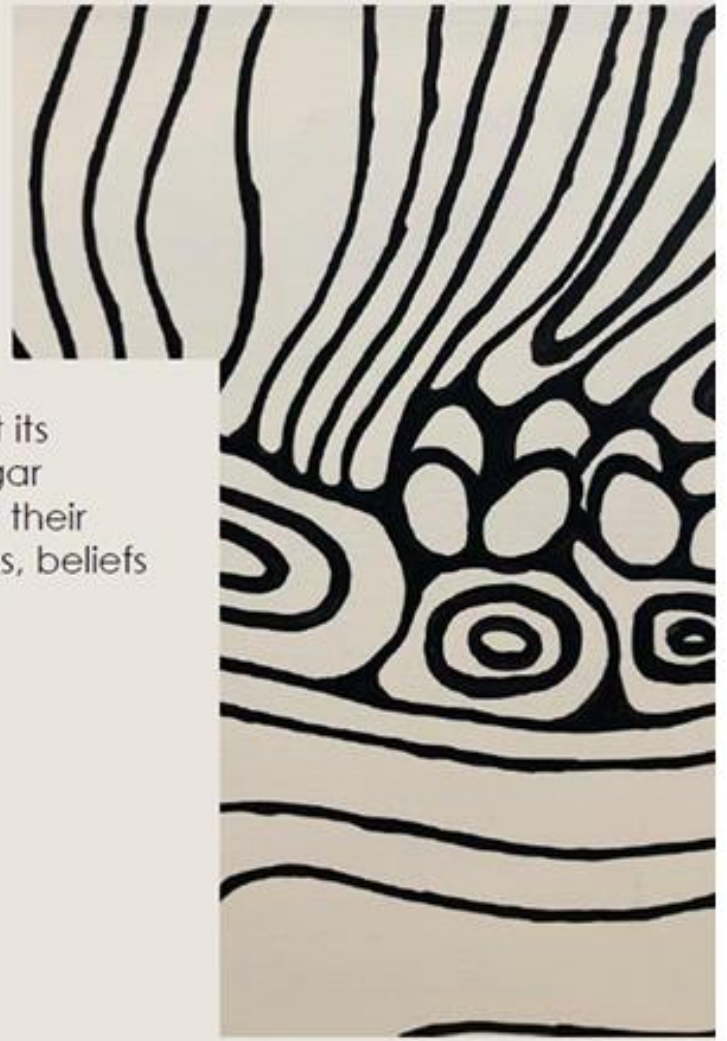
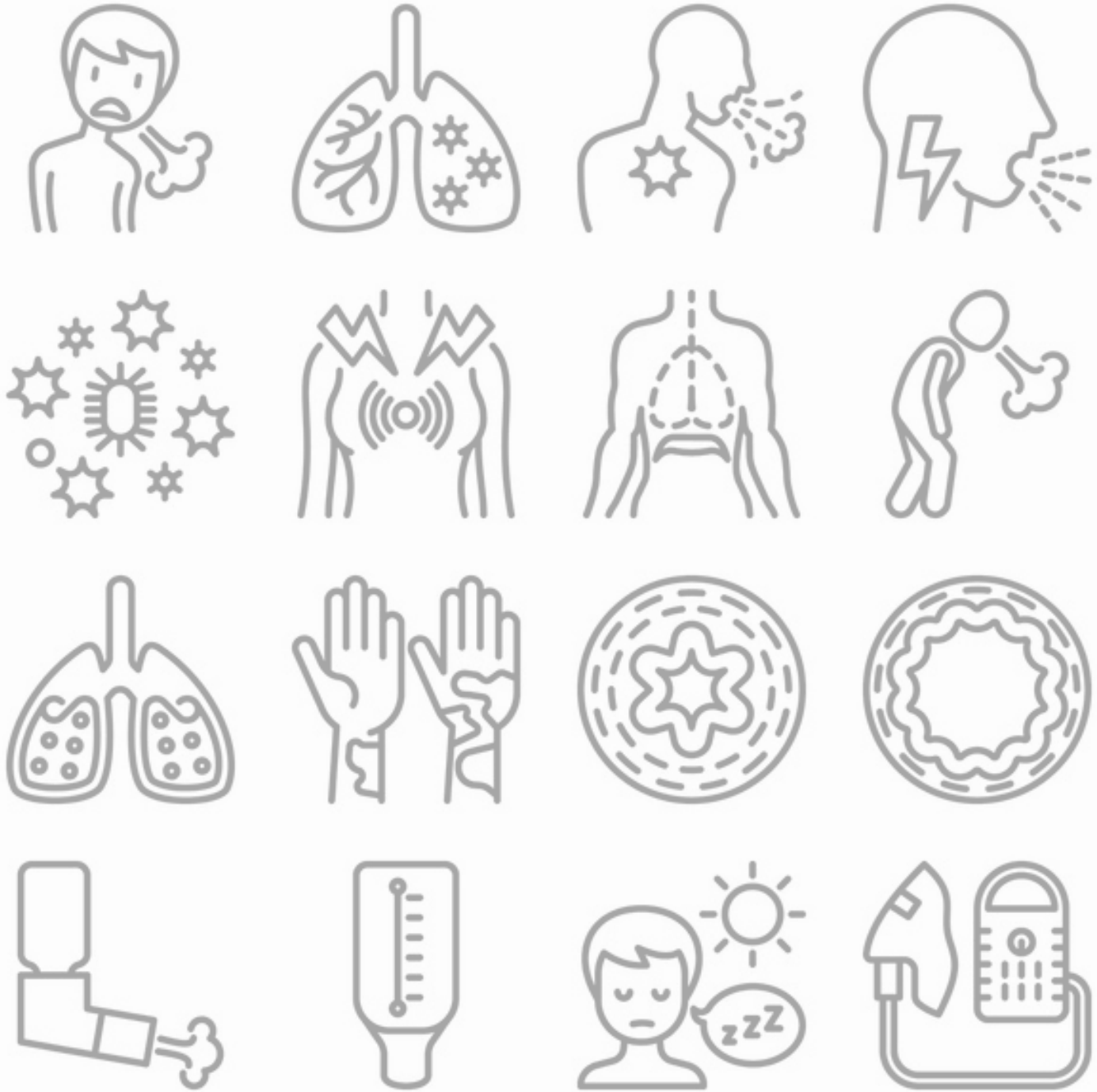
Acknowledgement of country

The University of Western Australia acknowledges that its campus is situated on Noongar land, and that Noongar people remain the spiritual and cultural custodians of their land, and continue to practise their values, languages, beliefs and knowledge.



Artist: Dr Richard Barry Walley OAM



Learning Outcomes

Learning objectives

1) Understand the classes and mechanisms of common respiratory drugs
2) Recognise common respiratory conditions treated with these drugs
3) Management of emergencies related to respiratory conditions in the dental setting
4) Understand drugs interactions with dental medications
5) Recognise oral and dental side effects of respiratory drugs
6) Applied knowledge to clinical scenarios

Introduction

Rationale for drug therapy

- Symptom control & relief
- Prevent exacerbation, acute asthma & death
- Improve & maintain lung function & QOL

Airflow obstruction

- Constriction of bronchioles
- Increased mucous production
- Increase oedema
- Problems: nasal cavity → alveoli

Pharmacotherapy

Aetiology

- Infection: viral, fungal, bacterial
- Immune: allergies, asthma
- Inflammatory: bronchitis, asthma, emphysema

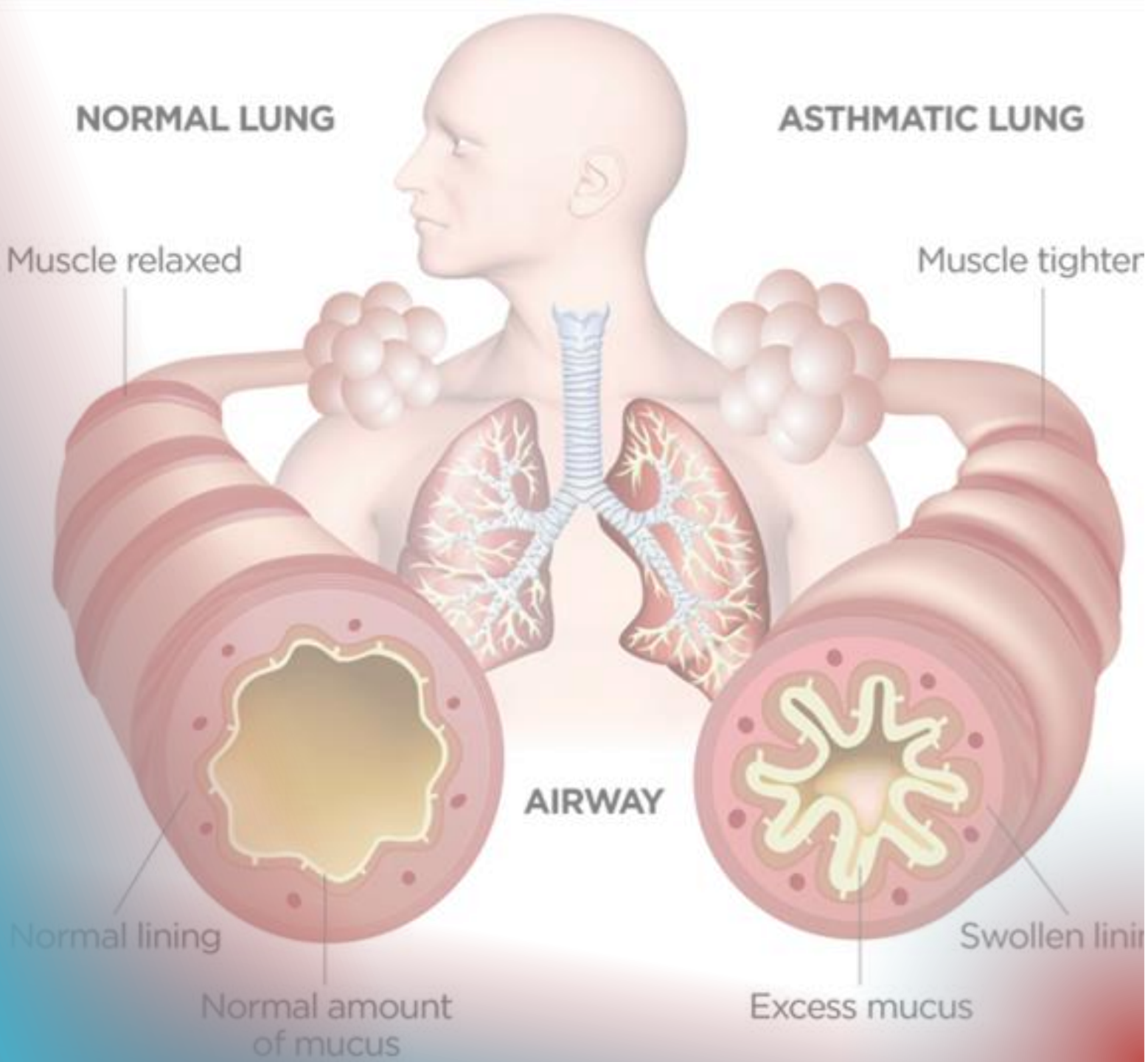
Drug therapy

- $Beta_2$ agonists
- Anticholinergics
- Theophylline
- Corticosteroids
- Cromones
- Other
  - Leukotriene receptor antagonist
  - Monoclonal antibody against IgE

Pathophysiology

Obstructive airway diseases

- Restricted expiratory airflow
  - Asthma
    - Reversible
    - Bronchospasm
    - Mucous hypersecretion
    - Oedema
  - COPD
    - A group of respiratory disease
    - Chronic & recurrent obstruction
    - Chronic bronchitis, emphysema
  - Cystic fibrosis
    - Inheritable
    - Abnormal secretions
    - Obstruct: AW & pancreatic ducts



Asthma

- **A chronic condition that inflames and narrows the airways in the lungs**
- **Reversible airway obstruction**
- **Characteristics**
  - Narrowing/complete obstruction
  - Extrinsic & intrinsic
  - Two phases of an acute attack
- Can affect people of all ages
- **Symptoms:** coughing, wheezing, shortness of breath, and chest tightness

Pathophysiology: Asthma

Extrinsic (Allergic)

- Aetiology: allergic nature
- Acute attack: early & late phase
- Triggers: grass, pollen, dust…

Early Phase (10-20mins)

- Trigger → release chemical mediators → vasodilation → increase permeability → viscous mucous → constriction bronchioles
- Mast cell degranulation → Mediators released
  - Histamine
  - Prostaglandin
  - Leukotrienes

Intrinsic (Non-allergic)

- Provoked by factors other than allergens
- Triggers
  - Sudden changes in weather
  - Infections
  - Emotional state

Late Phase (6-9hours)

- Eosinophils, macrophages, T-lymphocytes, neutrophils
- Inflammation
- AW hypersensitivity

- Asthma attacks can be divided into two phases: **the early phase** and **the late phase**.
- These phases reflect the timing and types of inflammatory responses in the airways after exposure to an allergen or irritant.

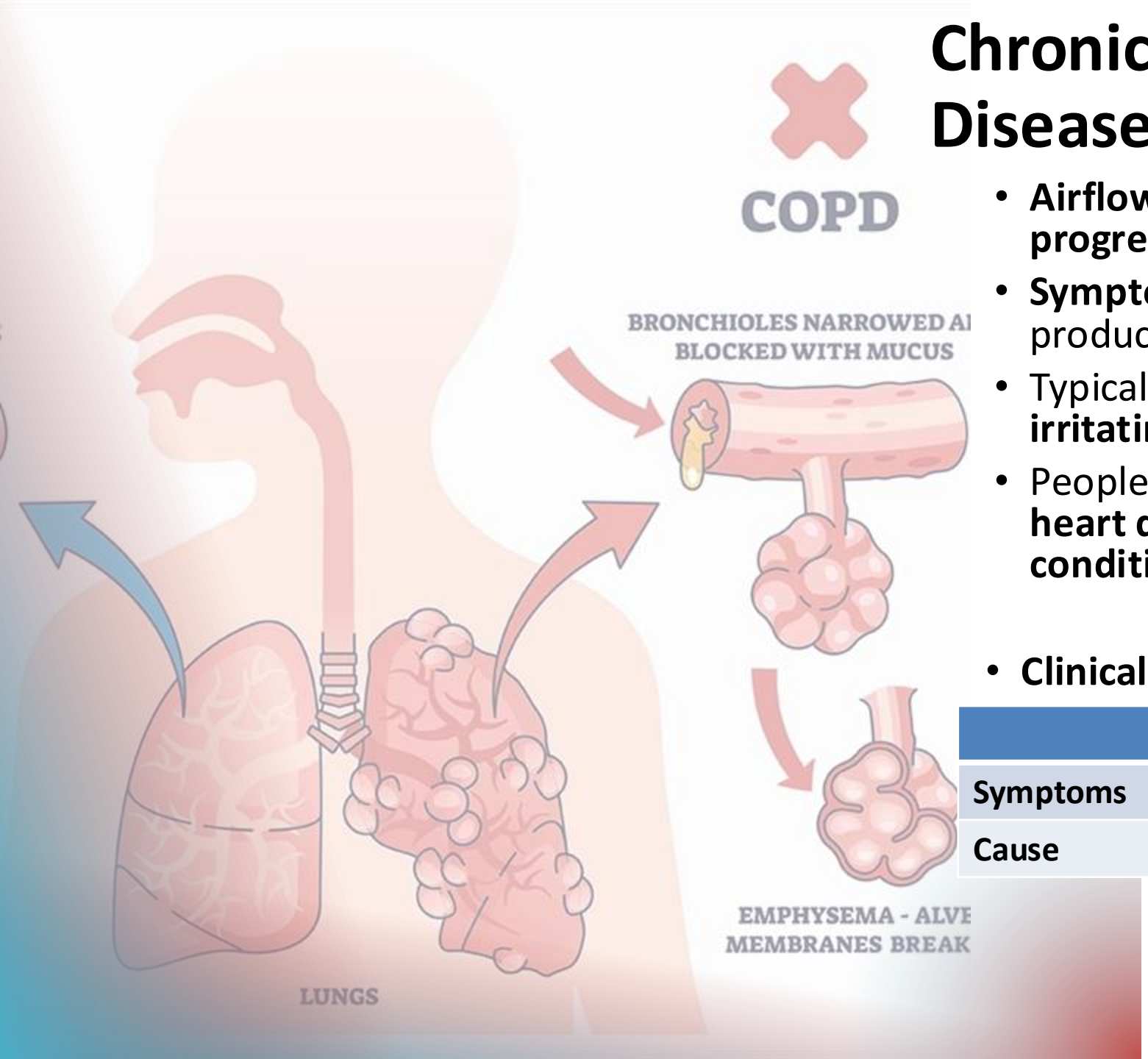
Early Phase (10-20 minutes)	Late Phase (6-9 hours)
IgE binds to receptors on mast cells ↓	Activated T_H2 lymphocytes release cytokines that recruit more proinflammatory cells ↓
Mast cells degranulate and release histamine, proteolytic enzymes, cytokines, leukotrienes, and prostaglandins ↓	Eosinophils Mast cells IgE-producing B cells ↓
Bronchoconstriction, vasodilation, and airway inflammation	Airway hyperresponsiveness, edema, mucus production, fibrosis, and airway remodeling

Symptoms:

Clinical presentation: Wheezing, Shortness of breath, Chest tightness, Coughing — Persistent Wheezing, Prolonged Shortness of breath, Continued Chest tightness, Ongoing Coughing

Treatment: **SABAs – albuterol (relax the bronchial muscles)** — **IC, LABAs, Leukotriene modifiers, in severe cases systemic corticosteroids**

Chronic Obstructive Pulmonary Disease (COPD)

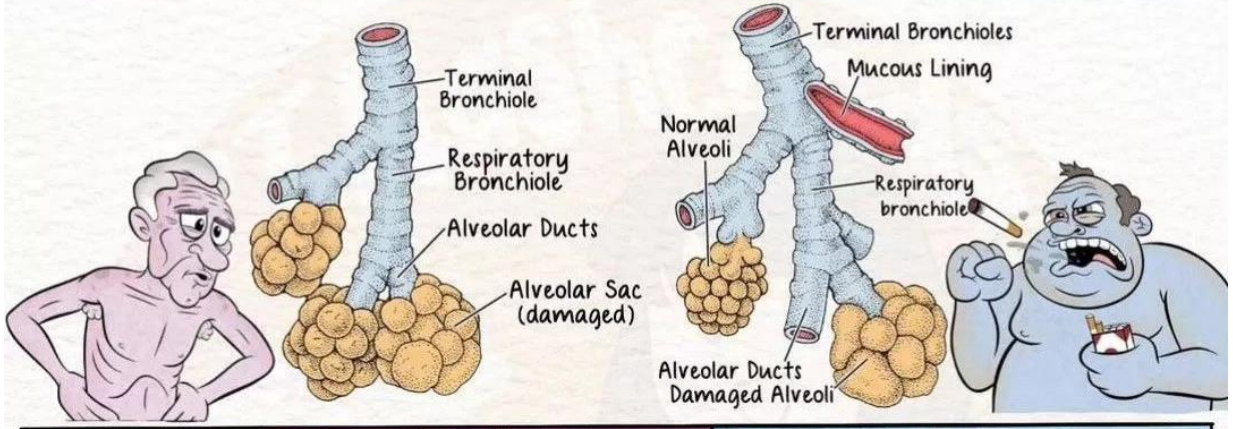


- **Airflow limitation in COPD is persistent, progressive & not fully reversible**
- **Symptoms:** breathing difficulty, cough, mucus production, wheezing
- Typically caused by **long-term exposure to irritating gases- cigarette smoke**
- People with COPD- **increased risk of developing heart disease, lung cancer and other conditions**

- **Clinical manifestations**

	Chronic Bronchitis	Emphysema
Symptoms	Chronic cough + phlegm	SOB, cough
Cause	Damaged bronchi	Damaged Alveoli

EMPHYSEMA vs. CHRONIC BRONCHITIS



	Emphysema "Pink Puffers"	Chronic Bronchitis "Blue Bloaters"
Usual Presentation	Shortness of breath and scant sputum production	Chronic productive cough
General Appearance	Thin, sometimes cachectic, with rosy skin tones	Often overweight, obese
Adventitious Sounds	Less common	Ronchi and Wheezes
Sputum	Scanty, Mucoid (Evaporated Milk)	Copious, Purulent (Condensed Milk)
Cough	Dyspnea before cough (less prominent)	Cough before dyspnea (more prominent)
Cor Pulmonale	Rare, except at the late stages	More prominent
Radiographic Findings	Hyper-inflated lungs Small heart Diaphragm: low & flat +/- bullae (pockets of air)	Normal sized lungs (R) Ventricular hypertrophy Normal shaped diaphragm (+) Dirty lung appearance
Other Findings	(+) Barrel Chest (+) Use of accessory muscles of respiration	(+) Cyanotic (+) Peripheral Edema

https://medizzy.com/feed/39973003

Drug Therapy

ASTHMA

- Short acting $Beta_2$ Agonist
- ICS
- Long acting $Beta_2$ agonist
  - Always with ICS
- Montelukast
- Omalizumab

COPD

- Short acting bronchodilators
  - SABA
  - SAMAs
- Long-acting bronchodilators
  - LABAs
  - LAMAs
- Corticosteroids
  - No role in monotherapy
- Other
  - Theophylline

Respiratory Medications

Relievers

- SABA (Short-acting β2 agonist)
- LABA (Long-acting β2 agonist with Rapid onset)

Preventers

- ICS (Inhaled Corticosteroids)
- Leukotriene Modifiers
- Mast Cell Stabilizers

Adjuvant

- LABA
- Theophylline
- Anti-immunoglobulin (IgE) – Omalizumab
- Anti-interleukin-5 (IL5) - Mepolizumab
- LAMA (Long-acting muscarinic antagonist)

Short acting Beta$_2$ Agonists – (SABAs) Relievers

- MOA: relax bronchial smooth muscle
- Indication
  - Sx relief of asthma & COPD
  - Prevention of exercise induced bronchoconstriction
- ADR
  - Tremor, palpitations, headache
  - Serious hypokalemia in high doses
- *Salbutamol (Ventolin/asmol)*
  - *100-200mcg prn*
- *Terbutaline (Bricanyl)*
  - *500-1500mcg prn*

Long acting Beta$_2$ Agonists (LABAs) Relievers

- MOA: relax bronchial smooth muscle
- Indication
  - Maintenance tx of asthma in patients on inhaled/oral CS
  - COPD
- ADR
  - Tremor, palpitations, headache
  - Serious hypokalemia in high doses
- *Eformoterol (Turbuhaler/Rapihaler)*
- *Indacaterol (capsules)*
- *Salmeterol (MDI/Accuhaler)*

Short acting anticholinergic (SAMAs)

- MOA
  - Relaxes airway smooth
  - Block M3 muscarinic receptor
  - Rapid bronchodilation (15-30 mins)
- Indication
  - Initial management of sx in mild COPD
  - Severe acute asthma attack when SABA is inadequate
- ADR
  - Dry mouth, throat irritation
- *Ipratropium (Atrovent)*

Long acting anticholinergic (LAMAs)

- MOA
  - Relaxes airway smooth
  - Block M3 muscarinic receptor
- Indication
  - Treatment of COPD
- ADR
  - Dry mouth, throat irritation
- *Tiotropium (Spiriva)*
- *Glycopyrronium (Seebri)*

Beta$_2$ agonists & anticholinergics Dental implications

- Anticholinergics: lower saliva secretions
  - Dry mouth → caries risks
- Combination w/ ICS
  - Oral candidiasis
- Patient factors
  - Sx control: increase inhaler use increases dental risks
  - Oral hygiene: poor oral hygiene predispose to increase caries risks

Xanthine Bronchodilator

- MOA
  - Relax smooth muscles in AW
  - Reduce AW responsiveness to histamine, adenosine, methacholine & allergens
- Indication
  - Severe AW obstruction, including acute asthma
  - Maintenance tx in severe asthma & COPD
- Side effects
  - Nausea, vomiting, GORD, headache, anxiety, tremor, palpitations
- *Aminophylline & theophylline*
- Not commonly used

PDE inhibitors
Dental implications

- Narrow therapeutic index
  - Know signs of adverse effects
- Drug interaction(s)
  - Acyclovir
  - Benzodiazepine
  - $Beta_2$ agonists
  - Macrolide Abs (alternative in penicillin allergy)
- Patient factors
  - Can they be placed in supine position?

Inhaled Corticosteroids

- MOA
  - Reduce AW inflammation and bronchial hyper-reactivity
- Indication
  - Maintenance tx of asthma and COPD
- Side effects
  - Dysphonia, oropharyngeal candidiasis, facial irritation w/ nebs
- Inhalations: single agent or combination w/ Beta$_2$ agonist
- Oral: acute severe asthma, not for prevention

Corticosteroids

Inhaled

- *Beclomethasone*
  - *Qvar*
- *Budesonide*
  - *Pulmicort*
- *Ciclesonide*
  - *Alvesco*
- *Fluticasone*
  - *Flixotide*

Oral

- *Hydrocortisone*
  - *Solu-cortef inj*
- *Methylprednisolone*
  - *Methyl-pred, solu-Medrol inj*
- *Prednisolone*
  - *Solone, predmix, redipred*

ICS in the dental setting

- Side effects
  - Oropharyngeal candidiasis
  - Increased susceptibility to infection*
  - Impaired wound healing*
  - *Prolonged oral dose
- Increase carries risks
- Pregnancy before 12 weeks linked w/ orofacial cleft
- Drug interaction
  - Budesonide, fluticasone, methylprednisolone + azole: increase steroid adverse effects
  - Aspirin: decrease salicylate concentration
  - NSAIDs + oral steroids: increase risks GI ulceration

Corticosteroids ADRs

- Infection
- Delayed wound healing
- Steroid rosacea
- Perioral dermatitis
- Skin atrophy
- Bruising
- Acne
- Facial flushing
- Pupura
- Depigmentation
- Telangiecstasia
- Steroid induced crushing's

Leukotriene receptor antagonist

- MOA
  - Inhibit cysteinyl leukotriene receptor
  - Antagonist AW smooth muscle contraction
- Indication
  - Maintenance tx of asthma
  - Prevention of exercise induced bronchoconstriction
- Side effects
  - Headache, nausea, vomiting, abdominal pain
- *Montelukast (singulair)*

Monoclonal antibody against IgE

- MOA
  - Reduces immune's system response to allergen
- Indication
  - Maintenance tx of mod-severe allergic asthma in patients tx w/ ICS and w/ raised serum IgE levels
- Side effects
  - Inj site rxn, rash, bleeding
- *Omalizumab*
  - *Xolair*

Other

- **Benralizumab (Fasenra 30ng inj)**
  - Binds to and blocks the interleukin-5 receptor
  - ADR: pharyngitis
- **Dupilumab (Dupixent 200mg, 300mg inj)**
  - Inhibits activity of the cytokines interleukin-4 and -13
  - ADR: labial herpes simplex
- **Mepolizumab (Nucala 100mg inj)**
  - Binds to interleukin-5 (IL-5), reducing the production and survival of eosinophils
  - ADR: infections, nasal congestion

Cromones, leuk. Receptor antag. & monoclonal anti IgE

in the dental setting

- **Medication factors**
  - No serious drug interactions
  - Adverse rxn relating to cough & throat irritation
  - Omalizumab: monitor bleeding
- **Patient factor: sx control of asthma**

Asthma & COPD in the dental setting

- **Medications side effects**
  - Dry mouth → caries risks
  - GORD
  - Oropharyngeal candidiasis
  - Enamel defects
  - Periodontal disease
- **Patient factors**
  - Precipitating factors: avoidance
  - Sx control
  - Analgesic considerations
- **Recognize signs & symptoms of acute attack**

Dental implications

- **Oral Health**
  - Preventative care
  - Mouth breathing
  - Reduced salivary flow
  - Increase risk dental decay
- **Patient education**
  - Regular check ups
  - Dietary advice
  - Monitor dry mouth & tx accordingly
  - Spacer device
  - Rinse after ICS

Implications for Dentistry (Continued.)

- **Hypoxia in COPD**: impairs oral health and delays wound healing
- **Breathing difficulties**: medications and physical limitations affect oral breathing
- **Xerostomia**: reduced saliva due to anticholinergics and β2 agonists
- **Inhaled corticosteroids**: risk of oral candidiasis
- *Preventive care*: rinse mouth after use, maintain regular brushing

Use of Oral NSAIDs in Uncontrolled Asthma

- Oral NSAIDs may worsen uncontrolled asthma
- Inhibit cyclooxygenase (COX) enzymes
- Leads to overproduction of cysteinyl leukotrienes (CysLT)
- Increases type 2 eosinophilic inflammation
- Results in increased bronchoconstriction and asthma exacerbation
- Management: Use inhaled corticosteroids ± long-acting β_2 agonists

NSAID-Exacerbated Respiratory Disease (NERD)

- Moderate-to-severe asthma
- Increased risk of chronic rhinosinusitis/nasal polyps
- NSAIDs (e.g., aspirin, ibuprofen) can worsen respiratory symptoms
- **Management:**
- Inhaled corticosteroids ± long-acting β2 agonists
- Acetaminophen preferred for pain relief over NSAIDs

Signs of poor asthma control

- Use of relivers >3x/week (not during times of illness/exercise)
- Sx of asthma on most days of the week
    - Wheezing, coughing etc
- Early-morning or night-time sx at least once a week
- Frequent exacerbation of asthma at least every 6wks
- Poor level of peak expiratory flow
    - Less than 80% of their best score
- Attacks may occur infrequently but are life threatening or severe
- Referral to MGP for assessment and medication review

Community first aid protocol

Rule of 4's

- Sit the patient comfortably in an upright position
- Give 4 puffs of salbutamol
- Give each puff one at a time, with 4 breaths after each puff
- Use a spacer if possible
- Wait 4 minutes
- If no improvement give 4 more puffs
- If still no improvement call 000 immediately
- Continue to give 4 puffs every 4 minutes until the ambulance arrives

Terbutaline / ICS+LABA

- Give 2 doses initially, wait 4 minutes then give 1 more dose
- If no improvement call 000 and continue to give 1 dose every 4 minutes

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Opioid cough suppressants

- MOA
  - Depress medullary cough centers
- Indication
  - Symptom relief in non-productive cough
- Side effects
  - Drowsiness, constipation, nausea, vomiting
- Precaution
  - Asthma
- Contra-indication
  - COPD
- *Codeine, dextromethorphan, dihydrocodeine, pholcodine*

Mucolytics

- MOA
  - Reduce mucous viscosity & aid expectoration
- Indication
  - Adjuvant in disease w/ excessive mucous production
- Side effects
  - Nausea, bronchospasm, cough
- Not for chronic bronchitis & COPD
- *Acetylcysteine, bromhexine*

Discontinued: Cromones

- MOA
  - Inhibit release of inflammatory mediators from mast cells
- Indication
  - Maintenance tx of asthma
  - Prevention of exercise induced bronchoconstriction
- Side effects
  - Cough, throat irritation, bitter taste, transient bronchospasms
- *Cromoglycate*
- *Nedocromil*