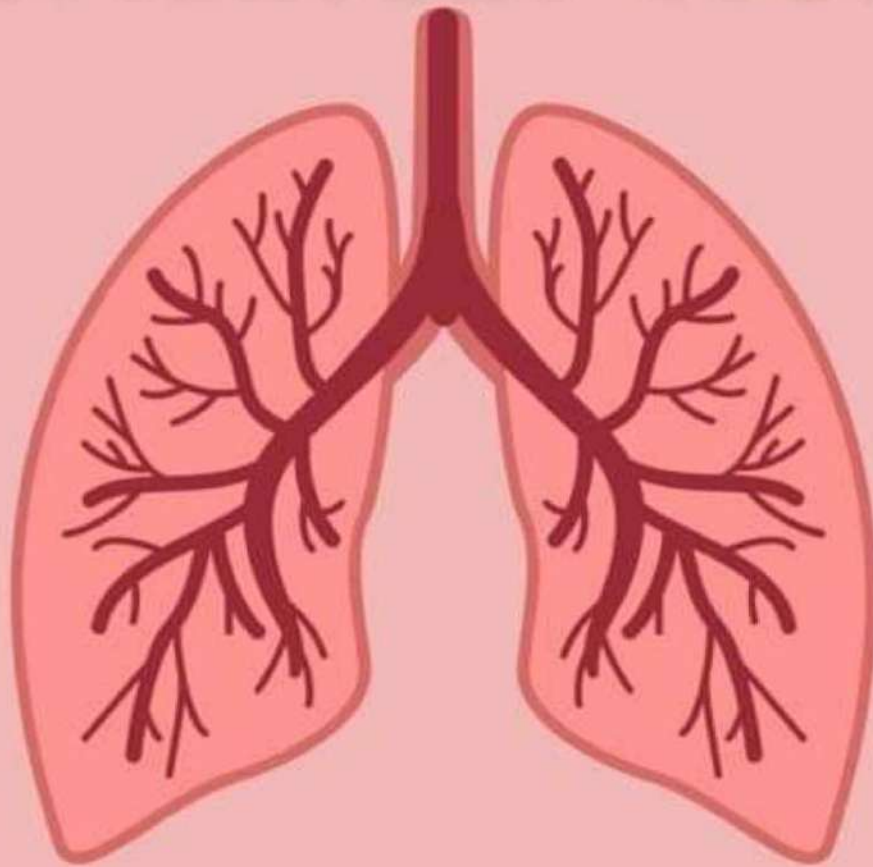




RESPIRATORY SYSTEM



SUBJECT : Pharmacology

LECTURE : 4 - part 1

DONE BY : Johainah Taha



Lecture 4: Treatment of allergic rhinitis (AR) and cough

Respiratory system
Second year
Medical school
Hashemite University
2nd semester 22/23
Sofian Al Shboul, MD, PhD.

محاضرة اليوم سهلة و لطيفة كثير 🧯 حاترك الكم اي مصدر رجعت اله و خصوصا الفيديوهات 🙌 و كمان ضفت فقرات الكتاب الي مو مكتوبة للاحتياط



Antihistamines - Learn with Visual Mnemonics! - YouTube



Visual Learner Studios uses visual mnemonics to teach pharmacology fast and efficiently. Website:...

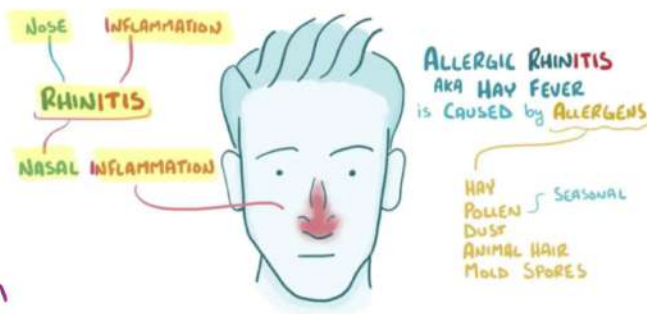
YouTube · VL Studios · Mar 10, 2016



Allergic rhinitis (AR)

• An **inflammation** of the mucous membranes of the **nose** and is characterized by:

1. Sneezing عطس
2. itchy nose/eyes حكة بالأنف أو العين
3. watery rhinorrhea سيلان الأنف
4. nasal congestion/itching احتقان الأنف
5. sometimes a nonproductive cough.



A non-productive cough, also known as a dry cough, refers to a cough that does not produce sputum

Definition & symptoms

- Caused by immunoglobulin E (IgE)-mediated reactions to inhaled allergens (over-reaction of the immune system)
- It is often **co-morbid with asthma** and/or **conjunctivitis**.
- 20 to 40 years old

Allergic rhinitis and asthma

If you have asthma, not treating your allergic rhinitis or hay fever symptoms adequately can lead to worsening of symptoms and increases the risk of a sudden asthma attack.

90% of people with asthma have allergic rhinitis

30% approximately of people with asthma have undiagnosed allergic rhinitis

Treating allergic rhinitis symptoms in people with asthma has been shown to reduce asthma exacerbations and A&E visits by up to **80%**

AllergyUK



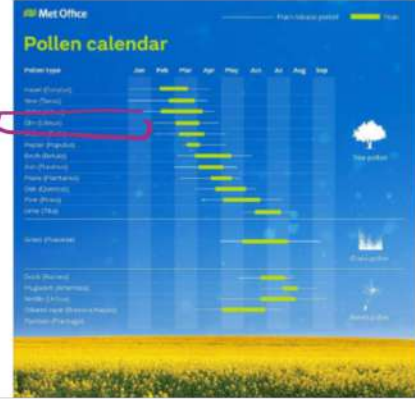
الأشخاص الي معهم allergic rhinitis يكون معهم كمان حساسية مع او او التهاب بال conjunctiva بالعين و ليس العكس

و ما في الها treatment و chronic، فكل الادوية بتعالج symptoms و ليس cause؛ السبب انها بتكون مرتبطة بجينات مهمة كثير (immune related) و ما بقدر اعمل الها inhibition مثل

IL33 - IL33R - IL13

Risk factors & triggers

- Known as “hay fever” ← القش والشعب
- An attack may be precipitated by inhalation of an allergen (such as dust, pollen, or animal dander). ← عيار ← نقاع ← وبر الحيوانات
- Genetic factors: IL33, IL33R and IL13. ← Immune related genes



The Allergy flare up at a specific time of the year

ال MET office هو مكتب للارصاد الجوية موجود في بيريطانيا بصدر هاد ال Pallon Calendar و بيحكيلي انه كل شهر كيف وضع الجو، لحتى الناس الي عندهم allergic rhinitis و asthma يكونوا عارفين متى بناسبهم يروحوا عالحدائق





• Sensitization is a process by which the immune system will produce the IgE antibody in response to certain types of particles or allergens it considered abnormal



Pathophysiology

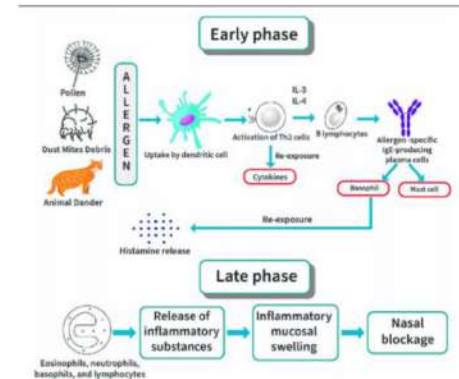
It is type 1 hypersensitivity



• First exposure to allergens (no symptoms) (Sensitization)

• DCs take up the allergen, process it present it to naive T cells which will activate and differentiate them into allergen-specific type 2 T helper cells (T_H2 cells) >> induce the activation of B cells >> plasma cells will produce allergen-specific IgE that binds to mast cells and basophils

• The mast cells release mediators, such as histamine, leukotrienes, and chemotactic factors that promote bronchiolar spasm and mucosal thickening from edema and cellular infiltration.



الذي بهم الدكتور بهاد السلايد انه نكون عارفين انواع ال cell mediated لانه
اكيد الادوية بتستهدفهم (ممكن يجي عليهم سؤال)

Histamine effects

- Histamine is present in all tissues
- High concentrations in mast cells and basophils
- Functions as a neurotransmitter in the brain
- Released by allergies, anaphylaxis and as a result of destruction of cells (cold, toxins from organisms, venoms from insects and spiders, and trauma)
- H1 receptor: smooth muscle contraction and increasing capillary permeability
- Can enhance the secretion of proinflammatory cytokines

H₁ Receptors

EXOCRINE EXCRETION
Increased production of nasal and bronchial mucus, resulting in respiratory symptoms.

BRONCHIAL SMOOTH MUSCLE
Constriction of bronchioles results in symptoms of asthma and decreased lung capacity.

INTESTINAL SMOOTH MUSCLE
Constriction results in intestinal cramps and diarrhea.

SENSORY NERVE ENDINGS
Causes itching and pain.

شايقين شو الهستامين بي عمل ؟؟ ال anti-histamine بي عمل عكسه

There are 4 types of Histamine Receptors :

H1: it is the main target of clinically use of drugs, it is expressed on vascular epithelium, smooth muscle cells, brain and peripheral nerve ending.

H2

H3

H4



Pharmacological treatments

Note that these drugs are specific for Allergic rhinitis



1. Intranasal corticosteroids
2. Antihistamines
3. α -Adrenergic agonists
4. Cromolyn and leukotriene receptor antagonists

ANTIHISTAMINES (H ₁ -RECEPTOR ANTAGONISTS)	
Azelastine ASTELIN [®] , ASTEPRO [®]	Allergic rhinitis
Cetirizine ZYRTEC	Allergic rhinitis
Desloratadine CLARINEX	Allergic rhinitis
Fexofenadine ALLEGRA	Allergic rhinitis
Loratadine CLARITIN	Allergic rhinitis
α -ADRENERGIC AGONISTS	
Oxymetazoline AFRIN, DRISTAN	Allergic rhinitis
Phenylephrine NEOSYNEPHRINE, SUDAFED PE	Allergic rhinitis
Pseudoephedrine SUDAFED	Allergic rhinitis
AGENTS FOR COUGH	

****The most effective drugs are corticosteroids that are given intranasally not by inhalation**



مهمة



Pharmacological treatments:

Corticosteroids

INHALED CORTICOSTEROIDS	
Beclomethasone BECLOMASE AQ7, QVAR	Allergic rhinitis, Asthma, COPD
Budesonide PULMICORT, BUDICORT*	Allergic rhinitis, Asthma, COPD
Ciclesonide ALVESCO, OMBASID*, ZETONIX*	Allergic rhinitis, Asthma
Fluticasone FLOMASE*, FLOVENT	Allergic rhinitis, Asthma, COPD
Mometasone ASMANEX, NASONEX*	Allergic rhinitis, Asthma
Triamcinolone NASACORT*	Allergic rhinitis, Asthma
Ipratropium ATROVENT	Allergic rhinitis, Asthma, COPD

- *** Nasal CS are the most effective medications for treatment of allergic rhinitis.
- Onset of action that ranges from 3 to 36 hours after first dose
- improve sneezing, itching, rhinorrhea, and nasal congestion.
- Systemic absorption is minimal, and adverse effects of treatment are localized (nasal irritation, nosebleed, sore throat, and, rarely, candidiasis)
- Patients should be instructed to **avoid deep** inhalation during administration into the nose, why? ^{تعليمات} To minimize systemic absorption
The target tissue is the nose
- For patients with chronic rhinitis, improvement may not be seen until 1 to 2 weeks after starting therapy.

*Intranasal corticosteroids examples: becomethasone, budesonide, fluticasone, ciclesonide, mometasone, and triamcinolone.

*To minimize systemic absorption, patients should be instructed to avoid deep inhalation during administration into the nose, because the target tissue is the nose, not the lungs or the throat. {local corticosteroids}

*Remember that the systemic corticosteroid are given orally or intramuscularly

* the first line treatment of chronic rhinitis is corticosteroids

@ **BBC FM Tried** to explain inhaled corticosteroids to asthma patients.

- B:** Budesonide
- B:** Beclomethasone
- C:** Ciclesonide
- F:** Fluticasone
- M:** Mometasone
- Tried:** Triamcinolone

هدول الطريقة
لحفظ الانوية



معلومة للإمتحان، الدكتور حكى انه ال corticosteroid الي اخدناهم بالاربع محاضرات حييجي عليهم سؤال بيجمع ما بين المحاضرات

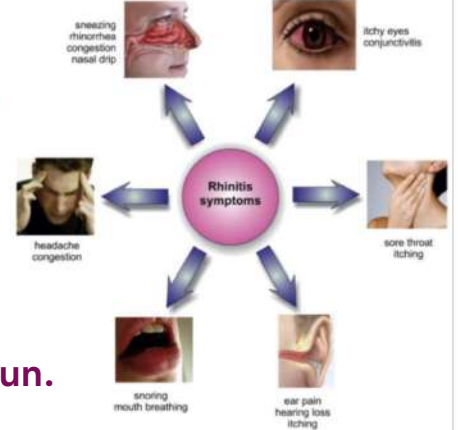


Pharmacological treatments:

2

Antihistamines

- Oral antihistamines (H1 receptor antagonists) have a **fast onset of action** and are useful for the **management of symptoms** of allergic rhinitis caused by **histamine release**, such as **sneezing**, **watery rhinorrhea**, and **itchy eyes/nose**.
- However, they are **more effective for prevention** of symptoms **in mild or intermittent disease**.
rather than treatment once symptoms have begun.
- **Drugs of choice in controlling the symptoms of allergic rhinitis**



*When we say Oral drug = slow onset usually + systemic effect
IV drug = rapid onset usually

*Oral antihistamines have a fast onset of action

حتكولي شو هالتناقض أحكيلكم مقارنة مع ال oral drug التانيين هم يعتبروا
سريعين و بشتغلوا خلال ساعات 🙌

and are useful for the management of symptoms of allergic rhinitis
caused by histamine release.

في عنا شرط مهم لحتى تشتغل ادوية ال (anti-histamine) و هو انه يكون في
histamine release

المعلومة جدا جدا مهمة 🙌

ملاحظة كمان مهمة و هي انه احنا ما بنستعمل ال Histamine بحالة وجود
attack بل بنستعملهم لحالات ال prevention ، مثال انا بعرف انه عندي حساسية و طالعة
يمكن فيه شجر لازم اوخد anti-histamine

اما بحالة وجود attack، فبعطي corticosteroids

ال Anti-histamine ال 2generations ، الاول بطلنا نستعمله الثاني مستعمل



Pharmacological treatments: Antihistamines

- Ophthalmic and nasal antihistamine delivery devices are available for targeted, topical tissue delivery.
- Suitable for patients with mild cases or ocular symptoms.

ملاحظة

مفادات الاحتقان

- Combinations of antihistamines with decongestants are effective when congestion is a feature of rhinitis, when patients have no response or incomplete control of symptoms with intranasal corticosteroids.

*Ophthalmic antihistamines and decongestants may be used for the treatment of hay fever, allergic reactions, and red eyes not caused by a bacterial infection. They reduce mucus formation and redness.

*Examples of topical intranasal antihistamines include olopatadine and azelastine.

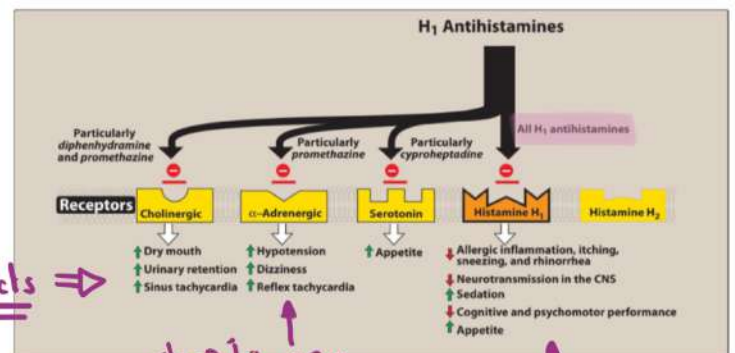
*Intranasal antihistamines provide increased delivery of the drug with fewer adverse effects.



Pharmacological treatments: Antihistamines (Actions)

- They do not influence the formation or release of histamine
- They block the receptor-mediated response of a target tissue.
- They can bind to cholinergic, adrenergic, or serotonin receptors >> additional effects unrelated to their ability to block H1 receptors.

Effects =>



الدكتور قرأ هـ دول

هـ دول بهين اكيـ

*The mechanism of action is believed to be a competitive antagonism of histamine binding to cellular receptors.

*It binds to H1 receptor .

*It can also binds to cholinergic, alpha-adrenergic and serotonin receptors and causes adverse effects

Pharmacological treatments: Antihistamines (Pharmacokinetics)

- Well absorbed after oral administration >> maximum serum levels occurring at 1-2 hours.
- First-generation half-life is 4 to 6 hours (Faster)
- Second-generation half-life is 12 to 24 hours (once-daily dosing)
- First-generation distributed in all tissues (CNS) → **They can cross the B.B.B, so they are not used nowadays**
- Metabolized by the liver **By Cyt P450**

Pharmacological treatments: Antihistamines (Adverse effects)

- First-generation have a low specificity, interacting with histamine muscarinic cholinergic, α -adrenergic, and serotonin receptors:
 1. Sedation **تخدير**
 2. Tachycardia
 3. Hypotension
 4. Vertigo **دوار**
 5. Increased appetite

*antihistamines that make you feel sleepy (most sedation) : chlorphenamine (Piriton), and diphenhydramine.

*non-drowsy antihistamines that are less likely to make you feel sleepy – such as acrivastine, cetirizine, fexofenadine and loratadine.

Pharmacological treatments: Antihistamines

- First generation:

1. Diphenhydramine
2. Chlorpheniramine

Most Sedation

- Internasal and/or eye drops:

1. Olopatadine
2. Azelastine

شرحنا عنهم فوق

- Second generation: → Can't cross B.B.B

1. Fexofenadine
2. Loratadine
3. Cetirizine
4. Levocetirizine

Least sedation

partial sedation

Sedation ال مهمة جداً وأكد عليها سؤال

****There are 2 generations for anti-histamine:**

*First-generation antihistamines, such as diphenhydramine and chlorpheniramine, are usually not preferred due to adverse effects, such as sedation, per-formance impairment, and other anticholinergic effects.

*The second-generation antihistamines (for example, fexofenadine, loratadine, desloratadine, cetirizine) are generally better tolerated.

Antihistamines - Learn with Visual Mnemonics! - YouTube



Visual Learner Studios uses visual mnemonics to teach pharmacology fast and efficiently. Website:...

YouTube · VL Studios · Mar 10, 2016



4 key moments in this video

هاد الفيديو على اليوتيوب بعظيم كحرف
لحفظ الاربويك

example :- Phenylephrine
Oxymetazoline
pseudoephedrine

Pharmacological treatments:

3 α -Adrenergic agonists (nasal decongestants)

- Short-acting (phenylephrine) constrict dilated arterioles in the nasal mucosa and reduce airway resistance.
- Rapid onset of action and show few systemic effects.
- NOT used in the long-term treatment of allergic rhinitis.
- Oral α -adrenergic agonists results in a longer duration of action but also increased systemic effects (increased blood pressure and heart rate)
- As with intranasal formulations, regular use of oral α -adrenergic agonists (phenylephrine and pseudoephedrine) alone in combination with antihistamines is not recommended.
- Side effects: tachycardia, palpitations, hypertension, constipation and nausea. اساك غثيان

α -Adrenergic agonists:

*Intranasal drugs.

*oxymetazoline -> Longer-acting.

*phenylephrin -> Short-acting

*intranasal formulations of α -adrenergic agonists should be used for no longer than 3 days due to the risk of rebound nasal congestion (rhinitis medicamentosa).

For this reason, the α -adrenergic agents are not used in the long-term

Pharmacological treatments:

4

Other agents (Cromolyn)

- Useful in allergic rhinitis, particularly when administered before contact with an allergen (**Prevention**).
- Dosing should begin at least 1 to 2 weeks prior to allergen exposure and should be used several times a day
- **Leukotriene receptor antagonists** may be a reasonable option in patients who also have **asthma**.
- An intranasal formulation of ipratropium is available to treat rhinorrhea associated with allergic rhinitis or the common cold. **It does not relieve** sneezing or nasal congestion.

سيلان الأنف

للعطس

احتقان الأنف

Other Agents :

1-Intranasal cromolyn:

الهدف من استعمالهم هو prevention لهيك بعطيهم قبل التعرض للallergen, و لحتى احصل على optimize effect لازم احصل عال dose قبل اسبوع او اسبوعين من التعرض للallergen و استخدمه عدة مرات يوميا

2-leukotriene receptor antagonists

هدول أدوية بتستهدف receptors اسمهم leukotriene receptors و هدول عبارة عن mediators للinflammation و allergic diseases لهيك احنا بنستخدم الAntagonists لنوقف عملهم بحالات الasthma They are effective for allergic rhinitis as monotherapy or in combination with other agents.

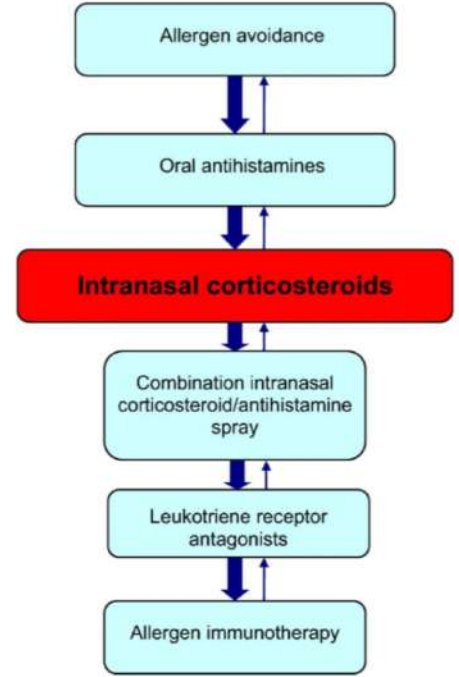
3-ipratropium

Intranasal drug

بستخدمه لعلاج ال rhinorrhea الي اله علاقة بال common cold او allergic rhinitis ولكن هو ما بخفف من شغلتين :

- 1- sneezing.
- 2- nasal congestion

- “Mild, intermittent allergic rhinitis can generally be managed effectively with avoidance measures and oral antihistamines. However, most patients presenting with allergic rhinitis have moderate-to-severe symptoms and, therefore, will require a trial of intranasal corticosteroids.”



<https://www.nature.com/articles/s41572-020-00227-0>

<https://aacijournal.biomedcentral.com/articles/10.1186/s13223-018-0280-7>

هذول مقالات لو بتحبوا تترسعو



Quiz Time

1-Histamine plays an important role in initiating the body's immune response to the presence of foreign antigens & pathogens. A primary source of histamine released during inflammatory conditions are:

- A- B cells
- B- Enterochromaffin-like cells
- C- Presynaptic nerve terminals
- D- Mast cells
- E- T lymphocytes

Answer : D

2-Use of this class of over-the-counter drugs has been associated with poor academic performance in children, an increased incidence of automobile accidents, increased work injuries & a significant decline in cognitive function in the elderly. A commonly used member of this drug class is:

- A- diphenhydramine
- B- fexofenadine
- C- loratadine
- D- nizatidine

Answer : A, first generation drug

3-A 24 year-old patient presents on a bright sunny Spring morning with a constellation of signs & symptoms that include a stuffy runny nose, sneezing, red, itchy & watery eyes, and a cough related to postnasal drip. A diagnosis of allergic rhinitis is made. In addition to a decongestant or corticosteroid spray, what other medication could you recommend that would counteract the effects related to histamine release, but have the least impact on mental status?

- A- brompheniramine
- B- chlorpheniramine
- C- diphenhydramine
- D- fexofenadine
- E- ranitidine

Answer : D

6- Mr Thibidoux arrives in your ER after suffering a gun-shot wound in a bar fight. After taking a brief history and exam, you decide to rapidly reduce his severe pain by administering i.v. morphine. Shortly thereafter Mr Thibidoux complains of feeling nauseous and itchy, and you notice that the skin on his neck & chest have become severely pink, when they were previously pale white. Which of the following would best reduce all of these symptoms if administered?

- A- adrenaline
- B- cimetidine
- C- cromolyn sodium
- D- diphenhydramine
- E- loratadine

Answer : D

5- Which is not a second generation antihistamine

- a) Cyclizine
- b) Fexofenadine
- c) Loratadine
- d) Acrivastine

Answer : A

6- Which agent is a preferred antihistamine for the management of allergic rhinitis?

- A. Chlorpheniramine
- B. Diphenhydramine
- C. Phenylephrine
- D. Cetirizine

Answer : D

7- Which category of allergic rhinitis medications is most likely to be associated with rhinitis medicamentosa (rebound nasal congestion) with prolonged use?

- A. Intranasal corticosteroid
- B. Intranasal decongestant
- C. Leukotriene antagonist
- D. Oral antihistamine

Answer: B

8- A 24-year-old woman presents to her primary care physician complaining of feeling sleepy all the time. She has a history of hay fever since the age of 9 years. She is currently taking an antihistamine but cannot remember the name. She says it controls her hay fever symptoms well. You suspect that her medication is causing her to feel sleepy. First generation antihistamines can cause drowsiness because they cross the blood–brain barrier and act on which receptor?

- (A) H1
- (B) H2
- (C) H3
- (D) H4

Answer : A

9- A 42-year-old man with HIV disease is hospitalized for refractory fungemia. He has begun on a course of caspofungin. After administration of the first intravenous dose, the patient develops flushing and sweats. What is the most likely mechanism of action for this finding?

- (A) Histamine release from mast cells
- (B) Pancreatic pseudocyst
- (C) Parathyroid adenoma
- (D) Parathyroid hyperplasia
- (E) Pheochromocytoma

Answer : A

10-A 27-year-old medical student has recurrent sinusitis and takes an over-the-counter agent. Unfortunately, he fell asleep while taking his final examination of the anatomy course. Which of the following agents is most likely to cause this adverse effect?

- (A) Doxycycline
- (B) Doxylamine
- (C) Doxazosin
- (D) Diphenhydramine
- (E) Hydroxyzine

Answer: D

11- A 15-year-old female presents to her primary care physician complaining of runny nose and itchy eyes. She said that she first had these symptoms during the spring a few years ago, but each year, they have been bothering her more. You know there are multiple ways to interfere with the signaling that is causing her symptoms. Which of the following drugs would prevent the release of the main chemical mediator in her case?

- (A) Cromolyn sodium
- (B) Diphenhydramine
- (C) Ranitidine
- (D) Loratadine
- (E) Theophylline

Answer : A

12- A 6-year-old boy is brought to his primary care physician with a history of hay fever and asthma. He usually has two to three attacks per week. For symptom control, he uses an albuterol inhaler, but his parents would like to try something more. They would like him to take something that would lessen the amount of attacks he has. Although corticosteroids would probably work best for prophylaxis, they are contraindicated in children. He is instead given montelukast. How does montelukast works?

- (A) Blocks leukotriene receptors
- (B) Blocks muscarinic acetylcholine receptors
- (C) Inhibits COX-1 and COX-2
- (D) Inhibits COX-2 only
- (E) Inhibits lipoxygenase

Answer: A

