**Question 1**

Which of the following drug is likely to offer the best response for a patient who presents to the ED with an acute exacerbation of COPD?

A Prednisolone

B Ipratropium

C Salmeterol

D Cromolyn

Explanation (B)

Salmeterol: slow onset, primarily preventative action

Cromolyn: Prevents acute bronchospasm, used prophylactically

Prednisolone: powerful prophylaxis of exacerbations

Ipratropium: Effective bronchodilator improves functional capacity.

Note: The mainstay of bronchodilator treatment in acute asthma is inhalation of short-acting beta-2-selective adrenergic agonists.

Inhaled anticholinergics

In accordance with current guidelines for asthma management prepared by the Expert Panel of the National Asthma Education and Prevention Program inhaled ipratropium be used in addition to inhaled SABA for patients with severe exacerbations who are in the emergency department.

There is still a debate if dual therapy is more effective than SABA alone, in patent with severe airflow obstruction.

Webs sources report that inhaled short-acting beta adrenergic agonists are the mainstay of therapy for an exacerbation of COPD because of their rapid onset of action and efficacy in producing bronchodilation. Inhaled anticholinergic drugs like ipratropium offer a possible added benefit. They are not superior to the SABA

The textbook reports that ipratropium appears to be AS effective as albuterol in patients with COPD who have at least partially reversible obstruction. Longer acting antimuscarinic (tiotropium) agents have been approved for maintenance therapy for COPD. They have shown to improve functional capacity of patients with COPD and to reduce frequency of exacerbations.

Also, antimuscarinic drugs appear to be slightly less effective in reversing asthmatic bronchospasm.

I am going to leave the answer as is, but it does not appear that ipratropium is superior to beta agonists in the treatment of COPD (rather as effective)

**Question 2**

Which of the following drugs does not possess bronchodilator activity?

A Atropine

B Adrenaline

C Theophylline

D Sodium cromoglycate

Explanation (D)

Sodium Cromoglycate has no effect on bronchial smooth muscle tone. It is ineffective in reversing asthmatic bronchospasm. It is used for the prophylactic treatment of exercise and allergen induced asthma. It inhibits cell activation by alteration in function of cell membrane chloride channels. It prevents mast cell degranulation.

**Question 3**

Regarding theophylline, which of the following is not an overdose effect?

A Hypokalaemia

B Seizures

C Tachycardia

D Hypocalcaemia

Explanation (D)

Chronic or subacute theophylline poisoning can occur as a result of accidental overmedication or use of a drug that interferes with theophylline metabolism (e.g., cimetidine, ciprofloxacin, and erythromycin. Theophylline toxicity includes: sinus tachycardia, tremor, vomiting and metabolic acidosis. Hypotension, tachycardia, hypokalaemia, and hyperglycaemia may also occur, probably owing to β2-adrenergic activation. (Mechanism poorly understood) but the effects can be ameliorated by β blockers. Cardiac arrhythmias include atrial tachycardias, premature ventricular contractions, and ventricular tachycardia. In severe poisoning (e.g., acute overdose with serum level > 100 mg/L), seizures often occur and are usually resistant to common anticonvulsants.

**Question 4**

Which of the following statements regarding Theophylline is correct?

A It reduces GFR

B It is a positive chronotrope and inotrope

C It has a Vd of 10L/kg

D It is thought to increase blood viscosity

Explanation (B)

Theophylline increases GFR and is thought to decrease blood viscosity. It is the most potent drug for bronchodilitation.

VD= 0.3-0.7L/Kg.

Theophylline is a non selective phosphodiesterase inhibitor. It has inotropic and chronotropic effects in the manner of milrinone (a PDE3 inhibitor) and vasodilatory effects in the manner of sildenafil (a PDE5 inhibitor) in addition to its bronchodilator effects

**Question 5**

The Beta 2 sympathomimetic with the longest duration of action is?

A Sotalol

B Salmeterol

C Isoprotenerol

D Terbutaline

Explanation (B)

Isoprotenerol is a β1 and β2 adrenoreceptor agonist which was commonly used to treat asthma before the more widespread use of salbutamol, which has more selective effects on the airways. Its primary use is for bradycardia or heart block. By activating β1 adrenergic receptor in the heart, it induces positive chronotropic, dromotropic, and inotropic effects. The plasma half-life for isoprotenerol is approximately two minutes.

Terbutaline is used as a fast-acting bronchodilator (often used as a short-term asthma treatment) and as a tocolytic to delay premature labour. The inhaled form of terbutaline starts working within 15 minutes and can last up to 6 hours.

Sotalol is a non-selective competitive beta-adrenergic receptor blocker that also exhibits Class III antiarrhythmic properties.

Salmeterol is a long-acting β₂ adrenergic receptor partial agonist used in the maintenance and prevention of asthma symptoms and maintenance of chronic obstructive pulmonary disease symptoms. Like femoterol (a full agonist), these agents achieve a long duration of action (>12hrs)

**Question 6**

Which is an effect of methylxanthines?

A Negative inotropic effect

B Stimulation of cell surface adenosine receptors

C Weak anti-diuresis

D Increased strength of skeletal muscle contraction

Explanation (D)

The methyxanthines have effects on the CNS, kidney, CVS, GIT and skeletal and smooth muscle. The therapeutic effect is not just confined to the airways (bronchodilation)-relaxation of smooth muscle via an increase in CAMP, they also strengthen the contractions of isolated skeletal muscles and have potent effects in improving contractility and reducing fatigue of the diaphragm in patients with COPD. They cause mild cortical arousal with increased alertness and deferral of fatigue. They cause both positive inotropic and chronotropic effects on the heart. They are weak diuretics. They inhibit surface cell adenosine receptors- these receptors cause smooth muscle airway contraction and promote histamine release. The third mechanism of action of Methylxantines is the enhancement of histone deacetylation, a process involved in corticosteroids mechanism of action.

**Question 7**

All of the following drugs cause DIRECT bronchodilation EXCEPT

A Theophylline

B Disodium cromoglycate

C Atropine

D Adrenaline

Explanation (B)

Disodium cromoglycate are only of value when taken prophylactically. When used as aerosols they inhibit both antigen and exercise induced asthma. Chronic usage slightly reduces the overall level of bronchial reactivity. These drugs however, have no effect on airway smooth muscle tone and are ineffective in reversing asthmatic bronchospams

**Question 8**

Salbutamol may cause all the following except

A Decreased PO2 initially

B Hyperkalaemia

C Weakness

D Skeletal muscle tremor

Explanation (B)

Salbutamol is used in the acute treatment of hyperkalemia. In children, following large amounts, salbutamol can produce severe vomiting.

A transient fall in PaO2 may occur due to vasodilatory effects of salbutamol. The vasodilating action may increase perfusion of poorly ventilated lung units, transiently decreasing arterial oxygen tension. This effect is usually small, but may occur with any bronchodilator. The significance of the drop depends on the initial PaO2 of the patient.

**Question 9**

Regarding Ipratropium, which of the following statements is correct?

A Inhibits mast cells

B Causes miosis

C It has an onset 3-5mins after administration

D Readily enters the CNS

Explanation (C)

Ipratropiums onset of action is 1-3 min and has a duration of action of 4-6hrs. It blocks acetylcholine causing bronchodilitation. It does not cause miosis nor does it enter the CNS

Extra:

Minimal systemic absorption Ipratropium is unable to cross the BBB being a quaternary ammonium derivative of atropine Nebulised ipratropium can precipitate glaucoma due to direct action on the eye Produces mydriasis and accommodation difficulties via the same direct mechanism that is prevented by using a mouthpiece The onset of action is slow - 30-60 mins to maximum effect, however the duration is long - 6-8 hours Cholinergic antagonists probably have little effect on mast cells, microvascular leak or chronic inflammatory response

Other sources report:

1-onset within 15mins peak effect 1-2 hours

2-The time course of action of ipratropium bromide also differs from the beta2-agonists in that although the onset of bronchodilator response is seen within three to five minutes of administration, peak response is not reached until 1.5 to 2 hours after inhalation. The duration of significant bronchodilator action is up to six hours.

I have thus changed the onset duration answer to 3-5min. Be aware that no one can agree and the current prescribed textbook does not give an onset time.

**Question 10**

How does Cromolyn reduce bronchial reactivity?

A Inhibiting eosinophil chemotactic factor

B Relaxing smooth muscle cells

C Inhibiting mediated mast cell degranulation.

D Direct bronchodilation

Explanation (C)

Cromolyn does not inhibit the IGE interaction with the agonist or the mast cell but rather once the complex is formed it prevents the degranulation of the mast cell

**Question 11**

Disodium cromoglycate has the following features

A When used regularly, it reduces airway hyperactivity

B They have the same potency as inhaled steroids

C It is useful in an acute asthma attack

D It reduces airway smooth muscle tone

Explanation (A)

The drug is not widely used anymore. They have no effect on airway smooth muscle tone and are ineffective in reversing asthmatic bronchospasm; they are only of value if taken prophylactically.

Their mechanism of action seems to involve a decrease in the release of mediators form mast cells. The drugs have no bronchodilator action but can prevent bronchoconstriction caused by a challenge with antigen to which the patient is allergic.

They do not have the same potency as inhaled steroids and the only way of determining if they are effective is to trial the patient for 4 weeks and see if their is a noticeable response

Note: Intal and Intal forte are used frequently by the respiratory physicians for rapid airflow induced asthma

**Question 12**

Which of the following asthma medications does not lead to direct smooth muscle relaxation?

A Ipratropium bromide

B Salbutamol

C Theophylline

D Disodium cromoglycate

Explanation (D)

The drug is not widely used anymore. They have no effect on airway smooth muscle tone and are ineffective in reversing asthmatic bronchospasm; they are only of value if taken prophylactically.

Their mechanism of action seems to involve a decrease in the release of mediators form mast cells. The drugs have no bronchodilator action but can prevent bronchoconstriction caused by a challenge with antigen to which the patient is allergic.

They do not have the same potency as inhaled steroids and the only way of determining if they are effective is to trial the patient for 4 weeks and see if their is a noticeable response

**Question 13**

Which is true regarding theophylline?

A Theophylline can cause seizure in toxic doses in the absence of preceding neurological symptoms

B Theophylline is positively inotropic and negatively chronotropic

C Theophylline is a mast cell stabilizer

D Theophylline does not cause smooth muscle relaxation

Explanation (A)

Theophylline produces direct bronchodilation. It inhibits the phosphodiesterase enzyme family. This results in higher concentration of cAMP and in some tissues- cGMP. This effect is the working theory as to the mechanism of smooth muscle relaxation in the bronchi and reduction in the immune and inflammatory activity of specific cells. At low concentrations the positive inotropic and chronotropic cardiac effects are due to an inhibition of presynaptic adenosine receptors in sympathetic nerves increasing catecholamine release at nerve endings. At higher (>10umol/L) concentrations the effects are associated with the inhibition of phosphodiesterase and increase in cAMP, which may result in an increased calcium influx. At much higher concentrations (>100umol/L) sequestration of calcium by the sarcoplasmic reticulum is impaired. Theophylline has a narrow therapeutic window. High levels >40mg/L may cause seizures or arrhythmias. Seizures may not be preceded by gastrointestinal or neurological warnings.

**Question 14**

Which of the following asthma drugs reduces bronchial reactivity?

A Omalizumab

B Theophylline

C Corticosteroids

D Ipratropium bromide

Explanation (C)

Corticosteroids reduce bronchial reactivity and reduces the frequency of exacerbations. Antimuscarinic drugs such as ipratropium bromide are effective bronchodilators. Omalizumab (an anti-IGE monoclonal antibody) inhibits the binding of IGE to mast cells but does not activate IGE already bound to these cells and thus does not provoke mast cell degranulation. Theophylline is an effective bronchodilator.

Note: cromolyn slightly reduces the overall bronchial reactivity. But these drugs have no effect on airway sooth muscle tone and are ineffective in reversing asthmatic bronchospasm. They are only of value when taken prophylactically

**Question 15**

Which of the following drugs is a bronchodilator?

A Ketamine

B Cromolyn

C Corticosteroids

D Muscarininc agonists

Explanation (A)

Muscarinic antagonists e.g. atropine cause bronchodilation. Corticosteroids do not relax airway smooth muscle directly but reduce bronchial reactivity and reduce the frequency of asthma exacerbations if taken regularly. Cromolyn has no effect on airway smooth muscle tone and is ineffective in reversing asthmatic bronchospasm. Ketamine relaxes bronchial smooth muscle and may be helpful in patients with reactive airways and those experiencing bronchoconstriction.

 Note: in the prescribed text, the introduction to drugs used in asthma, it reports that inhaled corticosteroids produce modest immediate bronchodilation. I do not agree with this.

Online sources report: Inhaled glucocorticoids suppress airway inflammation by activating anti-inflammatory genes, switching off inflammatory gene expression and inhibiting inflammatory cells. In addition they enhance beta 2 adrenergic signalling by increasing beta 2 receptor expression and function. This leads to increased beta 2 agonist effects (eg mast cell stabilisation), protection form the down-regulation of beta 2 receptor that is associated with long term beta 2 agonist administration and reversal or prevention of the uncoupling of beta 2 receptor from G protein, which is induced by some inflammatory mediators. The net effect is control of symptoms and signs in asthma patients.

Ketamine is the right answer