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Item 1 of 22
Question Id: 4080

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A 38-year-old man presents to the office for a health maintenance visit four weeks in advance of a one month trip to Egypt, where he plans to visit the major cities and landmarks. His past medical history is significant for hypertension, well-controlled on hydrochlorothiazide. He does not smoke and drinks alcohol only occasionally. This will be his first international trip. His vital signs are all within normal limits and his physical examination is unremarkable. Vaccination against which of the following would be of greatest benefit to this patient?

- A. Hepatitis A
- B. Cholera
- C. Yellow fever
- D. Rabies
- E. Meningococcus
- F. Pneumococcus

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Item 1 of 22
Question Id: 4080

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A 38-year-old man presents to the office for a health maintenance visit four weeks in advance of a one month trip to Egypt, where he plans to visit the major cities and landmarks. His past medical history is significant for hypertension, well-controlled on hydrochlorothiazide. He does not smoke and drinks alcohol only occasionally. This will be his first international trip. His vital signs are all within normal limits and his physical examination is unremarkable. Vaccination against which of the following would be of greatest benefit to this patient?

- ✔ A. Hepatitis A [72%]
- B. Cholera [3%]
- C. Yellow fever [17%]
- D. Rabies [1%]
- E. Meningococcus [4%]
- F. Pneumococcus [1%]

Correct

72%

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International travelers often require vaccination against infectious diseases that are uncommon in their home country but common in their destination area. The Centers for Disease Control (CDC) offer guidelines regarding which vaccinations are appropriate for various destination areas. For those traveling to North Africa, the CDC recommends administering the hepatitis A, hepatitis B, and typhoid vaccines as well as a polio booster vaccine. Of these, the most common vaccine-preventable infectious disease is hepatitis A. The risk of contracting hepatitis A is significant for those traveling to developing countries, and increases in proportion to the length of stay. The mortality from hepatitis A increases with age and approaches 3% in adults over age 55. North American and European countries are considered low-risk zones; most Asian and African countries are high-risk zones. A single dose of hepatitis A vaccine provides adequate protection for a young immunocompetent adult; the second dose should be administered for long-term immunity.

(Choice B) The CDC does not recommend routine vaccination against cholera for those traveling to any country.

(Choice C) Yellow fever is a mosquito-borne viral hemorrhagic fever endemic to tropical regions of sub-Saharan Africa and South America. Vaccination is in general recommended for those traveling to sub-Saharan African and equatorial South American countries.

(Choice D) Rabies vaccination is not required for entry into any country; however, it should be considered

Saharan Africa and South America. Vaccination is in general recommended for those traveling to sub-Saharan African and equatorial South American countries.

(Choice D) Rabies vaccination is not required for entry into any country; however, it should be considered for patients visiting developing countries who plan on spending a lot of time outdoors or in rural areas. Vaccination may be of greater benefit in children since they may be more likely to play with animals and less likely to report bites.

(Choice E) Meningococcal vaccination is required for people who are traveling to some Asian countries and to sub-Saharan Africa. This vaccine is legally required for pilgrims who make the Hajj to Mecca, Saudi Arabia.

(Choice F) The CDC recommends that the pneumococcal vaccine be administered to several age groups of individuals living within the United States (e.g. young children, those over age 65, and younger adults with specific comorbid chronic diseases). This particular patient does not fall into any of those groups.

Educational objective:

Hepatitis A is the most common vaccine-preventable disease among travelers. The hepatitis A vaccine should be considered for people anticipating travel to developing countries.

A 3-year-old girl is brought to the emergency department due to severe oral pain. The patient's pain began 2 weeks ago with discomfort while chewing, and has progressively worsened to refusing any oral intake. She had a similar episode of oral pain last year. Medical history includes 2 sinus infections and numerous episodes of cellulitis. Skin cultures from her previous infections isolated *Staphylococcus aureus* and *Streptococcus pyogenes*. Physical examination shows periodontal inflammation with ulceration and necrosis. Laboratory results are as follows:

Complete blood count

Hemoglobin	11.8 g/dL
Hematocrit	36%
Platelets	240,000/mm^3
Leukocytes	55,000/mm^3
Neutrophils	90%
Lymphocytes	8%
Monocytes	2%

Platelets	240,000/mm^3
Leukocytes	55,000/mm^3
Neutrophils	90%
Lymphocytes	8%
Monocytes	2%

Which of the following abnormalities is most likely present in this patient?

- A. Adenosine deaminase deficiency
- B. Complement deficiency
- C. Defective B lymphocyte maturation
- D. Defective intracellular killing
- E. Defective leukocyte adhesion

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Platelets	240,000/mm^3
Leukocytes	55,000/mm^3
Neutrophils	90%
Lymphocytes	8%
Monocytes	2%

Which of the following abnormalities is most likely present in this patient?

A. Adenosine deaminase deficiency [7%]
B. Complement deficiency [4%]
C. Defective B lymphocyte maturation [17%]
D. Defective intracellular killing [27%]
✔ E. Defective leukocyte adhesion [43%]

Correct

43%
Answered correctly

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Features of leukocyte adhesion deficiency

- Recurrent skin & mucosal bacterial infections (eg, omphalitis, periodontitis)
  - No pus (lack of neutrophils at inflammation site)
  - Poor wound healing
- Delayed umbilical cord separation (>21 days)
- Marked peripheral leukocytosis with neutrophilia

This child's presentation of recurrent bacterial infections, severe periodontitis, and marked leukocytosis is consistent with **leukocyte adhesion deficiency** (LAD). LAD is caused by defective integrins on the leukocyte surface, which normally allow neutrophils to adhere to vascular endothelium, exit the vasculature, and migrate to areas of infection or inflammation.

Lack of neutrophil migration in LAD results in recurrent **skin** (eg, cellulitis, abscess, omphalitis) and **mucosal** (eg, periodontal) **infections** as well as poor wound healing. Examination shows inflammation with a notable **lack of purulence**. Biopsy of infected tissue is devoid of neutrophils and culture often grows *Staphylococcus aureus* or Gram-negative bacilli. Peripheral serum studies show marked leukocytosis and **neutrophilia**, particularly during episodes of infection. Classically, the first presenting sign of LAD is delayed umbilical cord separation (age >3 weeks).

(Choice A) Adenosine deaminase deficiency is an autosomal recessive form of severe combined immunodeficiency, which is characterized by deficient formation of mature B and T lymphocytes. Severe combined immunodeficiency presents with severe infections and failure to thrive. Laboratory studies show marked lymphopenia.

(Choice B) Patients with complement deficiencies are at increased risk for disseminated bacterial infections, particularly with encapsulated bacteria (eg, *Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis)*. Cutaneous infections and neutrophilia are not seen.

(Choice C) Defective B lymphocyte maturation occurs in X-linked agammaglobulinemia (Bruton). Recurrent sinopulmonary and gastrointestinal infections with low B cell and immunoglobulin concentrations are typical. This female patient's history of periodontitis is inconsistent with X-linked agammaglobulinemia.

(Choice D) Chronic granulomatous disease (CGD) is a defect in intracellular killing due to impaired respiratory burst from activated phagocytes. Patients with CGD present with infections from catalase-positive organisms (eg, *Staphylococcus aureus, Serratia marcescens, Burkholderia cepacia*); *Streptococcus pyogenes* is catalase-negative and would be an unusual finding. In addition, patients with CGD do not have neutrophilia.

Educational objective:
Leukocyte adhesion deficiency presents with delayed umbilical cord separation, recurrent skin and mucosal

(Choice C) Defective B lymphocyte maturation occurs in X-linked agammaglobulinemia (Bruton). Recurrent sinopulmonary and gastrointestinal infections with low B cell and immunoglobulin concentrations are typical. This female patient's history of periodontitis is inconsistent with X-linked agammaglobulinemia.

(Choice D) Chronic granulomatous disease (CGD) is a defect in intracellular killing due to impaired respiratory burst from activated phagocytes. Patients with CGD present with infections from catalase-positive organisms (eg, *Staphylococcus aureus, Serratia marcescens, Burkholderia cepacia*); *Streptococcus pyogenes* is catalase-negative and would be an unusual finding. In addition, patients with CGD do not have neutrophilia.

Educational objective:

Leukocyte adhesion deficiency presents with delayed umbilical cord separation, recurrent skin and mucosal bacterial infections (without purulence), and severe periodontal disease. Marked leukocytosis with neutrophil predominance is common.

References

- Leukocyte adhesion deficiencies.

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A 6-week-old boy is seen in the office for routine follow-up after discharge from the neonatal intensive care unit. He was born at 31 weeks gestation to a 41-year-old woman via cesarean delivery for preeclampsia with severe features and breech presentation. The hospital course included brief oxygen supplementation via continuous positive airway pressure and nasal cannula and phototherapy for jaundice. The patient is now breastfeeding every 3 hours and gaining weight appropriately. Maternal prenatal laboratory studies were normal. Weight today is 3 kg (6.6 lb). Examination is unremarkable. The parents inquire about upcoming vaccines for their infant. Which of the following is the most accurate statement regarding immunization scheduling for this patient?

A. Immunizations are given according to the chronologic age
B. Immunizations are given according to the corrected gestational age
C. Immunizations are given when antibody testing confirms an immune response
D. Immunizations are given when weight ≥4 kg (8.8 lb)
E. Toxoid vaccines are given according to chronologic age, but live attenuated vaccines are given according to corrected gestational age

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Item 3 of 22
Question Id: 4479
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A 6-week-old boy is seen in the office for routine follow-up after discharge from the neonatal intensive care unit. He was born at 31 weeks gestation to a 41-year-old woman via cesarean delivery for preeclampsia with severe features and breech presentation. The hospital course included brief oxygen supplementation via continuous positive airway pressure and nasal cannula and phototherapy for jaundice. The patient is now breastfeeding every 3 hours and gaining weight appropriately. Maternal prenatal laboratory studies were normal. Weight today is 3 kg (6.6 lb). Examination is unremarkable. The parents inquire about upcoming vaccines for their infant. Which of the following is the most accurate statement regarding immunization scheduling for this patient?

✔ A. Immunizations are given according to the chronologic age [62%]

B. Immunizations are given according to the corrected gestational age [21%]

C. Immunizations are given when antibody testing confirms an immune response [0%]

D. Immunizations are given when weight ≥4 kg (8.8 lb) [2%]

E. Toxoid vaccines are given according to chronologic age, but live attenuated vaccines are given according to corrected gestational age [12%]

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Standard pediatric immunizations in the United States	
Inactivated (killed)	• Polio • Hepatitis A
Toxoid (inactivated toxin)	• Diphtheria, tetanus
Live attenuated	• Rotavirus • Measles • Mumps • Rubella • Varicella
Subunit/conjugate	• Hepatitis B • Pertussis • *Haemophilus influenzae* type B • Pneumococcal • Meningococcal • Human papillomavirus • Influenza (injection)

Premature infants are at high risk of complications from vaccine-preventable diseases due to immature immune

Premature infants are at high risk of complications from vaccine-preventable diseases due to immature immune systems. Vaccinations for preterm infants should not be delayed; they are safe and proven to induce an adequate antibody response to confer immunity. In addition, mild intercurrent illness is not a contraindication to vaccination. Therefore, medically stable premature infants should receive **routine immunizations** on the same schedule as full-term infants, based on their **chronologic age** (age since birth).

This patient's chronologic age is 6 weeks, so he should receive the hepatitis B (second dose), rotavirus, tetanus, diphtheria, acellular pertussis, *Haemophilus influenzae* type B, pneumococcal, and inactivated polio vaccines at 2 months chronologic age.

(Choice B) Corrected age, or age adjusted for gestation, is considered when assessing a premature infant's growth and developmental milestones, but it does not determine timing of vaccine administration.

(Choice C) Preterm infants can mount appropriate immunologic responses to vaccines. Measuring titers of IgG antibodies to evaluate responsiveness to antigens is unnecessary.

(Choice D) The first hepatitis B vaccine is administered when the patient weighs ≥2 kg (4 lb 6 oz), typically at birth. All other vaccines are administered based on chronologic age.

(Choice E) Live attenuated vaccines are withheld in immunocompromised patients. This infant displays no signs of immune compromise, so all vaccines can be administered based on chronologic age. The first dose of live measles, mumps, rubella, and varicella vaccines is typically administered around age 1 year.

Educational objective:

(Choice B) Corrected age, or age adjusted for gestation, is considered when assessing a premature infant's growth and developmental milestones, but it does not determine timing of vaccine administration.

(Choice C) Preterm infants can mount appropriate immunologic responses to vaccines. Measuring titers of IgG antibodies to evaluate responsiveness to antigens is unnecessary.

(Choice D) The first hepatitis B vaccine is administered when the patient weighs ≥2 kg (4 lb 6 oz), typically at birth. All other vaccines are administered based on chronologic age.

(Choice E) Live attenuated vaccines are withheld in immunocompromised patients. This infant displays no signs of immune compromise, so all vaccines can be administered based on chronologic age. The first dose of live measles, mumps, rubella, and varicella vaccines is typically administered around age 1 year.

Educational objective:

Preterm infants should receive routine immunizations according to chronologic age rather than age corrected for gestation. Live virus vaccines are withheld in immunocompromised patients, but mild intercurrent illness is not a contraindication to vaccination.

References

- Immunization of preterm infants.

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Question Id: 3197

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A 5-month-old boy is brought to the clinic due to fussiness and fever for 2 days. His medical history is significant for previous episodes of otitis media, oral candidiasis, and gastroenteritis due to rotavirus. The patient is at the third percentile for weight. His temperature is 39.3 C (102.8 F), pulse is 120/min, respiratory rate is 28/min, and blood pressure is 80/60 mm Hg. Physical examination shows an erythematous, bulging right tympanic membrane with poor mobility on pneumatic otoscopy. The lymph nodes are not palpable, and the tonsils are not visualized. Laboratory results are as follows:

Platelets	240,000/mm^3
Leukocytes	7,500/mm^3
Lymphocytes	5%
Immunoglobulins	
IgG	210 mg/dL
IgA	35 mg/dL
IgM	14 mg/dL
Lymphocytes	
	80/mm^3 (640-

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IgM	14 mg/dL
Lymphocytes	
CD4+ count	80/mm^3 (640-1,175/mm^3)
CD8+ count	70/mm^3 (335-875/mm^3)

Which of the following is the most likely etiology of this patient's condition?

- A. Bruton agammaglobulinemia
- B. Chronic granulomatous disease
- C. Common variable immunodeficiency
- D. Severe combined immunodeficiency
- E. Wiskott-Aldrich syndrome

Submit

IgM	14 mg/dL
Lymphocytes	
CD4+ count	80/mm³ (640-1,175/mm³)
CD8+ count	70/mm³ (335-875/mm³)

Which of the following is the most likely etiology of this patient's condition?

- A. Bruton agammaglobulinemia [9%]
- B. Chronic granulomatous disease [1%]
- C. Common variable immunodeficiency [10%]
- ✔ D. Severe combined immunodeficiency [75%]
- ✘ E. Wiskott-Aldrich syndrome [2%]

Incorrect
Correct answer

75%
Answered correctly

14 Seconds
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Severe combined immunodeficiency	
Etiology	• Gene defect leading to failure of T cell development • B cell dysfunction due to absent T cells
Inheritance	• X-linked recessive • Autosomal recessive
Clinical features	• Recurrent, severe viral, fungal, or opportunistic (ie, *Pneumocystis*) infections • Failure to thrive • Chronic diarrhea
Treatment	• Stem cell transplant

This patient has recurrent infections, failure to thrive, hypogammaglobulinemia, and markedly low T cell counts. These findings are consistent with **severe combined immunodeficiency** (SCID), a disorder of defective **T cell development** leading to severe **B cell dysfunction**. The absence of T cells causes severe defects in cellular immunity, increasing the risk for infection due to viruses, fungi, and opportunistic pathogens (eg, *Pneumocystis jirovecii*). The loss of CD4+ T cells also leads to B cell (humoral immunity) dysfunction, increasing the risk for sinopulmonary and gastrointestinal bacterial infections. In addition to infection, chronic **diarrhea** and **failure to thrive** in infancy as well as absence of lymphoid tissue on examination are typical.

sinopulmonary and gastrointestinal bacterial infections. In addition to infection, chronic **diarrhea** and **failure to thrive** in infancy as well as absence of lymphoid tissue on examination are typical.

Laboratory findings of SCID include lymphopenia and hypogammaglobulinemia. Stem cell transplant is the only treatment and should be performed as early as possible. Therefore, SCID is included in routine newborn screening in the United States and is detected by the absence of T cell receptor excision circles (circular DNA excreted by developing T cells in the thymus) in dried blood.

(Choice A) Bruton (or X-linked) agammaglobulinemia is characterized by absent B cells, low serum immunoglobulins, and normal T cell concentrations. Patients present with recurrent sinopulmonary and gastrointestinal infections; examination shows an absence of lymphoid tissue.

(Choice B) Chronic granulomatous disease is a defect of the NADPH oxidase in phagocytic cells, which leads to impaired killing of catalase-positive organisms (eg, *Staphylococcus aureus*, *Serratia marcescens*). Affected patients have recurrent skin and soft tissue infections but normal lymphocyte and immunoglobulin concentrations.

(Choice C) Common variable immunodeficiency (CVID) causes recurrent sinopulmonary or gastrointestinal bacterial infections due to hypogammaglobulinemia. In contrast to Bruton agammaglobulinemia, CVID is less severe and presents at a later age with normal T cell and B cell counts.

(Choice E) Wiskott-Aldrich syndrome, an X-linked recessive disease, presents in early infancy with eczema and bleeding (eg, post circumcision, bleeding from umbilical stump) due to thrombocytopenia, which is not present in this patient. T cell dysfunction and hypogammaglobulinemia worsen with age and present as bacterial, viral, and

patients have recurrent skin and soft tissue infections but normal lymphocyte and immunoglobulin concentrations.

(Choice C) Common variable immunodeficiency (CVID) causes recurrent sinopulmonary or gastrointestinal bacterial infections due to hypogammaglobulinemia. In contrast to Bruton agammaglobulinemia, CVID is less severe and presents at a later age with normal T cell and B cell counts.

(Choice E) Wiskott-Aldrich syndrome, an X-linked recessive disease, presents in early infancy with eczema and bleeding (eg, post circumcision, bleeding from umbilical stump) due to thrombocytopenia, which is not present in this patient. T cell dysfunction and hypogammaglobulinemia worsen with age and present as bacterial, viral, and opportunistic infections.

Educational objective:
Severe combined immunodeficiency is a life-threatening condition caused by defective T cell maturation. Affected patients present with failure to thrive, recurrent infections (viral, fungal, bacterial), and extremely low lymphocyte concentrations. Treatment requires stem cell transplantation.

References

- Primary immunodeficiency in the neonate: Early diagnosis and management.
- Severe combined immunodeficiency disorders.

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A 15-month-old boy is brought to the office due to 3 days of fever. In the past 9 months, he has had 4 episodes of otitis media and 2 episodes of lobar pneumonia, one of which required hospitalization and prolonged intravenous antibiotic therapy. The patient is at the 40th percentile for weight. His temperature is 38.2 C (100.8 F). Physical examination shows a bulging, erythematous tympanic membrane on the right side but is otherwise unremarkable. The patient's laboratory studies are as follows:

Leukocytes	8,000/mm^3
Neutrophils	6,000/mm^3
Lymphocytes	2,000/mm^3
CD4$^+$ T cells	1,150/mm^3 (640-1175/mm^3)
CD8$^+$ T cells	810/mm^3 (335-875/mm^3)
Immunoglobulins	
IgG	80 mg/dL
IgA	31 mg/dL
IgM	11 mg/dL
IgE	18 mg/dL

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CD8+ T cells	810/mm³ (335-875/mm³)
Immunoglobulins	
IgG	80 mg/dL
IgA	31 mg/dL
IgM	11 mg/dL
IgE	18 mg/dL

Which of the following is the most likely diagnosis for this patient?

A. Bruton agammaglobulinemia
B. Common variable immunodeficiency
C. DiGeorge syndrome
D. Severe combined immunodeficiency
E. Transient hypogammaglobulinemia of infancy

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CD8+ T cells	810/mm³ (335-875/mm³)
Immunoglobulins	
IgG	80 mg/dL
IgA	31 mg/dL
IgM	11 mg/dL
IgE	18 mg/dL

Which of the following is the most likely diagnosis for this patient?

- ✔ A. Bruton agammaglobulinemia [70%]
- ✘ B. Common variable immunodeficiency [19%]
- C. DiGeorge syndrome [0%]
- D. Severe combined immunodeficiency [4%]
- E. Transient hypogammaglobulinemia of infancy [4%]

Incorrect
Correct answer

70%
Answered correctly

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Humoral immunodeficiency syndromes					
Condition	**B cell count**	**IgG**	**IgA**	**IgM**	**IgE**
CD40 ligand deficiency (hyper-IgM syndrome)	Normal	↓	↓	↑	↓
Common variable immunodeficiency	Normal	↓	↓	↓	↓
Job syndrome (hyper-IgE syndrome)	Normal	Normal	Normal	Normal	↑
Selective IgA deficiency	Normal	Normal	↓	Normal	Normal
X-linked agammaglobulinemia	↓	↓	↓	↓	↓

This child has recurrent sinopulmonary infections, markedly **low serum immunoglobulins**, and **few B lymphocytes** (given by: Total lymphocytes – T cell lymphocytes = B cell lymphocytes; 2000-1960 = 40). These findings are consistent with **Bruton** agammaglobulinemia (or **X-linked agammaglobulinemia** [XLA]), a recessive disorder characterized by a defect in tyrosine kinase in B cells. This defect results in failed development of bone marrow pre-B cells into mature circulating B cells, which also leads to low immunoglobulin production.

This child has recurrent sinopulmonary infections, markedly **low serum immunoglobulins**, and **few B lymphocytes** (given by: Total lymphocytes – T cell lymphocytes = B cell lymphocytes; 2000-1960 = 40). These findings are consistent with **Bruton** agammaglobulinemia (or **X-linked agammaglobulinemia** [XLA]), a recessive disorder characterized by a defect in tyrosine kinase in B cells. This defect results in failed development of bone marrow pre-B cells into mature circulating B cells, which also leads to low immunoglobulin production.

When protection from maternally-derived transplacental IgG antibodies wanes at age 3-6 months, patients with XLA develop recurrent **sinopulmonary** (eg, acute otitis media, pneumonia) and **gastrointestinal** (eg, *Salmonella*, *Campylobacter*) infections that can be severe or chronic. Physical examination in older children with XLA shows underdeveloped lymphoid tissue (eg, tonsils, lymph nodes). However, these tissues are not prominent even in healthy children until after age 2 years. Therapy includes intravenous immunoglobulin administration and prophylactic antibiotics.

(Choice B) Common variable immunodeficiency (CVID) can present in a similar manner to XLA; however, patients with CVID present with less severe symptoms after adolescence. Serum immunoglobulin concentrations are decreased, but B cell concentrations are normal.

(Choice C) DiGeorge syndrome (22q11.2 deletion syndrome) can present with the classic triad of congenital heart disease, T cell deficiency, and hypocalcemia. Impaired T cell production leads to deficient cellular immunity (eg, recurrent viral and fungal infections). However, B cell concentrations are not affected.

(Choice D) Severe combined immunodeficiency (SCID) is caused by impaired T cell development and subsequent B cell dysfunction. Affected patients present with life-threatening bacterial, viral, fungal, and

disease, T cell deficiency, and hypocalcemia. Impaired T cell production leads to deficient cellular immunity (eg, recurrent viral and fungal infections). However, B cell concentrations are not affected.

(Choice D) Severe combined immunodeficiency (SCID) is caused by impaired T cell development and subsequent B cell dysfunction. Affected patients present with life-threatening bacterial, viral, fungal, and opportunistic infections in infancy. T and B cell concentrations are markedly decreased in SCID.

(Choice E) Transient hypogammaglobulinemia of infancy is characterized by decreased IgG, variable IgM, and normal IgA and B cell concentrations. Affected patients present with increased sinopulmonary and gastrointestinal infections that are usually mild rather than life-threatening. Immunoglobulin levels generally normalize by age 9-15 months.

Educational objective:
Bruton (X-linked) agammaglobulinemia presents with severe, recurrent sinopulmonary or gastrointestinal infections in late infancy. Serum immunoglobulins and B cell concentration are markedly low to absent.

References

- Overview of immunodeficiency disorders
- X-linked agammaglobulinemia.

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A 32-year-old woman comes to the office due to persistent cough and shortness of breath. She has had 3 episodes of pneumonia over the last 3 years. The patient had severe sinusitis a year ago and an episode of bloody diarrhea that required hospitalization 6 months ago. She usually responds to antibiotics but takes several days to clear the infection. No other family members have similar problems. The patient has not traveled outside of the United States. She does not use tobacco, alcohol, or illicit drugs and currently takes no medications. All of her immunizations are up to date. Blood pressure is 130/80 mm Hg and pulse is 90/min. BMI is 22 kg/m^2. Physical examination reveals fine crackles over the right lower lung field. No lower extremity edema is present. Neck palpation does not show any lymph node enlargement. Leukocyte count is 14,000/mm^3. HIV testing is negative. Chest x-ray reveals a right lower lobe infiltrate. Which of the following is most likely to reveal the cause of this patient's underlying disease process?

A. Measurement of CD4+ T lymphocyte count
B. Measurement of serum alpha-1 antitrypsin level
C. Methacholine challenge test
D. Quantitative measurement of serum immunoglobulin levels
E. Sweat chloride test

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Question Id: 4301

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A 32-year-old woman comes to the office due to persistent cough and shortness of breath. She has had 3 episodes of pneumonia over the last 3 years. The patient had severe sinusitis a year ago and an episode of bloody diarrhea that required hospitalization 6 months ago. She usually responds to antibiotics but takes several days to clear the infection. No other family members have similar problems. The patient has not traveled outside of the United States. She does not use tobacco, alcohol, or illicit drugs and currently takes no medications. All of her immunizations are up to date. Blood pressure is 130/80 mm Hg and pulse is 90/min. BMI is 22 kg/m^2. Physical examination reveals fine crackles over the right lower lung field. No lower extremity edema is present. Neck palpation does not show any lymph node enlargement. Leukocyte count is 14,000/mm^3. HIV testing is negative. Chest x-ray reveals a right lower lobe infiltrate. Which of the following is most likely to reveal the cause of this patient's underlying disease process?

A. Measurement of CD4+ T lymphocyte count [3%]
✗ B. Measurement of serum alpha-1 antitrypsin level [4%]
C. Methacholine challenge test [1%]
✓ D. Quantitative measurement of serum immunoglobulin levels [75%]
E. Sweat chloride test [15%]

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Common variable immunodeficiency	
Manifestations	• Recurrent respiratory (eg, pneumonia, sinusitis, otitis) & GI (eg, *Salmonella, Campylobacter*) infections • Autoimmune disease (eg, RA, thyroid disease) • Chronic lung disease (eg, bronchiectasis) • GI disorders (eg, chronic diarrhea, IBD-like conditions)
Diagnosis	• ↓↓ IgG, ↓ IgA/IgM • No response to vaccination
Management	• Immunoglobulin replacement therapy

GI = gastrointestinal; **IBD** = inflammatory bowel disease; **RA** = rheumatoid arthritis.

This patient with evidence of acute pneumonia (cough, shortness of breath, leukocytosis, right lower lobe infiltrate) and recent history of recurrent pneumonia, sinusitis, and bloody diarrhea likely has **common variable immunodeficiency (CVID)**. CVID is a collective diagnosis that includes a number of genetic defects resulting in **impaired B cell differentiation** and **hypogammaglobulinemia**.

CVID is one of the most common primary immunodeficiencies in adults and is characterized mainly by increased **susceptibility to bacterial infection**. Recurrent **respiratory infections** (eg, pneumonia, sinusitis, otitis) and **gastrointestinal infections** (eg, *Salmonella*, *Campylobacter*) are common, and the latter may lead to episodes of

CVID is one of the most common primary immunodeficiencies in adults and is characterized mainly by increased **susceptibility to bacterial infection**. Recurrent **respiratory infections** (eg, pneumonia, sinusitis, otitis) and **gastrointestinal infections** (eg, *Salmonella*, *Campylobacter*) are common, and the latter may lead to episodes of bloody diarrhea. Chronic giardiasis may occur, but opportunistic infections (eg, *Candida*, *Pneumocystis jirovecii*) are rare. Other characteristics of CVID include concomitant **autoimmune disease** (eg, hemolytic anemia, rheumatoid arthritis, pernicious anemia), inflammatory bowel-like disease, granuloma development, and increased risk for non-Hodgkin lymphoma. Enteropathy (eg, sprue-like illness) is common, and affected patients may present with malabsorption and weight loss.

Most cases of CVID are due to sporadic mutation, and family history of the disease is typically absent (as in this patient). The majority of patients are diagnosed in adulthood (age 20-45) due to a combination of variable presentation and diagnostic delay. Diagnosis is made by **quantitative measurement of immunoglobulin levels** (significantly reduced serum IgG with low levels of IgA and/or IgM) as well as by markedly reduced or absent immune response to vaccination.

(Choice A) Low CD4+ lymphocyte counts occur in DiGeorge syndrome and HIV infection and create susceptibility to opportunistic infection. DiGeorge syndrome typically manifests shortly after birth, and this patient is HIV negative.

(Choice B) Alpha-1 antitrypsin deficiency is an inherited disorder that leads to emphysema and liver damage but does not increase the risk of recurrent infections.

(Choice C) Methacholine challenge is used to diagnose asthma, which is not characterized by recurrent bacterial

(Choice A) Low CD4+ lymphocyte counts occur in DiGeorge syndrome and HIV infection and create susceptibility to opportunistic infection. DiGeorge syndrome typically manifests shortly after birth, and this patient is HIV negative.

(Choice B) Alpha-1 antitrypsin deficiency is an inherited disorder that leads to emphysema and liver damage but does not increase the risk of recurrent infections.

(Choice C) Methacholine challenge is used to diagnose asthma, which is not characterized by recurrent bacterial respiratory infections.

(Choice E) Sweat chloride test is used to diagnose cystic fibrosis (CF). Recurrent pneumonia and sinusitis can occur in CF; however, CF is often diagnosed prior to adulthood. In addition, although diarrhea and malabsorption may be seen (due to pancreatic insufficiency), bloody diarrhea would be unusual.

Educational objective:
Recurrent bacterial infections in an adult should raise suspicion for common variable immunodeficiency. Quantitative measurement of serum immunoglobulin levels is needed to establish the diagnosis.

References

- Clinical picture and treatment of 2212 patients with common variable immunodeficiency.

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Item 7 of 22
Question Id: 3980

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A 47-year-old diabetic woman comes to the physician due to the recent onset of tremors. She has undergone combined pancreatic and kidney transplantation secondary to end stage renal disease and diabetes. She takes multiple medications, including immunosuppressants. Her temperature is 36.1°C (97°F), blood pressure is 152/90 mm Hg, pulse is 78/min, and respirations are 16/min. Examination shows gum hypertrophy. Laboratory studies show:

Hb	13.0 g/dL
WBC	8,000/cmm
Serum Na	135 mEq/L
Serum K	5.3 mEq/L
BUN	26 mg/dL
Serum Creatinine	1.7 mg/dL

Which of the following immunosuppressants is most likely responsible for her presentation?

A. Tacrolimus

B. Cyclosporine

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WBC	8,000/cmm
Serum Na	135 mEq/L
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BUN	26 mg/dL
Serum Creatinine	1.7 mg/dL

Which of the following immunosuppressants is most likely responsible for her presentation?

- A. Tacrolimus
- B. Cyclosporine
- C. Azathioprine
- D. Mycophenolate

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Hb	13.0 g/dL
WBC	8,000/cmm
Serum Na	135 mEq/L
Serum K	5.3 mEq/L
BUN	26 mg/dL
Serum Creatinine	1.7 mg/dL

Which of the following immunosuppressants is most likely responsible for her presentation?

- ✗ A. Tacrolimus [25%]
- ✓ B. Cyclosporine [51%]
- C. Azathioprine [11%]
- D. Mycophenolate [10%]

Incorrect
Correct answer

51%
Answered correctly

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Cyclosporine is a commonly used immunosuppressant. It acts by *inhibiting the transcription of interleukin-2* and several other cytokines, mainly the T-helper lymphocytes.

Some of the most common side effects of cyclosporine are:

1. **Nephrotoxicity**: This is the most common and serious side effect. It may manifest as reversible acute azotemia or irreversible progressive renal disease. Hyperuricemia with accelerated gout, hyperkalemia, hypophosphatemia, and hypomagnesemia can be seen as manifestations of renal-induced dysfunction. Rarely, hemolytic uremic syndrome (HUS) may be seen.
2. **Hypertension**: This is due to renal vasoconstriction and sodium retention. It is generally seen in the first few weeks of therapy. Calcium channel blockers are the drugs of choice for treatment.
3. **Neurotoxicity**: This is often reversible. It manifests as headache, visual disturbances, seizure, mild tremors, akinetic mutism, etc.
4. **Glucose intolerance**: This is fairly common. Patients who are concurrently taking prednisone (steroids) might develop significant hyperglycemia.
5. **Infection**: Chronic therapy with cyclosporine is associated with infection in 40% of patients.
6. **Malignancy**: There is an increased risk of squamous cell carcinoma of the skin and lymphoproliferative diseases.
7. **Gingival hypertrophy** and **hirsutism**.
8. **GI manifestations**, such as anorexia, nausea, vomiting, and diarrhea: These are fairly common but mild.

(Choice A) Tacrolimus is a macrolide antibiotic produced by fungi. It has the same mechanism of action as

(Choice A) Tacrolimus is a macrolide antibiotic produced by fungi. It has the same mechanism of action as cyclosporine and has a similar toxicity profile (including nephrotoxicity and hyperkalemia); however, in contrast to cyclosporine, tacrolimus does not cause hirsutism or gum hypertrophy, and has a higher incidence of neurotoxicity, diarrhea, and glucose intolerance.

(Choice C) Azathioprine is a purine analog that is enzymatically converted to 6-mercaptopurine. It acts primarily by inhibiting purine synthesis. The major toxicity of azathioprine is dose-related diarrhea, leukopenia, and hepatotoxicity.

(Choice D) Mycophenolate is a reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH), which is the rate-limiting enzyme in de novo purine synthesis. The major toxicity of mycophenolate is bone marrow suppression.

Educational Objective:

Cyclosporine and tacrolimus have the same mechanism of action (calcineurin-inhibitors). The major side effects of cyclosporine include *nephrotoxicity, hyperkalemia, hypertension, gum hypertrophy, hirsutism, and tremor.* Tacrolimus has similar toxicities, except for hirsutism and gum hypertrophy.

*The major toxicity of azathioprine is dose-related diarrhea, leukopenia, and hepatotoxicity.
*The major toxicity of ***m****ycophenolate* is bone ***m****arrow* suppression.

*Extremely high yield question for the USMLE!!!

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Item 8 of 22
Question Id: 2134

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A 3-year-old boy is brought to the emergency department for 2 days of fever, cough, and worsening shortness of breath. His parents report that he recently recovered from prolonged diarrhea due to *Giardia* infection. His medical history is also significant for lobar pneumonia requiring hospitalization and recurrent ear infections treated with antibiotics since age 6 months. His temperature is 38.7 C (101.7 F), pulse is 140/min, and respirations are 60/min. Physical examination shows small tonsils and crackles in the lower lobe of the right lung. The child's growth is at the 40th percentile. Which of the following is the most likely cause of his recurrent infections?

A. Abnormal B lymphocyte maturation
B. Adenosine deaminase deficiency
C. Complement deficiency
D. Impaired oxidative burst
E. Thymic hypoplasia

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Item 8 of 22
Question Id: 2134

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- ✔ A. Abnormal B lymphocyte maturation [64%]
- ✘ B. Adenosine deaminase deficiency [15%]
- C. Complement deficiency [4%]
- D. Impaired oxidative burst [6%]
- E. Thymic hypoplasia [8%]

Incorrect
Correct answer
A

64%
Answered correctly

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Explanation

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X-linked agammaglobulinemia	
Clinical manifestations	• Recurrent sinopulmonary & gastrointestinal infections after age 6 months • Absence of lymphoid tissue on examination (eg, tonsils, lymph nodes)
Diagnosis	• ↓ Immunoglobulins & B cells • Normal T cell concentration • No response to vaccinations
Treatment	• Immunoglobulin replacement therapy • Prophylactic antibiotics if severe

This child's history of recurrent sinopulmonary and gastrointestinal infections beginning after age 6 months along with his small tonsils suggest **X-linked agammaglobulinemia** (XLA), or Bruton agammaglobulinemia. XLA is caused by a defect in tyrosine kinase that prevents the development of mature B cells. Low B cell concentrations lead to small or absent lymphoid tissue (eg, tonsils, adenoids) on physical examination and low or absent serum immunoglobulin concentrations. Infants with XLA are predisposed to recurrent **sinopulmonary** infections with encapsulated organisms such as *Haemophilus influenzae* and *Streptococcus pneumoniae* due to impaired humoral immunity response. The absence of IgA leads to increased risk for **gastrointestinal** infections (eg, *Giardia*). Patients usually present after age 6 months, when protection from maternally-acquired IgG begins to

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Giardia). Patients usually present after age 6 months, when protection from maternally-acquired IgG begins to wane.

Treatment of XLA is based on restoring serum immunoglobulin concentrations, which is accomplished by administering monthly **intravenous immunoglobulin**. Antibiotics are given for infections and may be given prophylactically if intravenous immunoglobulin alone is unsuccessful. Live vaccines are contraindicated in XLA; other vaccines are not contraindicated but are incapable of generating a meaningful antibody response in patients with XLA.

(Choice B) Adenosine deaminase deficiency is one of several gene defects resulting in impaired T cell development and causing severe combined immunodeficiency. Affected patients present with severe, recurrent viral, fungal (eg, *Candida*), and bacterial infections and failure to thrive.

(Choice C) Patients with complement deficiencies are at increased risk for disseminated bacterial infections, particularly with encapsulated bacteria (eg, *Streptococcus pneumoniae, Neisseria meningitidis*). *Giardia* infection is not associated with complement deficiencies.

(Choice D) Impaired oxidative burst occurs in chronic granulomatous disease. Patients with this disease have recurrent skin and pulmonary infections with catalase-positive organisms (eg, *Staphylococcus aureus, Serratia marcescens*).

(Choice E) Thymic hypoplasia is consistent with DiGeorge syndrome (22q11.2 microdeletion syndrome), which is characterized by hypocalcemia, cardiac defects, and failure to thrive in addition to recurrent infections.

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(Choice E) Thymic hypoplasia is consistent with DiGeorge syndrome (22q11.2 microdeletion syndrome), which is characterized by hypocalcemia, cardiac defects, and failure to thrive in addition to recurrent infections.

Educational objective:

X-linked agammaglobulinemia (Bruton agammaglobulinemia) results from a failure of B cell development. Affected patients have small or absent lymphoid tissue and experience recurrent sinopulmonary and gastrointestinal infections once protection from transplacental maternal antibody wanes.

References

- X-linked agammaglobulinemia.

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Item 9 of 22
Question Id: 12519
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An 8-year-old girl is brought to the office due to nasal congestion for 2 weeks. Her nasal discharge has become thick and green, and fever started today. On physical examination, the patient has mucopurulent nasal drip and tenderness over the maxillae. The remainder of the examination is normal. A diagnosis of acute sinusitis is made, and antibiotic therapy is initiated. The patient has had 2 prior episodes of sinusitis this year. Medical history is significant for a recent episode of *Giardia lamblia* infection and a hospitalization last year for *Streptococcus pneumoniae* bacteremia; prior to this, the patient was in good health. She has had asthma since age 3 but takes no medications other than bronchodilators as needed. Height and weight are currently at the 5th percentile for age. All immunizations are up to date. Her developmental milestones were achieved on time. Complete blood count is as follows:

Hemoglobin	12 g/dL
Platelets	180,000/mm^3
Leukocytes	7,500/mm^3

Which of the following will be important in long-term management of this patient?

- A. Antiviral and antifungal prophylaxis
- B. Cultured thymus transplant
- C. Hematopoietic stem cell transplant

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no medications other than bronchodilators as needed. Height and weight are currently at the 5th percentile for age. All immunizations are up to date. Her developmental milestones were achieved on time. Complete blood count is as follows:

Hemoglobin	12 g/dL
Platelets	180,000/mm^3
Leukocytes	7,500/mm^3

Which of the following will be important in long-term management of this patient?

A. Antiviral and antifungal prophylaxis
B. Cultured thymus transplant
C. Hematopoietic stem cell transplant
D. Immunomodulator therapy
E. Intravenous immunoglobulin infusion

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no medications other than bronchodilators as needed. Height and weight are currently at the 5th percentile for age. All immunizations are up to date. Her developmental milestones were achieved on time. Complete blood count is as follows:

Hemoglobin	12 g/dL
Platelets	180,000/mm^3
Leukocytes	7,500/mm^3

Which of the following will be important in long-term management of this patient?

- A. Antiviral and antifungal prophylaxis [10%]
- B. Cultured thymus transplant [2%]
- C. Hematopoietic stem cell transplant [21%]
- D. Immunomodulator therapy [10%]
- ✔ E. Intravenous immunoglobulin infusion [54%]

Correct

54% Answered correctly

10 Seconds Time Spent

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Common variable immunodeficiency	
Manifestations	• Recurrent respiratory (eg, pneumonia, sinusitis, otitis) & GI (eg, *Salmonella, Campylobacter*) infections • Autoimmune disease (eg, RA, thyroid disease) • Chronic lung disease (eg, bronchiectasis) • GI disorders (eg, chronic diarrhea, IBD-like conditions)
Diagnosis	• ↓↓ IgG, ↓ IgA/IgM • No response to vaccination
Management	• Immunoglobulin replacement therapy

GI = gastrointestinal; **IBD** = inflammatory bowel disease; **RA** = rheumatoid arthritis.

This girl has had episodes of sinusitis, streptococcal bacteremia, and *Giardia lamblia* infection, as well as failure to thrive and a history of asthma. Her presentation is most suggestive of **common variable immunodeficiency** (CVID). In CVID, abnormal B-cell differentiation results in deficiency of multiple immunoglobulin classes (IgG and either IgA, IgM, or both). Affected patients are at risk for recurrent respiratory infections, frequently from encapsulated organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Many patients have *Giardia lamblia* infection. In some cases in which T-cell immunity is also affected, patients are also at increased risk for enteroviral encephalitis. Failure to thrive and chronic respiratory problems (eg, asthma, bronchiectasis) are common. CVID can present in childhood (around puberty) or, more commonly, in adulthood (age 20-40)

encapsulated organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Many patients have *Giardia lamblia* infection. In some cases in which T-cell immunity is also affected, patients are also at increased risk for enteroviral encephalitis. Failure to thrive and chronic respiratory problems (eg, asthma, bronchiectasis) are common. CVID can present in childhood (around puberty) or, more commonly, in adulthood (age 20-40).

Management of CVID is focused on avoiding infection, so the mainstay of treatment is intravenous immunoglobulin infusion. Early initiation of therapy may prevent some complications of chronic infection. Patients with CVID have increased risk of autoimmune disease and certain malignancies regardless of treatment.

(Choice A) Antiviral and antifungal prophylaxis is important in the management of patients with certain impairments in cellular immunity, such as T-cell or phagocytic disorders (eg, chronic granulomatous disease, severe combined immunodeficiency [SCID]), or transplant patients receiving immunosuppressive medications. Because cellular immunity is usually adequate in CVID, patients do not routinely require antiviral or antifungal prophylaxis.

(Choice B) In DiGeorge syndrome, lack of thymic tissue prevents maturation of hematopoietic precursors, so cultured thymic transplant can be curative. However, DiGeorge syndrome typically presents with dysmorphic facial features, palatal defects, cardiac abnormalities, disorders of calcium metabolism, developmental delays, and lymphopenia.

(Choice C) Hematopoietic stem cell transplant is used in Wiskott-Aldrich syndrome and SCID. Wiskott-Aldrich syndrome, an X-linked condition characterized by impaired cytoskeleton changes, can cause recurrent infections but is also associated with eczema and microthrombocytopenia with bleeding. Although SCID can cause recurrent

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(Choice C) Hematopoietic stem cell transplant is used in Wiskott-Aldrich syndrome and SCID. Wiskott-Aldrich syndrome, an X-linked condition characterized by impaired cytoskeleton changes, can cause recurrent infections but is also associated with eczema and microthrombocytopenia with bleeding. Although SCID can cause recurrent infections and diarrhea, the infections typically begin early in infancy, diarrhea is typically chronic, and patients often have rash, leukopenia, and infection after live vaccines.

(Choice D) Immunomodulators such as interferon gamma are used in chronic granulomatous disease, which is due to impaired phagocyte function and causes recurrent skin infections, skin abscesses, lung abscesses, and fungal infections.

Educational objective:

Common variable immunodeficiency is a disorder in which B-cell differentiation is abnormal, leading to decreased production of multiple immunoglobulin classes. Patients are at risk for infections by encapsulated bacteria, *Giardia*, and enterovirus. Failure to thrive and chronic pulmonary disease are common features. Management is primarily by infusion of intravenous immunoglobulins to prevent severe infection.

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Item 10 of 22
Question Id: 3198

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A 2-year-old boy is brought to the clinic due to a "boil" on his right arm. His medical history includes 3 previous skin infections. The patient had a perianal abscess incised and drained at age 2 months after no improvement following a course of oral antibiotics; cultures grew *Staphylococcus aureus*. At age 7 months, he had a left inguinal lymphadenitis due to *Serratia marcescens*. Last year, the patient had a left calf abscess requiring surgical drainage; cultures grew *Burkholderia cepacia*. His temperature is 37.3 C (99.2 F). Physical examination shows an indurated, fluctuant mass on the lateral aspect of the patient's right arm. The remainder of his physical examination is unremarkable. Laboratory studies show normal leukocyte, platelet, and B and T cell concentrations. Which of the following is the most likely diagnosis?

- A. Chediak-Higashi syndrome
- B. Chronic granulomatous disease
- C. DiGeorge syndrome
- D. Leukocyte adhesion defect
- E. Wiskott-Aldrich syndrome

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Item 10 of 22
Question Id: 3198

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- ✗ A. Chediak-Higashi syndrome [5%]
- ✓ B. Chronic granulomatous disease [78%]
- C. DiGeorge syndrome [0%]
- D. Leukocyte adhesion defect [13%]
- E. Wiskott-Aldrich syndrome [1%]

Incorrect
Correct answer
B

78%
Answered correctly

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Chronic granulomatous disease	
Clinical features	• Majority of cases X-linked recessive • Recurrent pulmonary & cutaneous infections • Catalase-positive pathogens (eg, *Staphylococcus aureus*, *Serratia*, *Burkholderia*, *Aspergillus*)

Diagnosis	• Neutrophil function testing
	  ◦ Dihydrorhodamine 123 test
	  ◦ Nitroblue tetrazolium test

This patient's recurrent skin and soft tissue abscesses with a variety of catalase-positive organisms are consistent with **chronic granulomatous disease** (CGD). CGD is caused by a gene defect in the NADPH oxidase enzyme complex, leading to an inability to form hydrogen peroxide and impaired intracellular killing in phagocytes. Patients with CGD classically present with recurrent, severe **cutaneous** and **pulmonary infections** with **catalase-positive bacterial** and **fungal** organisms (eg, *Staphylococcus aureus*, *Serratia, Burkholderia*, *Aspergillus*, *Nocardia*). Other common infections include suppurative adenitis and osteomyelitis.

Leukocyte, platelet, and B and T cell concentrations are normal in CGD. The diagnosis is made by oxidative burst testing (eg, dihydrorhodamine or nitroblue tetrazolium testing) and confirmed by gene testing. Patients with CGD should receive antimicrobial prophylaxis with trimethoprim-sulfamethoxazole and itraconazole. Patients with severe phenotypes benefit from interferon-gamma injections.

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(Choice A) Chediak-Higashi syndrome is an autosomal recessive disorder characterized by partial oculocutaneous albinism and recurrent cutaneous infections. *Staphylococcus aureus* and *Streptococcus pyogenes* are common. This patient does not have albinism, and *Burkholderia* and *Serratia* infections are inconsistent with Chediak-Higashi syndrome.

(Choice C) DiGeorge (22q11.2 deletion) syndrome presents with dysmorphic facies, developmental delays, hypocalcemia, and decreased T cell concentration and function (due to thymic hypoplasia). This patient does not have dysmorphic features or lymphopenia.

(Choice D) Leukocyte adhesion deficiency is characterized by impaired neutrophil migration to the site of infection. Affected patients present with delayed umbilical cord separation, recurrent non-purulent skin infections, severe periodontitis, and marked neutrophilia, none of which are present in this patient.

(Choice E) Wiskott-Aldrich syndrome is an X-linked recessive disease characterized by eczema, thrombocytopenia, and recurrent infections. This patient has a normal platelet count and does not have eczema.

Educational objective:
Chronic granulomatous disease presents with recurrent cutaneous and pulmonary infections with catalase-positive organisms (eg, *Staphylococcus aureus*, *Serratia*). Abnormal oxidative burst (eg, dihydrorhodamine testing) is diagnostic.

References

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Question Id: 2769

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A 17-year-old boy is brought to the emergency department for evaluation of facial swelling. Mild swelling of his lips this morning progressed to severe diffuse facial swelling by the afternoon. The patient has had no fevers, recent infections, abdominal pain, vomiting, or other swelling. He is a junior in high school and has been very stressed this week due to midterm examinations. His mother says that he had a similar episode when he had a tooth extracted a year ago. The patient has no chronic medical problems and takes no medications. His father and paternal grandmother both have hypertension. On arrival, temperature is 36.9 C (98.4 F), blood pressure is 120/80 mm Hg, pulse is 82/min, and respirations are 18/min. Examination shows severe edema of the entire face; the patient is unable to open his eyes. The lungs are clear to auscultation, and neither stridor nor muffled voice is present. No rashes are detected. Mild edema of the hands is also seen. Which of the following best explains the pathophysiology of this patient's condition?

A. Antibody-mediated hypersensitivity
B. C1 inhibitor deficiency
C. Cell-mediated hypersensitivity
D. Drug-induced bradykinin elevation
E. IgE-mediated hypersensitivity
F. Immune complex–mediated hypersensitivity

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infections, abdominal pain, vomiting, or other swelling. He is a junior in high school and has been very stressed this week due to midterm examinations. His mother says that he had a similar episode when he had a tooth extracted a year ago. The patient has no chronic medical problems and takes no medications. His father and paternal grandmother both have hypertension. On arrival, temperature is 36.9 C (98.4 F), blood pressure is 120/80 mm Hg, pulse is 82/min, and respirations are 18/min. Examination shows severe edema of the entire face; the patient is unable to open his eyes. The lungs are clear to auscultation, and neither stridor nor muffled voice is present. No rashes are detected. Mild edema of the hands is also seen. Which of the following best explains the pathophysiology of this patient's condition?

- ✗ A. Antibody-mediated hypersensitivity [2%]
- ✓ B. C1 inhibitor deficiency [76%]
- C. Cell-mediated hypersensitivity [3%]
- D. Drug-induced bradykinin elevation [5%]
- E. IgE-mediated hypersensitivity [8%]
- F. Immune complex–mediated hypersensitivity [3%]

Incorrect
Correct answer

76%
Answered correctly

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Hereditary angioedema	
Pathophysiology	• C1 inhibitor deficiency/dysfunction • Excessive bradykinin
Clinical features	• Swelling (eg, face, extremities, genitalia) without urticaria • Laryngeal edema • Colicky abdominal pain, vomiting, diarrhea
Diagnosis	• Low C4 level • Low C1 inhibitor protein or function
Management	• C1 inhibitor concentrate

This patient has **hereditary angioedema**, a condition characterized by **recurrent edema** without associated pruritus or urticaria. This autosomal dominant disorder is typically caused by a **deficiency** in or dysfunction of **C1 inhibitor** (previously referred to as C1 esterase inhibitor). A **C1 inhibitor** defect leads to elevated **bradykinin**, which causes edema.

Hereditary angioedema typically presents in late childhood or adolescence with an acute onset of swelling after a dental procedure, **stress**, or trauma. The **face**, limbs, and genitalia are most commonly affected. **Bowel wall** edema presents as colicky abdominal pain, vomiting, and diarrhea. However, the most life-threatening risk is laryngeal edema, which can cause **laryngospasm** and airway obstruction.

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Diagnosis is confirmed by complement testing. Exaggerated cleavage of C4 by C1 complex causes **depressed C4 levels**, and low levels of C1 inhibitor protein or C1 inhibitor function confirm the diagnosis. Treatment of acute swelling typically involves C1 inhibitor concentrate; a bradykinin antagonist (eg, icatibant) or kallikrein inhibitor (eg, ecallantide) may be effective in resistant cases.

(Choice A) Antibody-mediated (type II) hypersensitivity is seen with immune hemolytic anemia and Rh hemolytic disease of the newborn. IgG or IgM antibodies react with cell-bound antigens, leading to complement activation and cell destruction. Swelling is not associated with type II reactions.

(Choice C) The most common examples of cell-mediated (type IV) hypersensitivity are the tuberculin skin test and allergic contact dermatitis. Direct contact of the allergen with the skin causes dermal inflammation and a localized rash after a latent period of 1-2 days.

(Choice D) ACE inhibitors can cause elevated bradykinin, resulting in angioedema; however, this patient takes no medications, and the development of these episodes following periods of stress (eg, dental procedure, examinations) makes hereditary angioedema more likely.

(Choice E) IgE-mediated (type I) hypersensitivity, as seen with anaphylaxis, is caused by mast cell and basophil degranulation. Acute onset of swelling may occur, but pruritus and urticaria are also expected.

(Choice F) Immune complex–mediated (type III) hypersensitivity can be seen in serum sickness. Antibody complexes activate the complement cascade wherever the immune complexes deposit. Joint swelling, fever, and rash are typical findings.

rash after a latent period of 1-2 days.

(Choice D) ACE inhibitors can cause elevated bradykinin, resulting in angioedema; however, this patient takes no medications, and the development of these episodes following periods of stress (eg, dental procedure, examinations) makes hereditary angioedema more likely.

(Choice E) IgE-mediated (type I) hypersensitivity, as seen with anaphylaxis, is caused by mast cell and basophil degranulation. Acute onset of swelling may occur, but pruritus and urticaria are also expected.

(Choice F) Immune complex–mediated (type III) hypersensitivity can be seen in serum sickness. Antibody complexes activate the complement cascade wherever the immune complexes deposit. Joint swelling, fever, and rash are typical findings.

Educational objective:
Hereditary angioedema results from deficiency or dysfunction of C1 inhibitor and is characterized by recurrent episodes of edema (eg, face, limbs, genitalia, bowel, larynx) without associated pruritus or urticaria.

References

- Hereditary and acquired C1-inhibitor-dependent angioedema: from pathophysiology to treatment.
- Hereditary angio-oedema.

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Question Id: 7494
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A 57-year-old woman comes to the emergency department with 12 hours of fever, chills, and severe generalized weakness. She also has discomfort in her right upper quadrant and has had 2 episodes of vomiting. The patient underwent a liver transplant for primary biliary cirrhosis 2 weeks ago and currently takes prednisone, tacrolimus, and mycophenolate. Temperature is 39.1 C (102.5 F), blood pressure is 85/55 mm Hg, and pulse is 130/min. Physical examination reveals tenderness in her right upper quadrant with mild guarding. Laboratory results are as follows:

Complete blood count	
Hemoglobin	10.8 g/dL
Platelets	450,000/mm^3
Leukocytes	28,800/mm^3
Serum chemistry	
Sodium	139 mEq/L
Potassium	4.1 mEq/L
Chloride	101 mEq/L
Bicarbonate	25 mEq/L

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Blood urea nitrogen	31 mg/dL
Creatinine	1.3 mg/dL
Calcium	9.2 mg/dL
Glucose	105 mg/dL

Liver function studies

Total bilirubin	1.3 mg/dL
Alkaline phosphatase	203 U/L
Aspartate aminotransferase	105 U/L
Alanine aminotransferase	63 U/L

Coagulation studies

INR	1.3

Which of the following is the most likely cause of this patient's condition?

A. Acute cellular rejection

B. *Aspergillus* infection

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Alkaline phosphatase	203 U/L
Aspartate aminotransferase	105 U/L
Alanine aminotransferase	63 U/L

Coagulation studies

INR	1.3

Which of the following is the most likely cause of this patient's condition?

A. Acute cellular rejection
B. *Aspergillus* infection
C. Bacterial infection
D. *Cytomegalovirus* infection
E. Epstein-Barr virus infection
F. Hyperacute rejection
G. Lymphoproliferative disorder

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Alanine aminotransferase	63 U/L

Coagulation studies

INR	1.3

Which of the following is the most likely cause of this patient's condition?

- A. Acute cellular rejection [53%]
- B. *Aspergillus* infection [1%]
- ✔ C. Bacterial infection [18%]
- ✘ D. *Cytomegalovirus* infection [20%]
- E. Epstein-Barr virus infection [0%]
- F. Hyperacute rejection [4%]
- G. Lymphoproliferative disorder [1%]

Incorrect
Correct answer

18%
Answered correctly

17 Seconds
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This patient underwent **liver transplantation** 2 weeks ago and now has right upper quadrant pain, high fever, hypotension, tachycardia, and significant leukocytosis, suggesting sepsis due to an ongoing **bacterial infection**.

Infections continue to be the major cause of morbidity and mortality in patients who have undergone liver transplantation. **Length of time since transplant** helps categorize the likely infectious organism as follows:

- **<1 month:** Bacterial causes from operative complications (eg, hepatic abscess, biliary leak, wound infection) or hospitalization (eg, intravascular catheter, external drain)
- **Months 1-6**: Opportunistic pathogens (eg, *Cytomegalovirus, Aspergillus, Mycobacterium tuberculosis*) in the setting of high-dose immunosuppressive medication
- **>6 months**: Immunosuppressants usually at maintenance levels. Patients primarily at risk for typical community-acquired pathogens (at a higher rate than the general population)

(Choice A) Acute cellular rejection occurs <90 days after transplantation and can cause fever, right upper quadrant pain, and elevations in liver function tests. However, this patient also has rapid-onset hemodynamic instability, making a bacterial infection more likely. In addition, although prednisone use can cause leukocytosis, significant leukocytosis and high fever are more likely to indicate bacterial infection.

(Choices B, D, and E) Opportunistic infections such as *Cytomegalovirus, Aspergillus*, and Epstein-Barr virus are most common 1-6 months post transplantation in the setting of high-dose immunosuppressive regiments. This patient had rapid-onset hemodynamic decompensation with significant leukocytosis 2 weeks post transplantation, making a bacterial cause more likely.

instability, making a bacterial infection more likely. In addition, although prednisone use can cause leukocytosis, significant leukocytosis and high fever are more likely to indicate bacterial infection.

(Choices B, D, and E) Opportunistic infections such as *Cytomegalovirus*, *Aspergillus*, and Epstein-Barr virus are most common 1-6 months post transplantation in the setting of high-dose immunosuppressive regiments. This patient had rapid-onset hemodynamic decompensation with significant leukocytosis 2 weeks post transplantation, making a bacterial cause more likely.

(Choice F) Hyperacute rejection is a relatively rare form of rejection due to an antibody/complement-mediated response (eg, ABO mismatch). This outcome manifests <1 week after transplantation.

(Choice G) Post-transplant lymphoproliferative disease is usually due to Epstein-Barr virus in the setting of chronic high-dose immunosuppression. Fever, weight loss, and fatigue are common presenting symptoms. This patient with significant leukocytosis and rapid-onset symptoms 2 weeks post transplantation likely has a bacterial infection.

Educational objective:

Infections are common in patients who undergo liver transplantation. Likely etiology can be discerned based on the length of time since transplantation. Most infections within the first month are due to bacterial causes; infections during months 1-6 are usually caused by opportunistic pathogens (in the setting of high-dose immunosuppression).

A 3-year-old boy is brought to the clinic due to 3 days of fever and painful swelling in his right groin. His medical history includes 4 previous episodes of cutaneous abscesses and a lung abscess due to *Staphylococcus aureus*, all of which required drainage and prolonged antimicrobial therapy. The boy's maternal uncle died in childhood from recurrent infections. The patient's temperature is 38.5 C (101.3 F). Physical examination shows an enlarged, tender, and fluctuant lymph node in the right inguinal area. There are several areas of scarring over previous drainage sites. The remainder of the physical examination is normal. Laboratory results are as follows:

Complete blood count	
Hematocrit	40%
Platelets	320,000/mm^3
Leukocytes	11,000/mm^3
Neutrophils	50%
Bands	10%
Lymphocytes	35%

Gram stain of fluid aspirated from the affected lymph node reveals numerous organism-filled, segmented neutrophils. Cultures grow *Aspergillus niger*. Which of the following tests would most likely confirm this patient's diagnosis?

Leukocytes	11,000/mm^3
Neutrophils	50%
Bands	10%
Lymphocytes	35%

Gram stain of fluid aspirated from the affected lymph node reveals numerous organism-filled, segmented neutrophils. Cultures grow *Aspergillus niger*. Which of the following tests would most likely confirm this patient's diagnosis?

- A. B cell concentrations
- B. CH50 assay
- C. Dihydrorhodamine test
- D. Fluorescence in situ hybridization
- E. Immunoglobulin levels
- F. T cell concentrations

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Leukocytes	11,000/mm^3
Neutrophils	50%
Bands	10%
Lymphocytes	35%

Gram stain of fluid aspirated from the affected lymph node reveals numerous organism-filled, segmented neutrophils. Cultures grow *Aspergillus niger*. Which of the following tests would most likely confirm this patient's diagnosis?

- A. B cell concentrations [5%]
- B. CH50 assay [5%]
- ✔ C. Dihydrorhodamine test [62%]
- ✘ D. Fluorescence in situ hybridization [4%]
- E. Immunoglobulin levels [13%]
- F. T cell concentrations [9%]

Incorrect

Chronic granulomatous disease	
Clinical features	• Majority of cases X-linked recessive • Recurrent pulmonary & cutaneous infections • Catalase-positive pathogens (eg, *Staphylococcus aureus*, *Serratia*, *Burkholderia*, *Aspergillus*)

Diagnosis	• Neutrophil function testing
	  ◦ Dihydrorhodamine 123 test
	  ◦ Nitroblue tetrazolium test

This patient's pulmonary abscess and recurrent cutaneous abscesses with organism-filled neutrophils are consistent with **chronic granulomatous disease** (CGD). CGD is a primary immunodeficiency syndrome caused by a mutation that prevents phagocytic oxidative burst (formation of H_2O_2) and therefore impairs intracellular killing by phagocytes. CGD is most commonly inherited in an X-linked recessive manner, as seen in this male patient with a male extended family member who had similar symptoms.

Patients with CGD experience **recurrent infections** starting early in life and are particularly susceptible to **catalase-positive** organisms (eg, *Staphylococcus aureus*, *Aspergillus*). The **lungs** (eg, pneumonia, empyema) and **skin/soft tissue** (eg, abscesses, lymphadenitis) are the most common sites of infection. Phagocytic cells filled with bacteria are a frequent finding on Gram stain. The diagnosis is initially made by **testing neutrophil function** via detection or absence of an oxidative burst (eg, dihydrorhodamine 123 or nitroblue tetrazolium test).

function via detection or absence of an oxidative burst (eg, dihydrorhodamine 123 or nitroblue tetrazolium test). Patients with CGD should receive lifelong antimicrobial prophylaxis, and interferon gamma can be used to boost intracellular killing in severe cases.

(Choices A and E) Low B cell concentrations and immunoglobulin levels are characteristic of X-linked (Bruton) agammaglobulinemia. Patients present with recurrent sinopulmonary and gastrointestinal infections. *Aspergillus* infections and bacteria-filled phagocytes are inconsistent with X-linked agammaglobulinemia.

(Choice B) CH50 assays are used to determine total complement concentration. Complement deficiencies present with recurrent infections from encapsulated bacteria, particularly *Neisseria*. *Staphylococcus aureus* and *Aspergillus* infections are inconsistent with complement deficiency.

(Choices D and F) T cell concentrations are markedly low in severe combined immunodeficiency as well as in 22q11.2 deletion (DiGeorge syndrome). DiGeorge syndrome, definitively diagnosed by fluorescence in situ hybridization, also presents with dysmorphic facies, developmental delays, and hypocalcemia (due to parathyroid hypoplasia).

Educational objective:
Chronic granulomatous disease is caused by impaired intracellular killing by phagocytes. Pneumonia, cutaneous abscesses, and suppurative adenitis are common. Diagnosis is made by neutrophil function testing (eg, dihydrorhodamine 123 or nitroblue tetrazolium testing).

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Question Id: 4258

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A 15-month-old full-term boy is brought to the clinic for a well-child examination. He has been eating and sleeping well and is meeting all developmental milestones. His day care center had an outbreak of pertussis 6 weeks ago that required it to close for a few days, but the patient has had no cough, nasal congestion, or rhinorrhea. At age 6 months, he had a generalized seizure that lasted approximately 2 minutes within hours of receiving the diphtheria–tetanus–acellular pertussis vaccine. He was taken to the emergency department for observation and discharged later that day. The patient has had no other seizures or medical concerns and takes no medications. His uncle has a history of childhood-onset epilepsy. Vital signs and physical examination are normal. The child is due for the fourth dose of the diphtheria–tetanus–acellular pertussis vaccine. Which of the following is the best next step in management of this patient?

A. Administer the diphtheria and tetanus toxoids; avoid the pertussis component
B. Administer the diphtheria–tetanus–acellular pertussis vaccine as scheduled
C. Administer only the tetanus toxoid at this time
D. Hold all immunizations containing diphtheria, tetanus, or pertussis components
E. Prescribe only postexposure prophylaxis antibiotics

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Item 14 of 22
Question Id: 4258

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✗ A. Administer the diphtheria and tetanus toxoids; avoid the pertussis component [11%]

✓ B. Administer the diphtheria–tetanus–acellular pertussis vaccine as scheduled [69%]

C. Administer only the tetanus toxoid at this time [1%]

D. Hold all immunizations containing diphtheria, tetanus, or pertussis components [10%]

E. Prescribe only postexposure prophylaxis antibiotics [7%]

Incorrect

69%

198 Seconds

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Diphtheria–tetanus–acellular pertussis immunization	
Components	• Diphtheria toxoid • Tetanus toxoid • Conjugated pertussis antigen (pertactin)
Schedule	• 5 doses given at ages: ◦ 2, 4 & 6 months ◦ 15-18 months ◦ 4-6 years
Contraindications	• Encephalopathy after previous dose • Anaphylaxis to vaccine component

The **diphtheria–tetanus–acellular pertussis (DTaP) vaccine** is a combination vaccine containing acellular pertussis antigen with diphtheria and tetanus toxoids. Combination vaccines are safe, effective at preventing infection, and beneficial in reducing the number of needlesticks required (resulting in decreased pain and improved compliance). Children should receive 5 doses of the inactivated DTaP vaccine at ages 2, 4, and 6 months; 15-18 months; and 4-6 years.

The risk of an adverse reaction to the DTaP vaccine is low and generally includes minor erythema/swelling at the injection site and/or fever. **Seizure**, triggered by fever or by the pertussis vaccine component, is **rare** and is typically short (<5 minutes) and self-limited, as in this child. Patients with a family history of febrile seizures or

The risk of an adverse reaction to the DTaP vaccine is low and generally includes minor erythema/swelling at the injection site and/or fever. **Seizure**, triggered by fever or by the pertussis vaccine component, is **rare** and is typically short (<5 minutes) and self-limited, as in this child. Patients with a family history of febrile seizures or epilepsy may be at increased risk. However, neither personal nor family history of seizures is a contraindication to immunization. Specifically, uncomplicated seizure following vaccine administration is **not a contraindication** to future vaccination. The benefit of DTaP vaccination, especially in the setting of a pertussis outbreak, outweighs the unlikely risk of significant side effects.

The DTaP vaccine is contraindicated in a few circumstances. When **anaphylaxis** develops following DTaP administration, the patient should not receive future doses **(Choice D)**. In addition, **unstable neurologic disorders** (eg, infantile spasms, uncontrolled epilepsy) and **encephalopathy** (ie, coma, decreased level of consciousness, prolonged seizures) within a week of DTaP vaccine administration are **contraindications** to the combination vaccine; as a result, diphtheria and tetanus toxoids should be administered without pertussis **(Choices A and C)**.

(Choice E) Postexposure antibiotic prophylaxis is indicated for close contacts (eg, household, day care) of anyone with pertussis within the last 21 days. Because this child was exposed to pertussis 6 weeks ago, prophylactic antibiotics are no longer required.

Educational objective:
Anaphylaxis, unstable neurologic disorders, and encephalopathy (eg, coma, decreased consciousness, prolonged seizures) within a week of administration of the diphtheria–tetanus–acellular pertussis vaccine are

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typically short (<5 minutes) and self-limited, as in this child. Patients with a family history of febrile seizures or epilepsy may be at increased risk. However, neither personal nor family history of seizures is a contraindication to immunization. Specifically, uncomplicated seizure following vaccine administration is **not a contraindication** to future vaccination. The benefit of DTaP vaccination, especially in the setting of a pertussis outbreak, outweighs the unlikely risk of significant side effects.

The DTaP vaccine is contraindicated in a few circumstances. When **anaphylaxis** develops following DTaP administration, the patient should not receive future doses **(Choice D)**. In addition, **unstable neurologic disorders** (eg, infantile spasms, uncontrolled epilepsy) and **encephalopathy** (ie, coma, decreased level of consciousness, prolonged seizures) within a week of DTaP vaccine administration are **contraindications** to the combination vaccine; as a result, diphtheria and tetanus toxoids should be administered without pertussis **(Choices A and C)**.

(Choice E) Postexposure antibiotic prophylaxis is indicated for close contacts (eg, household, day care) of anyone with pertussis within the last 21 days. Because this child was exposed to pertussis 6 weeks ago, prophylactic antibiotics are no longer required.

Educational objective:
Anaphylaxis, unstable neurologic disorders, and encephalopathy (eg, coma, decreased consciousness, prolonged seizures) within a week of administration of the diphtheria–tetanus–acellular pertussis vaccine are contraindications for future administration of pertussis-containing vaccines. However, uncomplicated seizures are not.

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Question Id: 3993

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An 18-year-old woman is brought to the emergency department with severe abdominal pain. Medical history includes asthma, eczema, and multiple episodes of pneumonia. Her temperature is 37.2 C (99 F), blood pressure is 90/60 mm Hg, and pulse is 128/min. Physical examination shows pallor and a tender, rigid abdomen. Laboratory studies reveal a hemoglobin concentration of 6.9 mg/dL and platelet count of 378,000/mm^3. Emergency laparotomy reveals a ruptured ectopic pregnancy. The patient receives a transfusion with blood type O, Rh-negative, packed red blood cells. During the transfusion, she experiences generalized hives and a drop in blood pressure to 70/40 mm Hg. The transfusion is stopped and intramuscular epinephrine is administered. Which of the following is the most likely diagnosis?

A. Bacterial contamination from transfusion
B. Blood group incompatibility
C. Cystic fibrosis
D. Hyper-IgM syndrome
E. Selective IgA deficiency
F. Wiskott-Aldrich syndrome
G. X-linked agammaglobulinemia

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is 90/60 mm Hg, and pulse is 128/min. Physical examination shows pallor and a tender, rigid abdomen. Laboratory studies reveal a hemoglobin concentration of 6.9 mg/dL and platelet count of 378,000/mm^3. Emergency laparotomy reveals a ruptured ectopic pregnancy. The patient receives a transfusion with blood type O, Rh-negative, packed red blood cells. During the transfusion, she experiences generalized hives and a drop in blood pressure to 70/40 mm Hg. The transfusion is stopped and intramuscular epinephrine is administered.

Which of the following is the most likely diagnosis?

- A. Bacterial contamination from transfusion [0%]
- ✗ B. Blood group incompatibility [9%]
- C. Cystic fibrosis [0%]
- D. Hyper-IgM syndrome [5%]
- ✓ E. Selective IgA deficiency [76%]
- F. Wiskott-Aldrich syndrome [5%]
- G. X-linked agammaglobulinemia [0%]

Incorrect
Correct answer

76%
Answered correctly

7 Seconds
Time Spent

09/13/2018
Last Updated

Selective IgA deficiency	
Epidemiology	• Most common primary immune deficiency
Clinical features	• Usually asymptomatic • Recurrent sinopulmonary & gastrointestinal infections • Associated with autoimmune disease (eg, celiac) & atopy (eg, asthma, eczema) • Anaphylaxis during transfusions
Diagnosis	• Low or absent IgA • Normal IgG, IgM levels, B cells
Treatment	• Supportive care • Medical alert bracelet for transfusion reactions (for severe deficiency)

This patient has a history of recurrent pneumonia, atopy (eg, asthma, eczema), and an anaphylactic reaction during blood transfusion. These findings are highly suggestive of **selective IgA deficiency**, the most common primary immunodeficiency. Serum IgA levels are low or undetectable due to failure of B cells to differentiate into IgA-secreting plasma cells; serum IgG and IgM levels are normal. Although most patients with IgA deficiency are asymptomatic, some have recurrent **sinopulmonary** (eg, sinusitis, pneumonia) and **gastrointestinal infections**

IgA-secreting plasma cells; serum IgG and IgM levels are normal. Although most patients with IgA deficiency are asymptomatic, some have recurrent **sinopulmonary** (eg, sinusitis, pneumonia) and **gastrointestinal infections** (eg, *Giardia*) due to absence of secretory IgA as a mucosal barrier. Concomitant atopic and autoimmune disorders (eg, systemic lupus erythematosus, celiac disease) are common.

Patients with severe IgA deficiency can form IgE antibodies directed against IgA (anti-IgA antibodies). When transfused with **blood products** (eg, red blood cells, platelets, fresh frozen plasma) containing small amounts of IgA, these patients can develop potentially fatal **anaphylaxis**. Therefore, patients with severe IgA deficiency should wear medical alert bracelets and receive blood products that are washed of residual plasma or from an IgA-deficient donor.

(Choice A) Bacterial contamination results from bacteria entering the blood component during processing. When these bacteria are introduced during the transfusion, they can cause septic shock (fever, chills, hypotension) but do not cause anaphylaxis.

(Choice B) Blood group (eg, ABO, Rh, minor antigen) incompatibility, which is less common with donor O-negative blood, causes an acute hemolytic reaction. Common findings are fever, flank pain, and hemoglobinuria, but not anaphylaxis.

(Choice C) Cystic fibrosis (CF) is characterized by abnormal sodium and chloride transport leading to pancreatic insufficiency and chronic, severe respiratory disease. Abnormal antibody production and transfusion reactions are not associated with CF.

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(Choice C) Cystic fibrosis (CF) is characterized by abnormal sodium and chloride transport leading to pancreatic insufficiency and chronic, severe respiratory disease. Abnormal antibody production and transfusion reactions are not associated with CF.

(Choices D and G) Patients with hyper-IgM syndrome (high IgM; low IgA, IgG) and X-linked (Bruton) agammaglobulinemia (low IgA, IgG, IgM) can also present with recurrent sinopulmonary infections in childhood. However, they do not develop anti-IgA antibodies and therefore do not experience anaphylaxis during transfusions.

(Choice F) Wiskott-Aldrich syndrome classically presents in infancy with recurrent sinopulmonary infections, eczema, and thrombocytopenia. It is not associated with anaphylaxis during transfusions. In addition, this patient's platelet count is normal.

Educational objective:
Selective IgA deficiency is the most common primary immune deficiency, and can present with recurrent sinopulmonary and gastrointestinal infections as well as atopic and autoimmune disease. With severe deficiency, production of anti-IgA antibodies can lead to anaphylaxis during blood transfusion.

References

- Selective IgA deficiency.

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A 1-year-old boy is admitted to the intensive care unit for severe respiratory distress and hypoxia requiring endotracheal intubation and mechanical ventilation. Medical history shows 2 prior episodes of pneumonia, chronic thrush, and tympanostomy tube placement for recurrent otitis media. His vaccinations are not fully up to date due to illness at the time of his well visits. The patient is at the 2nd percentile for height and weight. Physical examination shows diffuse crackles in both lungs. Laboratory results are as follows:

Complete blood count	
Leukocyte count	9,000/mm^3
Lymphocytes	5%
CD19+	low
CD3+	absent
Immunologic and rheumatologic studies	
HIV-1 antibody	negative
Immunoglobulins	
IgG	220 mg/dL
IgA	45 mg/dL

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Immunologic and rheumatologic studies

HIV-1 antibody	negative
Immunoglobulins	
IgG	220 mg/dL
IgA	45 mg/dL
IgM	18 mg/dL

Which of the following is the best long-term treatment for this patient?

A. Antiretroviral therapy
B. Broad-spectrum antibiotics
C. Catch-up vaccinations
D. Intravenous immunoglobulin
E. Stem cell transplantation

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Immunologic and rheumatologic studies

HIV-1 antibody	negative
Immunoglobulins	
IgG	220 mg/dL
IgA	45 mg/dL
IgM	18 mg/dL

Which of the following is the best long-term treatment for this patient?

- A. Antiretroviral therapy [1%]
- B. Broad-spectrum antibiotics [4%]
- C. Catch-up vaccinations [3%]
- D. Intravenous immunoglobulin [18%]
- ✔ E. Stem cell transplantation [72%]

Correct

72% Answered correctly

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Severe combined immunodeficiency	
Etiology	• Gene defect leading to failure of T cell development • B cell dysfunction due to absent T cells
Inheritance	• X-linked recessive • Autosomal recessive
Clinical features	• Recurrent, severe viral, fungal, or opportunistic (ie, *Pneumocystis*) infections • Failure to thrive • Chronic diarrhea
Treatment	• Stem cell transplant

This patient has recurrent and severe infections, failure to thrive, and lymphopenia (CD19+ = B cells, CD3+ = T cells). These findings are consistent with **severe combined immunodeficiency** (SCID). SCID is a severe primary immunodeficiency caused by one of several gene defects leading to failure of **T cell development**. Without cellular immunity, patients with SCID are at high risk for infections with viruses, fungi (eg, *Candida* [thrush]), and opportunistic pathogens (eg, *Pneumocystis jirovecii*). The loss of helper T cell function also causes B cell dysfunction (ie, impaired humoral immunity) and recurrent sinopulmonary bacterial infections (eg,

This patient has recurrent and severe infections, failure to thrive, and lymphopenia (CD19+ = B cells, CD3+ = T cells). These findings are consistent with **severe combined immunodeficiency** (SCID). SCID is a severe primary immunodeficiency caused by one of several gene defects leading to failure of **T cell development**. Without cellular immunity, patients with SCID are at high risk for infections with viruses, fungi (eg, *Candida* [thrush]), and opportunistic pathogens (eg, *Pneumocystis jirovecii*). The loss of helper T cell function also causes B cell dysfunction (ie, impaired humoral immunity) and recurrent sinopulmonary bacterial infections (eg, pneumonia, otitis media). In addition to infection, **failure to thrive** and chronic diarrhea in infancy are typical.

Stem cell transplantation is the only definitive therapy and should be performed as early as possible. Replacement of defective immature T cells with normal hematopoietic cells allows the development of a functional immune system. SCID is usually fatal in early childhood unless transplantation is performed.

(Choice A) Antiretroviral therapy is used to treat patients with HIV infection. Perinatal HIV infection can present in a similar manner (eg, recurrent and severe infections, failure to thrive, lymphopenia) to SCID, but this patient's HIV test is negative.

(Choices B and D) Intravenous immunoglobulin and broad-spectrum antibiotic therapy are short-term management options for SCID while awaiting transplantation. Intravenous immunoglobulin can be used for long-term therapy in certain humoral immunodeficiency syndromes (eg, X-linked agammaglobulinemia, common variable immunodeficiency).

(Choice C) Live, attenuated vaccines (eg, measles-mumps-rubella, varicella) are contraindicated in SCID as they can cause severe or fatal disease. Inactivated vaccines are not contraindicated but will not result in protective

test is negative.

(Choices B and D) Intravenous immunoglobulin and broad-spectrum antibiotic therapy are short-term management options for SCID while awaiting transplantation. Intravenous immunoglobulin can be used for long-term therapy in certain humoral immunodeficiency syndromes (eg, X-linked agammaglobulinemia, common variable immunodeficiency).

(Choice C) Live, attenuated vaccines (eg, measles-mumps-rubella, varicella) are contraindicated in SCID as they can cause severe or fatal disease. Inactivated vaccines are not contraindicated but will not result in protective immunity due to poor humoral response.

Educational objective:
Severe combined immunodeficiency presents in infancy with severe infections, failure to thrive, and chronic diarrhea. Absence of T cells and dysfunctional B cells are diagnostic. Treatment requires urgent stem cell transplantation.

References

- Transplantation of hematopoietic stem cells in human severe combined immunodeficiency: Long-term outcomes.

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A 60-year-old man with chronic obstructive pulmonary disease comes to the emergency department with severe dyspnea, a productive cough, and fever for the last 3 days. His temperature is 39.4 C (103 F), blood pressure is 110/62 mm Hg, pulse is 120/min, and respirations are 35/min. His chest x-ray shows a right lower-lobe infiltrate. Sputum examination shows gram-positive cocci. The patient is given intravenous antibiotics and eventually improves. On hospital discharge, he is offered a polysaccharide vaccine that can help prevent future occurrences of his infection. This vaccine induces immunity by which of the following mechanisms?

A. Increased mucosal IgA production
B. Natural killer cell response
C. Relatively T-cell-independent B-cell response
D. Proliferation of CD8+ T cells
E. T-cell-dependent B-cell response with memory B-cell production

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✗ A. Increased mucosal IgA production [3%]

B. Natural killer cell response [1%]

✓ C. Relatively T-cell-independent B-cell response [30%]

D. Proliferation of CD8+ T cells [2%]

E. T-cell-dependent B-cell response with memory B-cell production [62%]

Incorrect
Correct answer
C

30%
Answered correctly

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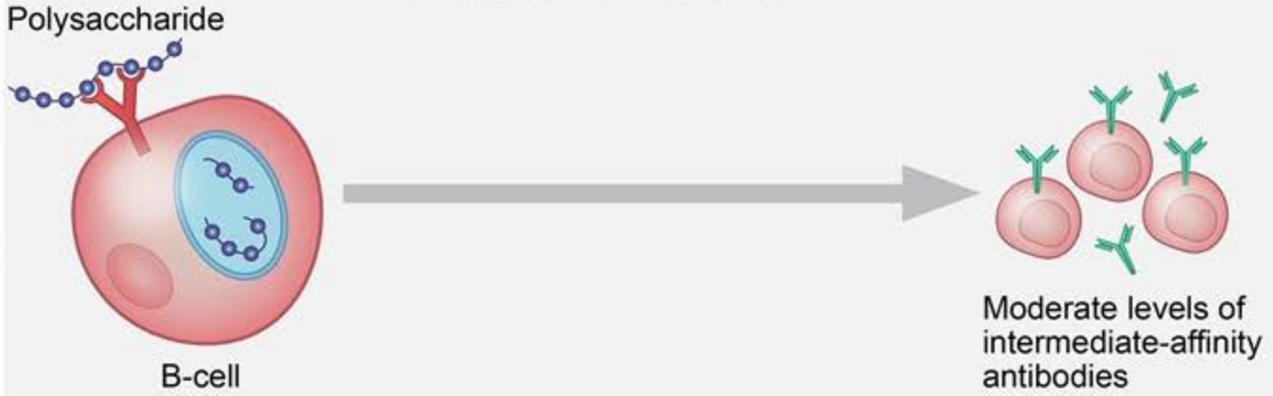
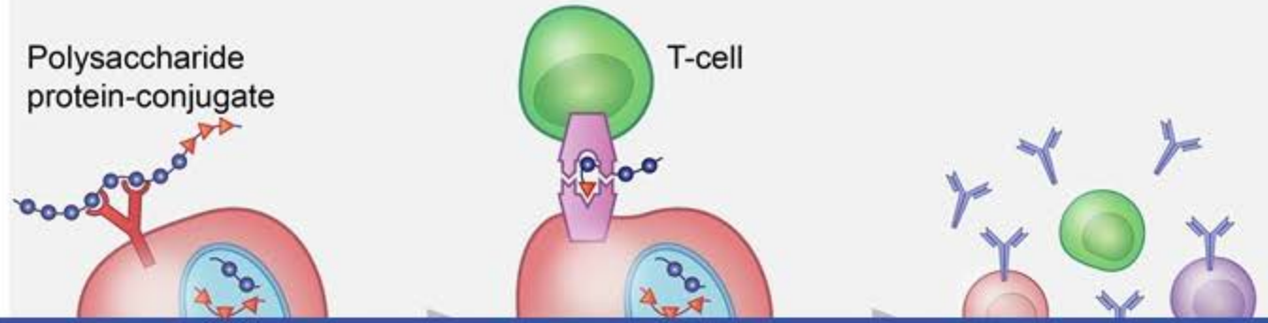
Polysaccharide vaccine



Advantages

- ↓ Incidence of replacement strains due to lack of mucosal immunity

Conjugate vaccine



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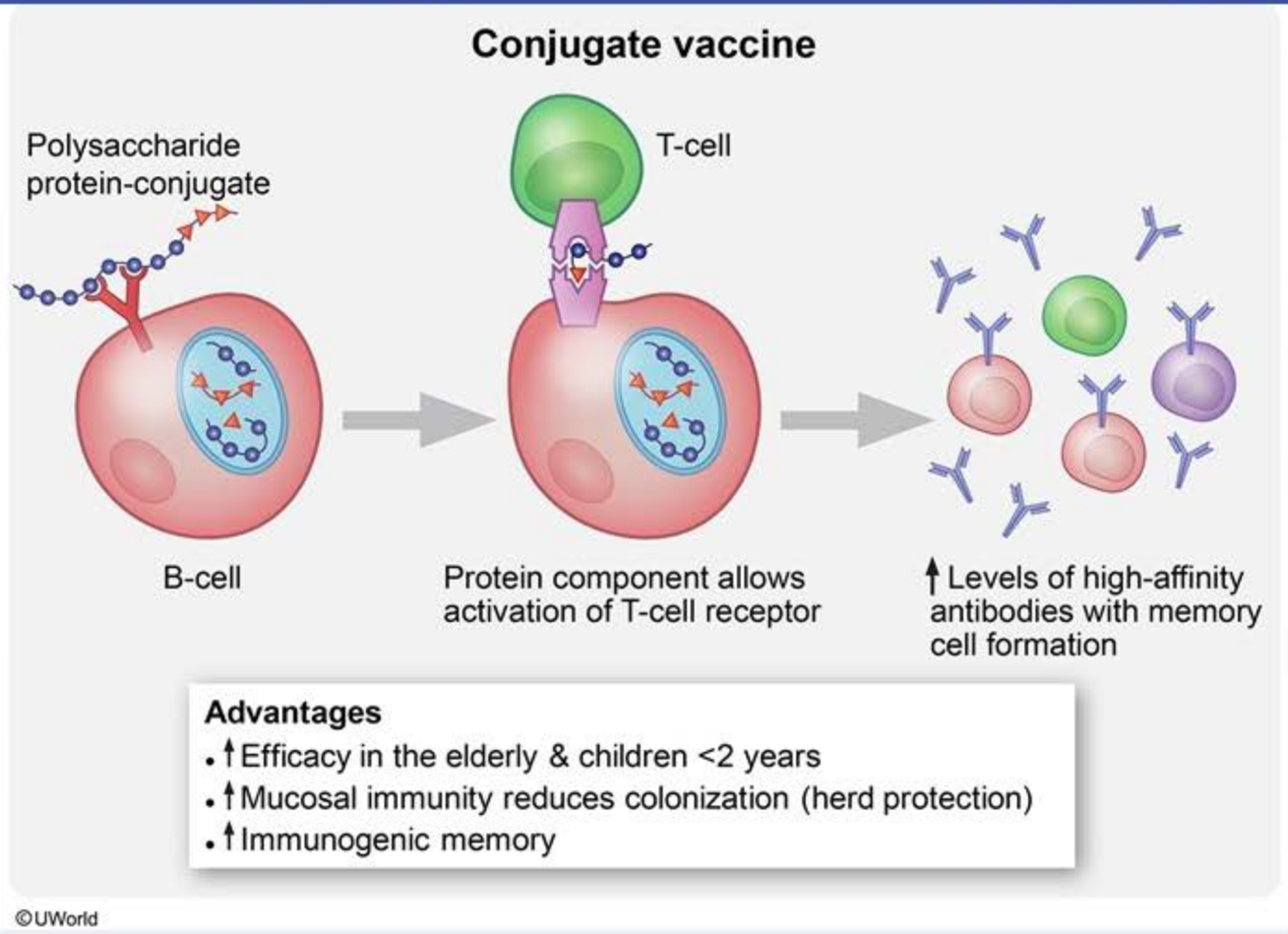

This patient has **pneumococcal pneumonia**, which is caused by a variety of *Streptococcus pneumoniae* serotypes. Each infectious serotype produces a distinct capsular polysaccharide, and anti-capsular antibodies formed during an immune response provide immunity against only a single serotype. As such, at-risk patients are

This patient has **pneumococcal pneumonia**, which is caused by a variety of *Streptococcus pneumoniae* serotypes. Each infectious serotype produces a distinct capsular polysaccharide, and anti-capsular antibodies formed during an immune response provide immunity against only a single serotype. As such, at-risk patients are given a pneumococcal vaccine containing multiple capsular antigens. Two types of vaccines are currently available for use in the United States:

1. **Pneumococcal polysaccharide vaccine** (PPSV23) contains capsular material from 23 serotypes that have historically been responsible for the majority of pneumococcal infections. Because polysaccharides alone cannot be presented to T cells, the vaccine induces a relatively T-cell-independent B-cell response that is less effective in young children and the elderly.

2. **Pneumococcal conjugate vaccine** (PCV13) consists of capsular polysaccharides from 13 of the most common serotypes that have been covalently attached to inactivated diphtheria toxin protein. This polysaccharide-protein conjugate induces a T-cell-dependent B-cell response, resulting in improved immunogenicity due to the formation of higher-affinity antibodies and memory cells **(Choice E)**.

Routine administration of the PCV13 is recommended for **all infants and young children**. PPSV23 is administered to **adults age <65 with predisposing comorbidities** (eg, chronic heart or lung disease, diabetes mellitus, cirrhosis). **Immunocompromised patients** and **all individuals age >65** should receive both vaccines to maximize protection.

(Choice A) Certain vaccines induce a predominantly IgA (mucosal) response. An example is the oral polio vaccine, which promotes the secretion of anti-poliovirus IgA antibodies into the gastrointestinal tract

maximize protection.

(Choice A) Certain vaccines induce a predominantly IgA (mucosal) response. An example is the oral polio vaccine, which promotes the secretion of anti-poliovirus IgA antibodies into the gastrointestinal tract.

(Choice B) The natural killer (NK) cell response is a component of the body's innate immunity. NK cells are lymphocytes that can nonspecifically recognize stressed and abnormal cells. They attack principally cancer cells and virus-infected cells. NK cells are not involved in the immune response to vaccines.

(Choice D) Proliferation of CD8+ T cells occurs mainly in response to intracellular pathogens. Certain live attenuated vaccines, such as the measles (MMR) and intranasal influenza vaccines, produce a predominately CD8+ T-cell response.

Educational objective:

The 23-valent pneumococcal vaccine contains capsular polysaccharides and induces a relatively T-cell-independent B-cell response. In contrast, the 13-valent pneumococcal vaccine contains capsular polysaccharides conjugated to a protein antigen, which allows for a more robust T-cell-dependent B-cell response.

References

- Review: current and new generation pneumococcal vaccines

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A 62-year-old man comes to the office with a 4-week history of itchy, dry skin on the hands. He has experienced scaly, cracking skin at the dorsum of both hands extending to the fingers. The patient has tried moisturizer lotions with some relief, but the symptoms are persistent. Medical history is notable for seasonal allergies, hypertension, benign prostatic hyperplasia, and an occasional herpes rash on his upper lip following upper respiratory infections. He works as a dentist and does not use tobacco, alcohol, or illicit drugs. Examination shows dry, crusted, and irritated skin with erythema at the fingers, finger webs, and dorsum of the hands, as shown in the image. A few vesicles are noted at the finger webs. No other skin lesions are seen. Which of the following is the most likely diagnosis?

- A. Contact dermatitis
- B. Herpetic whitlow
- C. Psoriasis
- D. Scabies
- E. Tinea manuum

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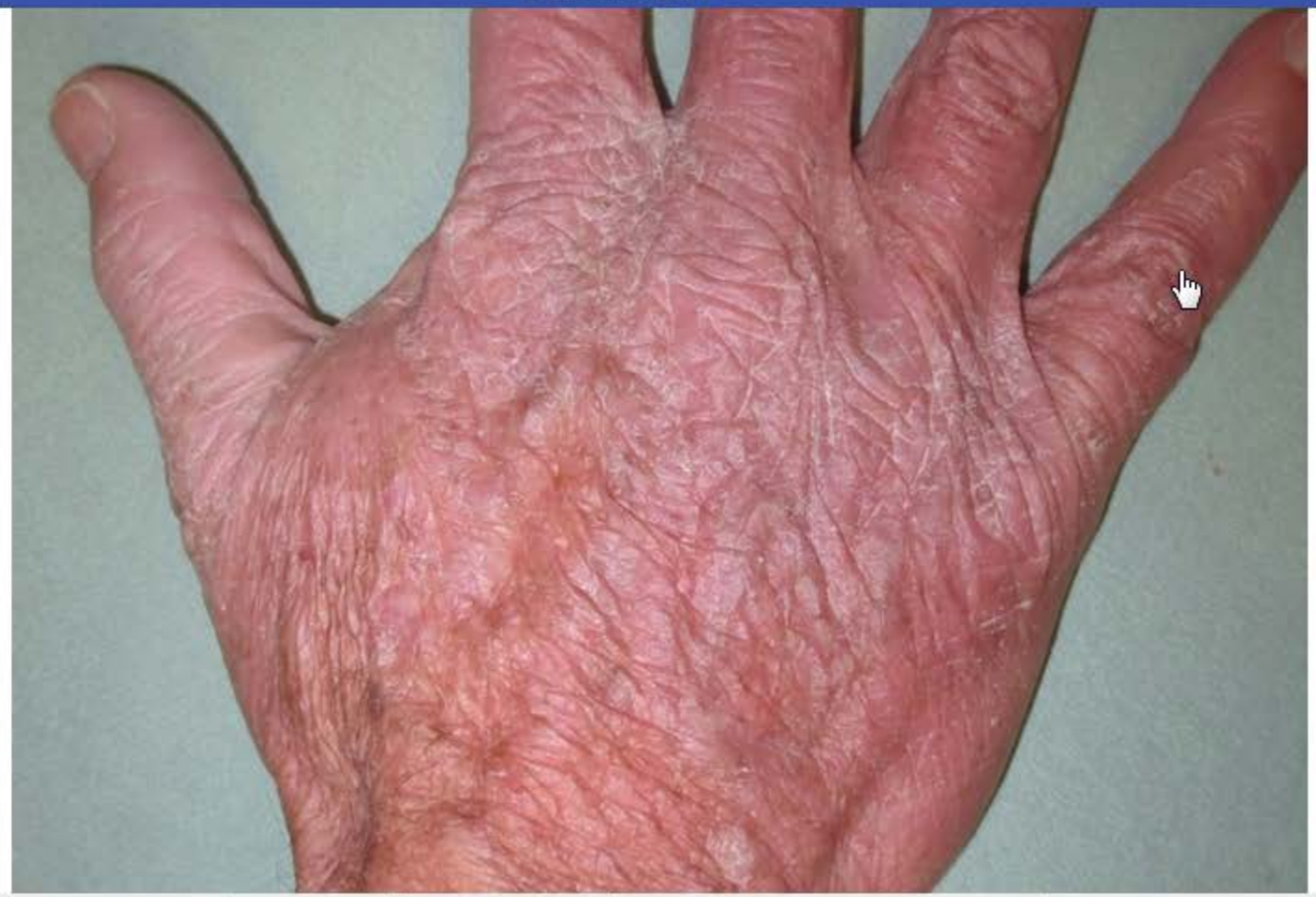

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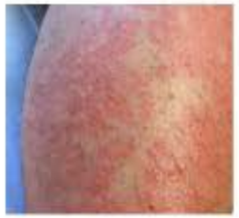
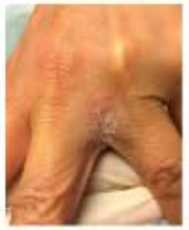
Contact dermatitis

	Allergic	Irritant
		
Pathophysiology	Type IV hypersensitivity	Physical or chemical irritation
Triggers	• Poison oak/ivy/sumac • Nickel • Rubber/latex • Leather dyes • Medications	• Soaps/detergents • Chemicals • Acid/alkali
Appearance	• Primarily on exposed skin, well demarcated • Erythema • Papules/vesicles • Chronic lichenification	• Commonly on hands • Erythema • Fissures

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This patient with a scaly, pruritic rash on the hands has **irritant contact dermatitis** (ICD), possibly due to frequent hand washing as a dentist. ICD is a localized inflammatory reaction that can be triggered by a variety of chemicals, solvents, cleaning products, or acidic/alkaline solutions. ICD is **nonimmunologically mediated** but can resemble allergic contact dermatitis with pruritus, erythema, local swelling, and vesicles. Symptoms can develop acutely (within hours of exposure) but are often **chronic**, leading to excoriations, hyperkeratosis, and fissuring of involved skin.

Emollients and use of **protective barriers** can often relieve symptoms. However, identification and avoidance of the offending agent are also essential, although this is frequently challenging, as many common household and occupational products can contribute to symptoms. The diagnosis of ICD (and allergic contact dermatitis) is usually based on **clinical findings**, but if initial measures do not clear the rash, skin biopsy may be required for confirmation.

(Choice B) Herpetic whitlow is due to inoculation of herpes simplex virus into broken skin. Patients experience tingling and burning of the hand associated with a localized vesicular rash. Symptoms would not be bilateral and symmetric.

(Choice C) Palmoplantar psoriasis causes thickened erythematous plaques with fissuring on the palms and/or soles, often with scaling. Features that would differentiate palmoplantar psoriasis from contact dermatitis include typical psoriatic scaling, nail changes, and the presence of psoriasis elsewhere on the body.

(Choice D) Typical scabies lesions are small, erythematous, papules and irregular burrows. They predominantly involve the finger webs, flexural surfaces, belt line, and buttocks. More diffuse skin involvement can be seen in

(Choice C) Palmoplantar psoriasis causes thickened erythematous plaques with fissuring on the palms and/or soles, often with scaling. Features that would differentiate palmoplantar psoriasis from contact dermatitis include typical psoriatic scaling, nail changes, and the presence of psoriasis elsewhere on the body.

(Choice D) Typical scabies lesions are small, erythematous, papules and irregular burrows. They predominantly involve the finger webs, flexural surfaces, belt line, and buttocks. More diffuse skin involvement can be seen in crusted scabies, but this is typically seen in immunocompromised individuals.

(Choice E) Tinea manuum is a superficial fungal infection of the hands. It typically presents as pruritic, hyperkeratotic patches on the palms or annular erythematous lesions resembling tinea corporis on the dorsum of the hands and finger webs. Most patients have concurrent tinea pedis.

Educational objective:

Irritant contact dermatitis can be triggered by a variety of chemicals, solvents, cleaning products, or acidic/alkaline solutions. It is nonimmunologically mediated but can resemble allergic contact dermatitis with pruritus, erythema, local swelling, and vesicles. Chronic symptoms include excoriations, hyperkeratosis, and fissuring of skin.

References

- Hand dermatitis: review of etiology, diagnosis, and treatment.

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Emollients and use of **protective barriers** can often relieve symptoms. However, identification and avoidance of

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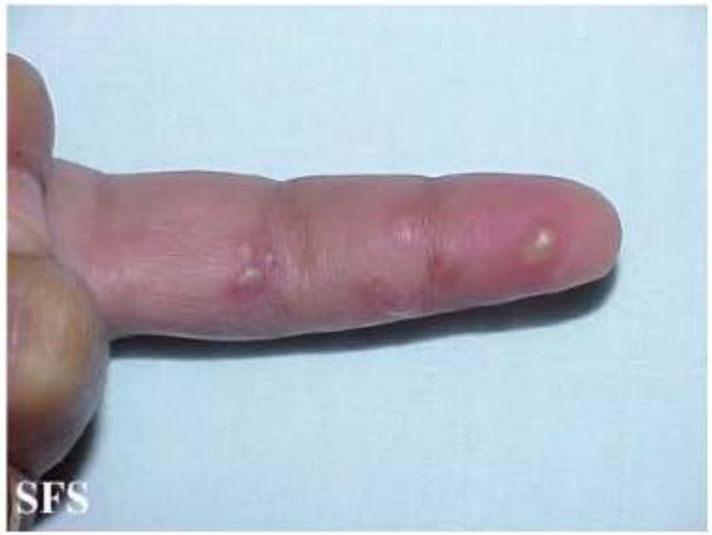

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Emollients and use of **protective barriers** can often relieve symptoms. However, identification and avoidance of

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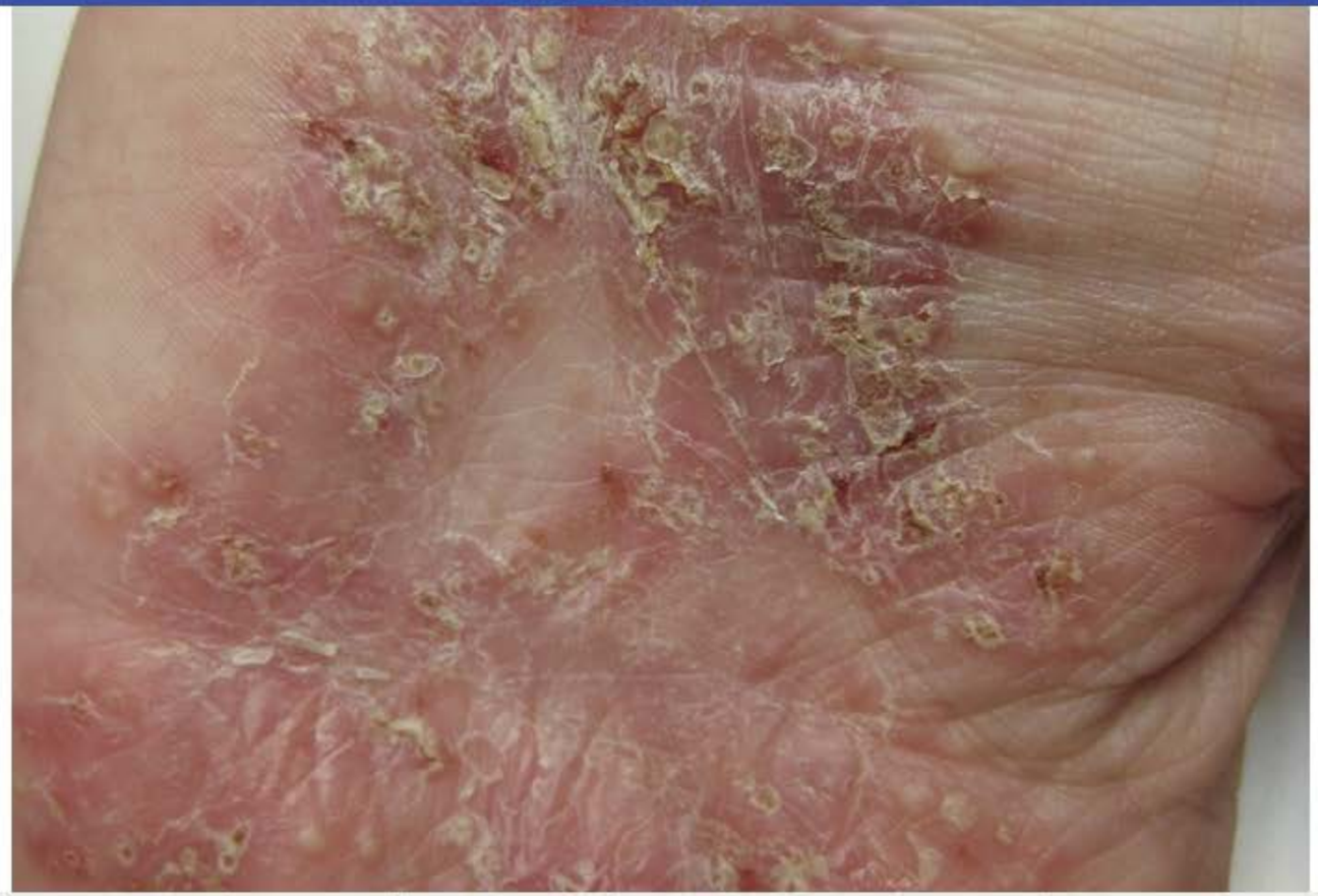

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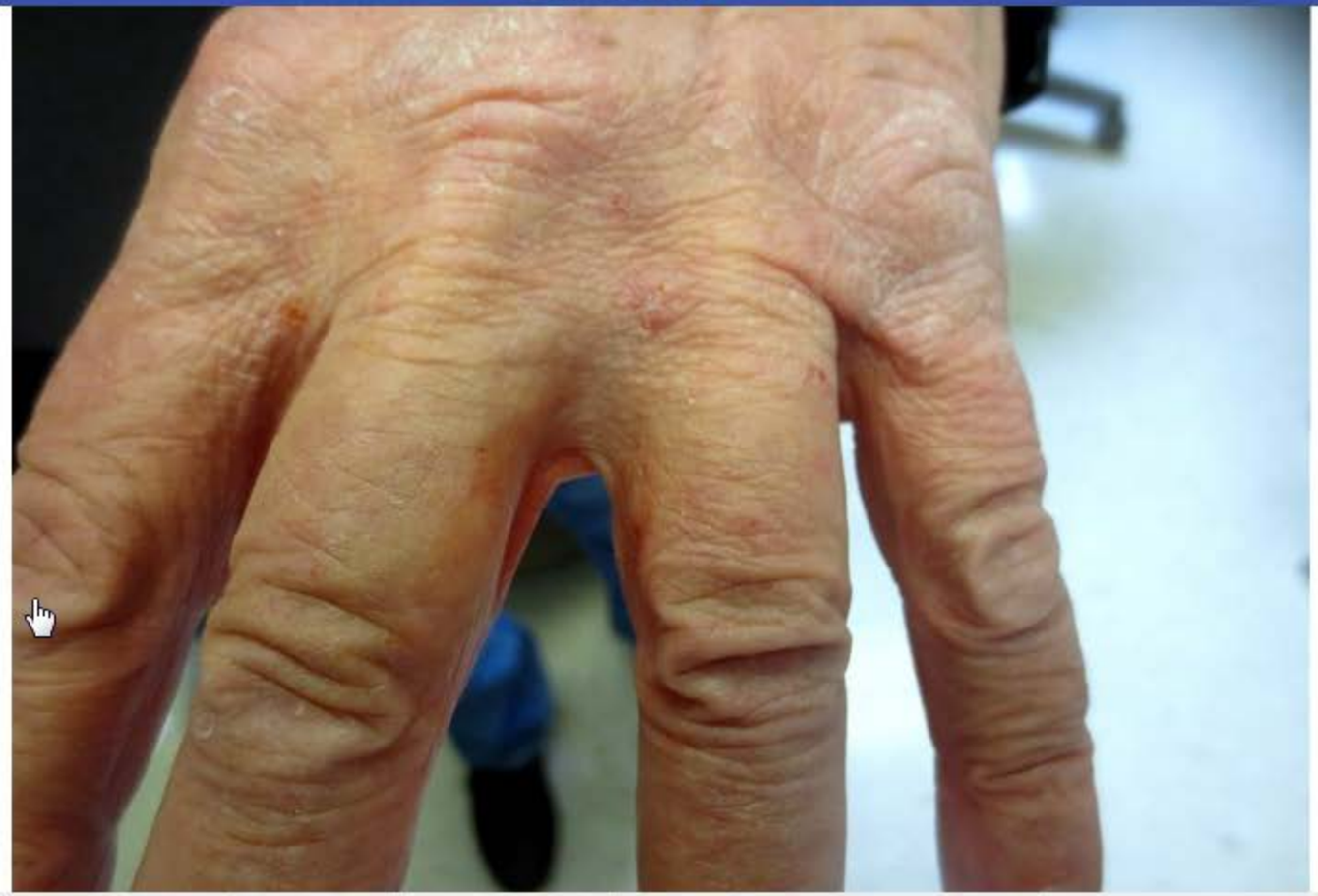

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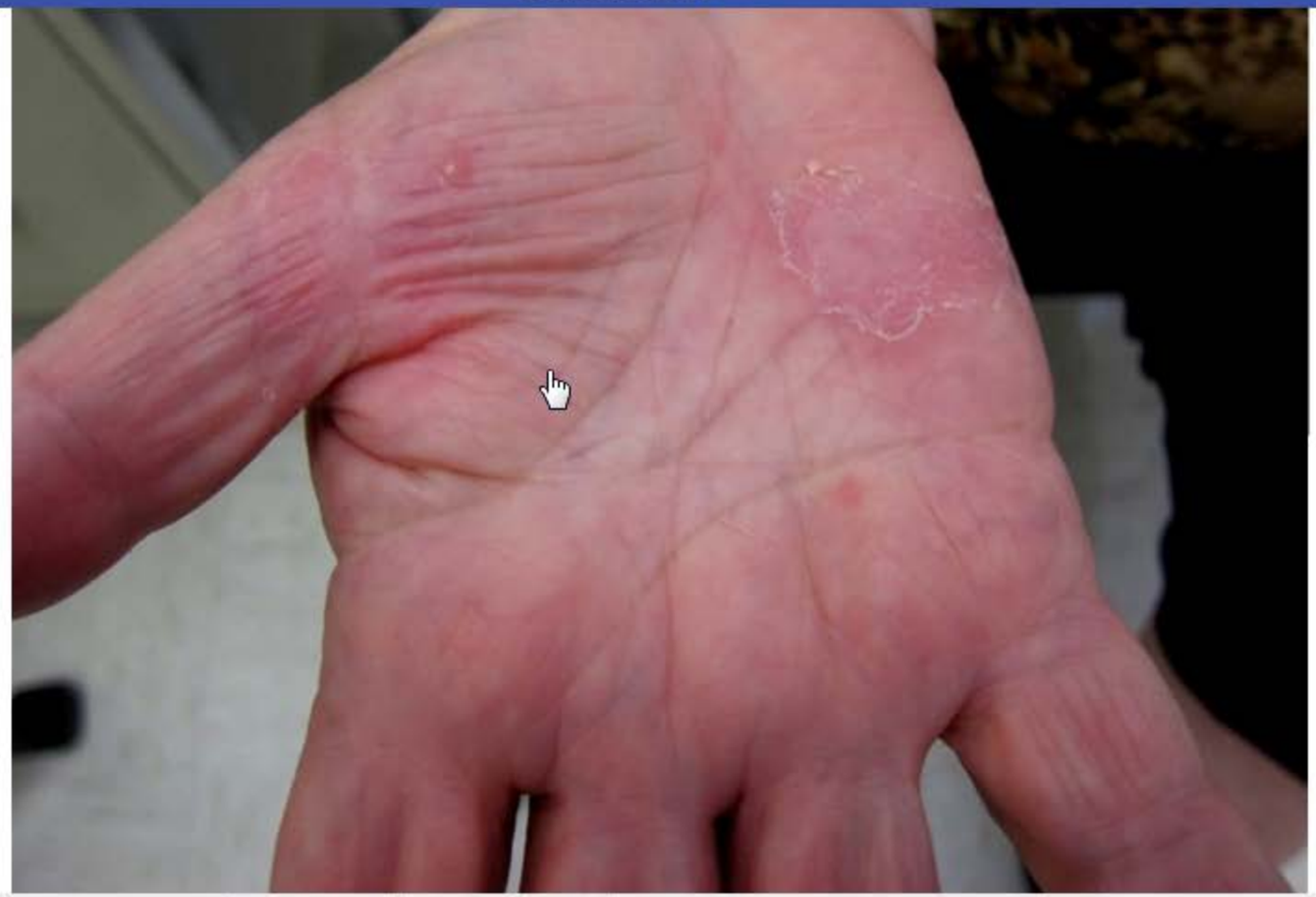

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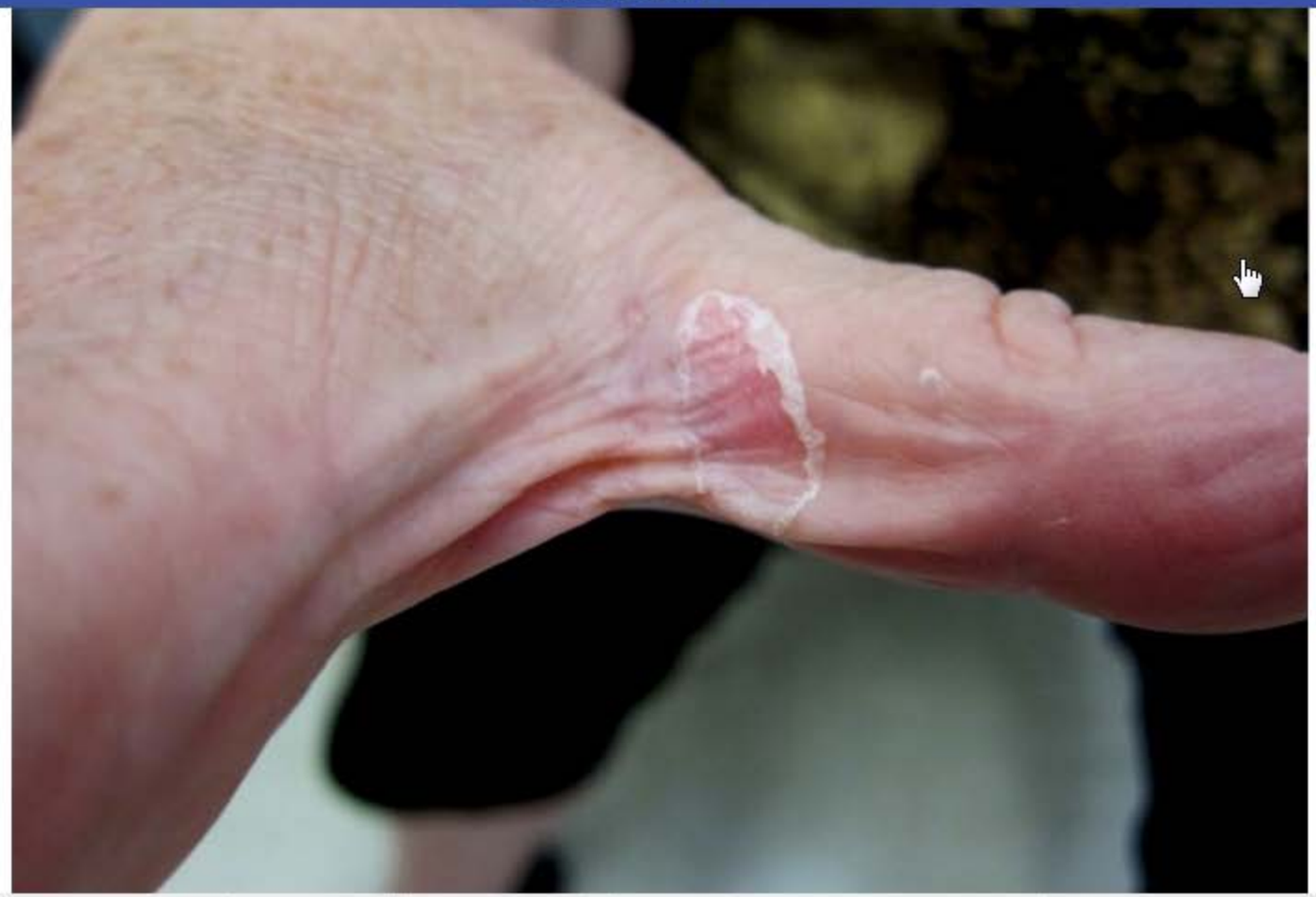

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A 50-year-old man comes to the emergency department due to acute onset respiratory difficulty. He also has periorbital, circumoral and facial edema. He denies any itching or skin rash. Two weeks ago, he experienced chest pain, profuse sweating and anxiety, and was subsequently admitted to the cardiac intensive care unit. At that time, his ECG showed ST segment elevation and Q waves in the inferior leads. He was taken to the catheterization lab and had an angioplasty with stent done for 100% occlusion of the right coronary artery. He was discharged with the following medications: aspirin, clopidogrel, metoprolol, enalapril, simvastatin and isosorbide mononitrate. In the ED, his pulse is 102/min, blood pressure is 110/70 mmHg, respirations are 24/min and temperature is 36.8°C (98.4°F). Which of the following is most likely responsible for his present symptoms?

- A. Metoprolol
- B. Isosorbide
- C. Clopidogrel
- D. Aspirin
- E. Enalapril
- F. Simvastatin

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A 50-year-old man comes to the emergency department due to acute onset respiratory difficulty. He also has periorbital, circumoral and facial edema. He denies any itching or skin rash. Two weeks ago, he experienced chest pain, profuse sweating and anxiety, and was subsequently admitted to the cardiac intensive care unit. At that time, his ECG showed ST segment elevation and Q waves in the inferior leads. He was taken to the catheterization lab and had an angioplasty with stent done for 100% occlusion of the right coronary artery. He was discharged with the following medications: aspirin, clopidogrel, metoprolol, enalapril, simvastatin and isosorbide mononitrate. In the ED, his pulse is 102/min, blood pressure is 110/70 mmHg, respirations are 24/min and temperature is 36.8°C (98.4°F). Which of the following is most likely responsible for his present symptoms?

- A. Metoprolol [6%]
- B. Isosorbide [10%]
- ✗ C. Clopidogrel [2%]
- D. Aspirin [7%]
- ✓ E. Enalapril [71%]
- F. Simvastatin [2%]

Incorrect

71% | 5 Seconds | 07/04/2018

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ACE inhibitors are the most common cause of acquired angioedema. Patients present with edema in the face, mouth, lips, tongue, glottis and larynx. Laryngeal edema can cause airway obstruction and be life threatening. Angioedema occurs due to the pro-inflammatory action of bradykinin, which promotes edema, inflammation and the sensation of pain. Angiotensin converting enzyme (ACE) is also known as kininase; it functions to degrade bradykinin. When ACE is inhibited, levels of bradykinin increase, thereby leading to angioedema.

ACE inhibitors are usually started on the first post-infarction day in non-hypotensive patients, and patients typically present with angioedema within days to weeks after starting therapy (as in this patient). However, it is important to note that angioedema from ACE inhibitors can occur at ANYTIME, not just within weeks of starting the medication. The first step in management of angioedema is to check for airway compromise and vasomotor instability, which require subcutaneous epinephrine administration if present. If airway obstruction fails to respond to epinephrine, an emergency tracheostomy is done. The ACE-inhibitor should be stopped immediately.

(Choice A) The common adverse effects of beta-blockers (metoprolol) are bradycardia, AV block, bronchoconstriction (clinically significant in patients with asthma and COPD), and male sexual dysfunction.

(Choice B) Nitrates can cause headaches, hypotension and development of tolerance to the drug with continuous use.

(Choice C) Clopidogrel uncommonly causes adverse reactions, the most significant of which is thrombotic thrombocytopenic purpura.

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(Choice B) Nitrates can cause headaches, hypotension and development of tolerance to the drug with continuous use.

(Choice C) Clopidogrel uncommonly causes adverse reactions, the most significant of which is thrombotic thrombocytopenic purpura.

(Choice D) Aspirin and NSAIDs can cause allergic angioedema. It typically happens immediately after exposure and it is accompanied by itching and skin rash (urticaria).

(Choice F) Statins are associated with hepatotoxicity and myopathy.

Educational objective:
ACE inhibitors are the most common cause of acquired angioedema. It is important to note that angioedema from ACE inhibitors can occur at ANYTIME, not just within weeks of starting the medication. Other adverse effects of ACE inhibitors are cough, hyperkalemia, and precipitation of acute renal failure in patients with bilateral renal artery stenosis.

References

- Angiotensin-converting enzyme inhibitors and angioedema.

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A 14-month-old boy is admitted to the hospital for treatment of pneumonia. He has a fever, cough, and increased labored breathing. Sick contacts include multiple children in day care who have had a "cold." The boy's mother is concerned about him "frequently being ill" as he had 3 episodes of bronchiolitis during infancy and pneumococcal pneumonia 2 months ago that required intubation and hospitalization in the intensive care unit. The patient also had tympanostomy tubes recently placed for recurrent otitis media. He takes no medications and his vaccinations are up to date. Weight is 7 kg (15.4 lb, <3rd percentile). Temperature is 39.6 C (103.3 F), blood pressure is 90/50 mm Hg, pulse is 128/min, and respirations are 38/min. On examination, the patient appears listless and is in mild respiratory distress. Both ear canals contain purulent drainage. Crackles are heard in the left lung base. Laboratory results are as follows:

Complete blood count

Hemoglobin	12.6 g/dL
Platelets	260,000/μL
Leukocytes	9,000/μL
Neutrophils	40%
Lymphocytes	50%

Immunoglobulins

Immunoglobulins	
IgG	250 mg/dL (normal, 700-1,500 mg/dL)
IgA	24 mg/dL (normal, 60-400 mg/dL)
IgM	450 mg/dL (normal, 60-300 mg/dL)
CD4/CD8 ratio	2.2 (normal, 1-4)
HIV-1 antibody	negative

Which of the following is the most likely diagnosis in this patient?

- A. Bruton agammaglobulinemia
- B. Common variable immunodeficiency
- C. Hyper-IgM syndrome
- D. IgA deficiency
- E. Medical child abuse
- F. Selective IgG subclass deficiencies
- G. Transient hypogammaglobulinemia of infancy

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IgM	450 mg/dL (normal, 60-300 mg/dL)
CD4/CD8 ratio	2.2 (normal, 1-4)
HIV-1 antibody	negative

Which of the following is the most likely diagnosis in this patient?

- A. Bruton agammaglobulinemia [8%]
- B. Common variable immunodeficiency [6%]
- ✔ C. Hyper-IgM syndrome [76%]
- D. IgA deficiency [5%]
- E. Medical child abuse [0%]
- F. Selective IgG subclass deficiencies [0%]
- G. Transient hypogammaglobulinemia of infancy [0%]

Correct

76% Answered correctly

12 Seconds Time Spent

10/11/2018 Last Updated

Primary humoral deficiencies		
Diagnosis	**Clinical features**	**Laboratory findings**
X-linked agammaglobulinemia	Recurrent &/or severe sinopulmonary infections with viruses & encapsulated bacteria	↓ or absent B cells ↓ Immunoglobulins
Common variable immunodeficiency		Normal B cells ↓ Immunoglobulins
IgA deficiency		Normal B cells ↓ IgA
Hyper-IgM syndrome		Normal B cells ↓ IgG & IgA ↑ IgM
IgG subclass deficiency		Normal B cells ↓ IgG

Mild respiratory infections are common in childhood and can occur up to 10 times a year, especially with day care exposure. This child has **severe** and **recurrent sinopulmonary infections** (including intubation, tympanostomy

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Mild respiratory infections are common in childhood and can occur up to 10 times a year, especially with day care exposure. This child has **severe** and **recurrent sinopulmonary infections** (including intubation, tympanostomy tubes, and poor growth) that are concerning for **humoral immunodeficiency**. Complete blood count with differential, lymphocyte T and B cell subsets, and serum IgG, IgA, and IgM are important screening tests. HIV infection should also be excluded.

In this patient, the **low serum IgA and IgG** in combination with the **markedly elevated IgM** is concerning for hyper-IgM syndrome, which is due to an **X-linked** genetic defect in the **CD40 ligand**. The CD40 ligand is present on T cells and binds to CD40 expressed on B cells, which induces a change in B cell production of IgM to other immunoglobulins (class switching). The absence of the CD40 ligand prevents class switching, leading to elevated IgM levels and a deficiency of all other immunoglobulin types. CD40 ligand deficiency also inhibits plasma cell formation, which contributes to poor response to infection and immunization.

Patients with hyper-IgM syndrome have recurrent sinopulmonary infections (eg, acute otitis media, pneumonia, sinusitis) with encapsulated bacteria. They also tend to have more frequent viral infections and increased risk of opportunistic infections, such as *Pneumocystis jirovecii* pneumonia. Growth impairment can result from high energy expenditure and poor intake during illness. Treatment includes antibiotic prophylaxis and interval administration of intravenous immunoglobulin.

(Choice A) Bruton (or X-linked) agammaglobulinemia presents in a similar manner to the other humoral immunodeficiency syndromes. It is characterized by low IgG, IgM, and IgA as well as low or absent B lymphocytes; B cell concentration is normal in hyper-IgM syndrome.

(Choice B) Common variable immunodeficiency is characterized by low levels of IgG, IgM, and IgA in the setting of a normal B lymphocyte count. It is most commonly diagnosed in adolescents or young adults.

(Choice D) Selective IgA deficiency is one of the most common immunodeficiency syndromes. Most patients are asymptomatic, but some have recurrent respiratory, gastrointestinal, and/or urogenital infections. Serum IgA is low, whereas IgM is normal.

(Choice E) Medical child abuse (also known as factitious disorder imposed by another, or formerly called Munchausen syndrome by proxy) is a form of child abuse during which a caregiver induces illness (eg, putting contaminated material in a child's ears) or fabricates a history of recurrent symptoms. The child may undergo repeated procedures, medication courses, and/or hospitalizations with no objective abnormalities detected.

(Choice F) Patients with selective IgG subclass deficiencies usually have recurrent infections, low or normal total IgG, and normal IgM.

(Choice G) The normal physiologic nadir of maternally derived antibody is age 3-6 months in term infants. Low serum IgG levels after age 6 months is termed transient hypogammaglobulinemia of infancy, and it usually resolves by age 12 months. B and T lymphocyte counts and IgA and IgM levels are normal.

Educational objective:
Primary humoral immunodeficiency syndromes present with recurrent or severe sinopulmonary infections. Hyper-IgM syndrome is due to a defect in the CD40 ligand and is characterized by high IgM levels, low IgG and IgA, and normal lymphocyte populations.

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Item 21 of 22
Question Id: 8951

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A 6-month-old girl is brought to the physician for a well-child visit and routine vaccinations. She is exclusively breastfed and urinating and stooling normally. One month ago, she was hospitalized for intussusception that was reduced successfully by air enema. The child lives with her mother, brother, and maternal aunt in a small apartment. Her brother has autism and her aunt is pregnant. Vital signs are normal. On examination, she has mild nasal congestion and clear rhinorrhea. The remainder of the examination is normal. Her mother is very concerned about potential side effects of vaccinations. Which of the following is a contraindication to rotavirus vaccination?

- A. Administration of inactivated immunizations on the same day
- B. Exclusive breastfeeding
- C. Family history of autism
- D. Personal history of intussusception
- E. Pregnant household member
- F. Viral upper respiratory infection

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Item 21 of 22
Question Id: 8951

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A 6-month-old girl is brought to the physician for a well-child visit and routine vaccinations. She is exclusively breastfed and urinating and stooling normally. One month ago, she was hospitalized for intussusception that was reduced successfully by air enema. The child lives with her mother, brother, and maternal aunt in a small apartment. Her brother has autism and her aunt is pregnant. Vital signs are normal. On examination, she has mild nasal congestion and clear rhinorrhea. The remainder of the examination is normal. Her mother is very concerned about potential side effects of vaccinations. Which of the following is a contraindication to rotavirus vaccination?

✗ A. Administration of inactivated immunizations on the same day [4%]

B. Exclusive breastfeeding [0%]

C. Family history of autism [0%]

✓ D. Personal history of intussusception [54%]

E. Pregnant household member [18%]

F. Viral upper respiratory infection [20%]

Incorrect
Correct answer

54%
Answered correctly

5 Seconds
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Contraindications to rotavirus vaccine
• Anaphylaxis to vaccine ingredients • History of intussusception • History of uncorrected congenital malformation of the gastrointestinal tract (eg, Meckel's diverticulum) • Severe combined immunodeficiency disease

Rotavirus is the most common cause of gastroenteritis in infants and young children worldwide. The virus is **highly contagious** and is transmitted by the **fecal-oral route** through direct contact and through fomites. The typical course of illness consists of fever, vomiting, and **watery osmotic diarrhea**. Affected children often suffer from severe dehydration.

The rotavirus vaccine is the best defense against rotavirus gastroenteritis and prevents most cases of infection. The vaccine series is typically administered at **age 2-6 months** and has dramatically reduced the incidence of rotavirus-related hospitalizations and deaths globally. This **live attenuated virus vaccine** (LAVV) can be administered safely with routine inactivated vaccinations. Although the vaccine is generally well tolerated, caregivers should be advised about the small risk of **intussusception**. The mechanism is not clear but may be related to rates of viral replication in the intestines. Infants with a history of intussusception should not receive the vaccine. In most other infants, the benefit of disease prevention outweighs the low probability of intussusception. Therefore, vaccination against rotavirus is recommended in the absence of contraindications (Table).

Although there have been newer versions of the rotavirus vaccine, a history of intussusception (previously considered a precaution to vaccine administration) is still currently considered a contraindication.

(Choice A) In general, the administration of multiple vaccinations in a single office visit is safe and increases vaccine compliance and optimal protection at a young age. LAVVs can be administered on the same day (eg, measles-mumps-rubella and varicella); however, because such vaccines need to replicate to result in an immune response, administration of subsequent LAVVs should be delayed by ~4 weeks due to possible interference of immune response.

(Choice B) In comparison to formula-fed infants, breastfed infants produce higher levels of antibodies in response to vaccinations. Feeding regimen has no impact on vaccine safety.

(Choice C) Vaccinations are not associated with the development of autism-spectrum disorders.

(Choice E) Live virus vaccinations should not be administered to pregnant women due to theoretical risk of fetal infection. However, **live virus vaccinations can be safely administered to household contacts** of pregnant women because the virus is weak and not contagious. Vaccination of household contacts reduces the potential spread of infection to patients who cannot receive vaccinations.

(Choice F) Vaccines can be administered safely during minor illnesses (eg, upper respiratory infections). They should be postponed until recovery from moderate or severe illnesses as manifestations of the underlying illness can be incorrectly attributed to the vaccine and vice versa.

Educational objective:

women because the virus is weak and not contagious. Vaccination of household contacts reduces the potential spread of infection to patients who cannot receive vaccinations.

(Choice F) Vaccines can be administered safely during minor illnesses (eg, upper respiratory infections). They should be postponed until recovery from moderate or severe illnesses as manifestations of the underlying illness can be incorrectly attributed to the vaccine and vice versa.

Educational objective:

The rotavirus vaccine effectively prevents most cases of rotavirus gastroenteritis. It is contraindicated in patients with a history of intussusception due to the risk of this side effect.

References

- Rotavirus vaccine and health care utilization for diarrhea in U.S. children.
- Risk of intussusception after monovalent rotavirus vaccination.
- Intussusception risk after rotavirus vaccination in U.S. infants.
- Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP).
- Prenatal and infant exposure to thimerosal from vaccines and immunoglobulins and risk of autism.

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Item 22 of 22
Question Id: 3236

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A 34-year-old woman brings her 2 children, ages 4 and 3, to the pediatrician for routine physical examinations. This is their first visit as they recently moved from another state. Medical records indicate that no immunizations have been given. The mother proudly explains, "My children are wonderfully healthy on their own and have no need for these artificial vaccines." The physician fully discusses the principles and benefits of immunization as well as the inherent risks and potential consequences of not being immunized. The physician recommends that the children be given all age-appropriate vaccinations today. The mother remains convinced that immunizations cause more harm than good and steadfastly refuses vaccination of her children. Which of the following is the most appropriate next step in management?

A. Document in the medical chart that the risks and benefits of vaccination have been explained
B. Explain that physicians are obligated to report cases of vaccine refusal to the local health department
C. Obtain a court order for immunization of the children, in the interest of the children and public health
D. Proceed with immunizations today, to protect the children and public health
E. Request to speak with the children's father

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Item 22 of 22
Question Id: 3236

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A 34-year-old woman brings her 2 children, ages 4 and 3, to the pediatrician for routine physical examinations. This is their first visit as they recently moved from another state. Medical records indicate that no immunizations have been given. The mother proudly explains, "My children are wonderfully healthy on their own and have no need for these artificial vaccines." The physician fully discusses the principles and benefits of immunization as well as the inherent risks and potential consequences of not being immunized. The physician recommends that the children be given all age-appropriate vaccinations today. The mother remains convinced that immunizations cause more harm than good and steadfastly refuses vaccination of her children. Which of the following is the most appropriate next step in management?

- ✔ A. Document in the medical chart that the risks and benefits of vaccination have been explained [88%]
- B. Explain that physicians are obligated to report cases of vaccine refusal to the local health department [5%]
- C. Obtain a court order for immunization of the children, in the interest of the children and public health [1%]
- D. Proceed with immunizations today, to protect the children and public health [0%]
- E. Request to speak with the children's father [3%]

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It is estimated that over 90% of children in the United States have received all major vaccinations by the time they enter school, and public health personnel continue their efforts to increase this number. "Herd immunity" is an extremely successful principle whereby the disease resistance of the vaccinated majority indirectly confers protection on the disease-susceptible minority, preventing morbidity from major illness. Individuals who are unvaccinated or partially vaccinated remain at increased risk and can affect the strength of herd immunity, which is exemplified by recent outbreaks in pertussis and measles.

Currently, all states allow medical exemption from vaccination (eg, allergy to vaccine components). Some states also allow for exemption based on a parent's religious and/or personal beliefs. If a child is unvaccinated and is not exempt, he/she may not be able to enroll in day care or school, depending on the state. The physician must **respect** the **mother's decision** but is obligated to **inform** her about the health-associated **risks** and benefits as well as the potential consequences (school enrollment). The discussion should be fully **documented** in the medical record.

(Choice B) Physicians do not report cases of vaccination refusal. Although health departments are interested in recording the incidence of specific conditions (eg, measles), they do not track or enforce immunization against such diseases.

(Choice C) Although there are opposing views and much controversy regarding the risks and benefits of vaccination, court orders are generally reserved for cases in which parents refuse life-saving treatment for children. Court-mandated vaccinations could be appropriate in the case of disease outbreak, for instance. However, a physician generally would not pursue a court order as a preventive measure when the risk of acquiring

(Choice C) Although there are opposing views and much controversy regarding the risks and benefits of vaccination, court orders are generally reserved for cases in which parents refuse life-saving treatment for children. Court-mandated vaccinations could be appropriate in the case of disease outbreak, for instance. However, a physician generally would not pursue a court order as a preventive measure when the risk of acquiring an illness is quite low.

(Choice D) Immunizing the children without consent from the mother would be appropriate only if they were in imminent danger.

(Choice E) The physician could ask what the father thinks of vaccination, as part of the discussion, but not in an attempt to undermine the mother's authority. There has been no mention of the children's father and it is not clear whether he is involved in their lives. Therefore, insisting on speaking with the father could be perceived as patronizing and jeopardize any existing doctor-patient relationship.

Educational objective:
Physicians must respect parents' medical decisions for their children, with the exception of refusal of life-saving treatment. Physicians must counsel parents about the health risks of refusing vaccination and document the discussion in the medical chart. In addition, physicians should be aware of the vaccination exemption laws in their state.

References