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Item 22 of 26 Question Id: 762

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A 5-year-old boy with severe, recurrent respiratory infections is undergoing evaluation. Sputum studies reveal intracellular bacteria. Further testing shows that the patient's T cells lack the IL-12 receptor. Supplementation with which of the following substances would most likely improve this patient's condition?

- A. Early complement components (2%)
- B. GM-CSF (5%)
- C. Immunoglobulins (7%)
- D. Interferon-gamma (78%)
- E. Interleukin-4 (5%)

Omitted  
Correct answer  
D

78%  
Answered correctly

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Version

### Explanation

T cell subsets		
	TH1	TH2
Immunity	Cell-mediated	Humoral (antibody-mediated)
Function	Activate macrophages & CD8 <sup>+</sup> T cells	Activate B cells, promote class-switching

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	TH1	TH2
<b>Immunity</b>	Cell-mediated	Humoral (antibody-mediated)
<b>Function</b>	Activate macrophages & CD8 <sup>+</sup> T cells	Activate B cells, promote class-switching
<b>Cytokines</b>	IL-2, IFN- $\gamma$ , lymphotoxin $\beta$	IL-4, 5, 10, & 13
<b>Result</b>	Cytotoxicity; delayed hypersensitivity	Secretion of antibodies

IFN = interferon.

Helper T cells that have not yet contacted antigens are called **naive (Th0) cells** and have T-cell receptors (TCRs) and CD4 proteins on their surface. An **antigen-MHC class II complex** on an antigen-presenting cell (eg, macrophage, dendritic cell) can activate a naive Th cell by interacting with both TCR and CD4. The activated T cell then differentiates into either a Th1 or Th2 cell.

If the antigen is presented by a macrophage, the macrophage will produce **IL-12**, which stimulates differentiation into **Th1** cells. A deficiency of IL-12 receptors on naive T cells prevents differentiation into Th1 cells, which produce interferon-gamma (**IFN- $\gamma$** ). IFN- $\gamma$  is responsible for activation of the macrophage and CD8<sup>+</sup> cytotoxic response against intracellular organisms, such as **mycobacteria**. Therefore, individuals with an IL-12 receptor deficiency are susceptible to severe, persistent mycobacterial infections. Administration of IFN- $\gamma$  improves the immune response to mycobacterium in these patients.

**(Choices A and B)** Both complement and GM-CSF (granulocyte-macrophage colony-stimulating factor) play a part in the immune response against pathogens such as mycobacterium. However, patients with an IL-12

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If the antigen is presented by a macrophage, the macrophage will produce **IL-12**, which stimulates differentiation into **Th1** cells. A deficiency of IL-12 receptors on naive T cells prevents differentiation into Th1 cells, which produce interferon-gamma (**IFN- $\gamma$** ). IFN- $\gamma$  is responsible for activation of the macrophage and CD8 $^{+}$  cytotoxic response against intracellular organisms, such as **mycobacteria**. Therefore, individuals with an IL-12 receptor deficiency are susceptible to severe, persistent mycobacterial infections. Administration of IFN- $\gamma$  improves the immune response to mycobacterium in these patients.

**(Choices A and B)** Both complement and GM-CSF (granulocyte-macrophage colony-stimulating factor) play a part in the immune response against pathogens such as mycobacterium. However, patients with an IL-12 receptor deficiency are unable to produce sufficient IFN- $\gamma$  and therefore would not be able to mount a sufficient immune response to mycobacterium without IFN- $\gamma$  supplementation.

**(Choices C and E)** Formation of Th2 cells is induced by IL-4, which also plays a role in B cell differentiation and the production of immunoglobulins. Administration of immunoglobulins or IL-4 would improve the immune response against extracellular bacteria or viruses but would not be effective in stimulating an immune response against intracellular bacteria such as mycobacterium.

### Educational objective:

IL-12 stimulates the differentiation of naive Th0 cells into Th1 cells. Patients with IL-12 receptor deficiency are susceptible to severe mycobacterial infections due to the inability to mount a strong cell-mediated granulomatous immune response; therefore, they require treatment with IFN- $\gamma$ .

Immunology

Allergy & Immunology

Cell mediated immunity

Subject

System

Topic

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Item 23 of 26 Question Id: 569

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A 57-year-old woman with autosomal dominant polycystic kidney disease develops end-stage renal disease and undergoes deceased-donor kidney transplantation. During the operation, the surgeon notices that the graft becomes cyanotic and mottled soon after its blood vessels are connected with those of the recipient. Blood flow to the graft ceases, and no urine is produced. Which of the following best explains the findings observed by the surgeon?

- A. Activation of recipient T lymphocytes (12%)
- B. Antibody recognition of graft HLA components (60%)
- C. Degranulation of recipient mast cells and basophils (12%)
- D. Donor T lymphocyte-mediated vasculopathy (11%)
- E. Severe renal graft atherosclerosis (3%)

Omitted  
Correct answer  
B

60%  
Answered correctly

01 sec  
Time Spent

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### Explanation

#### Transplant rejection reactions

Type of rejection	Onset time	Etiology	Morphology

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Transplant rejection reactions			
Type of rejection	Onset time	Etiology	Morphology
Hyperacute	Minutes to hours	<ul style="list-style-type: none"> <li>Preformed recipient antibodies against graft antigens</li> </ul>	<ul style="list-style-type: none"> <li>Gross mottling &amp; cyanosis</li> <li>Arterial fibrinoid necrosis &amp; capillary thrombotic occlusion</li> </ul>
Acute	Usually <6 months	<ul style="list-style-type: none"> <li>Exposure to donor antigens induces activation of naive immune cells</li> <li>Predominantly <b>cell-mediated</b></li> </ul>	<ul style="list-style-type: none"> <li><b>Cellular:</b> lymphocytic interstitial infiltrate &amp; endotheliitis</li> <li>Humoral: C4d deposition, neutrophilic infiltrate, necrotizing vasculitis</li> </ul>
Chronic	Months to years	<ul style="list-style-type: none"> <li>Chronic low-grade immune response refractory to immunosuppression</li> <li>Mixed cell-mediated and humoral</li> </ul>	<ul style="list-style-type: none"> <li>Vascular wall thickening &amp; luminal narrowing</li> <li>Interstitial fibrosis &amp; parenchymal atrophy</li> </ul>

This patient is experiencing **hyperacute rejection** of a renal transplant. Hyperacute rejection is an **antibody-mediated reaction** (ie, [type II hypersensitivity](#)) caused by **preformed IgG antibodies** in the recipient that are directed against donor antigens. These are commonly anti-HLA antibodies (eg, formed during prior blood transfusion or pregnancy) or ABO blood group antibodies.

Hyperacute rejection is usually diagnosed in the operating room when the kidney becomes **cyanotic and**

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Hyperacute rejection is usually diagnosed in the operating room when the kidney becomes **cyanotic and mottled** after anastomosis of the donor and recipient blood vessels. Perfusion through the transplanted organ ceases immediately due to antibody- and complement-mediated vascular injury with subsequent **thrombotic occlusion**. This rapidly leads to ischemic necrosis of the glomeruli and renal cortex with little to **no urine output** and irreversible **graft loss**.

To minimize the risk of hyperacute rejection, donor and recipient ABO and HLA cross-matching is performed prior to renal transplantation.

**(Choice A)** Activation of recipient T lymphocytes is the primary mechanism of acute organ transplant rejection. Recipient T cells are sensitized by donor graft antigens, leading to cell-mediated (ie, [type IV hypersensitivity](#)) rejection that typically occurs within 6 months after transplant. This type of rejection is generally reversible with increased doses of immunosuppression.

**(Choice C)** Degranulation of mast cells and basophils occurs during a [type I hypersensitivity](#) reaction (eg, allergic response), which is not involved in organ transplant rejection.

**(Choice D)** Graft versus host disease occurs when donor T lymphocytes recognize recipient antigens, leading to vasculitis and tissue damage that frequently affects the skin, liver, and gastrointestinal tract. The risk is highest with allogeneic hematopoietic stem cell transplantation.

**(Choice E)** Atherosclerotic stenosis of the transplanted renal artery can occur over time, but it would not cause acute graft ischemia with cyanosis and mottling at the time of transplant surgery.

#### Educational objective:

Hyperacute rejection is caused by preformed antibodies in the recipient that recognize and attack donor antigens (ie, type II hypersensitivity). These are often anti-ABO blood group or anti-HLA antibodies. Vascular injury and capillary thrombotic occlusion lead to rapid ischemic necrosis of the renal graft, often evidenced by gross

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**(Choice A)** Activation of recipient T lymphocytes is the primary mechanism of acute organ transplant rejection. Recipient T cells are sensitized by donor graft antigens, leading to cell-mediated (ie, [type IV hypersensitivity](#)) rejection that typically occurs within 6 months after transplant. This type of rejection is generally reversible with increased doses of immunosuppression.

**(Choice C)** Degranulation of mast cells and basophils occurs during a [type I hypersensitivity](#) reaction (eg, allergic response), which is not involved in organ transplant rejection.

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**(Choice E)** Atherosclerotic stenosis of the transplanted renal artery can occur over time, but it would not cause acute graft ischemia with cyanosis and mottling at the time of transplant surgery.

### Educational objective:

Hyperacute rejection is caused by preformed antibodies in the recipient that recognize and attack donor antigens (ie, [type II hypersensitivity](#)). These are often anti-ABO blood group or anti-HLA antibodies. Vascular injury and capillary thrombotic occlusion lead to rapid ischemic necrosis of the renal graft, often evidenced by gross cyanosis and mottling immediately following graft perfusion.

### References

- [The major histocompatibility complex in transplantation.](#)

Immunology  
Subject

Allergy & Immunology  
System

Transplant rejection  
Topic

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Item 24 of 26 Question Id: 750

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A 23-year-old man comes to the physician with dysuria and increased urinary frequency. He is an active duty member of the US military and recently returned from sub-Saharan Africa, where he had been stationed for the last year. The patient's symptoms have persisted for several months and have failed to resolve following antibiotic treatment. His blood eosinophil count is elevated. Urine microscopy shows schistosome eggs. He is started on praziquantel and experiences improvement in his symptoms. The elevated eosinophils in this patient contribute to the host defense against schistosomiasis through which of the following mechanisms?

- A. Antibody-dependent cell-mediated cytotoxicity (43%)
- B. B lymphocyte chemotaxis (8%)
- C. Complement activation (11%)
- D. Immediate hypersensitivity (29%)
- E. MHC class I antigen processing (6%)

Omitted  
Correct answer  
A

43%  
Answered correctly

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Time Spent

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### Explanation

#### Parasitic killing by eosinophils

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### Parasitic killing by eosinophils

Eosinophil

IgG

Surface antigen

Release of granule proteins and reactive oxygen species

Helminth

Fc receptor

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Eosinophils perform the following functions:

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### Eosinophils perform the following functions:

- **Parasitic defense:** Eosinophil proliferation and activation during multicellular parasitic infection is stimulated by **IL-5** produced by  $T_{H}2$  and mast cells (not to be confused with IL-4, which stimulates IgE production). When a parasite invades the mucosa or enters the bloodstream, it is coated by IgG and IgA antibodies that bind the Fc receptors located on the eosinophil cell surface. This triggers eosinophil degranulation and release of cytotoxic proteins (eg, **major basic protein**) and reactive oxygen intermediates, substances that damage and destroy antibody-bound parasites. This mechanism is an example of **antibody-dependent cell-mediated cytotoxicity** (ADCC), which is also used by macrophages, neutrophils, and natural killer cells.
- **Type I hypersensitivity reactions:** Eosinophils also synthesize prostaglandins, leukotrienes, and cytokines that contribute to the inflammation seen in **late-phase** type 1 hypersensitivity and chronic allergic reactions.

**(Choice B)** Eosinophils contain a diverse number of immunomodulatory cytokines that are important for directing the  $T_{H}2$  immune response; but they do not significantly affect B cell chemotaxis.

**(Choice C)** Complement activation is an important step in antibody-mediated (type II) and immune complex mediated (type III) hypersensitivity reactions. Complement does not play a prominent role in the destruction of parasites by eosinophils.

**(Choice D)** Immediate (type I) hypersensitivity reactions are primarily mediated by mast cells and basophils. These cells possess Fc receptor-bound IgE on their membranes. Eosinophils contribute to late-phase type 1 hypersensitivity, but this is an allergic response that would not be protective against schistosomiasis.

**(Choice E)** Eosinophils can phagocytose parasitic antigens and present them in association with MHC class II molecules to stimulate helper T lymphocytes. In contrast, MHC class I antigen processing is involved in inducing



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that contribute to the inflammation seen in **late-phase** type 1 hypersensitivity and chronic allergic reactions.

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**(Choice D)** Immediate (type I) hypersensitivity reactions are primarily mediated by mast cells and basophils. These cells possess Fc receptor-bound IgE on their membranes. Eosinophils contribute to late-phase type 1 hypersensitivity, but this is an allergic response that would not be protective against schistosomiasis.

**(Choice E)** Eosinophils can phagocytose parasitic antigens and present them in association with MHC class II molecules to stimulate helper T lymphocytes. In contrast, MHC class I antigen processing is involved in inducing a cytotoxic T lymphocyte response against intracellular pathogens (eg, viruses).

### Educational objective:

Eosinophils play a role in host defense during multicellular parasitic infection. When stimulated by antibodies bound to a parasitic organism, they destroy the parasite via antibody-dependent cell-mediated cytotoxicity with enzymes from their cytoplasmic granules. Another function of eosinophils is regulation of type I hypersensitivity reactions.

### References

- IgE, mast cells, basophils, and eosinophils.

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Item 25 of 26 Question Id: 544

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A 3-year-old boy experiences recurrent sinusitis and an episode of severe pneumonia. As part of his evaluation, *Candida* extract is injected intradermally. Forty-eight hours later, he returns to the clinic with a firm nodule measuring 16 mm in diameter where the extract was injected. Which of the following cell types is most likely responsible for the reaction observed in this patient?

- A. B lymphocytes (4%)
- B. Eosinophils (2%)
- C. Mast cells (4%)
- D. Neutrophils (8%)
- E. T lymphocytes (80%)

Omitted  
Correct answer  
E

80%  
Answered correctly

02 secs  
Time Spent

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Version

### Explanation

This patient with recurrent infection is undergoing a delayed-type hypersensitivity **skin test** to screen for **cellular immunodeficiency**. This procedure involves intradermal injection of an antigen to which the patient has already been exposed (ie, *Candida* extract). Development of an area of induration (ie, tissue firmness) surrounding the injection site indicates a positive response and demonstrates effective cellular immunity. Skin testing can also be used as a control in patients with suspected tuberculosis exposure to ensure that the lack of response is not

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This patient with recurrent infection is undergoing a delayed-type hypersensitivity **skin test** to screen for **cellular immunodeficiency**. This procedure involves intradermal injection of an antigen to which the patient has already been exposed (ie, *Candida* extract). Development of an area of induration (ie, tissue firmness) surrounding the injection site indicates a positive response and demonstrates effective cellular immunity. Skin testing can also be used as a control in patients with suspected tuberculosis exposure to ensure that the lack of response is not caused by anergy.

Contact dermatitis, granulomatous inflammation, and reactive skin testing (eg, tuberculin skin test, *Candida* extract skin reaction) are all examples of [type IV \(delayed type\) hypersensitivity](#) reactions. When reexposed to an antigen, previously sensitized **T lymphocytes** proliferate and release inflammatory cytokines that promote cell-mediated cytotoxicity (CD8<sup>+</sup> T cells) and/or macrophage recruitment and activation. The resulting tissue damage and swelling is typically evident **24-48 hours** after exposure.

**(Choice A)** Antibody production by activated B lymphocytes (eg, plasma cells) plays a central role in type I, II, and III [hypersensitivity reactions](#). The timeframe of these reactions can be immediate (type I: eg, anaphylaxis, allergies) or variable (types II and III: eg, most autoimmune disorders, serum sickness).

**(Choice B)** Eosinophils are phagocytic cells that play a role in the defense against parasitic organisms. These cells are present in small numbers in the bloodstream but are often found in increased numbers in the affected tissues of patients with type I hypersensitivity responses (eg, asthma, allergies).

**(Choice C)** Mast cells are granulocytes that are the primary mediators of type I (immediate) hypersensitivity reactions (eg, allergies). Sensitized mast cells degranulate and release inflammatory mediators (eg, histamine, prostaglandins) when allergen-specific IgE cross-link on the mast cell Fc receptors, causing rapid swelling and tissue damage.

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**(Choice A)** Antibody production by activated B lymphocytes (eg, plasma cells) plays a central role in type I, II, and III hypersensitivity reactions. The timeframe of these reactions can be immediate (type I: eg, anaphylaxis, allergies) or variable (types II and III: eg, most autoimmune disorders, serum sickness).

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**(Choice C)** Mast cells are granulocytes that are the primary mediators of type I (immediate) hypersensitivity reactions (eg, allergies). Sensitized mast cells degranulate and release inflammatory mediators (eg, histamine, prostaglandins) when allergen-specific IgE cross-link on the mast cell Fc receptors, causing rapid swelling and tissue damage.

**(Choice D)** Neutrophils are the primary phagocytes of the innate immune system and play an ancillary role in some hypersensitivity reactions. Neutrophil deficiency or dysfunction can lead to severe infections without evidence of a significant immune response (eg, pus, infiltrates, erythema).

#### Educational objective:

Type IV (delayed) hypersensitivity reactions (eg, *Candida* extract skin test, contact dermatitis) are characterized by erythema and induration that develops 24-48 hours after repeat exposure to an antigen. T lymphocytes mediate the inflammation in these reactions through cytokine release, CD8<sup>+</sup> cytotoxicity, and macrophage recruitment.

Immunology

Subject

Allergy & Immunology

System

Hypersensitivity reactions

Topic

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A 57-year-old woman comes to the emergency department due to cough and hemoptysis. The patient also reports several months of fatigue and joint pain. Physical examination is notable for crusting of the nasal mucosa, lung crackles, and scattered palpable purpura over the lower extremities. Chest x-ray reveals bilateral, diffuse alveolar infiltrates. Laboratory studies show normocytic anemia, red blood cell casts and protein in the urine, and positive c-ANCA. After a confirmatory biopsy, treatment with rituximab infusion is planned. This medication is most likely to improve this patient's condition via which of the following mechanisms?

- A. Blockade of T-cell costimulation (12%)
- B. Depletion of B cells (68%)
- C. Disruption of leukocyte migration (3%)
- D. Inhibition of cytoplasmic kinase (3%)
- E. Interruption of cytokine function (11%)

Omitted  
Correct answer  
B

68%  
Answered correctly

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Time Spent

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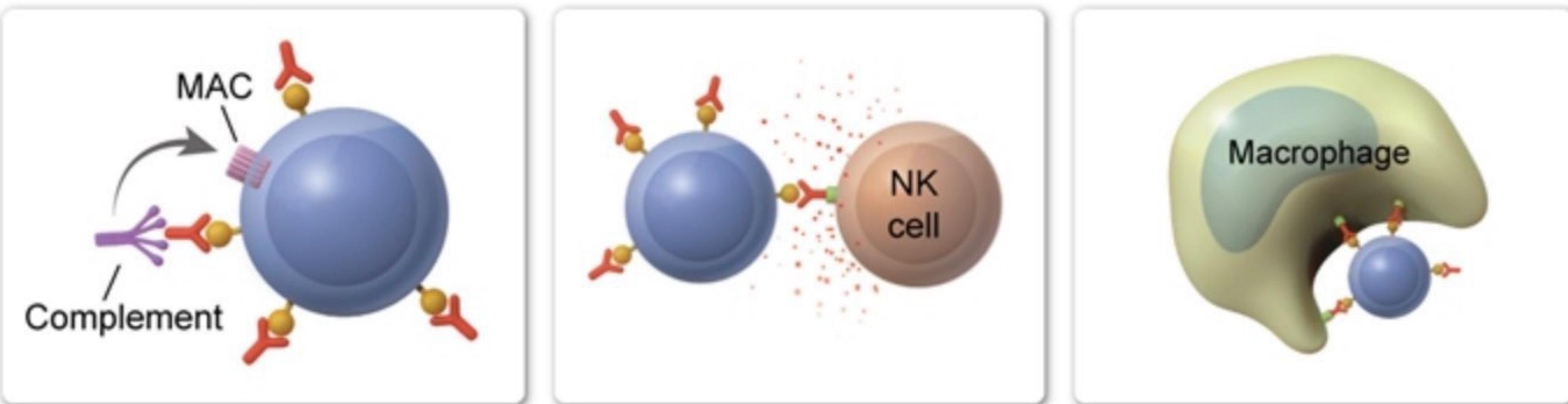
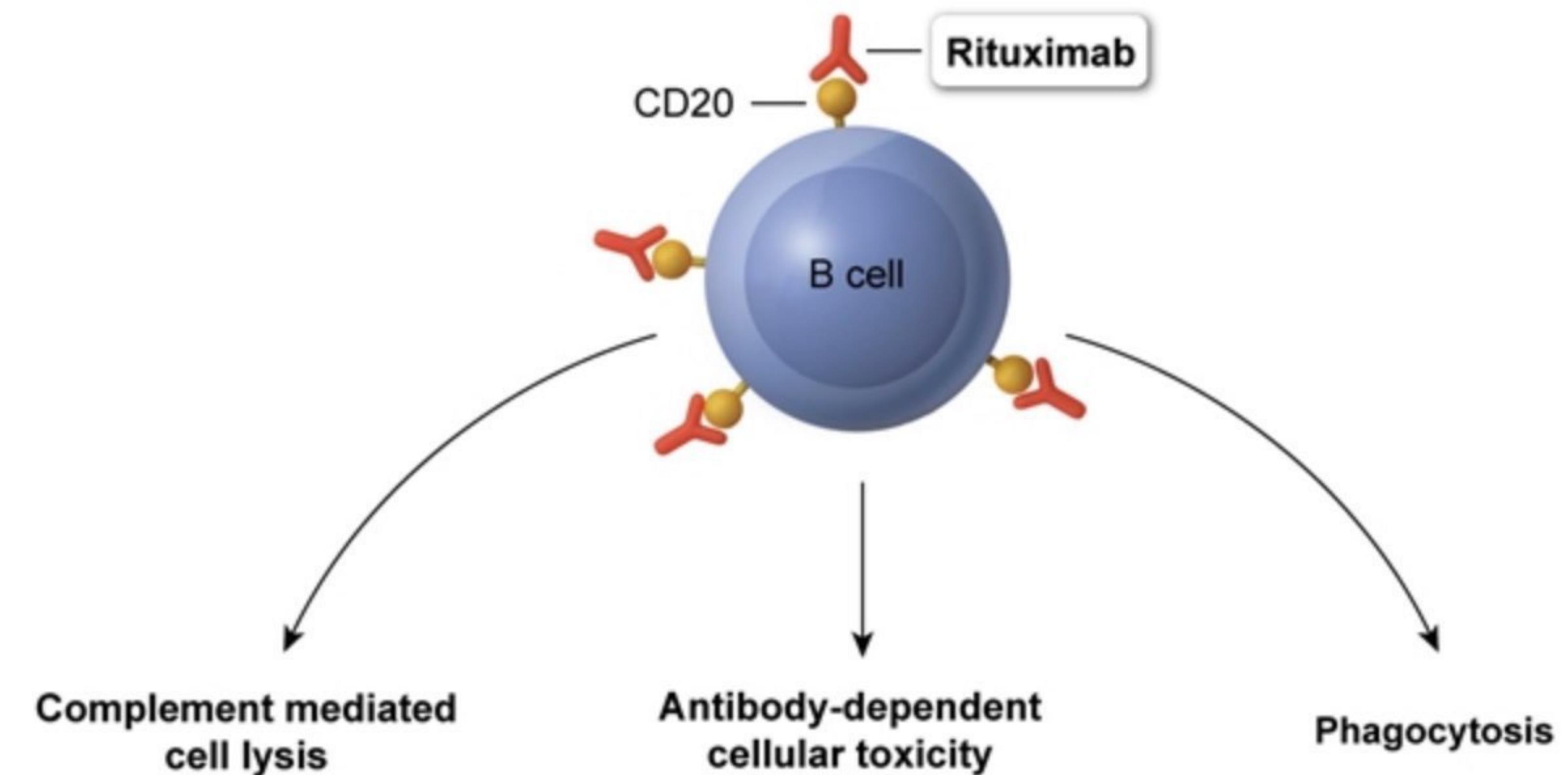
### Explanation

#### Rituximab mechanism of action





### Rituximab mechanism of action



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Complement mediated cell lysis      Antibody-dependent cellular toxicity      Phagocytosis

MAC  
Complement

NK cell

Macrophage

B cell depletion

MAC = membrane attack complex; NK cell = natural killer cell.

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This patient's clinical picture is consistent with **granulomatosis with polyangiitis (GPA)**, a c-ANCA-positive inflammatory vasculitis that primarily attacks the upper/lower respiratory tract, kidneys, and skin. Molecular and immunologic advances have led to a dramatic expansion in treatments for chronic systemic inflammatory diseases such as GPA; treatments are generally classified as follows:

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MAC = membrane attack complex; NK cell = natural killer cell.

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- **Cytokine inhibitors:** These bind free inflammatory cytokines or block cytokine receptors on cell surfaces; they target tumor necrosis factor (eg, infliximab, etanercept), IL-1, IL-6, IL-17, or IL-12/23 (**Choice E**).
- **T-cell costimulation inhibitors:** Two steps are required to activate cytotoxic T cells. The T cell must bind a specific antigen on the major histocompatibility complex type 1 of an antigen-presenting cell, and then the T cell must be costimulated by the interaction between the T-cell surface receptor CD28 and the antigen-presenting cell surface ligand CD80/86. T-cell costimulatory inhibitors (eg, abatacept) block the CD28 receptor on the cytotoxic T cell, which prevents T-cell costimulation and causes T-cell anergy (**Choice A**).
- **B-cell depletion or inhibition:** Because B cells generate inflammatory cytokines, promote T-cell activation, and differentiate into plasma cells that generate autoantibodies, medications that inhibit B-cell activation (eg, belimumab) or deplete B-cell populations (eg, **rituximab**) are highly effective in many systemic inflammatory disorders.

Rituximab is an **IgG monoclonal antibody against CD20**, a surface molecule present on developing and mature **B cells**. Binding of rituximab to CD20 results in Fc receptor–mediated B-cell cytotoxicity and antibody-dependent B-cell phagocytosis, which **significantly reduces the B-cell population**. Although existing plasma cells are unaffected (they do not express CD20), the reduction in total B-cell population significantly improves inflammatory symptoms. However, depletion of B cells also increases the risk for severe and recurrent bacterial infections, a major adverse effect of therapy.

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Rituximab is an **IgG monoclonal antibody against CD20**, a surface molecule present on developing and mature **B cells**. Binding of rituximab to CD20 results in Fc receptor-mediated B-cell cytotoxicity and antibody-dependent B-cell phagocytosis, which **significantly reduces the B-cell population**. Although existing plasma cells are unaffected (they do not express CD20), the reduction in total B-cell population significantly improves inflammatory symptoms. However, depletion of B cells also increases the risk for severe and recurrent bacterial infections, a major adverse effect of therapy.

**(Choice C)** Natalizumab is a monoclonal antibody against integrin, an adhesion molecule that mediates leukocyte interaction with the endothelium and subsequent leukocyte attachment/migration into tissue. Natalizumab is used in relapsing-remitting multiple sclerosis.

**(Choice D)** Cytoplasmic kinases (eg, Janus kinase) transmit inflammatory cytokine receptor binding to the nucleus. Rituximab does not operate via this mechanism, but new therapies that target these intracellular signaling pathways are under development.

#### Educational objective:

Rituximab is a monoclonal antibody directed against CD20, a cell surface receptor on developing and mature B cells. Binding of rituximab to CD20 results in B-cell cytotoxicity and phagocytosis, which reduces the B-cell population. This reduces inflammatory symptoms in a wide range of rheumatologic diseases.

Immunology  
Subject

Allergy & Immunology  
System

Biologic agents  
Topic

# Anaphylaxis and allergic reactions

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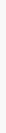
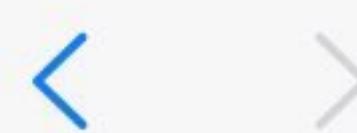
The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 52-year-old woman comes to the emergency department with pain and redness affecting her left leg. The patient's symptoms began 2 days ago and have progressed to the point where she cannot walk without experiencing severe pain. Physical examination shows a large, erythematous area with indistinct margins over her left leg. The area feels hot and indurated and is exquisitely tender. She is admitted to the hospital for severe left leg cellulitis and is started on intravenous cefazolin. Several minutes after the infusion is started, she experiences shortness of breath, diffuse itching, and dizziness. Her blood pressure is 64/38 mm Hg and heart rate is 130/min. On examination, there is a diffuse erythematous skin rash and bilateral wheezing is heard on lung auscultation.

### Item 1 of 2

Which of the following is most likely to be elevated in this patient's serum as a result of her medication reaction?

- A. Alkaline phosphatase
- B. Calcitonin
- C. Collagenase
- D. Myeloperoxidase
- E. Tryptase



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## Item 2 of 2

The patient's anaphylactic reaction is determined to be mediated by antigen-specific IgE antibodies attached to high-affinity receptors on the surface of mast cells and basophils. Which of the following mechanisms is most likely to trigger vasoactive substance release by these cells?

- A. Antibody-receptor covalent binding
- B. Antibody-receptor dissociation
- C. Receptor aggregation
- D. Receptor detachment from the cell surface
- E. Receptor internalization

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Item 4 of 19 Question Id: 19115

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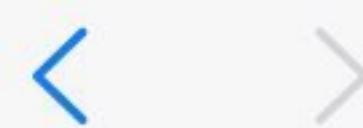
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UWorld USMLE

A 42-year-old woman is hospitalized due to fever and chills after a hemodialysis session. The patient has a history of end-stage kidney disease due to IgA nephropathy and recently began intermittent dialysis through a tunneled catheter. Medical history includes depression, for which she takes citalopram. Temperature is 38.4 C (101.1 F), blood pressure is 130/80 mm Hg, and pulse is 94/min. There is no erythema or tenderness at the catheter site, and the remainder of the physical examination shows no abnormalities. Blood cultures are obtained, and empiric vancomycin and ceftazidime are initiated. While receiving the intravenous vancomycin infusion, the patient reports a burning, itching sensation. Vital signs are unchanged, but repeat examination shows an erythematous rash involving the face and neck. She reports no history of drug allergy but has never received these antibiotics. Which of the following is the most likely underlying cause of this patient's current condition?

- A. Bacterial product release
- B. Cross-reacting antibodies
- C. Direct mast cell activation
- D. Drug-specific antibodies
- E. Serotonergic drug interaction

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A 1-year-old boy is brought to the office for a health maintenance visit. He has had no significant health issues and is growing well. The patient is up to date with recommended vaccinations and has had no prior vaccine-related adverse events. He has no known allergies. Physical examination shows no abnormalities. The patient receives the first dose of the subcutaneous measles-mumps-rubella vaccine. The next day, his mother calls the office because the patient has a temperature of 38 C (100.4 F) and has been irritable since the vaccination. The immunization site is mildly red, swollen, and tender; there is no other skin rash. Which of the following cells and effector mechanisms is most likely involved in pathogenesis of this patient's current condition?

- A. CD4<sup>+</sup> T cells and CD40 ligand
- B. CD8<sup>+</sup> T cells and perforins
- C. Dendritic cells and MHC II
- D. Macrophages and IL-6
- E. Plasma cells and IgM

[Proceed To Next Item](#)

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UWorld USMLE

A 62-year-old man is found dead in his apartment. An autopsy shows diffuse cerebral edema, laryngeal edema, and hyperinflated lungs. Which of the following is the most likely cause of death in this patient?

- A. Acute myocardial infarction
- B. Anaphylaxis
- C. Chronic obstructive pulmonary disease exacerbation
- D. Meningococcal meningitis
- E. Seizures

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UWorld USMLE

A 62-year-old woman undergoes hip replacement surgery. The patient has a history of advanced hip osteoarthritis that limits her daily activities. She has no other medical conditions and no known drug allergies. After appropriate preoperative evaluation, total hip arthroplasty is performed under general anesthesia. The intraoperative course is uncomplicated, and after recovery from anesthesia, patient-controlled intravenous morphine is started for pain control. Several minutes later, the patient reports generalized itching. Physical examination reveals hypotension, tachycardia, and mild bilateral wheezing but no rashes. Which of the following drug effects is most likely responsible for this patient's current condition?

- A. Decreased myocardial contractility
- B. Decreased sympathetic output
- C. Direct mast cell degranulation
- D. Formation of drug-IgE complexes
- E. Increased 5-lipoxygenase activity

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UWorld USMLE

A 22-year-old woman comes to the emergency department after development of a diffuse pruritic rash following a meal at a buffet restaurant an hour ago. She also felt light-headed and nearly fainted. The patient has no prior medical conditions and takes no medications. Temperature is 37 C (98.6 F), blood pressure is 96/52 mm Hg, pulse is 126/min, and respirations are 16/min. Physical examination shows mild lip swelling; the tongue appears normal. Heart auscultation demonstrates regular tachycardia without extraneous sounds. Lung sounds are clear with normal work of breathing. Skin examination shows confluent urticaria on the neck, shoulders, and abdomen. Intravenous fluids are begun, and intramuscular epinephrine is administered immediately. In addition to its effect on airway and circulation, this medication is most likely to improve this patient's condition through which of the following mechanisms?

- A. Blockade of tissue histamine receptors
- B. Decreased IgE Fc receptors on mast cells
- C. Decreased leukotriene synthesis in leukocytes
- D. Decreased mediator release from mast cells
- E. Decreased number of circulating eosinophils

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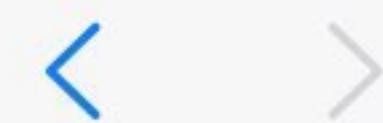
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UWorld USMLE

A 5-year-old child is brought to the emergency department by his parents for right arm pain. The patient reports that he was playing hide and seek outside and felt a sharp pain on his arm while hiding in some thick bushes. His parents suspect that something had stung him. Physical examination shows an edematous and erythematous plaque with mild central pallor. A residual stinger, located central to the lesion, is readily extracted. The physical examination is otherwise not significant. Which of the following substances is most likely directly responsible for the skin findings observed in this patient?

- A. C3b
- B. IL-2
- C. Histamine
- D. Lysozyme
- E. TNF- $\alpha$

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A 75-year-old man comes to the urgent care center with acute onset of a pruritic rash after eating strawberries. The patient has no associated swelling in or around the mouth, no wheezing, and no difficulty breathing. Past medical history is notable for coronary artery disease, for which he takes atorvastatin, lisinopril, aspirin, and metoprolol. He also has a history of allergy to dog and cat dander. The patient does not use alcohol or tobacco. His family reports that he lives alone and his functional status has been declining. He walks with a cane, has poor vision, and is frequently forgetful. The patient also has occasional dizziness when standing up and a history of frequent falls. Which of the following would be the most appropriate medication to treat this patient's acute symptoms?

- A. Chlorpheniramine
- B. Diphenhydramine
- C. Hydroxyzine
- D. Loratadine
- E. Promethazine

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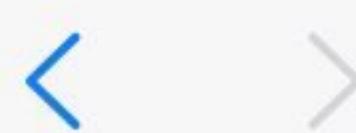
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UWorld USMLE

A 12-year-old girl is being evaluated for recurrent episodes of self-limited colicky abdominal pain and nausea lasting several days. She was also recently hospitalized for an episode of difficulty breathing. The patient has no significant past medical history, but her mother has a history of attacks of severe abdominal pain and diarrhea. Physical examination is unremarkable. Laboratory evaluation reveals decreased serum complement C4 and C1 esterase inhibitor levels. Which of the following drugs is contraindicated in this patient?

- A. Captopril
- B. Furosemide
- C. Methotrexate
- D. Metoprolol
- E. Penicillin

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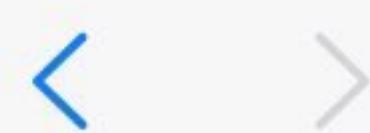
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Settings

A 25-year-old woman is brought to the emergency department 40 minutes after being stung by several wasps. She reports throat tightness and dizziness. She has no chronic medical conditions and takes no medication. Blood pressure is 80/40 mm Hg, pulse is 120/min, and respirations are 32/min. Examination shows diffuse erythematous plaques over the trunk and 1+ pitting edema of the ankles. Which of the following is the most likely cause of this patient's hypotension?

- A. Chemical mediator-induced decreased myocardial contractility
- B. Chemical mediator-induced increased vascular permeability
- C. Impaired endogenous sympathetic nerve activity
- D. Toxin-mediated decreased myocardial contractility
- E. Toxin-mediated increased capillary permeability

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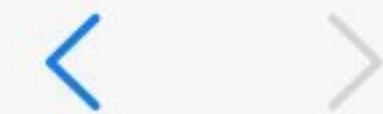
Text Zoom

Settings

A 56-year-old woman comes to the emergency department with facial swelling and difficulty breathing. She woke up today with a "feeling of fullness" in her lips, and 2 hours later her husband said that her lips looked puffy. There is no itching or skin rash. The patient has had no similar symptoms before. She has a history of gastroesophageal reflux disease and takes Lansoprazole daily. She also began taking lisinopril 2 months ago for hypertension. The patient's blood pressure is 135/75 mm Hg. On examination, there is moderate swelling of her lips and tongue. Mild audible stridor without wheezing is present. Which of the following is the most likely mechanism responsible for this patient's symptoms?

- A. Bradykinin accumulation
- B. Hereditary C1-esterase inhibitor deficiency
- C. IgE-dependent mast cell degranulation
- D. Increased renin secretion
- E. Nonimmune mediated mast cell degranulation

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Settings

An 8-year-old girl is brought to the emergency department due to "not feeling well." The patient was at an outdoor picnic and began experiencing nausea, vomiting, abdominal cramps, and watery diarrhea 30 minutes ago. She also reports feeling dizzy. The patient has no prior medical conditions and takes no medications. Temperature is 37 C (98.6 F), blood pressure is 60/30 mm Hg, pulse is 140/min, and respirations are 28/min. On physical examination, the patient appears pale and listless. There is faint bilateral wheezing. The abdomen is soft and nontender. Scattered wheals are present. Which of the following is most responsible for this patient's current condition?

- A. Gram-negative bacterial endotoxin
- B. Gram-positive bacterial exotoxin
- C. Kallikrein-generated bradykinin
- D. Mast cell-derived histamine
- E. Vasoactive intestinal peptide

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UWorld USMLE

A 19-year-old woman comes to the office to discuss treatment options for seasonal sneezing, rhinorrhea, and nasal congestion. She has had these symptoms for the past few springs and summers but is now willing to "try anything" to allow her to concentrate on her upcoming final exams. The patient has no significant medical history, takes no medications, and has no drug allergies. Vital signs are within normal limits and physical examination reveals mild bilateral pale and boggy nasal turbinates with copious clear mucus. Fluticasone, an intranasal glucocorticoid, is prescribed. Which of the following is the most likely mechanism of action of this drug?

- A. Apoptosis of tissue eosinophils
- B. Antagonism of leukotriene receptors
- C. Binding and removal of circulating IgE
- D. Reduced differentiation of regulatory T cells (Treg)

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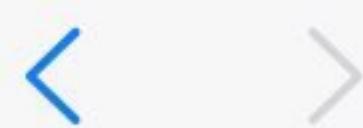
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UWorld USMLE

A 7-year-old boy is brought to the office due to sudden onset of facial swelling 2 hours ago. He has had no itching or pain other than a sore throat over the last 2 days, for which he has taken acetaminophen. The patient has had similar episodes of facial swelling that resolved spontaneously after a few days. Temperature is 37 C (98.6 F), blood pressure is 100/78 mm Hg, pulse is 95/min, and respirations are 24/min. Examination shows nonpitting edema of the cheeks, lips, and tongue; there is no tenderness or erythema. Which of the following studies is most likely to be abnormal?

- A. Eosinophil count
- B. Serum C4 level
- C. Serum C8 level
- D. Serum IgA level
- E. Serum IgE level

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An 11-year-old girl is brought to the office for a health maintenance visit. She feels well and has no chronic medical conditions. As part of routine care, the patient receives a first dose of the quadrivalent meningococcal conjugate vaccine and the 9-valent human papillomavirus vaccine. Five minutes later, while being escorted to the waiting area, the patient appears pale and reports feeling dizzy. She immediately loses consciousness, but a fall is prevented by the health care provider. Blood pressure is 70/40 mm Hg and pulse is 46/min. On physical examination, the patient has normal lung and heart sounds. There is no rash. Which of the following is the most likely cause of this patient's syncope?

- A. Delayed-type hypersensitivity reaction to the vaccine
- B. Excessive cytokine response to vaccine microbial components
- C. IgE-mediated hypersensitivity reaction to vaccine allergen
- D. Stress-induced cardioinhibitory and vasodepressor response
- E. Systemic invasion by live attenuated microbial agents

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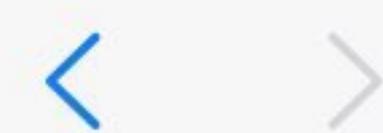
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UWorld USMLE

A 36-year-old woman with fistulizing perianal Crohn disease comes to the office for a follow-up appointment. Eight weeks ago, the patient began receiving intermittent injections of infliximab, a chimeric human-mouse monoclonal antibody targeted against tumor necrosis factor-alpha. She reports improvement in fistula discharge and discomfort but has experienced fever, diffuse joint pain, and an itchy rash 5-7 days after each of the recent treatments. The symptoms spontaneously resolve after 2-3 days. The patient has no other medical conditions and has no history of drug allergies. A delayed drug reaction due to formation of antibodies against foreign drug components is suspected. Which of the following mechanisms is most likely responsible for resolution of these drug reactions?

- A. Activation of the mononuclear phagocyte system
- B. Apoptosis of tissue mast cells and eosinophils
- C. Clearance of intact drug molecules by kidneys
- D. Endocytosis and degradation of mast cell-bound IgE
- E. Regulatory T-cell-mediated cytotoxic T-cell suppression

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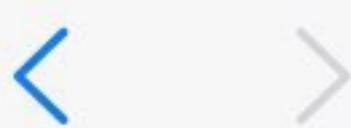
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Settings

A 21-year-old woman comes to the office due to recurrent episodes of self-limited, colicky abdominal pain. She also had an episode of facial swelling that resolved spontaneously. The patient has no other significant past medical history and takes no medications. Examination is unremarkable. Evaluation shows that her complement protein C1, even when not attached to an antigen-antibody complex, is excessively cleaving C2 and C4. Which of the following is most likely increased in this patient?

- A. Antinuclear antibody titer
- B. Antistreptolysin O titer
- C. Bradykinin
- D. Free hemoglobin
- E. Renin

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Settings

A 57-year-old male with suspected bacterial pneumonia is admitted to the hospital and given ceftriaxone and azithromycin for treatment. Soon after the first dose of ceftriaxone, he complains of difficulty breathing, abdominal cramps, and lightheadedness. His current blood pressure is 70/50 mmHg, while his heart rate is 120/min. Physical examination reveals a diffuse maculopapular rash. Which of the following drugs should be administered next to this patient?

- A. Corticosteroids (11%)
- B. Epinephrine (65%)
- C. Norepinephrine (7%)
- D. Dobutamine (4%)
- E. Diphenhydramine (10%)

Omitted

Correct answer

B



65%

Answered correctly



54 secs

Time Spent



2023

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### Explanation

Dyspnea, hypotension, and tachycardia soon after administration of  $\beta$ -lactam antibiotics are suggestive of anaphylactic shock. Hypotension occurs in anaphylactic shock secondary to collapse of peripheral vascular resistance, increases in vascular permeability, and leakage of capillary fluid. Stimulation of the smooth muscle tone within the bronchial wall, along with an increase in bronchial secretion, causes