Pharmacology of the Respiratory System

Part 1: Agents used to treat cough

Basic information

- Cough is one of the most common symptoms seen in clinical practice.
- The initial stimulus arises in the bronchial mucosa, where irritation results in stimulation of "Cough" receptors, which are specialized stretch receptors. Afferent impulses reach the cough center in the medulla via the vagus nerve and trigger a cough reflex.
- Cough may be acute (<3 weeks), subacute (3-8 weeks) or chronic (>8 weeks).

Causes of cough:

- **Acute cough:** respiratory infection is the most common cause.
- **Chronic cough:**
  - Upper airway cough syndrome (post-nasal drip): due to allergic rhinitis, chronic sinusitis or tonsillitis. It is the most common cause of chronic cough.
  - Bronchial asthma: the 2nd most common cause.
  - Gastoesophageal reflux disease (GERD).
  - Other causes: ACEIs, lung tumors, CHF.

MANAGEMENT OF COUGH

- **Specific treatment:** directed to the cause of cough e.g. antibiotics for respiratory infections.
- **Non-specific treatment:**
  - **Antitussives:** are used to stop dry cough.
  - **Mucolytics and expectorants:** are used in productive cough to liquefy bronchial secretions and facilitate their removal.

COUGH SUPPRESSANTS (ANTITUSSIVES)

Definition: they are drugs that reduce the frequency or intensity of coughing.

Peripheral antitussives: they ↓ afferent impulses of the cough reflex.

- **Steam inhalation with menthol or tincture benzoin compound**

– It is one of the best and easy ways to relieve acute cough. Inhaling water steam with or without medications (e.g. menthol) helps flush out mucus and moisturizes dry, irritated air passages. The efficacy of added medication is not proved.

- **Benzonatate**

– It is a glycerol derivative chemically related to the local anesthetic **procaine**. It depresses peripheral cough receptors at the lung by local anesthetic effect.

Central antitussives: they inhibit cough center in the medulla.

- **Opioids: Codeine and hydrocodone**

– They are *natural* derivatives of morphine. They directly inhibit the cough center in the medulla at doses that are lower than those needed for analgesia.
– They are generally not recommended because of adverse effects.

Adverse effects

– **D**rowsiness and constipation.
– Drug **d**ependence if used for long duration.
– Respiratory **d**epression in large doses. Children less than 5 years old are more sensitive to respiratory depression so, codeine is not recommended to children < 5 years.

N.B.
Some antihistamines (diphenhydramine) have antitussive activity, the mechanism is unknown. It has undesirable **atropine-like effect** → drying of mucosal secretions.

- **Opioid isomers: Dextromethorphan**

– It is *synthetic* L-isomer of opioids.
– It has selective central antitussive action with **very few** opioid effects (i.e. **less** addiction liability, analgesic action, respiratory depression, or constipation).
– High doses can cause neuropsychiatric effects e.g. sedation and hallucinations.

MUCOLYTICS

Definition: they are agents that reduce viscosity of respiratory secretions without increasing their amount.

■ Bromhexine

– Bromhexine acts on the mucus at the formative stages within the mucus-secreting cells. It disrupts the structure of acid mucopolysaccharide fibers in mucoid sputum and produces a less viscous mucus, which is easy to expel.
– Because bromhexine can disrupt the gastric mucosal barrier, it should be avoided in patients with peptic ulcer.

■ Ambroxol

– It stimulates synthesis and release of surfactant by type II pneumocytes. Surfactant acts as an anti-glue factor by reducing the adhesion of mucus to the bronchial wall.

■ *N*-Acetylcysteine and carbocyseine

– Acetylcysteine has free sulfhydryl (-SH) groups that break disulfide bonds in mucus and reduces its viscosity.
– Unlike acetylcysteine, carbocysteine does not act directly on mucus but rather, it affects the structural components of mucus.

Therapeutic uses of mucolytics

- Chronic respiratory diseases: chronic bronchitis, emphysema, bronchiectasis and cystic fibrosis.
- Post-operative and post-traumatic pulmonary complications.
- Chronic sinusitis and chronic otitis media.
- **N.B.** Intravenous *N*-acetylcysteine is used as an antidote for acetaminophen (paracetamol) toxicity (quite apart from its mucolytic activity).

EXPECTORANTS

Definition: drugs that increase water content and amount of the respiratory secretions. This action facilitates the removal of respiratory secretions.

Adequate hydration is the single most important measure to encourage expectoration. Using an expectorant in addition may produce the desired result.

■ Potassium iodide

– Iodides accumulates in the bronchial glands and stimulate secretion of low viscosity watery mucous.
– The use of iodides is accompanied by wide range of **side effects** including unpleasant (metallic) taste, increase lacrimal and salivary secretions, painful salivary swelling, hypothyroidism, and skin eruptions (rash).

■ **Guaifenesin**

– It is one of the most widely used over-the-counter (OTC) expectorants. It increases bronchial fluid secretions by unclear mechanism.

■ **Other expectorants**

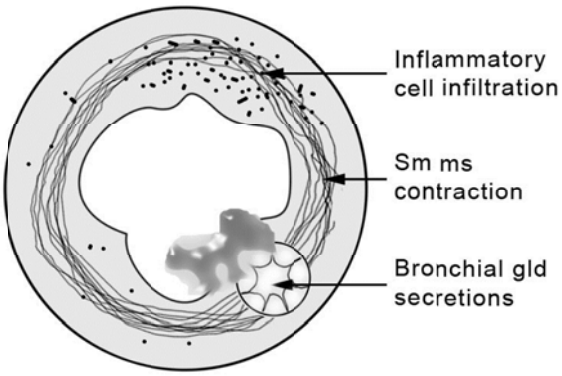
– Many other traditional expectorants (e.g., ammonium chloride, tincture ipecacuanha, herbal remedies) are found in numerous OTC cough mixtures. Their efficacy is doubtful, particularly in the dosages of most preparations.

Part 2: Therapy of bronchial asthma

Definition: *Asthma* is a chronic inflammatory disorder of the airways causing airflow obstruction and recurrent episodes of wheezing, breathlessness, chest tightness, and coughing.

Pathogenesis

Frequent exposure to allergic stimuli causes infiltration of the bronchial wall by acute and chronic **inflammatory cells.** These cells release many **inflammatory cytokines** e.g. histamine, adenosine, PGs, LTs, PAF, etc. leading to:



– Hypertrophy of airway smooth ms
– Increased mucus secretion that is difficult to expel.
– Congestion and edema of the respiratory mucosa.

Predisposing factors

- **Recurrent respiratory infection:** the most important factor.
- **Genetic factors:** asthma occurs in families with positive history of allergy.
- **Psychological factors:** are present in 40 % of asthmatics.

Clinical presentation

■ **Chronic asthma**

– There is dyspnea, chest tightness, coughing (particularly at night), and expiratory wheezing.

Drugs that cause bronchoconstriction in asthmatic patients

- Cholinomimetic drugs.
- Non-selective β- blockers.
- Histamine releasers e.g. morphine, trimetaphan, curare, penicillins.
- Adenosine
- NSAIDs

– Patients can present with mild intermittent symptoms that require no medications or only occasional short-acting inhaled β2-agonists to severe symptoms despite multiple medications.

- **Acute severe asthma**

– Uncontrolled asthma can progress to an acute state in which inflammation, airway edema, mucus accumulation, and severe bronchospasm that is poorly responsive to bronchodilator therapy.
– There are severe dyspnea, inspiratory wheezing, cyanosis; the patient may be able to say only a few words with each breath.

MANAGEMENT OF ASTHMA

BRONCHODILATORS

3 groups of bronchodilator drugs:

- **β-adrenergic agonists.**
- **Muscarinic receptor blockers: ipratropium.**
- **Xanthines**: **theophylline.**

β-adrenergic agonists

Classification

- **Non-selective β-receptor agonists:** e.g. adrenaline, isoprenaline and ephedrine. They are rarely used as bronchodilators.
- **Selective β2 agonists:**
  Short acting: salbutamol, terbutaline, fenoterol (duration 3-4 hrs).
  Long acting: salmeterol and formoterol (duration 12 hrs).

Mechanism of action

- Stimulation of bronchial β_2 receptors → ↑ cAMP → bronchodilatation.
- Stimulation of β_2 receptors in the mast cells → ↓ histamine release
- They ↓ bronchial inflammation and wall edema.

Administration

- In acute asthma: short acting β_2 agonists are given by inhalation or i.v infusion.
- In chronic asthma: long acting β_2 agonists are given orally or by inhalation.

Adverse effects

– **T**achycardia and arrhythmia due to:
  – *Reflex from hypotension (caused by VD of sk ms BV).*

  - *Direct activation of cardiac β_1 (due to loss of selectivity in high doses).*
- Tremors of skeletal ms and nervousness.
- Tolerance with prolonged use *(requiring temporary cessation of the drug).*
- Hypokalemia *(due to shift of K^+ from blood to cells).*

Muscarinic antagonists: Ipratropium bromide

- **Atropine** blocks M_3 receptors in airway ms leading to bronchodilatation through unopposed β_2 action, but it is **not used for treatment of asthma** because:
  - It is non-selective M_3 blocker leading to many side effects e.g. dry mouth and urine retention.
  - It can cross BBB and causes CNS side effects e.g. sedation.
  - It causes excessive dryness of bronchial secretions making it difficult to expel
- **Ipratropium is more preferred than atropine because:**
  - It is more selective muscarinic blocker than atropine.
  - It is quaternary ammonium compound that can't cross BBB.
  - Does not cause excessive dryness of bronchial secretions.
- **Ipratropium is not sufficient alone for bronchodilatation.** It is usually combined with **β_2 agonists** to get synergistic effect.

Methylxanthines

Classification

- **Natural:** e.g. caffeine, theophylline, and theobromine.
- **Semisynthetic:** e.g. aminophylline (salt of theophylline).

For asthma, the most commonly used xanthine is **theophylline.**

Mechanism and pharmacological effects

- Xanthines are adenosine **A receptor antagonists** leading to:
  - Bronchodilatation (block bronchoconstrictor effect of adenosine).
  - CNS stimulation (block the inhibitory effect of adenosine on the CNS)
  - ↓ mediator release from mast cells.
  - ↑ AV conduction.
- They inhibit **phosphodiestrase** enzyme (PDE3 and PDE4) → ↑ cAMP leading to:
  - Bronchodilatation (PDE4).
  - ↑ cardiac contractility and arrhythmogenic action (PDE3).
  - VC of cerebral and VD of peripheral vessels.
  - Relaxation of most smooth muscles (GIT, biliary, ureteric, etc).
  - Diuresis.

Therapeutic uses

- **Respiratory uses:**

– Acute severe asthma: aminophylline may be given by **slow i.v. infusion** 250 mg i.v. (at least over 15 minutes to avoid syncope or cardiac arrest), followed by maintenance i.v infusion of 0.7 mg/kg/h.
– Chronic bronchial asthma: sustained release tablets of theophylline 100-300 mg/day or rectal suppository of aminophylline can be given.

Evidence

In acute asthma, IV aminophylline is not likely to result in any additional bronchodilation compared to standard care with inhaled bronchodilators and steroids.

- **CNS uses:**

– To reverse CNS depression.
– To delay physical and mental fatigue (caffeine).
– Treatment of migraine (caffeine + ergotamine): to increase VC of cerebral blood vessels and increase absorption of ergotamine from GIT.
– Neonatal apnea syndrome: caffeine is the agent of choice.

- **CVS uses:**

– Acute pulmonary edema due to acute left sided HF.

Adverse effects

– **CNS:** irritability, headache, insomnia, nervousness and convulsions.
– **CVS:** palpitations, tachycardia, and arrhythmias. **Rapid i.v. injection** can cause hypotension, syncope and **cardiac arrest.**
– **GIT:** nausea, anorexia, **hyperacidity** and reactivation of peptic ulcer.

Precautions

- Aminophylline must be given by slow i.v.i. (at least over 15 minutes to avoid sudden syncope or cardiac arrest).
- Used with caution in severe cardiac disease, severe hypoxemia, and renal and hepatic disease and in elderly and neonates.
- They should not be given to patients with peptic ulcer.

Drug interactions

- **Enzyme inhibitors** (cimetidine and erythromycin) → ↑ serum levels of methylxanthines and ↑ their toxicity (arrhythmia).
- **Enzyme inducers** (smoking, rifampin) → ↓ their serum levels and reduce their effect.

Evidence

There is increased risk of arrhythmia when using both β2 agonist and xanthines in the same time because both drugs are arrhythmogenic.

REDUCTION OF BRONCHIAL INFLAMMATION

Corticosteroids

Mechanism of action

Corticosteroids can effectively ↓ bronchial inflammation and **hyperreactivity** through:

- They inhibit B cell function → ↓ antigen-antibody reaction.
- They inhibit T cell functions → ↓ mediators and cytokine release.
- They inhibit macrophage activity and stabilize lysosomal membranes.
- They inhibit mast cells → ↓ histamine release and capillary permeability.
- They inhibit phospholipase A2 enzyme →↓ synthesis of PGs & LTs.
- Corticosteroids cause up-regulation of β2 receptors.

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Why NSAIDs can not be given in bronchial asthma?

Because NSAIDs inhibit *Cox* enzyme but NOT *lipooxygenase* enzyme leading to accumulation of LTs which are potent bronchoconstrictors.

Use in asthma

- Acute severe asthma: **hydrocortisone** 200 mg given by i.v. injection**.** It may be repeated every 4 h if necessary.
- Chronic bronchial asthma: oral **prednisolone** 20 mg/d or **dexamethazone** 4-8 mg/d, or by inhalation (**beclomethasone**).
- **Inhaled corticosteroids (e.g. beclomethazone):** should be considered the 1st choice in newly diagnosed asthma. They have the following advantages:
  - Their efficacy is equal to inhaled β_2 agonists.
  - Minimal systemic side effects.

Adverse effects

- **If used systemically:** …..see endocrine chapter.
- **If used by inhalation:** → **oropharyngeal candidiasis.** It could be avoided by:
  - Mouth wash and gargle after each inhalation.
  - Candida infection can be treated by **nystatin mouthwash** or **amphotricin-B lozenges.**

Precautions

- They must be **withdrawn gradually** to avoid acute Addisonian crisis.
- **Diet** should be rich in K^+ and proteins and low in NaCl and carbohydrates.
- **Continuous check** for any increase in weight, edema, sugar in urine or BP.
- If the patient develops **acute infection**, he must be treated by adequate antibiotics with decreased dose of steroid.

PROPHYLACTIC TREATMENT

The following classes of drugs are not bronchodilators but are used to reduce frequency of asthma exacerbations.

Leukotriene inhibitors:

Zafirlukast and montelukast

- They **block leukotriene (LTD4) receptors.**
- Zafirlukast is given twice daily but montelukast is given once daily.

Zileuton

- It inhibits 5-lipooxygenase enzyme →↓ leukotriene synthesis.
- Zileuton is microsomal P450 inhibitor and can inhibit the metabolism of many drugs e.g. warfarin and theophylline.

- In clinical trials, leukotriene inhibitors reduced frequency of asthma exacerbations as equal to corticosteroids.
- Montelukast is approved to control asthma in children.

Mast cell stabilizers:

Cromolyn and nedocromil

- Cromolyn sodium (disodium cromoglycate) and nedocromil are poorly soluble drugs and should be given as micronized powder through spinhaler.
- They inhibit mast cell degranulation by unclear mechanism probably by altering the function of **chloride channels** in the mast cell membrane.
- They were used to reduce frequency of attacks **(i.e. prophylactic treatment)** in some allergic conditions e.g. bronchial asthma, allergic rhinitis, and allergic conjunctivitis.
- Their use now becomes **very limited** and has been largely replaced by leukotriene inhibitors.
- **Adverse effects** occur at site of administration e.g. local irritation of the throat, chest tightness, and bronchospasm.

N.B.

Mast cell stabilizers are not given during the acute attack. If given during the acute attacks, they may aggravate bronchospasm.

Ketotifen

- It is a 2nd generation antihistamine and a mast cell stabilizer.
- It is used as eye drops to treat **allergic conjunctivitis**, and orally as a prophylactic treatment in bronchial asthma and other seasonal allergies.

OTHER DRUGS USED IN TREATMENT OF BRONCHIAL ASTHMA

- **Expectorants and mucolytics:** to reduce mucus viscosity.

- **Mixture of oxygen (20%) and helium (80%): Heliox**
  - Helium is an inert gas. Its low density facilitates O_2 diffusion through obstructed airways → ↓ work of breathing.

- **Anti-IgE monoclonal antibodies: Omalizumab**
  - Omalizumab is a new drug that inhibits the binding of IgE to mast cells and prevents mast cell degranulation. It may also inhibit IgE synthesis by B cells.
  - It reduces frequency and severity of asthma even when the dose of corticosteroids is reduced.

Stepwise approach for treatment of chronic asthma

The management of stable asthma is now well established with a stepwise approach:

Step 1:	Inhaled short-acting B2 agonist (SABA) as required
Step 2:	Add inhaled steroid at 400 mcg/day
Step 3:	▪ Add inhaled long-acting B2 agonist (LABA) ▪ Still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day
Step 4:	▪ increase inhaled steroid up to 2000 mcg/day ▪ Add a 4th drug e.g. Leukotriene antagonist, SR theophylline, oral B2 agonist tablets.
Step 5:	▪ Use oral steroid tablet in lowest dose in addition to the high dose inhaled steroid (2000 mcg/day). ▪ Refer the patient for specialist care.

Treatment of acute severe asthma (status asthmatics)

Definition: acute severe asthma (status asthmatics) is a condition in which bronchodilators are poorly effective in relieving the attack.

Management

- Hospital admission.
- **Oxygen:** to maintain peripheral capillary O2 saturation (SpO2) between 94-98%.

- **β2 agonists:** use high dose by inhalation.
- Add **ipratropium bromide** by inhalation to the β2 agonists.
- **Hydrocortisone:** 200 mg i.v. / 6hs.
- Consider a single dose of **IV magnesium sulphate** (1.2-2 g over 20 min) to patients who failed to respond to initial inhaled bronchodilator therapy.
- Correction of acidosis and dehydration by i.v. fluids.

In acute severe asthma, IV **aminophylline** is not likely to result in any additional bronchodilation compared to standard care with inhaled bronchodilators and steroids.

Routine prescription of **antibiotics** is not indicated for patients with acute asthma.

Part 3: Oxygen therapy

Basic information

Arterial blood gases (ABG): normal values and interpretation

Parameter	Normal range	Interpretation
pH	7.34 – 7.44	– Acidosis ↓ binding of O2 to Hb (tissue hypoxia) – Alkalosis ↑ binding of O2 to Hb.
Arterial O2 saturation at ambient air **SaO2**	94 –100 %	– At open air, SaO2 must be > 94% and PaO2 >80 mm Hg (or 10.6 kPa). – **Hypoxemia** means SaO2 < 90% and/or PaO2 <60 mm Hg (or 8 kPa). At this level, supplemental oxygen should be administered. – At a PaO2 < 30 mmHg, the patient is at risk of death and must be oxygenated immediately.
Arterial O2 partial pressure **PaO2**	80 – 100 mmHg (10.6 –13 kPa)	
Arterial CO2 partial pressure **PaCO2**	35 – 45 mmHg (4.5 – 6 kPa)	– High value (**respiratory acidosis**) denotes hypoventilation problem (e.g. COPD). – Low value (**respiratory alkalosis**) denotes hyperventilation problem.
$HCO3^-$	22 – 26 mmol/L	– Low value denotes **metabolic acidosis**. – High value denotes **metabolic alkalosis**.

N.B.

- **Hypoxia:** low oxygen level at the tissues.
- **Hypoxemia:** low oxygen level in the arterial blood.

OXYGEN THERAPY

Key points

- Oxygen is stored either in liquid or gaseous form in metal cylinders (green tanks). Oxygen concentrators are also available for long term home use; they extract oxygen from air using electric current.
- Oxygen is commonly delivered to the patient through nasal cannula or face mask.
- Diagnosis of hypoxemia is done either by pulse oximeter (easy) or by arterial blood gas analysis (see table for reference ranges).
- Dyspnea does not necessarily indicate hypoxemia. Severe hypoxemia can be present without dyspnea and vice versa.

Pulse oximeter

Indications of oxygen therapy

Oxygen should not be used routinely unless there is evidence of hypoxia.

- **Acute hypoxic conditions:** acute MI, acute pulmonary edema, carbon monoxide poisoning, cardiac and respiratory arrest, low COP and metabolic acidosis (bicarbonate <18mmol/L).
- **Chronic hypoxic conditions** (long-term oxygen therapy): e.g. COPD and CHF.

Monitoring and stopping

- ABG or oximetry should be done within 2 hours of starting oxygen therapy and oxygen delivery is adjusted accordingly.
- Oxygen should be stopped when SaO2 > 92% while the patient is breathing at room air.
- For patients with COPD, the oxygen saturation target should not exceed 92% to avoid CO2 retention (see below).

Dangers, adverse effects and precautions

– Fire and explosions: (safety measures are required).
– Irritation of nose, pharynx and trachea.
– Inhibition of mucociliary function → ↓ tracheal outflow of mucous.
– CO2 toxicity:

- In patients with COPD who receive supplementary O2, CO2 retention can occur through 2 mechanisms:
  - Increase O2 saturation of blood reduces deoxygenated Hb which carries CO2 in blood (in the form of bicarbonate).
  - In patients with COPD, hypoxia is the main stimulant of respiration (hypoxic drive). If 100% O2 was administered, hypoxia is corrected and the hypoxic drive is lost leading to CO2 retention.
- CO2 retention can lead to headache, drowsiness (narcosis) or even death.
- Prevention: In people with COPD, CO2 toxicity can be prevented by careful control of the supplemental oxygen. Just enough oxygen is given to maintain an oxygen saturation of 88 - 92%.

– Retrolental fibroplasias: high concentration of O_2 in neonates (<32 weeks) stimulates fibrous tissue formation posterior to the eye lens and permanent blindness. So, O_2 should be used only when needed and its concentration must not exceed 35-40% in premature infants.

– Pulmonary oxygen toxicity: high O2 concentrations (> 60%) given for >48 hours can damage alveolar membrane and cause alveolar edema.

Notes

Review Questions

- Discuss different drugs used in the treatment of **cough.**
- Discuss the different lines of treatment of **bronchial asthma.**
- Discuss pharmacology of **xanthenes:** classification, mechanism of action, pharmacologic effects, therapeutic uses, and side effects.
- Mention uses of mucolytics.
- Mention precautions during the use of methylxanthines.
- Mention precautions during the use of corticosteroids in BA.
- Mention the main side effects of oxygen therapy.
- Mention the main side effects of selective beta-2 agonists.
- Mention the main lines of treatment of status asthmaticus.
- Mention 3 drugs causing bronchoconstriction and mention the mechanisms.

Mention the pharmacodynamic principles underlying the use of:

– Beta-2 agonists in bronchial asthma.
– Methylxanthines in bronchial asthma.
– Montelukast for prophylaxis of bronchial asthma.
– Acetylcystiene in chronic bronchitis.

Mention the rationale of the following combinations:

– Oxygen with helium in chronic obstructive lung disease.
– Corticosteroids with beta-2 agonists in bronchial asthma.

Of each of the following questions, select ONE BEST answer:

1. Which of the following mucolytics act by breaking disulfide bonds of proteoglycans, which causes depolymerization and reduction of viscosity of sputum?
A. Acetylcysteine
B. Iodides
C. Trypsin
D. Water vapor
E. Licorice

2. Which of the following drugs is a methylxanthine used in the treatment of bronchial asthma?
A. Salbutamol
B. Ipratropium
C. Theophylline
D. Pentoxifylline
E. Dipyridamole

3. The mechanism of methylxanthines action in bronchial asthma is:
A. Inhibition of the enzyme phosphodiesterase
B. Beta2 -adrenoreceptor stimulation
C. Inhibition of the production of inflammatory cytokines
D. Inhibition of M-cholinoreceptors
E. Inhibition of leukotriene receptors

4. Which of the following drugs can decrease the effect of leukotrienes in the inflamed tissue?
A. Zileuton
B. Montelukast
C. Theophylline
D. Loratidine
E. Cromoglycate

5. Which of the following drugs can decrease the concentration of leukotrienes in the inflamed tissue?
A. Zileuton
B. Montelukast
C. Theophylline
D. Loratidine
E. Cromoglycate

6. Indicate the expectorant which increase lung surfactant:
A. Sodium benzoate
B. Trypsin
C. Ambroxol
D. Tincture Ipecacucnha
E. Iodides

7. Which one is considered the major side effect of Theophylline:
A. Bradycardia
B. Arrhythmia
C. Depression of respiratory center
D. Elevation of the arterial blood pressure
E. Depression of mood

8. Choose the drug belonging to class mast cell stabilizers:
A. Zileuton
B. Zafirlucast
C. Epinephrine
D. Salbutamol
E. Sodium cromoglycate

9. Which of the following drugs can disrupt mucus synthesis within bronchial glandular cells?
A. Potassium iodide
B. Acetylcystiene
C. Bromhexine
D. Trypsin
E. Ambroxol

10. Which of the following is not a recognized action of terbutaline?
A. Diuretic effect.
B. Cardiac arrhythmia.
C. Skeletal muscle tremors.
D. Smooth muscle relaxation.
E. Tachycardia.

11. Disodium cromoglycate has as its major action:
A. Smooth muscle relaxation in the bronchi.
B. Stimulation of cortisol release by the adrenals.
C. Block of calcium channels in the lymphocytes.
D. Block of mediator release from mast cells.
E. Block of cAMP synthesis in the basophils.

12. The following may induce bronchospasm EXCEPT:
A. Propranolol.
B. Morphine.
C. Aspirin
D. Captopril
E. Theophylline.

13. Which of the following drugs given for cardiovascular indications might complicate the management of asthma in the same patient?
A. Hydralazine.
B. Verapamil.
C. Nitroglycerine
D. Quinidine.
E. Propranolol.

14. Methylxanthines:
A. Cause decreased gastric acid secretion.
B. Are potent diuretics in most patients.
C. Cause increase in mental alertness and even insomnia in some patients.
D. Are potent vasoconstrictors.
E. Cause fatigue of respiratory muscles

15. Theophylline is therapeutically useful in asthma because:
A. It has no significant effects on the heart.
B. It stimulates the respiratory center.
C. It increases mediator release from mast cells.
D. It is a potent stimulant of beta-receptors.
E. It increases cAMP without desensitizing receptors in bronchioles

16. In status asthmaticus, all are true EXCEPT:
A. Salbutamol and ipratropium may be given by nebulized aerosol
B. IV aminophylline is useful.
C. Hydrocortisone is preferred to prednisolone for initial therapy.
D. Humidified oxygen should be given.
E. Morphine provides useful sedation

17. All of the following drugs are central antitussives EXCEPT:
A. Codeine
B. Pholcodeine
C. Noscapine
D. Dextromethrphane
E. Ticture benzoin Co.

18. In designing a dosage regimen for aminophylline all are true EXCEPT:
A. Children (ages 3-12 y) have faster clearance of this drug than adults or infants
B. Patients with history of cardiac disease should be carefully monitored, because aminophylline may induce ventricular extrasystoles and other arrhythmias
C. Excessive doses result in skeletal muscle tremors and CNS excitation.
D. The use of tobacco by the patient inhibits the metabolism of aminophylline.
E. Erythromycin increases the serum levels of theophylline.

19. Ipratropium bromide is:
A. Derivative of phenylephrine.
B. Less effect on sputum viscosity.
C. Tertiary amine
D. Given by inhalation, oral and parenteral routes
E. More effective bronchodilator than B2 agonist

20. Disodium cromoglycate, all are true EXCEPT:
A. Is well absorbed from the GIT.
B. Stabilizes mast cells and prevent their degranulation.
C. Is inhaled as a powder for prophylaxis of bronchial asthma.
D. Can cause bronchconstriction during administration.
E. Can be used in the treatment of allergic rhinitis.

21. All of the following drugs are mucolytics EXCEPT:
A. Bromhexine
B. Iodides
C. Acetylcysteine
D. Ambroxol
E. Ketotifen

22. Oropharyngeal candidiasis is a common side effect of which of the following:
A. Inhaled beta-2 agonists
B. Inhaled ipratropium
C. Inhaled corticosteroids
D. Inhaled disodium cromoglycate
E. Oxygen

23. Oropharyngeal candidiasis could be treated by:
A. Liquorice lozenge
B. Amphotericin-B lozenge
C. Ampicillin
D. Aminoglycosides
E. Steam inhalation

24. Which of the following statements is NOT true:
A. Antitussives decrease the amount and liquefy bronchial secretions.
B. Peripheral antitussives are used when the cough arises above the larynx
C. Mucolytics used in the treatment of productive cough to liquefy copious bronchial secretion.
D. Iodides can be used as expectorant and mucolytic
E. Inhalation of water vapor or adequate intake of water is an excellent mucolytic & expectorant.

25. Combination of B2 agonists and ipratropium can lead to:
A. Antagonistic effect.
B. Additive effect.
C. Potentiating effect.
D. Synergistic effect.
E. No effect

26. The Symptoms of allergen-mediated asthma result from which of the following?
A. Increased release of mediators from mast cells
B. Increased adrenergic responsiveness of the airways
C. Increased vascular permeability of bronchial Tissue
D. Decreased calcium influx into the mast cells
E. Decreased prostaglandin production

27. Drugs that can dilate bronchi during an acute asthmatic attack include all of the following except
A. Epinephrine
B. Terbutaline
C. Nedocromil
D. Theophyline
E. Ipratropium

28. Which of the following is a prophylactic agent that appears to stabilize mast cells?
A. Aminophyline
B. Cromolyn
C. Epinephrine
D. Ipratropium
E. Metaproterenol

29. Which of the following has overdose toxicity that includes insomnia, arrhythmias, and convulsions?
A. Aminophylline
B. Cromolyn
C. Epinephrine
D. Ipratropium
E. Metaproterenol

30. Which of the following is a very long acting β2 – selective agonist that is used for asthma prophylaxis?
A. Aminophyline
B. Cromolyn
C. Epinephrine
D. Ipratropium
E. Salmeterol

31. In the emergency department, the preferred first-line therapy for asthma exacerbation is
A. Theophyline
B. A beta2-agonist
C. A corticosteroid
D. Cromolyn sodium
E. An antihistamine

32. A drug administered by inhalation of powder as a prophylactic for asthma
A. Ephedrine
B. Disodium cromolyn
C. Isoproterenol
D. Ocytriphylline
E. Epinephrine

33. When administering oxygen to a hypoxemic patient with COPD, the target oxygen saturation level would be:

A. 94 – 98%
B. 92 – 94%
C. 88 – 92%
D. 60%
E. 100%

34. Regarding oxygen therapy, one statement is true:

A. Severe dyspnea does not necessarily indicate hypoxia.
B. Oxygen should be started immediately to all acutely ill patients.
C. Oxygen should be stopped as soon as oxygen saturation reaches 88% in room air.
D. Acidosis increases binding of oxygen to hemoglobin.
E. Oxygen therapy reduces mortality in acute myocardial infarction.

35. Which of the following drugs given for cardiovascular indications might precipitate bronchospasm in asthmatic patients?

A. Hydralazine.
B. Verapamil.
C. Nitroglycerine
D. Quinidine.
E. Adenosine.

Answers

1 A	7 B	13 E	19 B	25 D	31 B
2 C	8 E	14 C	20 A	26 A	32 B
3 A	9 C	15 E	21 E	27 C	33 C
4 B	10 A	16 E	22 C	28 B	34 A
5 A	11 D	17 E	23 B	29 A	35 E
6 C	12 E	18 D	24 A	30 E	