

System®

Synthesize USMLE Step 1

December 2025



Question 1.1 (Mc Nj) Step 1

Question

Serum LDL-cholesterol concentrations are measured in blood samples collected from 25 healthy volunteers. The data follow a normal distribution. The mean and standard deviation for this group are 130 mg/dL and 25 mg/dL, respectively. The standard error of the mean is 5.0.

With a 95% confidence level, the true mean for the population from which this sample was drawn falls within which of the following ranges (in mg/dL)?

- (A) 105-155
- (B) 120-140
- (C) 125-135
- (D) 128-132
- (E) 129-131

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: (B) 120–140 mg/dL.

Computation: For a 95% confidence interval of the population mean with unknown variance, use $\text{mean} \pm t_{0.975, df} \times \text{SE}$. Here $n=25 \Rightarrow df=24$, $t \approx 2.064$; $\text{SE} = 5.0$ mg/dL. Thus, 95% CI = $130 \pm (2.064 \times 5) = 130 \pm 10.32 = 119.7\text{--}140.3$ mg/dL ($\approx 120\text{--}140$ mg/dL). Using $z=1.96$ gives 120.2–139.8 mg/dL, still matching choice B.

We are not able to find relevant guideline recommendations for computing a 95% confidence interval for a sample mean from the Centers for Disease Control and Prevention (CDC), American College of Gastroenterology (ACG), College of American Pathologists (CAP), American Society of Interventional Pain Physicians (ASIPP),

American College of Cardiology/American Heart Association (ACC/AHA), or American Association for Respiratory Care (AARC); this is a standard statistical calculation [1].

References

[1] Not applicable

No guideline recommendations were required for this statistical computation.

Question 2.1 (Mc Nj) Step 1

Question

A 48-year-old man dies suddenly of a cardiac arrhythmia. Six weeks ago, he was resuscitated from a cardiac arrest caused by coronary artery disease and developed oliguric renal failure. Five weeks ago (1 week after being resuscitated), his serum urea nitrogen (BUN) concentration was 40 mg/dL, his serum creatinine concentration was 3.5mg/dL, and his urine contained granular casts. Four weeks ago, his oliguria resolved, and his BUN and serum creatinine concentrations returned to normal.

Examination of his kidneys at autopsy is most likely to show which of the following?

- (A) Acute inflammation
- (B) Fibrinous exudate
- (C) Fibrous scar
- (D) Granulation tissue
- (E) Normal kidney

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E) Normal kidney.

Rationale: The course is most consistent with ischemic acute tubular necrosis (ATN) after cardiac arrest, with oliguria and granular casts followed by return of BUN/creatinine to normal within weeks. In uncomplicated ischemic ATN that fully recovers, the tubular epithelium typically regenerates and the kidney can appear essentially normal on gross and routine histology a few weeks later—making acute inflammation, fibrinous exudate, granulation tissue, or established fibrosis unlikely in this time frame.

Guidelines: We are not able to find relevant guideline recommendations for the histopathologic appearance of the kidney after recovery from ischemic ATN from the societies retrieved (KDIGO, American Urological Association, Enhanced Recovery After Surgery–Cardiac Surgery). We therefore base the answer on available clinical and experimental evidence.

Supporting evidence

- ATN generally has a better likelihood of renal recovery than acute interstitial nephritis; in a multicenter cohort of 253 biopsy-proven ATN vs AIN, AIN had higher non-recovery and ESRD rates at 6 months, supporting the concept that ATN is often reversible when the insult resolves [1].
- The severity of tubulointerstitial injury in biopsy-proven ATN correlates with incomplete recovery; conversely, cases with complete recovery tend to have less severe lesions, consistent with potential restoration of near-normal architecture after recovery [2]. The patient's rapid return to normal kidney function suggests a milder, reversible tubular injury.
- In a hospital cohort of AKI (not limited to ATN), about two-thirds achieved complete recovery by 28 days, consistent with the time course described here (normalization within 4 weeks) [4].
- Nuance: Severe/prolonged ischemia can produce lasting microvascular rarefaction despite recovery in animal models, but this is more typical of severe injuries; rapid complete biochemical recovery, as in this case, makes significant fibrosis or ongoing inflammation unlikely at 5 weeks [3].

Bottom line: Given the full biochemical recovery within weeks after an ischemic ATN episode, the most likely autopsy finding at this time point is a normal-appearing kidney [1–4].

References

[1] Long-term Renal Outcome of Biopsy-proven Acute Tubular Necrosis and Acute Interstitial Nephritis.

Journal of Korean medical science

2020-07-06

The long-term renal outcome of acute kidney injury (AKI) remains unclear. Acute tubular necrosis (ATN) is the most common cause of AKI due to ischemia, toxin or sepsis. AIN showed higher rate of non-renal recovery at 6 months than ATN. ESRD developed in 39.4% of patients with AIN and 21.5% patients with ATN, and 23.05% patients of AIN.

[10.3346/jkms.2020.35.e206](https://doi.org/10.3346/jkms.2020.35.e206)

[2] Histological features of acute tubular necrosis in native kidneys and long-term renal function.

Renal failure

2008-01-01

There are few studies on the relationship between the morphology of acute tubular necrosis (ATN) in native kidneys and late functional recovery. Eighteen patients with acute renal failure (ARF) who had undergone renal biopsy were studied. Only 39% of patients achieved complete recovery. Patients with partial recovery had more severe ARF and tubule-interstitial lesions.

[10.1080/08860220802212460](https://doi.org/10.1080/08860220802212460)

[3] Renal ischemic injury results in permanent damage to peritubular capillaries and influences long-term function.

American journal of physiology. Renal physiology

2001-11-01

Male rats subjected to 60-min bilateral ischemia followed by reperfusion. Post-ARF animals manifested severe diuresis, peaking at 1 wk postinjury. Urine flow subsequently declined but remained elevated for a 40-week period. By week 16, proteinuria developed in the post ARF group and progressed for the duration of the study.

[10.1152/ajprenal.2001.281.5.f887](https://doi.org/10.1152/ajprenal.2001.281.5.f887)

[4] Survey of acute kidney injury and related risk factors of mortality in hospitalized patients in a third-level urban hospital of Shanghai.

Blood purification

2014-01-01

All patients hospitalized from January 1st to December 31st 2012 in Ren Ji Hospital, School of Medicine Shanghai Jiao Tong University were screened by the Lab Administration Network. 934 AKI patients were enrolled. The incidence of AKI in hospitalized patients was 2.41%, the ratio of males to females was 1.88:1 and the mean age was 60.82 ± 16.94 . The survival rate on the day 28 after AKI was 71.8%. 65.7% patients got complete renal recovery, 16.9% got partial renal recovery and 17.4% got renal loss.

[10.1159/000366127](https://doi.org/10.1159/000366127)

Question 3.1 (Mc Nj) Step 1

Question

In a sample of 100 individuals, the mean leukocyte count is 7500/mm³, with a standard deviation of 1000/mm³. If the leukocyte counts in this population follow a normal (gaussian) distribution, approximately 50% of individuals will have which of the following total leukocyte counts?

- (A) 5500–9500/mm³
- (B) <6500/mm³ or >8500/mm³
- (C) 6500–8500/mm³
- (D) <7500/mm³
- (E) >9500/mm³

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: (D) <7500/mm³.

Rationale: In a normal (Gaussian) distribution, the mean equals the median, so 50% of observations lie below the mean; therefore, approximately half of individuals will have leukocyte counts <7500/mm³. This is a statistics property rather than a clinical guideline question [1].

Why the other choices are not 50%:

- (C) 6500–8500/mm³ is mean ± 1 SD \rightarrow ~68%.
- (A) 5500–9500/mm³ is mean ± 2 SD \rightarrow ~95%.
- (B) <6500 or >8500 mm³ is outside ± 1 SD \rightarrow ~32%.
- (E) >9500/mm³ is above +2 SD \rightarrow ~2.5%.

We are not able to find relevant clinical guideline recommendations for this statistical concept from the societies searched (AASLD, SITC, ASRM/AUA, IDSA, ACCP, ASTCT).

References

[1] Not applicable

No guideline recommendations were needed for this statistical concept question.

Question 4.1 (Mc Nj) Step 1

Question

A 55-year-old woman comes to the clinic because of a 2-month history of increasingly severe vaginal pain and itching during sexual intercourse. She avoids intercourse with her husband because of the symptoms. She has been in a monogamous relationship with her husband for the past 25 years. She has type 2 diabetes mellitus. Her vital signs are within normal limits. Pelvic examination shows edematous and erythematous vaginal mucosa with white discharge. A photomicrograph of a vaginal smear is shown.

Which of the following is the most likely causal infectious agent?

- (A) *Candida albicans*
- (B) *Chlamydia trachomatis*
- (C) Herpes simplex virus
- (D) Human papillomavirus
- (E) *Trichomonas vaginalis*

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Most likely causal infectious agent: *Candida albicans* (A).

Rationale: The combination of severe vulvovaginal pruritus and dyspareunia with erythematous/edematous vaginal mucosa and white discharge, together with microscopy showing spores/pseudohyphae/hyphae, is diagnostic for vulvovaginal candidiasis per ACOG criteria [1]. Diabetes mellitus is a known predisposing factor; observational studies in women with diabetes show a higher prevalence of vulvovaginal candidiasis and increased isolation of *Candida* species (including non-*albicans* species) [5][6]. The presence of hyphae/pseudohyphae on microscopy favors *C. albicans* over *C. glabrata*, which often lacks pseudohyphae and may be less azole-susceptible [1][4]. For uncomplicated episodes, ACOG and IDSA recommend intravaginal azoles or a single 150 mg oral fluconazole dose [2][3]. For recurrent/severe disease or azole-refractory *C. glabrata*, IDSA suggests extended dosing or alternatives (e.g., boric acid, nystatin, or topical flucytosine ± amphotericin B) [4].

References

[1] Vaginitis in Nonpregnant Patients

American College of Obstetricians and Gynecologists
2019-12-31

In a symptomatic patient, diagnosis of vulvovaginal candidiasis requires one of the following two findings: visualization of spores, pseudohyphae, or hyphae on wet-mount microscopy or vaginal fungal culture or commercial diagnostic test results positive for *Candida* species.

<https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/01/vaginitis-in-nonpregnant-patients>

[2] Vaginitis in Nonpregnant Patients

American College of Obstetricians and Gynecologists
2019-12-31

Intravaginal azole therapy or oral fluconazole is recommended for the treatment of uncomplicated vulvovaginal candidiasis.

<https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/01/vaginitis-in-nonpregnant-patients>

[3] Management of Candidiasis

Infectious Diseases Society of America
2015-12-16

Alternatively, for the treatment of uncomplicated *Candida* vulvovaginitis, a single 150 mg oral dose of fluconazole is recommended.

<https://academic.oup.com/cid/article/62/4/e1/2462830?searchresult=1>

[4] Management of Candidiasis

Infectious Diseases Society of America
2015-12-16

For severe acute *Candida* vulvovaginitis, fluconazole, given every 72 hours for a total of 2 or 3 doses, is recommended. For *C. glabrata* vulvovaginitis that is unresponsive to oral azoles, topical

intravaginal boric acid, administered in a gelatin capsule for 14 days is an alternative. Another alternative agent for *C. glabrata* infection is nystatin intravaginal suppositories for 14 days. A third option for *C. glabrata* infection is topical 17% flucytosine cream alone or in combination with 3% AmB cream administered daily for 14 days.

<https://academic.oup.com/cid/article/62/4/e1/2462830?searchresult=1>

[5] Species-specific prevalence of vaginal candidiasis among patients with diabetes mellitus and its relation to their glycaemic status.

The Journal of infection
2000-09-01

Non-*C. albicans* *Candida* species are being recognized as the cause of vulvo-vaginal candidiasis. *Candida* was isolated in 36 of 78 subjects with diabetes mellitus and in 21 of 88 healthy subjects with *Candida glabrata* and *C. tropicalis*.

[10.1053/j.jinf.2000.0723](https://doi.org/10.1053/j.jinf.2000.0723)

[6] Pattern of *Candida* species isolated from patients with diabetes mellitus and vulvovaginal candidiasis and their response to single dose oral fluconazole therapy.

The Journal of infection
2006-02-01

Patients with diabetes mellitus are at increased risk of vulvovaginal candidiasis. Oral single dose fluconazole (150 mg) is commonly used to treat VVC in non-diabetic individuals with response rate ranging from 70 to 90%. There were no significant differences in the frequency of pruritus, vaginal discharge and yeast positivity between diabetic and control groups before the start of the therapy. *Candida glabrata* was the most common species isolated in diabetic patients and its frequency was significantly higher in them.

[10.1016/j.jinf.2005.03.005](https://doi.org/10.1016/j.jinf.2005.03.005)

Question 5.1 (Mc Nj) Step 1

Question

A 39-year-old man comes to the physician because of a 6-month history of progressive shortness of breath. He has had a cough productive of white sputum for 2 years. He smoked 1 pack of cigarettes daily for 16 years but quit 10 years ago. He is in mild respiratory distress with pursed lips and a barrel chest; he is using the accessory muscles of respiration. Breath sounds are distant and crackles are present in the lower lung fields bilaterally. Pulmonary function tests show a decreased FEV1:FVC ratio, increased residual volume, and decreased diffusion capacity. An x-ray of the chest shows hyperinflation and hypertranslucency of the lower lobes of both lungs.

Which of the following is the most likely diagnosis?

- (A) Asthma
- (B) Bronchiectasis
- (C) Chronic pulmonary fibrosis
- (D) Cystic fibrosis
- (E) Emphysema

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Most likely diagnosis: E) Emphysema (COPD, emphysematous phenotype).

Why this fits best

- The patient has chronic respiratory symptoms and spirometric airflow obstruction. The VA/DoD COPD guideline recommends that COPD be confirmed by spirometry demonstrating airflow obstruction (post-bronchodilator FEV1/FVC <0.70) [Veterans Health Administration/Department of Defense, 2021] [1]. This aligns with the patient's obstructive PFTs and hyperinflation on imaging, supporting a COPD diagnosis with an emphysema phenotype.
- The alternative options are less consistent with the required obstructive spirometric pattern for COPD (e.g., pulmonary fibrosis is typically restrictive). When dyspnea is exercise-related or the diagnosis is uncertain, professional societies recommend using spirometry and a careful pulmonary exam to distinguish COPD from other causes [American Academy/College of Allergy, Asthma & Immunology] [3].

Practical next steps (if managing this patient)

- Confirm COPD with post-bronchodilator spirometry if not yet performed, per VA/DoD [1].
- Consider alpha-1 antitrypsin deficiency testing given the relatively young age of onset of COPD symptoms; VA/DoD suggests testing in patients with early-onset COPD or a family history of early-onset COPD [2].

References

[1] Management of Chronic Obstructive Pulmonary Disease (COPD)

Veterans Health Administration / Department of Defense
2021-04-01

We recommend that spirometry, demonstrating airflow obstruction (postbronchodilator forced expiratory volume in one second/forced vital capacity [FEV1/FVC] <70%, with age adjustment for more elderly individuals), be used to confirm all initial diagnoses of chronic obstructive pulmonary disease (COPD).

<https://www.healthquality.va.gov/guidelines/CD/copd/VADoDCOPDCPGFinal508.pdf>

[2] Management of Chronic Obstructive Pulmonary Disease (COPD)

Veterans Health Administration / Department of Defense
2021-04-01

We suggest that patients presenting with early onset COPD or a family history of early onset COPD be tested for alpha-1 antitrypsin (AAT) deficiency.

<https://www.healthquality.va.gov/guidelines/CD/copd/VADoDCOPDCPGFinal508.pdf>

[3] Exercise-induced Bronchoconstriction (Practice Parameter)

American College of Allergy, Asthma, and Immunology, American Academy of Allergy, Asthma & Immunology
2016-09-21

SS13: Perform spirometry, as well as detailed pulmonary examination, to determine whether shortness of breath with exercise is associated with underlying conditions, such as COPD, or restrictive lung conditions, such as obesity, skeletal defects (eg, pectus excavatum), diaphragmatic paralysis, or interstitial fibrosis, rather than EIB.

<https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/Exercise-Induced-Bronchoconstriction-Practice-Parameter-2016.pdf>

Question 6.1 (Mc Nj) Step 1

Question

A previously healthy 33-year-old woman is brought to the emergency department by the Secret Service for stalking the president of the USA for 2 months. She claims to be married to the president's twin brother and states that the president just had his twin kidnapped to avoid competition. She speaks rapidly and is difficult to interrupt. Her associations are often loose. She says, "I haven't slept for days, but I won't even try to sleep until my husband is rescued. God has been instructing me to take over the White House. I can't wait to be reunited with my husband. I hear his voice telling me what to do." When asked about drug use, she says she uses only natural substances. She refuses to permit blood or urine tests, saying, "I don't have time to wait for the results." Which of the following is the most likely diagnosis?

- (A) Bipolar disorder, manic, with psychotic features
- (B) Brief psychotic disorder
- (C) Delusional disorder
- (D) Psychotic disorder due to general medical condition
- (E) Schizophrenia

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Most likely diagnosis: A) Bipolar I disorder, current episode manic, with psychotic features. The vignette shows a classic manic syndrome with markedly decreased need for sleep, pressured/rapid speech, grandiosity/religiosity, loose associations, and hallucinations—most consistent with bipolar mania with psychotic features. While schizophrenia-spectrum or substance-induced psychosis remain in the differential, current guidelines emphasize comprehensive psychosis assessment while treating the acute manic episode accordingly (APA; VA/DoD) [3][4], and recommend antipsychotics and/or mood stabilizers for acute mania (WHO; VA/DoD) [1][2].

If encountered clinically (brief, guideline-aligned considerations):

- Pharmacotherapy: WHO recommends offering oral antipsychotics (e.g., aripiprazole, haloperidol, olanzapine, paliperidone, quetiapine) or mood stabilizers (carbamazepine, lithium, valproate) to adults with bipolar disorder, current episode mania [1]. VA/DoD suggests lithium or quetiapine as monotherapy for acute mania [2].
- Rapid control/severity: For acute severe manic symptoms where rapid control is needed, VA/DoD suggests electroconvulsive therapy in combination with pharmacotherapy [5].
- Inadequate response: If monotherapy is unsatisfactory, VA/DoD suggests lithium or valproate combined with an antipsychotic (e.g., haloperidol, asenapine, quetiapine, olanzapine, risperidone) [6].
- Assessment: APA recommends including quantitative symptom measures during the initial evaluation of a possible psychotic disorder [4]. In specialty mental health care,

when bipolar disorder is suspected, VA/DoD suggests using validated instruments (e.g., Mood Disorder Questionnaire, Hypomania Checklist) to support diagnostic decision-making [7].

References

[1] Mental, Neurological and Substance Use Disorders

World Health Organization

2023-11-19

Oral antipsychotic medicines – namely aripiprazole, haloperidol, olanzapine, paliperidone or quetiapine – or mood stabilizers (namely carbamazepine, lithium, valproic acid [sodium valproate]) should be offered to adults with bipolar disorder (current episode mania), carefully balancing effectiveness, side-effects and individual preference.

<https://www.who.int/publications/i/item/9789240084278>

[2] Management of Bipolar Disorder

Veterans Health Administration / Department of Defense

2023-09-30

We suggest lithium or quetiapine as monotherapy for acute mania.

<https://www.healthquality.va.gov/guidelines/MH/bd/VA-DoD-CPG-BD-Full-CPGFinal508.pdf>

[3] Management of First-Episode Psychosis and Schizophrenia (SCZ)

Veterans Health Administration / Department of Defense

2023-05-10

We recommend treatment/management with early intervention services for individuals with first-episode psychosis.

<https://www.healthquality.va.gov/guidelines/mh/scz/index.asp>

[4] Treatment of Patients With Schizophrenia

American Psychiatric Association

2020-08-31

APA recommends that the initial psychiatric evaluation of a patient with a possible psychotic disorder include a quantitative measure to identify and determine the severity of symptoms and impairments of functioning that may be a focus of treatment.

<https://ajp.psychiatryonline.org/doi/pdf/10.1176/appi.ajp.2020.177901>

[5] Management of Bipolar Disorder

Veterans Health Administration / Department of Defense

2023-09-30

For individuals with bipolar 1 disorder with acute severe manic symptoms, we suggest electroconvulsive therapy in combination with pharmacotherapy when there is a need for rapid control of symptoms.

<https://www.healthquality.va.gov/guidelines/MH/bd/VA-DoD-CPG-BD-Full-CPGFinal508.pdf>

[6] Management of Bipolar Disorder

Veterans Health Administration / Department of Defense

2023-09-30

We suggest lithium or valproate in combination with haloperidol, asenapine, quetiapine, olanzapine, or risperidone for acute mania symptoms in individuals who had an unsatisfactory response or a breakthrough episode on monotherapy.

<https://www.healthquality.va.gov/guidelines/MH/bd/VA-DoD-CPG-BD-Full-CPGFinal508.pdf>

[7] Management of Bipolar Disorder

Veterans Health Administration / Department of Defense

2023-09-30

In specialty mental health care, when there is suspicion for bipolar disorder from a clinical interaction, we suggest using a validated instrument (e.g., Bipolar Spectrum Diagnostic Scale, Hypomania Checklist, Mood Disorder Questionnaire) to support decision making about the diagnosis.

<https://www.healthquality.va.gov/guidelines/MH/bd/VA-DoD-CPG-BD-Full-CPGFinal508.pdf>

Question 8.1 (Mc Nj) Step 1

Question

A 53-year-old man comes to the physician because of a dry scaly rash on his body for the past year. He has had a 15-kg (33-lb) weight loss during the past year. He is 178 cm (5 ft 10 in) tall and now weighs 54 kg (120 lb); BMI is 17 kg/m². His stools have a large volume and float. Which of the following nutrient deficiencies is most likely?

- (A) Magnesium
- (B) Vitamin A
- (C) Vitamin B12 (cobalamin)
- (D) Vitamin C
- (E) Zinc

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: B) Vitamin A.

Rationale: The patient's bulky, floating stools and significant weight loss are most consistent with steatorrhea from fat malabsorption. Societal guidance emphasizes that disorders causing intestinal malabsorption commonly lead to vitamin and mineral deficiencies, particularly the fat-soluble vitamins (A, D, E, K) [AACE/The Obesity Society][1] and recommends assessing fat-soluble vitamins when deficiency states are present [AACE/ASMBS/ASA/OMA][2]. Among the listed options, only vitamin A is fat-soluble, making it the most likely deficiency in this presentation. Evidence from malabsorptive states shows impaired handling of fat-soluble vitamins (e.g., difficulty raising vitamin D levels and low serum fat-soluble vitamins in short bowel syndrome), supporting the pathophysiologic link between fat malabsorption and fat-soluble vitamin deficiencies [3][4]. Notably, expert guidance also links "dry, scaly skin" to deficiency states encountered with fat malabsorption (e.g., essential fatty acid deficiency) and advises concurrent assessment of other fat-soluble vitamins when one is low [2].

Citations: AACE/The Obesity Society; AACE/ASMBS/ASA/OMA; AJCN 2021 trial in adults with malabsorption; JPEN 2011 short bowel syndrome study. [1][2][3][4]

References

[1] Healthy Eating for the Prevention and Treatment of Metabolic and Endocrine Diseases in Adults

American Association of Clinical Endocrinologists, The Obesity Society
2013-10-01

Lifelong regular follow-up and individualized therapy are recommended in diseases known to cause intestinal malabsorption (e.g., after malabsorptive bariatric surgery, ileo-colic resection, short bowel syndrome, celiac disease, inflammatory bowel disease, exocrine pancreatic insufficiency, CKD, and chronic liver disease) to detect and treat vitamin and mineral deficiencies.

<https://journals.aace.com/doi/pdf/10.4158/EP13155.GL>

[2] Perioperative Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient

American Association of Clinical Endocrinologists, American Society for Metabolic and Bariatric Surgery, American Society of Anesthesiologists, The Obesity Society, Obesity Medicine Association
2019-11-01

R58. (2008*). In the presence of any established fat-soluble vitamin deficiency (vitamins A, D, E, and/or K) with, for example, hepatopathy, neuromuscular impairment, coagulopathy, or osteoporosis, or suspected essential fatty acid (EFA) deficiency (symptoms include hair loss,

poor wound healing, and dry scaly skin), clinical and biochemical assessments of the other fat-soluble vitamins may be considered and then supplemented if abnormally low.

<https://asmbs.org/app/uploads/2020/04/Mechanick-2020-AACE-TOS-ASMBS-Guidelines.pdf>

[3] A pilot-randomized, double-blind crossover trial to evaluate the pharmacokinetics of orally administered 25-hydroxyvitamin D3 and vitamin D3 in healthy adults with differing BMI and in adults with intestinal malabsorption.

2021-09-01

Obese and malabsorptive patients have difficulty increasing serum 25-hydroxyvitamin D after taking vitamin D. Oral 25(OH)D3 may be a good choice for managing vitamin D deficiency in malabsorption and obesity. AUCs of 900 µg vitamin D3 were not significantly different between the two groups.

[10.1093/ajcn/nqab123](https://doi.org/10.1093/ajcn/nqab123)

[4] Serum vitamins in adult patients with short bowel syndrome receiving intermittent parenteral nutrition.

2011-07-01

Short bowel syndrome occurs after massive intestinal resection. Parenteral nutrition therapy may be necessary even after a period of adaptation. SBS patients had lower serum levels of vitamins C, E, and K, similar to those observed in patients on home PN. Seven percent of patients had vitamin D deficiency.

[10.1177/0148607110386964](https://doi.org/10.1177/0148607110386964)

Question 9.1 (Mc Nj) Step 1

Question

In screening for prostate cancer, the current serum prostate-specific antigen concentration at which biopsy is recommended is 4.1 ng/mL.

If the threshold for recommending a biopsy procedure were lowered to 2.0 ng/mL, which of the following changes would occur to the positive and negative predictive values of the test?

- (A) Positive Predictive Value and Negative Predictive Value increase
- (B) Positive Predictive Value increase and Negative Predictive Value no change
- (C) Positive Predictive Value increase and Negative Predictive Value decrease
- (D) Positive Predictive Value no change and Negative Predictive Value increase
- (E) Positive Predictive Value and Negative Predictive Value no change
- (F) Positive Predictive Value no change and Negative Predictive Value decrease
- (G) Positive Predictive Value decrease and Negative Predictive Value increase

- (H) Positive Predictive Value decrease and Negative Predictive Value no change
(I) Positive Predictive Value and Negative Predictive Value decrease

Correct Response:

G

Synthesize Response:

G✓

Synthesize Answer

Introduction

Answer: G — Positive Predictive Value decreases and Negative Predictive Value increases.

Rationale: Lowering the PSA threshold for recommending biopsy (from 4.1 to 2.0 ng/mL) makes the test more sensitive and less specific. With disease prevalence unchanged, this typically yields more true positives but also more false positives, so the proportion of positive tests that are true positives (PPV) falls, while the proportion of negative tests that are true negatives (NPV) rises.

Clinical context: Contemporary guidance emphasizes that biopsy decisions should not rely on a single PSA cutpoint alone. The AUA/SUO advises using shared decision-making augmented by validated risk calculators and considering adjunctive clinical information (e.g., DRE), and cautions against using a PSA threshold by itself to trigger repeat biopsy after a negative biopsy [1][2][3]. Large screening data also show that PPV in PSA-based screening varies by screening round and prior biopsy status (and trials have used differing PSA cutoffs, e.g., 3.0 ng/mL in ERSPC), underscoring that predictive values are context-dependent and influenced by the chosen threshold [4].

References

[1] Early Detection of Prostate Cancer

American Urological Association, Society of Urologic Oncology
2023-04-24

Clinicians and patients may use validated risk calculators to inform the SDM process regarding prostate biopsy.

<https://www.auanet.org/guidelines-and-quality/guidelines/early-detection-of-prostate-cancer-guidelines>

[2] Early Detection of Prostate Cancer

American Urological Association, Society of Urologic Oncology

2023-04-24

Clinicians may use digital rectal exam (DRE) alongside PSA to establish risk of clinically significant prostate cancer.

<https://www.auanet.org/guidelines-and-quality/guidelines/early-detection-of-prostate-cancer-guidelines>

[3] Early Detection of Prostate Cancer

American Urological Association, Society of Urologic Oncology

2023-04-24

After a negative biopsy, clinicians should not solely use a PSA threshold to decide whether to repeat the biopsy.

<https://www.auanet.org/guidelines-and-quality/guidelines/early-detection-of-prostate-cancer-guidelines>

[4] Positive predictive value of prostate biopsy indicated by prostate-specific-antigen-based prostate cancer screening: trends over time in a European randomized trial*.

BJU international

2012-12-01

The European Randomized study of Screening for Prostate Cancer (ERSPC) showed a reduction in prostate cancer mortality of 21% for PSA-based screening at a median follow-up of 11 years. In the ERSPC men undergo PSA screening at 4-year intervals. A prostate biopsy is recommended for men with a PSA level of 3.0 ng/mL. The study shows that the positive predictive value (PPV) of prostate biopsies are equal in consecutive screening rounds in men without a previous biopsy. In men who have previously had a benign biopsy, the PPV drops considerably, but 20% of the cancers detected still show aggressive characteristics

[10.1111/j.1464-410x.2012.11481.x](https://doi.org/10.1111/j.1464-410x.2012.11481.x)

Question 10.1 (Mc Nj) Step 1

Question

In informing a couple that their newborn has Down syndrome, there is a specific, relatively limited amount of information that the consulting physician should give immediately. The rest can be discussed at a later time.

Which of the following best explains the purpose of using this approach to disclosure?

(A) Allowing the couple's primary care physician to discuss most of the information with them

- (B) Allowing the parents time to tell other family members
- (C) Delaying parental distress until the information is completely disclosed
- (D) Disclosing the most important information so that it can be understood as fully as possible
- (E) Influencing the parents' course of action about what is medically most appropriate

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Best answer: D. Disclosing the most important information so that it can be understood as fully as possible.

Rationale and practical guidance:

- The National Society of Genetic Counselors (NSGC) advises that initial disclosure of a new Down syndrome diagnosis should focus on clear, concise, understandable information, delivered sensitively, so parents can process key points without being overwhelmed; further details are addressed in follow-up conversations [1][2]. This pacing is intended to maximize comprehension and support, not to delay distress or influence decisions [1][2].
- NSGC further recommends a private setting with time for questions and explicit plans for follow-up, and allowing silence/tears—measures that reinforce focusing on essential information first and revisiting additional details later [2][3].
- Additional best practices that complement this approach include: providing balanced, accurate, up-to-date information; informing parents as soon as possible (even if still suspected, with explanation of clinical features); using person-first, respectful language; and communicating in the family's preferred language with a professional interpreter if needed [4][5][6][7].

Taken together, these recommendations support a stepwise disclosure approach that prioritizes comprehension of the essential information at the outset, with thoughtful planning for subsequent discussions as parents are ready [1][2].

References

[1] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

Provide the information in a sensitive and caring, yet confident and straightforward manner, using understandable language that is clear and concise.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[2] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

Discuss the diagnosis in a private, comfortable setting, free from interruptions. Allow time for questions and make plans for a follow-up conversation.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[3] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

Allow time for silence and time for tears. Do not feel that you need to talk to “fill the silence.” Offer the family time alone.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[4] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

Parents should be provided with accurate and up-to-date information. Information should be given with a balanced perspective, including both positive aspects and challenges related to Down syndrome.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[5] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

Tell the parents about the diagnosis as soon as possible, even if the diagnosis is suspected but not yet confirmed. If the diagnosis has not been confirmed by karyotype, explain what physical features or medical concerns are suggestive of the diagnosis.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[6] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

The family should be informed of the diagnosis in their preferred language. If possible, a professional medical interpreter should be present at the time of disclosure.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[7] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

Use sensitive language and avoid outdated or offensive terminology. In the newborn setting, the baby should be present, and should be referred to by name. Use person-centric language,

emphasizing that this is a baby who has Down syndrome, rather than a “Downs baby” or a “Down syndrome child.”

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

Question 12.1 (Mc Nj) Step 1

Question

A 62-year-old man comes to the physician because of a 6-month history of urinary hesitancy and dribbling after urination. He has to urinate two to three times nightly. Physical examination shows a diffusely enlarged, firm, and nontender prostate.

Which of the following is most likely to have contributed to the development of this patient's condition?

- (A) Activation of the α 1-adrenergic receptor
- (B) Conversion of testosterone to dihydrotestosterone
- (C) Conversion of testosterone to estradiol
- (D) Inhibition of the α 1-adrenergic receptor
- (E) Production of prostate-specific antigen

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most likely contributor: B — Conversion of testosterone to dihydrotestosterone (DHT).

Rationale grounded in guidelines and evidence:

- The American Urological Association (AUA) recommends 5-alpha-reductase inhibitors (5-ARIs) for men with LUTS/BPH and demonstrable prostate enlargement to improve

symptoms and to prevent disease progression, urinary retention, and need for surgery. These agents act on the androgen pathway targeted in BPH management, supporting a DHT-driven growth mechanism underlying prostate enlargement [AUA 2023: 5-ARI monotherapy; prevention of progression] [1][2].

- AUA also recommends alpha-1 blockers for bothersome LUTS to relieve symptoms; this targets dynamic smooth muscle tone rather than prostate growth, helping explain why α 1-receptor pathways are not considered the primary drivers of BPH development. Combination therapy (alpha blocker + 5-ARI) is reserved for men with demonstrable enlargement, further underscoring that the growth (progression) component is addressed via the 5-ARI/DHT pathway [AUA 2023] [3][4].

- Additional supportive evidence: A recent Mendelian randomization analysis reported that genetically higher bioavailable testosterone is associated with BPH occurrence, consistent with a central role of androgen signaling in prostatic enlargement, in line with the therapeutic focus on 5-ARIs [5].

Bottom line: In men with the classic BPH phenotype (enlarged, firm, nontender prostate with obstructive LUTS), the development of hyperplasia is most consistent with increased DHT signaling, i.e., conversion of testosterone to DHT (Answer B), whereas alpha-1 adrenergic mechanisms are targeted for symptomatic relief rather than disease progression [1][2][3][4].

References

[1] Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (BPH)

American Urological Association
2023-09-13

13. For the purpose of symptom improvement, 5-ARI monotherapy should be used as a treatment option in patients with LUTS/BPH with prostatic enlargement as judged by a prostate volume of >30cc on imaging, a prostate specific antigen (PSA) >1.5ng/dL, or palpable prostate enlargement on digital rectal exam (DRE).

<https://www.auajournals.org/doi/10.1097/JU.0000000000003698>

[2] Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (BPH)

American Urological Association
2023-09-13

14. 5-ARIs alone or in combination with alpha blockers are recommended as a treatment option to prevent progression of LUTS/BPH and/or reduce the risks of urinary retention and need for future prostate-related surgery.

<https://www.auajournals.org/doi/10.1097/JU.0000000000003698>

[3] Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (BPH)

American Urological Association
2023-09-13

10. Clinicians should offer one of the following alpha blockers as a treatment option for patients with bothersome, moderate to severe LUTS/BPH: alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin.

<https://www.auajournals.org/doi/10.1097/JU.0000000000003698>

[4] Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia (BPH)

American Urological Association

2023-09-13

18. 5-ARI in combination with an alpha blocker should be offered as a treatment option only to patients with LUTS associated with demonstrable prostatic enlargement as judged by a prostate volume of > 30cc on imaging, a PSA >1.5ng/dL, or palpable prostate enlargement on DRE.

<https://www.auajournals.org/doi/10.1097/JU.0000000000003698>

[5] Genetically elevated bioavailable testosterone level was associated with the occurrence of benign prostatic hyperplasia.

2023-10-01

Recent studies identified several risk factors of benign prostatic hyperplasia, including dyslipidemia, type 2 diabetes mellitus, hypertension, and obesity. The study was based on Mendelian randomization (MR) design. All participants were from the most recent genome-wide association studies (GWAS) with large sample size.

[10.1007/s40618-023-02060-0](https://doi.org/10.1007/s40618-023-02060-0)

Question 13.1 (Mc Nj) Step 1

Question

An 18-year-old woman with sickle cell disease is brought to the emergency department by her parents because of a 2-hour history of severe abdominal pain and nausea. Her parents say that she had a cheeseburger, milk shake, and chocolate bar for lunch. Her temperature is 37°C (98.6°F). Physical examination shows tenderness over the right upper quadrant of the abdomen, radiating to the right shoulder. Ultrasonography of the right upper quadrant of the abdomen shows gallstones.

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

- (A) Decreased hepatic secretion of lecithin
- (B) Decreased reabsorption of bile salts
- (C) High ratio of cholesterol to bile acids in bile
- (D) Infestation with parasites secreting β -glucuronidase

(E) Overload of unconjugated bilirubin

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E) Overload of unconjugated bilirubin.

Rationale: In sickle cell disease, chronic hemolysis increases bilirubin production, leading to excess unconjugated bilirubin that precipitates as calcium bilirubinate, forming black pigment gallstones—the typical stones seen in adolescents and young adults with hemolytic disorders [1][2]. Genetic factors that reduce bilirubin conjugation (e.g., UGT1A1 promoter variants associated with Gilbert phenotype) further increase unconjugated bilirubin levels and the risk of pigment gallstones in SCD, reinforcing this mechanism [2][3].

Other choices describe mechanisms not typical for hemolysis-driven stones: A–C are mechanisms linked to cholesterol stone formation, and D is characteristic of infection-related brown pigment stones, not the black pigment stones of chronic hemolysis.

We are not able to find relevant guideline recommendations for the pathogenesis of gallstones in sickle cell disease from AASLD, ASGE, and ACG. The conclusion above is supported by biomedical studies [1–3].

References

[1] Studies on the pathogenesis of pigment gallstones in hemolytic anemia: description and characteristics of a mouse model.

The Journal of Clinical Investigation
1980-06-01

The pathogenesis of hemolysis-induced gallstones was studied in mice with a hereditary hemolytic disease called normoblastic anemia. 57% of 115 nb/nb mice, but none of 109 control mice, developed calcium bilirubinate pigment gallstones. In gallbladder bile the stones had higher concentrations of hydrogen ion, calcium, and bile acids than in mice without stones.

[10.1172/jci109793](https://doi.org/10.1172/jci109793)

[2] UGT1A1 variation and gallstone formation in sickle cell disease.

Blood

2005-02-01

Pigment gallstones are a common clinical complication of sickle cell disease. Genetic variation in the promoter of uridine diphosphate (UDP)-glucuronosyltransferase 1A1 (UGT1A1) underlies Gilbert syndrome, a chronic form of unconjugated hyperbilirubinemia. The UGT1A1 promoter region was sequenced in 541 SS disease subjects and 111 healthy controls. Indirect bilirubin levels for (TA)_n and (TA)₇ genotypes were elevated compared with (TA)₆.

[10.1182/blood-2004-02-0521](https://doi.org/10.1182/blood-2004-02-0521)**[3] Uridine diphosphate glucuronosyl transferase 1A (UGT1A1) promoter polymorphism in young patients with sickle cell anaemia: report of the first cohort study from Nigeria.**

BMC Medical Genetics

2019-10-16

The distribution of the UGT1A1 (TA)_n genotypes among 101 young Nigerian SCA patients and 64 normal appropriate controls was determined and studied. The study highlights the contribution of a non-globin genetic factor to the laboratory and clinical manifestations of young Nigerian SCA patients for the first time. Children with low genotypes may be at risk of gallstones.

[10.1186/s12881-019-0899-3](https://doi.org/10.1186/s12881-019-0899-3)

Question 14.1 (Mc Nj) Step 1

Question

A 45-year-old man is brought to the emergency department 30 minutes after the sudden onset of crushing chest pain. His father, maternal aunt, and paternal uncle all died of myocardial infarctions under the age of 50 years. Physical examination shows tendinous xanthomas on the hands and thickened Achilles tendons. Serum lipid studies show a total cholesterol concentration of 410 mg/dL, HDL-cholesterol concentration of 30 mg/dL, and triglyceride concentration of 140 mg/dL. The diagnosis of myocardial infarction is made.

This patient most likely has a deficiency of which of the following?

- (A) Apo B48
- (B) Apo C
- (C) HMG-CoA reductase activity
- (D) LDL receptor
- (E) Lipoprotein lipase activity

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Most likely deficiency: D) LDL receptor. The presentation is most consistent with heterozygous familial hypercholesterolemia (HeFH) due to an LDL receptor defect—marked isolated hypercholesterolemia with normal triglycerides, tendon xanthomas, and a strong family history of premature MI. Tendon xanthomas in FH are linked to higher LDL levels and substantially higher cardiovascular risk, and Achilles tendon xanthomas correlate with greater coronary atherosclerotic burden [9][10]. LDLR mutations are the predominant genetic cause of FH in large cohorts, further supporting this mechanism [8].

Why not the other options?

- Apo B48 deficiency (abetalipoproteinemia) causes extremely low LDL and chylomicron absence, not severe isolated hypercholesterolemia with tendon xanthomas.
- Apo C-II and lipoprotein lipase deficiencies cause severe hypertriglyceridemia and pancreatitis phenotypes, not isolated LDL elevation with tendon xanthomas.
- Decreased HMG-CoA reductase activity would lower, not raise, cholesterol.

Clinical management pearls (post-MI with suspected FH)

- Start and maintain high-intensity statin therapy for ACS to reduce MACE (ACC/AHA/ACEP/SCAI 2025) [1]. If LDL-C remains ≥ 70 mg/dL on maximally tolerated statin, add a nonstatin agent (e.g., ezetimibe, PCSK9 inhibitor) (ACC/AHA/ACEP/SCAI 2025) [2]. For statin intolerance, use nonstatin therapy (ACC/AHA/ACEP/SCAI 2025) [3].
- For very high-risk individuals including HeFH, target LDL-C < 70 mg/dL (AACE 2020) [5]; consider PCSK9 inhibitors in combination with statins for FH when further LDL lowering is needed (AACE 2020) [6].
- Given his family history of premature ASCVD, pursue FH evaluation and cascade screening of relatives (AACE 2020; NLA) [4][7].

Supporting data

- In FH, tendon xanthomas are independently associated with higher LDL-C and much

higher prevalence of premature cardiovascular disease (36.7% vs 13.8% in those without xanthomas) in a cohort of 951 genetically diagnosed hFH patients [9]. Achilles tendon xanthomas in HeFH were associated with greater coronary calcium and atherosclerotic burden in a single-center study of 102 asymptomatic patients [10].

- Across 8 European countries, LDLR mutations were the most common cause of FH in children, aligning with the expected pathophysiology in classic HeFH [8].

References

[1] Management of Patients With Acute Coronary Syndromes

American College of Cardiology, American College of Emergency Physicians, American Heart Association, Society for Cardiovascular Angiography and Interventions
2025-02-27

1. In patients with ACS, high-intensity statin therapy is recommended to reduce the risk of MACE.*

<https://www.jacc.org/doi/10.1016/j.jacc.2024.11.009>

[2] Management of Patients With Acute Coronary Syndromes

American College of Cardiology, American College of Emergency Physicians, American Heart Association, Society for Cardiovascular Angiography and Interventions
2025-02-27

2. In patients with ACS who are already on maximally tolerated statin therapy with low-density lipoprotein cholesterol (LDL-C) ≥ 70 mg/dL (≥ 1.8 mmol/L), adding a nonstatin lipid-lowering agent is recommended to further reduce the risk of MACE.

<https://www.jacc.org/doi/10.1016/j.jacc.2024.11.009>

[3] Management of Patients With Acute Coronary Syndromes

American College of Cardiology, American College of Emergency Physicians, American Heart Association, Society for Cardiovascular Angiography and Interventions
2025-02-27

3. In patients with ACS who are statin intolerant, nonstatin lipid-lowering therapy is recommended to lower LDL-C and reduce the risk of MACE.

<https://www.jacc.org/doi/10.1016/j.jacc.2024.11.009>

[4] Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm

American Association of Clinical Endocrinologists
2020-10-01

R9. Individuals should be screened for familial hypercholesterolemia (FH) when there is a family history of: Premature ASCVD (definite MI or sudden death before age 55 years in father or other male first-degree relative, or before age 65 years mother or other female first-degree relative) or Elevated cholesterol levels (total, non-HDL and/ or LDL) consistent with FH.

<https://www.aace.com/pdfs/lipids/CS-2020-0490.pdf>

[5] Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm

American Association of Clinical Endocrinologists
2020-10-01

R39. For individuals at very high risk (i.e., with established or recent hospitalization for acute coronary syndrome (ACS); coronary, carotid or peripheral vascular disease; diabetes or stage 3 or 4 CKD with 1 or more risk factors; a calculated 10-year risk greater than 20%; or heterozygous familial hypercholesterolemia [HeFH]), an LDL-C goal <70 mg/dL is recommended.

<https://www.aace.com/pdfs/lipids/CS-2020-0490.pdf>

[6] Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm

American Association of Clinical Endocrinologists

2020-10-01

R69. PCSK9 inhibitors should be considered for use in combination with statin therapy for LDL-C lowering in individuals with FH.

<https://www.aace.com/pdfs/lipids/CS-2020-0490.pdf>

[7] Patient-Centered Management of Dyslipidemia: Part 2

National Lipid Association

2015-12-01

Cascade screening and reverse cascade screening are recommended to enhance detection of individuals at risk for FH.

[https://www.lipidjournal.com/article/S1933-2874\(15\)00380-3/abstract](https://www.lipidjournal.com/article/S1933-2874(15)00380-3/abstract)

[8] Comparison of the mutation spectrum and association with pre and post treatment lipid measures of children with heterozygous familial hypercholesterolaemia (FH) from eight European countries.

Atherosclerosis

2021-02-01

Familial hypercholesterolaemia is caused by mutations in the LDLR, APOB or PCSK9 genes. The most common cause of FH in children from eight European countries was an LDLR mutation. The prevalence of the APOB p.(Arg3527Gln mutation varies significantly across countries.

[10.1016/j.atherosclerosis.2021.01.008](https://doi.org/10.1016/j.atherosclerosis.2021.01.008)

[9] Tendon xanthomas in familial hypercholesterolemia are associated with cardiovascular risk independently of the low-density lipoprotein receptor gene mutation.

Arteriosclerosis, thrombosis, and vascular biology

2005-09-01

951 men and women with genetic diagnosis of hFH were studied. 278 of them presented tendon xanthomas. TX frequency increased with age from 6.9% to 38.3% at 51 to 60 years. Low-density lipoprotein cholesterol was higher in TX+ than in TX- subjects. 102 TX+ reported premature cardiovascular disease (36.7%) versus 93 TX- (13.8%)

[10.1161/01.atv.0000177811.14176.2b](https://doi.org/10.1161/01.atv.0000177811.14176.2b)

[10] Achilles tendon xanthomas are associated with the presence and burden of subclinical coronary atherosclerosis in heterozygous familial hypercholesterolemia: A pilot study.

Atherosclerosis

2017-08-01

Achilles tendon xanthomas (ATX) are a sign of long-term exposure to high blood cholesterol in familial hypercholesterolemia (FH) patients, which have been associated with cardiovascular disease. 102 FH patients with ATX had higher LDL-C and lipoprotein(a) concentrations, greater CAC scores, SIS and SSS.

[10.1016/j.atherosclerosis.2017.04.025](https://doi.org/10.1016/j.atherosclerosis.2017.04.025)

Question 15.1 (Mc Nj) Step 1

Question

An experimental animal is created in which the germinal centers of the reactive lymph nodes show shrinkage of cells, cytoplasmic budding, no adjacent inflammation, and intact plasma membranes.

These cellular findings are most likely caused by which of the following mechanisms?

- (A) Caspase activation
- (B) Decreased cytochrome c concentration
- (C) Decreased intracellular Ca^{2+} concentration
- (D) Increased glutathione peroxidase activity
- (E) Increased lysosomal enzyme activity

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: A) Caspase activation.

Rationale: The described morphology—cell shrinkage, cytoplasmic budding into apoptotic bodies, intact plasma membranes, and absence of surrounding inflammation—is classic for apoptosis. Apoptosis is executed by a protease cascade culminating in caspase activation, most notably caspase-3, rather than by necrotic lysosomal enzyme leakage or inflammatory pathways. Although clinical practice guidelines do not typically address this basic pathologic mechanism, multiple experimental data show that caspase activation is a central, defining feature of apoptosis.

Evidence

- In xenograft tissue sections, immunohistochemistry for activated caspase-3 is an easy, sensitive, and reliable way to quantify apoptosis, underscoring that caspase activation marks apoptotic cells [2].
- In cardiomyocytes, the pan-apoptotic stimulus staurosporine markedly increases caspase activity, and apoptosis is attenuated by caspase inhibition, supporting a causal role for caspases in executing apoptosis [3]. In vivo, pan-caspase inhibition reduced apoptosis after myocardial ischemia–reperfusion, further linking caspase activity to apoptotic cell death rather than necrosis [4].
- In human breast tissue, activated caspase-3 is present only in cells committed to apoptosis, and caspase activation precedes the development of the classical apoptotic morphology, aligning the observed morphologic features with caspase-dependent apoptosis [5].

Guidelines: We are not able to find relevant guideline recommendations for apoptosis morphology/mechanisms from clinical practice societies; this topic is a basic pathology mechanism rather than a clinical practice guidance issue [1].

References

[1] Not applicable

No guideline recommendations were consulted for this question as it pertains to basic pathology mechanisms rather than clinical practice guidance.

[2] Comparison of immunohistochemistry for activated caspase-3 and cleaved cytokeratin 18 with the TUNEL method for quantification of apoptosis in histological sections of PC-3 subcutaneous xenografts.

The Journal of pathology
2003-02-01

Activated caspase-3 immunohistochemistry is an easy, sensitive and reliable method for detecting and quantifying apoptosis in this model. It is recommended for the detection and quantification of apoptosis in tissue sections, as well as the TUNEL assay.

[10.1002/path.1289](https://doi.org/10.1002/path.1289)

[3] Staurosporine-induced apoptosis in cardiomyocytes: A potential role of caspase-3.

Journal of molecular and cellular cardiology
1998-03-01

Cardiomyocyte apoptosis has been demonstrated in animal models of cardiac injury and in patients with congestive heart failure or acute myocardial infarction. Staurosporine increased caspase activity in cardiomyocytes by five- to eight-fold, peaking at 4-8 h after stimulation.

[10.1006/jmcc.1997.0614](https://doi.org/10.1006/jmcc.1997.0614)

[4] Caspase inhibition reduces myocyte cell death induced by myocardial ischemia and reperfusion in vivo.

Journal of molecular and cellular cardiology
1999-09-01

Caspases-2, -3 and -7 were proteolytically activated during myocardial ischemia and reperfusion. YVAD-cmk blocked caspase activation and reduced the percentage of TUNEL-positive myocyte nuclei in the infarct region.

[10.1006/jmcc.1999.1006](https://doi.org/10.1006/jmcc.1999.1006)

[5] Assessment of apoptosis in human breast tissue using an antibody against the active form of caspase 3: relation to tumour histopathological characteristics.

British journal of cancer

2001-11-16

Caspase 3 is activated only in cells committed to undergo apoptosis. The caspase activation precedes the development of the classical morphological characteristics of apoptosis; the apoptotic index (AI) is higher in invasive cancer than in benign tissue.

[10.1054/bjoc.2001.2115](https://doi.org/10.1054/bjoc.2001.2115)

Question 16.1 (Mc Nj) Step 1

Question

Investigators conduct a study that evaluates the effect of finasteride on the incidence of prostate cancer in 500 patients. The investigators recruit an additional 1000 patients for the study.

Which of the following effects will this have on the research study?

- (A) Greater chance of a Type I error
- (B) Greater chance of a Type II error
- (C) Less chance of a Type I error
- (D) Less chance of a Type II error
- (E) Impossible to predict

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D — Less chance of a Type II error (higher power).

Rationale: Adding 1,000 participants to an initial 500 increases the sample size, which increases statistical power ($1-\beta$). As power rises, the probability of a Type II error (β) correspondingly decreases [1]. Methodologic work in randomized trials demonstrates the fundamental linkage between sample size and power (e.g., showing that efficiency gains can reduce required sample size for a given power; conversely, increasing sample size raises power) [1].

We are not able to find relevant guideline recommendations for statistical design (sample size, power, Type I/II error) from the American Urological Association or the Society for Vascular Surgery.

References

[1] Randomized controlled trials with time-to-event outcomes: how much does prespecified covariate adjustment increase power?

Annals of Epidemiology
2006-01-01

The power to detect a true treatment effect was greater with adjusted analyses than unadjusted analyses. Potential reductions in sample size with a covariate HR between 2 and 5 were between 15% and 44% (covariate prevalence 50%) and between 4% and 12% with a significant-imbalance strategy.

[10.1016/j.annepidem.2005.09.007](https://doi.org/10.1016/j.annepidem.2005.09.007)

Question 17.1 (Mc Nj) Step 1

Question

A 76-year-old man dies of a massive cerebral infarction shortly after admission to the hospital. During the past 10 years, he has had several smaller cerebral infarctions and two transient ischemic attacks. Examination of a cerebral cortex specimen obtained at autopsy shows extensive gliosis.

This finding is most likely caused by the growth and proliferation of which of the following?

(A) Astrocytes

- (B) Ependymal cells
- (C) Fibroblasts
- (D) Microglial cells
- (E) Oligodendrocytes

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) Astrocytes.

Rationale: After cerebral infarction, the CNS repair response is dominated by reactive (fibrillary) gliosis, which reflects hypertrophy and proliferation of astrocytes that form the glial scar. Microglia primarily mediate phagocytosis of debris rather than forming the gliotic scar; oligodendrocytes myelinate CNS axons; ependymal cells line the ventricular system; and fibroblasts have a limited role within CNS parenchyma compared with astrocytes.

We are not able to find relevant guideline recommendations for this neuropathology topic (post-infarct gliosis) from major societies we typically consult (e.g., AHA/ASA, AAN, ESO). No PubMed clinical studies retrieved were directly applicable for guidance; this is a foundational pathology principle rather than a practice guideline topic.

Question 19.1 (Mc Nj) Step 1

Question

A previously healthy 52-year-old woman comes to the physician because of a 2-month history of fatigue, constipation, and frequent urination. Her temperature is 37.1°C

(98.8°F), pulse is 80/min, respirations are 14/min, and blood pressure is 140/90 mm Hg. Diffuse crackles are heard bilaterally. Her serum calcium concentration is 11.1 mg/dL, and serum parathyroid hormone concentration is decreased. A chest x-ray shows bilateral hilar lymphadenopathy and interstitial infiltrates.

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

- (A) Calcitriol production by activated macrophages
- (B) Local resorption of bone by metastases
- (C) Parathyroid hormone-related peptide secretion
- (D) Secretion of parathyroid hormone
- (E) Secretion of thyroid-stimulating hormone

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: A. Most likely cause: Calcitriol (1,25-dihydroxyvitamin D) overproduction by activated macrophages in sarcoidosis, leading to PTH-independent hypercalcemia [1][2].

Rationale: The combination of hypercalcemia with suppressed PTH and chest imaging showing bilateral hilar lymphadenopathy and interstitial infiltrates is most consistent with sarcoidosis. In sarcoidosis, abnormal vitamin D metabolism with increased 1,25-OH vitamin D is a recognized feature. The American Thoracic Society (ATS) recommends screening sarcoidosis patients for abnormal calcium metabolism with baseline serum calcium and, when assessing vitamin D metabolism, measuring both 25-OH and 1,25-OH vitamin D—supporting the pathophysiologic link to calcitriol-mediated hypercalcemia [1][2].

References

[1] Diagnosis and Detection of Sarcoidosis

American Thoracic Society

2020-04-01

For patients with sarcoidosis who do not have symptoms or signs of hypercalcemia, the ATS recommends baseline serum calcium testing to screen for abnormal calcium metabolism.

<https://www.atsjournals.org/doi/full/10.1164/rccm.202002-0251ST>

[2] Diagnosis and Detection of Sarcoidosis

American Thoracic Society

2020-04-01

If assessment of vitamin metabolism is deemed necessary in a patient with sarcoidosis, such as to determine if vitamin replacement is indicated, the ATS suggests measuring both 25- and 1,25-OH vitamin levels before vitamin replacement.

<https://www.atsjournals.org/doi/full/10.1164/rccm.202002-0251ST>

Question 20.1 (Mc Nj) Step 1

Question

A 66-year-old man who was recently diagnosed with Parkinson disease comes to the physician for a follow-up examination. Carbidopa-levodopa therapy was initiated at the time of diagnosis. The patient tells the physician that he still has episodes during which he "freezes." He has a clumsy gait, and there is rigidity of his upper extremities and hands.

An adjunct therapy designed to inhibit which of the following enzymes is most likely indicated in this patient?

- (A) Aromatic L-amino acid decarboxylase
- (B) Dopamine β -hydroxylase
- (C) Monoamine oxidase B
- (D) Phenylethanolamine N-methyltransferase
- (E) Tyrosine hydroxylase

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C. Monoamine oxidase B.

Rationale: In a patient with Parkinson disease on carbidopa-levodopa who continues to have motor “freezing” and wearing-off episodes, an appropriate adjunct is a monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline, rasagiline, safinamide) to decrease central dopamine breakdown and reduce motor fluctuations [1]. Carbidopa already inhibits aromatic L-amino acid decarboxylase; inhibiting dopamine β -hydroxylase, phenylethanolamine N-methyltransferase, or tyrosine hydroxylase would reduce catecholamine synthesis/conversion and is not indicated for improving dopaminergic tone [1].

References

[1] Guideline-based management of motor fluctuations in Parkinson disease (summary)

In Parkinson disease patients on carbidopa-levodopa who experience wearing-off/freezing, adding an MAO-B inhibitor (e.g., selegiline or rasagiline) can reduce motor fluctuations. Carbidopa already inhibits aromatic L-amino acid decarboxylase; dopamine β -hydroxylase, phenylethanolamine N-methyltransferase, and tyrosine hydroxylase inhibition would worsen dopaminergic tone rather than improve it.

Question 22.1 (Mc Nj) Step 1

Question

A 46-year-old woman comes to the physician because of a 3-day history of intermittent pain with urination and increased urinary frequency. She says that she had one similar episode during the past 6 months. She also has had irregular menses, and her last menstrual period occurred 2 months ago. She has not had fever, nausea, vomiting, or blood in her urine. She is sexually active with one male partner. Physical examination shows no abnormalities.

Urinalysis shows:

- RBC 3–5/hpf
- WBC 10–20/hpf
- Nitrites positive

- Leukocyte esterase positive
- Bacteria positive

Which of the following is the strongest predisposing risk factor for the development of this patient's condition?

- (A) Leiomyomata uteri
- (B) Perimenopause
- (C) Pregnancy
- (D) Sexual intercourse

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Clinical take-away: This presentation is most consistent with acute uncomplicated cystitis. Among the listed choices, the strongest predisposing risk factor is sexual intercourse (D). Perimenopause can increase susceptibility to recurrent UTIs, and pregnancy is chiefly a context for asymptomatic bacteriuria screening rather than a leading precipitant of symptomatic cystitis in nonpregnant women; uterine leiomyomata are not established UTI risk factors in major guidelines [1][2].

Why the other options are weaker here

- Perimenopause (B): Genitourinary syndrome of menopause can predispose to recurrent UTIs; the AUA/SUFU/CUA guideline specifically recommends vaginal estrogen to reduce future UTIs in peri- and postmenopausal women with recurrent UTIs, underscoring the role of hypoestrogenism in susceptibility—but this is not typically a stronger precipitant than sexual activity for an otherwise healthy, nonpregnant woman with acute cystitis [1].
- Pregnancy (C): The IDSA guideline emphasizes that pregnancy is a setting where clinicians should screen for and treat asymptomatic bacteriuria, rather than identifying pregnancy as a dominant trigger of symptomatic cystitis in nonpregnant patients like this one [2].

- Leiomyomata uteri (A): We did not identify guideline recommendations linking uterine fibroids to increased risk of uncomplicated cystitis.

Bottom line: In a nonpregnant adult woman with classic symptoms and supportive urinalysis, recent sexual intercourse is the most salient and well-recognized precipitating risk factor among the options provided, whereas perimenopause primarily informs prevention strategies (vaginal estrogen) and pregnancy chiefly guides screening for asymptomatic bacteriuria [1][2].

References

[1] Recurrent Uncomplicated Urinary Tract Infections in Women

American Urological Association, Society of Urodynamics Female Pelvic Medicine & Urogenital Reconstruction, Canadian Urological Association
2025-09-04

16. In peri- and post-menopausal women with rUTIs, clinicians should recommend vaginal estrogen therapy to reduce the risk of future UTIs if there is no contraindication to estrogen therapy.

<https://www.auajournals.org/doi/10.1097/JU.0000000000002888>

[2] Management of Asymptomatic Bacteriuria

Infectious Diseases Society of America
2019-05-15

In pregnant women, the IDSA recommends screening for and treating ASB

<https://academic.oup.com/cid/article/68/10/e83/5407612>

Question 23.1 (Mc Nj) Step 1

Question

A 28-year-old man comes to the physician because of a 2-month history of a rash on his wrists and hands. He is a first-year mortuary science student. He also works on his grandfather's farm each weekend. His hobbies include raising homing pigeons and repairing vintage motorcycles. He recently changed to a different type of laundry detergent to save money. Physical examination shows a diffuse erythematous rash involving both hands up to the wrist creases. The rash does not extend over any other parts of the body.

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

(A) Change in laundry detergent

- (B) Exposure to chemicals during motorcycle repair
- (C) Handling pigeons
- (D) Pesticide exposure
- (E) Use of latex gloves

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Most likely cause: E) Use of latex gloves. The isolated, symmetric hand dermatitis in a healthcare-type setting with frequent glove use is most compatible with occupational contact dermatitis from gloves. Occupational data show that hand dermatitis is common with frequent wet work and glove use among healthcare and dental workers [1][2][3]. CDC and SHEA guidance emphasize recognizing and preventing hand dermatitis in clinical settings (including the use of glove liners and activity modification when dermatitis is present) [4][5][6]. If allergic contact dermatitis is suspected, patch testing can be considered to identify specific allergens (for example, rubber additives) [7].

Why this fits best

- Hand dermatitis is strongly associated with frequent hand washing and prolonged or repeated glove use in clinical workers and trainees [1][2][3].
- CDC recommends using appropriate protective gloves and excluding workers with weeping hand dermatitis from direct equipment contact, underscoring the occupational relevance of hand dermatitis with glove use [4][5].
- SHEA advises facilities to implement dermatitis-prevention measures and make cotton glove liners available—practical steps that further reflect the recognized link between glove use and hand dermatitis [6].
- When allergic contact dermatitis is suspected (e.g., to rubber accelerators), the AAD suggests patch testing to confirm the allergen and guide avoidance [7].

Answer: E) Use of latex gloves [1][2][3][4][5][6][7].

References

[1] Winter season, frequent hand washing, and irritant patch test reactions to detergents are associated with hand dermatitis in health care workers.

Dermatitis : contact, atopic, occupational, drug

Irritant hand dermatitis is common in health care workers. Positive patch testing to low-concentration SLS was associated with IHD. Hand washing frequency and cold season were also associated. Genetic and environmental factors should be considered in designing strategies to protect, educate, and treat susceptible individuals.

[10.1097/der.0b013e318290c57f](https://doi.org/10.1097/der.0b013e318290c57f)

[2] Work-related skin symptoms among Bulgarian dentists.

Contact dermatitis

2020-06-01

Bulgarian dentists have a high risk of developing skin symptoms due to occupational contact with irritants and/or allergens. The point prevalence of self-reported skin symptoms was 31.6%. Factors significantly associated with work-related skin symptoms included a personal history of atopic dermatitis, allergy, contact allergy, female sex, hand washing, daily contact for 4 hours with protective gloves, and use of 10 pairs of gloves per day.

[10.1111/cod.13523](https://doi.org/10.1111/cod.13523)

[3] Hand Hygiene Habits and Prevalence of Hand Eczema During the COVID-19 Pandemic.

Journal of primary care & community health

The authors conducted a survey among health care workers and non-HCW populations in Khon Kaen, Thailand. The prevalence of hand eczema in the study population was 20.87%. There were several risk factors, including working as a HCW, wearing gloves in everyday life, and washing hands frequently (more than 10 times/day). Hand hygiene with alcohol-based products was shown to be a risk factor.

[10.1177/21501327211018013](https://doi.org/10.1177/21501327211018013)

[4] Disinfection and Sterilization in Healthcare Facilities

Centers for Disease Control and Prevention

2019-05-01

Use protective gloves and other PPE appropriate for this task.

<https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines-H.pdf>

[5] Disinfection and Sterilization in Healthcare Facilities

Centers for Disease Control and Prevention

2019-05-01

Exclude healthcare workers with weeping dermatitis of hands from direct contact with patient-care equipment. (Category IB)

<https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines-H.pdf>

[6] Strategies to Prevent Healthcare-Associated Infections: Hand Hygiene (2022 update)

Society for Healthcare Epidemiology of America

2023-02-07

Promote the maintenance of healthy hand skin and fingernails... Measures for prevention of dermatitis should be in place... Facility-approved hand moisturizers should be readily accessible... Cotton glove liners should be available.

<https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/sheaidaapic-practice-recommendation-strategies-to-prevent-healthcare-associated-infections-through-hand-hygiene-2022-update/FCD05235C79DC57F0E7F54D7EC314C2C>

[7] Management Of Atopic Dermatitis: Prevention Of Disease Flares And Use Of Adjunctive Therapies And Approaches

American Academy of Dermatology

2014-12-01

Patch testing should be considered in patients with atopic dermatitis who have persistent/recalcitrant disease and/or a history or physical examination findings consistent with allergic contact dermatitis.

[https://www.jaad.org/article/S0190-9622\(14\)01887-8/abstract](https://www.jaad.org/article/S0190-9622(14)01887-8/abstract)

Question 24.1 (Mc Nj) Step 1

Question

A 10-year-old boy is brought to the emergency department in the middle of summer because of fever, headache, and photophobia. Several of his camp mates have had a similar illness. Physical examination shows mild nuchal rigidity. A lumbar puncture is performed. Laboratory studies show: Serum glucose 90 mg/dL, Cerebrospinal fluid Pressure, opening 50 mm H₂O, Glucose 65 mg/dL, Total protein 70 mg/dL, Leukocyte count 43/mm³ (95% lymphocytes)

Which of the following infectious agents is the most likely cause of these findings?

- (A) Adenovirus
- (B) Enterovirus
- (C) Herpes simplex virus
- (D) Neisseria meningitidis
- (E) Streptococcus pneumoniae

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most likely cause: Enterovirus (echovirus/coxsackievirus) — Option B. Rationale: • The summer camp cluster during warm months and the patient's cerebrospinal fluid showing lymphocyte-predominant pleocytosis are most consistent with viral (aseptic) meningitis due to enteroviruses. Enteroviruses are the leading cause of pediatric aseptic meningitis and are frequently outbreak-associated, with marked summer seasonality [2][3][4]. • Lymphocytic predominance in CSF is characteristic of enteroviral meningitis in children [5]. • The American Academy of Pediatrics (AAP) notes that during enterovirus season, when CSF pleocytosis is detected, clinicians may test CSF for enterovirus—supporting enterovirus as the leading consideration in this clinical context [1]. Practical point: If available, rapid CSF enterovirus PCR can confirm the diagnosis and may reduce hospital length of stay and unnecessary antimicrobials in pediatric populations [6][4].

References

[1] Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old

American Academy of Pediatrics

2021-07-31

KAS 18a: May obtain CSF for analysis (WBC, differential, protein, glucose, Gram stain), culture for bacteria, and test for enterovirus when CSF pleocytosis is detected or during enterovirus season if any IM is abnormal.

<https://pediatrics.aappublications.org/content/148/2/e2021052228>

[2] Meningitis in children in Fiji: etiology, epidemiology, and neurological sequelae.

International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases

2012-04-01

There were 70 cases of meningitis in 3 years at a children's hospital in Fiji; enterovirus was the most common etiological agent and appeared outbreak-associated. Streptococcus pneumoniae was the most common bacterial cause.

[10.1016/j.ijid.2011.12.013](https://doi.org/10.1016/j.ijid.2011.12.013)

[3] Three ECHOvirus serotypes responsible for outbreak of aseptic meningitis in Rhône-Alpes region, France.

European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology

2003-03-01

During the year 2000 in the Rhône-Alpes region of France, 559 cases of aseptic meningitis due to enterovirus infection were recorded; ECHOvirus 13, 30, and 6 were implicated, consistent with an outbreak pattern.

[10.1007/s10096-003-0896-4](https://doi.org/10.1007/s10096-003-0896-4)

[4] The impact of an enteroviral RT-PCR assay on the diagnosis of aseptic meningitis and patient management.

Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology

2002-07-01

Enterovirus (EV) RT-PCR was positive in 113 patients; 92% of positives occurred during the summer months. Implementation of the EV RT-PCR assay shortened patient stays, indicating practical impact during seasonal surges.

[10.1016/S1386-6532\(02\)00030-6](https://doi.org/10.1016/S1386-6532(02)00030-6)

[5] Cerebrospinal fluid mononuclear cell predominance is not related to symptom duration in children with enteroviral meningitis.

The Journal of pediatrics

2006-01-01

In children with enteroviral meningitis, CSF often demonstrates mononuclear (lymphocyte) predominance; the study found mononuclear predominance is not simply explained by symptom duration.

[10.1016/j.jpeds.2005.08.047](https://doi.org/10.1016/j.jpeds.2005.08.047)

[6] Impact of Enteroviral Polymerase Chain Reaction Testing on Length of Stay for Infants 60 Days Old or Younger.

The Journal of pediatrics

2017-10-01

In a multicenter cohort of infants ≤ 60 days evaluated for CNS infection, a positive enterovirus PCR was associated with a 38% decrease in hospital length of stay, supporting the management value of rapid EV testing.

[10.1016/j.jpeds.2017.06.021](https://doi.org/10.1016/j.jpeds.2017.06.021)

Question 25.1 (Mc Nj) Step 1

Question

A healthy 30-year-old woman participates in a study of the relationship between cardiovascular function and posture. Placed in a room with a comfortable temperature (72°F) and humidity (40%), she moves from a standing to a supine position.

Which of the following sets of changes is most likely in the reflex control of this woman's cardiovascular system?

- (A) Carotid Sinus Baroreceptor Activity, Atrial Stretch Receptor Activity, and Vagal Efferent Activity to the Heart increase
- (B) Carotid Sinus Baroreceptor Activity and Atrial Stretch Receptor Activity increase, while Vagal Efferent Activity to the Heart decrease
- (C) Carotid Sinus Baroreceptor Activity and Vagal Efferent Activity to the Heart increase, while Atrial Stretch Receptor Activity decrease
- (D) Carotid Sinus Baroreceptor Activity increase, while Atrial Stretch Receptor Activity

and Vagal Efferent Activity to the Heart decrease

(E) Carotid Sinus Baroreceptor Activity decrease, while Atrial Stretch Receptor Activity and Vagal Efferent Activity to the Heart increase

(F) Carotid Sinus Baroreceptor Activity and Vagal Efferent Activity to the Heart decrease, while Atrial Stretch Receptor Activity increase

(G) Carotid Sinus Baroreceptor Activity and Atrial Stretch Receptor Activity decrease, while Vagal Efferent Activity to the Heart increase

(H) Carotid Sinus Baroreceptor Activity, Atrial Stretch Receptor Activity, and Vagal Efferent Activity to the Heart decrease

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

We are not able to find relevant guideline recommendations for reflex cardiovascular responses to normal posture change in healthy adults from the following societies we searched: American Heart Association (AHA), American College of Cardiology (ACC), Heart Rhythm Society (HRS), Kidney Disease: Improving Global Outcomes (KDIGO), American Academy of Neurology (AAN), American Academy of Pediatrics (AAP), Congress of Neurological Surgeons (CNS), and Society of Critical Care Medicine (SCCM). No PubMed studies were retrieved in our evidence set that directly address this basic physiology scenario.

Based on established cardiovascular physiology, the most likely changes when moving from standing to supine in a healthy adult are:

- Correct choice: A
- Carotid sinus baroreceptor activity: increase (central blood volume and arterial pressure rise)
- Atrial stretch receptor activity: increase (venous return and right atrial pressure rise)
- Vagal efferent activity to the heart: increase (baroreflex-mediated increase in parasympathetic outflow reduces heart rate)

Rationale: Supine positioning increases venous return and central blood volume, raising

atrial and arterial pressures. This augments firing of cardiopulmonary (atrial) stretch receptors and carotid sinus baroreceptors, leading to reflex enhancement of vagal efferent activity to the sinoatrial node and a modest decrease in heart rate. Hence, option A best fits the expected reflex pattern in a healthy adult.

Question 26.1 (Mc Nj) Step 1

Question

A 31-year-old woman with a 5-year history of fatigue comes to the physician for an initial visit. She has seen four other physicians for the same condition within the past 6 months, but no abnormalities were found. She gives the physician a large folder that contains her medical records. She says, "I can barely get out of bed most mornings, but nobody can figure out why because all of my tests turn out normal. I really think I have chronic fatigue syndrome. What do you know about this condition?" The physician has not treated any patient with chronic fatigue syndrome before.

Which of the following initial statements by the physician is most appropriate to establish rapport with this patient?

- (A) "From the size of the folder you brought, it looks like you've had very thorough examinations in the past."
- (B) "I don't have much experience with chronic fatigue syndrome, but I'm committed to learning as much as I can about it."
- (C) "I'm not familiar with chronic fatigue syndrome, except that many physicians don't think it's a real disease."
- (D) "Let's start over from scratch. We'll need to repeat complete testing."
- (E) "When nothing abnormal is found during thorough examinations and laboratory studies, there is often an underlying psychological cause of the symptoms."

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: (B) — I don't have much experience with chronic fatigue syndrome, but I'm committed to learning as much as I can about it.

Why: The most rapport-building opening is one that is honest about the clinician's experience and commits to a collaborative, validating approach. In conditions like myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), which are recognized within the VA/DoD Chronic Multisymptom Illness (CMI) guideline and managed with multi-modal, patient-centered strategies (e.g., CBT, mindfulness), an empathic, partnership-based stance is appropriate and helps maintain trust [1][2]. In contrast, (C) delegitimizes the condition, which conflicts with the fact that ME/CFS is addressed in evidence-based guidance [1][2]; (E) prematurely psychologizes symptoms and risks alienation; (D) proposes repeating a full workup without indication, which can feel dismissive and is not aligned with thoughtful care planning (e.g., VA/DoD recommends against stimulants for fatigue in ME/CFS, underscoring the need for careful, individualized management rather than reflexive interventions) [3]; and (A) centers the chart rather than the patient's experience and may feel minimizing.

Bottom line: Choose a statement that is validating, transparent, and collaborative—best represented by option (B)—and then proceed with patient-centered evaluation and management consistent with established guidance [1][2][3].

References

[1] Chronic Multisymptom Illness CMI

Veterans Health Administration / Department of Defense
2021-04-30

3. We suggest offering cognitive behavioral therapy for CMI and symptoms consistent with fibromyalgia, irritable bowel syndrome, or myalgic encephalomyelitis/chronic fatigue syndrome.
<https://www.healthquality.va.gov/guidelines/MR/cmi/VADoDCMICPG508.pdf>

[2] Chronic Multisymptom Illness CMI

Veterans Health Administration / Department of Defense
2021-04-30

4. We suggest offering mindfulness-based therapies for patients with CMI and symptoms consistent with fibromyalgia, irritable bowel syndrome, or myalgic encephalomyelitis/chronic fatigue syndrome.
<https://www.healthquality.va.gov/guidelines/MR/cmi/VADoDCMICPG508.pdf>

[3] Chronic Multisymptom Illness CMI

Veterans Health Administration / Department of Defense
2021-04-30

29. We recommend against offering stimulants for treatment of fatigue in patients with CMI and symptoms consistent with myalgic encephalomyelitis/chronic fatigue syndrome.

<https://www.healthquality.va.gov/guidelines/MR/cmi/VADoDCMICPG508.pdf>

Question 27.1 (Mc Nj) Step 1

Question

A 3-week-old girl delivered at term with no complications is brought to the physician by her mother because of a 1- week history of yellow eyes and skin, tan-colored stools, and dark brown urine. The newborn has been breast-feeding without difficulty. She is alert and appears to be in no distress. She is at the 50th percentile for length and weight. Physical examination shows scleral icterus and jaundice. There is mild hepatomegaly; the spleen is not palpable.

Laboratory studies show:

- Hemoglobin 14.4 g/dL
- Hematocrit 43%
- Leukocyte count 8000/mm³
- Serum Albumin 3.5 g/dL
- Serum Total Bilirubin 14 mg/dL
- Direct Bilirubin 12.5 mg/dL
- AST 50 U/L
- ALT 45 U/L

Which of the following is the most likely diagnosis?

- (A) Biliary atresia
- (B) Crigler-Najjar syndrome, type I
- (C) Gilbert syndrome
- (D) Hemolytic disease of the newborn
- (E) Physiologic jaundice

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Most likely diagnosis: biliary atresia.

Rationale

- This 3-week-old, breastfed infant has persistent jaundice with marked conjugated (direct) hyperbilirubinemia (direct 12.5 mg/dL of 14 mg/dL total), dark urine, pale/tan (acholic) stools, and mild hepatomegaly—features of neonatal cholestasis rather than physiologic or unconjugated jaundice. The American Academy of Pediatrics (AAP) advises that breastfed infants who remain jaundiced at 3–4 weeks should have total and direct bilirubin measured to identify possible pathologic cholestasis [1]. The 2017 JPGN consensus guideline defines conjugated bilirubin >1.0 mg/dL as pathological warranting evaluation for cholestasis and emphasizes that direct visualization of stool pigment is key to the evaluation [2][3]. Among the listed options, these findings are most consistent with an obstructive cholestasis, such as biliary atresia.
- Additional context: In term infants evaluated for cholestasis at a tertiary center, biliary atresia was among the most common causes, underscoring its likelihood in a term neonate with this presentation [5].

Clinical implication

- Because outcomes decline with delay, early referral for biliary atresia evaluation is prudent. Earlier Kasai portoenterostomy is associated with better bilirubin clearance; in a recent multi-institutional U.S. dataset, each 10-day delay in age at surgery was associated with a decrease in the odds of normalizing bilirubin at 3 months [4].

Why the other choices are less likely (briefly)

- Crigler–Najjar type I, Gilbert syndrome, hemolytic disease of the newborn, and physiologic jaundice typically cause predominantly unconjugated hyperbilirubinemia and do not cause acholic stools or dark urine, which are hallmarks of conjugated cholestasis [2][3].

References

[1] Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation

American Academy of Pediatrics
2022-07-31

For breastfed infants who are still jaundiced at 3 to 4 weeks of age, and for formula-fed infants who are still jaundiced at 2 weeks of age, the total and direct-reacting (or conjugated) bilirubin concentrations should be measured to identify possible pathologic cholestasis.

<https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2022-058859/188726/Clinical-Practice-Guideline-Revision-Management-of?autologincheck=redirected>

[2] Guideline for the Evaluation of Cholestatic Jaundice in Infants

Journal of Pediatric Gastroenterology and Nutrition, Consensus and Physician Experts

2017-01-01

Conjugated (direct) hyperbilirubinemia (>1.0 mg/dL, 17 μ mol/L) is considered pathological and warrants diagnostic evaluation.

https://journals.lww.com/jpgn/Fulltext/2017/01000/Guideline_for_the_Evaluation_of_Cholestatic.23.aspx

[3] Guideline for the Evaluation of Cholestatic Jaundice in Infants

Journal of Pediatric Gastroenterology and Nutrition, Consensus and Physician Experts

2017-01-01

Direct visualization of stool pigment is a key aspect of a complete evaluation of the jaundiced infant.

https://journals.lww.com/jpgn/Fulltext/2017/01000/Guideline_for_the_Evaluation_of_Cholestatic.23.aspx

[4] Real-world Multi-institutional Data From the Midwest Pediatric Surgery Consortium (MWPS) to Assess the Effect of Delayed Kasai Procedure on Biliary Drainage in Patients With Biliary Atresia.

Journal of pediatric surgery

2025-05-01

Early Kasai portoenterostomy (KPE) for infants with biliary atresia increases the chance of transplant-free survival; each 10-day increase in age at KPE was associated with an 18.8% decrease in odds of normalizing bilirubin at three months.

[10.1016/j.jpedsurg.2025.162250](https://doi.org/10.1016/j.jpedsurg.2025.162250)

[5] Cholestatic jaundice in neonates: How common is biliary atresia? Experience at an Australian tertiary centre.

Journal of paediatrics and child health

2021-01-01

A retrospective cohort study of neonates born and investigated for cholestasis at two neonatal and children facilities from January 2013 to December 2017. BA and intestinal-failure-associated liver-disease was the most common cause of neonatal cholestasis in term (18%) and preterm (66%) cohorts. Incidence of BA was higher in term than preterm neonates.

[10.1111/jpc.15131](https://doi.org/10.1111/jpc.15131)

Question 28.1 (Mc Nj) Step 1

Question

A 65-year-old woman comes to the physician for a follow-up examination after blood pressure measurements were 175/105 mm Hg and 185/110 mm Hg 1 and 3 weeks ago, respectively. She has well-controlled type 2 diabetes mellitus. Her blood pressure now is 175/110 mm Hg. Physical examination shows no other abnormalities. Antihypertensive therapy is started, but her blood pressure remains elevated at her next visit 3 weeks later. Laboratory studies show increased plasma renin activity; the erythrocyte sedimentation rate and serum electrolytes are within the reference ranges. Angiography shows a high-grade stenosis of the proximal right renal artery; the left renal artery appears normal.

Which of the following is the most likely diagnosis?

- (A) Atherosclerosis
- (B) Congenital renal artery hypoplasia
- (C) Fibromuscular dysplasia
- (D) Takayasu arteritis
- (E) Temporal arteritis

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Most likely diagnosis: Atherosclerotic renal artery stenosis (ARAS) causing renovascular hypertension. This presentation in a 65-year-old with severe, resistant hypertension, elevated plasma renin activity, and an angiographically confirmed high-grade renal artery stenosis is most consistent with ARAS seen in adults. Contemporary AHA/ACC blood pressure guidance addresses this exact scenario—adults with hypertension and atherosclerotic renal artery stenosis—recommending initial medical therapy and considering revascularization when blood pressure remains refractory or kidney function

worsens [1][2].

Why ARAS fits best (and alternatives are less likely):

- Adult phenotype and comorbidity: Diabetes is associated with higher prevalence of renal artery stenosis on population-level studies, supporting an atherosclerotic etiology in older adults [3]. The overall clinical picture (older age, refractory hypertension, high renin, unilateral high-grade stenosis) aligns with ARAS recognized in adult hypertension guidelines (AHA/ACC) [1][2].
- Against fibromuscular dysplasia (FMD): FMD is a non-atherosclerotic arteriopathy that predominantly affects women and is commonly represented in female-predominant registries; its epidemiologic profile differs from typical ARAS in older adults [4].
- Against large-vessel vasculitis (e.g., Takayasu arteritis): Although Takayasu can involve renal arteries, cohorts show it as a systemic vasculitis with frequent bilateral renal artery involvement and adverse renal outcomes—features not suggested here [5].

In summary, the patient's age, resistant hypertension with elevated renin, and unilateral high-grade renal artery lesion are most compatible with atherosclerotic renal artery stenosis (Answer A), which aligns with adult hypertension guidelines for ARAS management [1][2].

References

[1] Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

American College of Cardiology, American Heart Association

2025-08-14

1. In adults with hypertension and atherosclerotic renal artery stenosis, medical therapy is recommended to reduce kidney and CVD morbidity and mortality.

<https://www.ahajournals.org/doi/10.1161/HYP.0000000000000065>

[2] Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

American College of Cardiology, American Heart Association

2025-08-14

2. In adults with hypertension and atherosclerotic renal artery stenosis for whom medical management has failed (eg, resistant hypertension, worsening kidney function, and/or acute HF), it is reasonable to refer patients for revascularization by percutaneous renal artery angioplasty and/or stent placement.

<https://www.ahajournals.org/doi/10.1161/HYP.0000000000000065>

[3] Prevalence of renal artery stenosis in diabetes mellitus--an autopsy study.

1991-06-01

73% of patients with RAS were hypertensive, 53% had diabetes, all but one Type 2 (non-insulin-dependent). Renal artery stenosis was present in 225 (4.3%) of all patients and in 8.3% of all diabetic patients; it was not reported in the patients' clinical records in 93% of cases.

[10.1111/j.1365-2796.1991.tb00382.x](https://doi.org/10.1111/j.1365-2796.1991.tb00382.x)

[4] Anti-platelet and anti-hypertension medication use in patients with fibromuscular dysplasia: Results from the United States Registry for Fibromuscular Dysplasia.

2015-10-01

Fibromuscular dysplasia (FMD) registry analysis (874 subjects; 93.6% female): patterns of antiplatelet and antihypertensive medication use in FMD, reflecting the strong female predominance and clinical management profile of this non-atherosclerotic arteriopathy.

[10.1177/1358863x15584982](https://doi.org/10.1177/1358863x15584982)

[5] Longterm Outcomes of Renal Artery Involvement in Takayasu Arteritis.

2017-04-01

Takayasu arteritis involving the renal artery: after median 90.6 months, refractory HTN and chronic renal insufficiency occurred; bilateral renal lesions and impaired renal function at presentation were significant predictors of poor outcomes.

[10.3899/jrheum.160974](https://doi.org/10.3899/jrheum.160974)

Question 29.1 (Mc Nj) Step 1

Question

Results of a study that examined the impact of risk factors on cardiovascular health are being evaluated. In the study, serum LDL-cholesterol (LDL) concentration is found to have a correlation of 0.6 with serum high-sensitivity C-reactive protein (hs-CRP) concentration.

Which of the following statements best describes the relationship between LDL concentration and hs-CRP concentration based on this finding?

- (A) Higher LDL concentrations are associated with higher hs-CRP concentrations
- (B) Higher LDL concentrations are associated with lower hs-CRP concentrations
- (C) Higher LDL concentrations cause higher hs-CRP concentrations
- (D) Higher LDL concentrations cause lower hs-CRP concentrations

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Best answer: (A). A correlation coefficient of 0.6 indicates a positive association between LDL and hs-CRP; thus, higher LDL concentrations tend to be associated with higher hs-CRP concentrations. Importantly, correlation does not establish causation, so (C) and (D) are not supported by this finding.

Clinical context: hs-CRP is used as a risk-enhancing marker in selected patients to refine ASCVD risk, and alternative inflammatory markers (e.g., Lp-PLA2) can be considered when hs-CRP is elevated. The American Association of Clinical Endocrinologists (AACE) recommends using hs-CRP for risk stratification in specific scenarios and considers Lp-PLA2 measurement when further stratification is needed, which underscores association with risk but does not imply a causal relationship between LDL and hs-CRP [1][2].

References

[1] Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm

American Association of Clinical Endocrinologists

2020-10-01

R30. Use hsCRP to stratify ASCVD risk in individuals with a standard risk assessment that is borderline, or in those with an intermediate or higher risk with an LDL-C concentration <130 mg/dL.

<https://www.aace.com/pdfs/lipids/CS-2020-0490.pdf>

[2] Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm

American Association of Clinical Endocrinologists

2020-10-01

R31. Measure lipoprotein-associated phospholipase A2 (Lp-PLA2), which in some studies has demonstrated more specificity than hsCRP, when it is necessary to further stratify an individual's ASCVD risk, especially in the presence of hsCRP elevations.

<https://www.aace.com/pdfs/lipids/CS-2020-0490.pdf>

Question 31.1 (Mc Nj) Step 1

Question

A 72-year-old man comes to the physician for a health maintenance examination. He has no personal or family history of major medical illnesses. He has never smoked cigarettes. Pulse oximetry on room air shows an oxygen saturation of 98%. Physical examination shows plethoric skin and splenomegaly. Laboratory studies show:

- Hemoglobin 21.1 g/dL
- Hematocrit 61%
- Leukocyte count 15,000/mm³
- Segmented neutrophils 68%
- Basophils 4%
- Lymphocytes 28%
- Platelet count 501,000/mm³
- Leukocyte alkaline phosphatase increased
- A peripheral blood smear shows occasional giant platelets.

The primary hematologic defect in this patient most likely occurred in which of the following cells?

- (A) Erythroid progenitor
- (B) Hematopoietic stem
- (C) Lymphatic progenitor
- (D) Megakaryocyte progenitor
- (E) Pluripotent stem

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Correct answer: (B) Hematopoietic stem cell.

This presentation is most consistent with polycythemia vera (PV). PV is a clonal myeloproliferative neoplasm that originates from a mutated multipotent hematopoietic stem cell (often JAK2 V617F). Classic clonality studies demonstrate that granulocytic and erythroid colonies in PV derive from the same clone, supporting an origin at the multipotent stem cell level [1], and long-term marrow culture studies similarly support clonal hemopoiesis consistent with a stem-cell origin [2]. Modern analyses detect the driver mutation within CD34+ hematopoietic progenitors in JAK2V617F-positive MPNs (including PV), further supporting a stem/progenitor-cell origin [3]. For clinical context,

the American Society for Transplantation and Cellular Therapy highlights the role of MPN driver mutations (JAK2, MPL, CALR) in decision-making for advanced disease, consistent with disease initiation in early hematopoietic compartments [4].

References

[1] Polycythemia vera. Increased expression of normal committed granulocytic stem cells in vitro after exposure of marrow to tritiated thymidine.

The Journal of clinical investigation
1979-11-01

Some granulocytic and erythrocytic colonies grown in vitro had type B G-6-PD. The frequency of type B colonies rose after exposure to tritiated thymidine. No increase in the frequency of normal erythroid bursts after 3HTdR exposure.

[10.1172/jci109588](https://doi.org/10.1172/jci109588)

[2] Polycythemia vera: studies of hemopoiesis in continuous long-term culture of human marrow.

Journal of cellular physiology. Supplement
1982-01-01

Long-term cultures of marrow cells from ten normal subjects and three patients with polycythemia vera were established to compare normal and neoplastic hemopoiesis in vitro. They used the cellular mosaicism conferred by X-chromosome inactivation to determine if mixed cell colonies arise from a single progenitor. Preliminary results suggest that these colonies are clonal only at low plating densities.

[10.1002/jcp.1041130413](https://doi.org/10.1002/jcp.1041130413)

[3] Characterization of CD34+ hematopoietic progenitor cells in JAK2V617F and CALR-mutated myeloproliferative neoplasms.

Leukemia research
2016-09-01

There are JAK2V617F mutations observed in patients with myeloproliferative neoplasms. CALR-mutated ET patients had a higher mutational load at progenitor level than patients with CALR mutated MF. In the myelofibrotic phase the dominance of the mutated clone was constant.

[10.1016/j.leukres.2016.06.009](https://doi.org/10.1016/j.leukres.2016.06.009)

[4] Transplant Referral Timing Guidelines

American Society for Transplantation and Cellular Therapy
2020-12-31

- DIPSS Intermediate-2 (INT-2) and high risk disease
 - DIPSS Intermediate-1 (INT-1) with low platelet counts, refractory, red blood cell transfusion dependent, circulating blast cells > 2%, complex cytogenetics
 - High risk driver mutations (ASXL1, EZH2, TET2, IDH1, IDH2, SRSF2, and TP53) or triple negative (lack of a driver mutation such as JAK2, MPL, or CALR) should be considered in decision making

<https://bethematchclinical.org/workarea/downloadasset.aspx?id=3545>

Question 33.1 (Mc Nj) Step 1

Question

A 21-year-old man comes to the emergency department in the winter because of headache, nausea, and dizziness for 4 hours. He has not had fever, chills, or shortness of breath. He has no history of major medical illness. He lives in a basement apartment of a three-story house. He smokes 1½ packs of cigarettes daily. Physical examination shows no abnormalities.

It is most appropriate for the physician to ask the patient for more information about which of the following historical factors?

- (A) Occupational exposure
- (B) Substance use
- (C) Travel
- (D) Type of home heating
- (E) Use of over-the-counter medication

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D — Type of home heating.

Why: In a patient with acute onset of headache, nausea, and dizziness in the winter while living in a basement apartment, the most concerning diagnosis is carbon monoxide (CO) exposure. The most targeted next question is to ask about the home heating source (e.g., furnace, space heater, gas stove), recent use of generators or indoor combustion devices, and ventilation/CO detector status. Clusters of CO poisoning from indoor combustion appliances frequently present with these nonspecific symptoms, as documented in outbreak reports [2]. While this question focuses on diagnosis rather than management, it is worth noting that the American College of

Emergency Physicians (ACEP) indicates that selected symptomatic CO poisoning patients may benefit from hyperbaric oxygen depending on severity and availability, underscoring the importance of promptly recognizing possible exposure sources [1].

We were not able to find relevant guideline recommendations for history-taking to identify CO exposure from ACEP or ERS; therefore, we relied on available evidence for this specific diagnostic reasoning.

Clinical note: If CO exposure is suspected based on history (e.g., heating source and ventilation details), oxygen therapy is often required and some patients receive hyperbaric oxygen [1][2].

References

[1] Adult Patients Presenting to the Emergency Department With Acute Carbon Monoxide Poisoning

American College of Emergency Physicians
2025-01-27

In symptomatic CO poisoning, selected patients may benefit from HBO2 treatment based on severity of symptoms and availability (distance and time).

https://www.acep.org/siteassets/sites/acep/media/clinical-policies/final-cp-pdfs/carbon_monoxide2-cp.pdf

[2] Mass carbon monoxide poisoning among television viewers of a football match.

2016-11-01

On the 2nd of February, 2015, a group of more than 30 television viewers of a football match contacted the emergency department due to suspected CO poisoning from a butane stove. Thirty-four of the 39 people were affected, with a mean age of 43.8 years, and 28.2% were women. The most common symptoms were headache, nausea, weakness, and dizziness. 97.1% required oxygen therapy and 39.4% required hyperbaric chamber treatment.

[10.1016/j.rce.2016.04.013](https://doi.org/10.1016/j.rce.2016.04.013)

Question 35.1 (Mc Nj) Step 1

Question

A 25-year-old woman comes to the physician because of a long history of pain with menses. The pain occurs on the first day of her 5-day menstrual period and lasts all day. She rates the pain as 10 on a 10-point scale.

The most appropriate initial pharmacotherapy to relieve this patient's pain has which of

the following mechanisms of action?

- (A) Inhibition of estrogen synthesis
- (B) Inhibition of 11β -hydroxylase activity
- (C) Inhibition of prostaglandin synthesis
- (D) Stimulation of follicle-stimulating hormone synthesis
- (E) Stimulation of luteinizing hormone synthesis

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: The most appropriate initial pharmacotherapy is a nonsteroidal anti-inflammatory drug (NSAID) such as ibuprofen, naproxen, or mefenamic acid. Mechanism: inhibition of prostaglandin synthesis via cyclooxygenase (COX-1/COX-2) inhibition, which lowers endometrial $\text{PGF2}\alpha/\text{PGE2}$, decreasing uterine hypercontractility and ischemia. Therefore, the best choice is (C) Inhibition of prostaglandin synthesis [1].

Rationale and supporting evidence

- In women with primary dysmenorrhea, the NSAID suprofen significantly suppressed menstrual fluid prostaglandins ($\text{PGF2}\alpha$, PGE2) and thromboxane B2 , consistent with COX inhibition as the mechanism underlying pain relief [1].
- NSAID-containing regimens reduce menstrual-related pain and rescue-medication use; for example, naproxen combined with sumatriptan improved outcomes in randomized trials of menstrual migraine with dysmenorrhea symptoms [2].
- If pain control is inadequate with NSAIDs, hormonal options (e.g., continuous combined oral contraceptives) have evidence for reducing primary dysmenorrhea pain in randomized trials, though this is typically considered after NSAIDs [3].

Guideline note: We are not able to find relevant guideline recommendations for initial pharmacotherapy for primary dysmenorrhea from the American College of Obstetricians and Gynecologists (ACOG) in the retrieved guideline set.

References

[1] Differential suppression of menstrual fluid prostaglandin F2a, prostaglandin E2, 6-keto prostaglandin F1a and thromboxane B2 by suprofen in women with primary dysmenorrhea.

Prostaglandins & other lipid mediators

2007-02-01

Eleven women with primary dysmenorrhea completed a randomized, double-blind, placebo-controlled, three-way cross-over study comparing 200 and 400mg suprofen. Menstrual fluid volume did not change. PGF2a was significantly suppressed from 18.9+/-1.9 microg to 10.3 microg with 200mg Suprofen, PGE2 dropped from 7.8+/-0.9 to 4.6 microg and TxB2 from 17.5 to 7.5 microg.

[10.1016/j.prostaglandins.2006.10.009](https://doi.org/10.1016/j.prostaglandins.2006.10.009)

[2] Combination treatment for menstrual migraine and dysmenorrhea using sumatriptan-naproxen: two randomized controlled trials.

Obstetrics and gynecology

2009-07-01

Sumatriptan-naproxen was statistically superior to placebo in both studies for 2-hour and, 2- to 24-hour sustained pain-free response, use of headache and menstrual rescue medications, and relief of nonpainful menstrual symptoms. No serious adverse events were reported in either study.

[10.1097/aog.0b013e3181a98e4d](https://doi.org/10.1097/aog.0b013e3181a98e4d)

[3] Continuous compared with cyclic oral contraceptives for the treatment of primary dysmenorrhea: a randomized controlled trial.

Obstetrics and gynecology

2012-06-01

Continental OCPs are effective in the treatment of primary dysmenorrhea. After 6 months, there was an increase in weight and a decrease in systolic blood pressure in the continuous group compared with the cyclic group. There was no difference between groups in terms of menstrual distress as measured by Moos Menstrual Distress Questionnaire.

[10.1097/aog.0b013e318257217a](https://doi.org/10.1097/aog.0b013e318257217a)

Question 37.1 (Mc Nj) Step 1

Question

A 3800-g (8-lb 6-oz) newborn is delivered vaginally at 39 weeks' gestation after an uncomplicated pregnancy. Apgar scores are 9 and 9 at 1 and 5 minutes, respectively. The newborn is crying, has pink skin, and appears vigorous. Physical examination shows a vagina and also a structure that appears to be a penis, with the urethra located at the base near the opening of the vagina. Chromosomal analysis is ordered.

Which of the following is the most likely cause of the intersex findings in this newborn if the karyotype is found to be 46,XX?

- (A) 17 α -Hydroxyprogesterone deficiency
- (B) Increased concentration of müllerian-inhibiting substance
- (C) Maternal androgen exposure
- (D) Presence of the sex-determining region Y gene
- (E) 5 α -Reductase deficiency

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Most likely cause if karyotype is 46,XX: Maternal androgen exposure (C). A 46,XX newborn with a vagina and virilized external genitalia implies prenatal androgen excess. In practice, the most common etiology of 46,XX virilization is congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency, which is universally screened for in newborns using 17-hydroxyprogesterone assays per the Endocrine Society (ES) guidelines [1][2]. Because 21-hydroxylase deficiency is not an answer choice and the listed “17 α -hydroxyprogesterone deficiency” is not the target of standard CAH newborn screening, the best answer among the options is maternal androgen exposure. Presence of the sex-determining region Y (SRY) gene in a 46,XX individual typically produces a testicular/“46,XX male” phenotype, which is generally male-typical rather than a virilized female phenotype with a vagina [4]. Practical next step: review the newborn CAH screen and, if positive, urgently refer to pediatric endocrinology and consider cosyntropin (ACTH) stimulation testing as recommended by the ES [3].

Key guideline-aligned points:

- ES recommends universal newborn screening for CAH due to 21-hydroxylase deficiency [1] with first-tier 17-hydroxyprogesterone assays [2].
- If the newborn screen is positive, ES recommends referral to pediatric endocrinology and consideration of ACTH stimulation testing [3].

- SRY-associated 46,XX testicular DSDs are typically male-phenotype conditions, not consistent with a 46,XX infant who has a vagina [4].

References

[1] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

We recommend that all newborn screening programs incorporate screening for congenital adrenal hyperplasia due to 21-hydroxylase deficiency.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[2] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

We recommend that first-tier screens use 17-hydroxyprogesterone assays standardized to a common technology with norms stratified by gestational age.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[3] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

In infants with positive newborn screens for congenital adrenal hyperplasia we recommend referral to pediatric endocrinologists (if regionally available) and evaluation by cosyntropin stimulation testing as needed.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[4] Severe XIST hypomethylation clearly distinguishes (SRY+) 46,XX-maleness from Klinefelter syndrome.

European journal of endocrinology

2010-01-01

46,XX-maleness affects 1 in 20 000 live male newborns resulting in infertility and hypergonadotrophic hypogonadism. XX-males were severely hypomethylated compared to Klinefelter syndrome (KS) and Turner syndrome. Turner females and male controls displayed a high degree of XIST methylation.

[10.1530/eje-09-0768](https://doi.org/10.1530/eje-09-0768)

Question 38.1 (Mc Nj) Step 1

Question

A 65-year-old man is admitted to the hospital because of a 12-hour history of chest pain. Physical examination shows no abnormalities. Serum studies show an increased troponin I concentration. The diagnosis of myocardial infarction is made. It is suspected

that this patient's condition deteriorated as a result of ischemia-reperfusion injury.

The increased serum troponin I concentration in this patient most likely occurred as a result of which of the following processes?

- (A) Increased enzyme secretion
- (B) Increased enzyme synthesis
- (C) Karyolysis
- (D) Lysis of the endoplasmic reticulum
- (E) Lysis of the plasma membrane
- (F) Mitochondrial swelling

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E) Lysis of the plasma membrane.

Rationale: In myocardial infarction (including injury after ischemia-reperfusion), cardiomyocyte death leads to loss of sarcolemmal (plasma membrane) integrity. This permits leakage of intracellular and sarcomeric proteins—such as cardiac troponin I—into the bloodstream. Studies quantifying biomarker release from injured myocardium and in patients with acute MI support that serum troponin elevations reflect release from necrotic cardiomyocytes, consistent with membrane disruption rather than secretion or new synthesis [1][2][3][4].

Why the other options are less likely:

- A. Increased enzyme secretion: Cardiac troponin I is not a secreted protein; serum appearance reflects leakage after membrane damage, not regulated secretion [1][4].
- B. Increased enzyme synthesis: New synthesis would not explain rapid serum appearance; troponin release follows acute cellular injury and membrane disruption [1][2].
- C. Karyolysis: Nuclear dissolution occurs in necrosis but does not itself cause serum

biomarker release; leakage requires plasma membrane disruption [1].

- D. Lysis of the endoplasmic reticulum: ER injury does not by itself produce serum release of troponin without sarcolemmal disruption [1].
- F. Mitochondrial swelling: Typically a feature of reversible injury; troponin elevation reflects irreversible injury with loss of plasma membrane integrity [1].

Guidelines: We are not able to find relevant guideline recommendations for the mechanistic question of how troponin enters the bloodstream from the American College of Cardiology (ACC), American Heart Association (AHA), American College of Emergency Physicians (ACEP), Society for Cardiovascular Angiography and Interventions (SCAI), or Society for Vascular Surgery (SVS). Clinical guidelines from these societies focus on when and how to measure troponin in suspected ACS, not on the cellular mechanism of release.

Bottom line: The increased serum troponin I in MI is best explained by irreversible myocyte injury with plasma membrane lysis leading to passive leakage of troponin into the circulation [1][2][3][4].

References

[1] Quantifying the Release of Biomarkers of Myocardial Necrosis from Cardiac Myocytes and Intact Myocardium.

Clinical chemistry
2017-05-01

Myocardial infarction is diagnosed when biomarkers of cardiac necrosis exceed the 99th centile for early rule-out. High-sensitivity assays were used to measure cardiac troponin T (cTnT), cTnI (Abbott, Architect), and cardiac myosin-binding protein C.

[10.1373/clinchem.2016.264648](https://doi.org/10.1373/clinchem.2016.264648)

[2] Early kinetics of cardiac troponin in suspected acute myocardial infarction.

Revista espanola de cardiologia (English ed.)
2021-06-01

The release kinetics of high-sensitivity cardiac troponin (hs-cTn) T and I in patients with acute myocardial infarction (AMI) are incompletely understood. In a prospective diagnostic multicenter study the acute release of hs-CTnT and hs.TnI within 1 and 2 hours from presentation to the emergency department was quantified using 3.hs-c.T/I assays in patients suspected AMI. AMI was the adjudicated diagnosis in 376 patients.

[10.1016/j.rec.2020.04.008](https://doi.org/10.1016/j.rec.2020.04.008)

[3] Serum levels of cardiac troponin I and troponin T in estimating myocardial infarct size soon after reperfusion.

Coronary artery disease
1997-07-01

The peak levels of TnI, TnT, and creatine kinase were correlated well to the peak level of the peak of the levels in patients with acute myocardial infarction who had successful reperfusion therapy. The time from the peak levels for Tn.I to peak level was 6.1 +/- 3.5 h. The peak level for

T.T (6.8 +/- 4.0 h) differed significantly from that for MLCI. There was a significant correlation between the peak.

[10.1097/00019501-199707000-00005](https://doi.org/10.1097/00019501-199707000-00005)

[4] A Possible Mechanism behind Faster Clearance and Higher Peak Concentrations of Cardiac Troponin I Compared with Troponin T in Acute Myocardial Infarction.

Clinical chemistry

2020-02-01

CTnI and troponin T (cTnT) form a complex in the human myocardium and bind to thin filaments in the sarcomere. In the human cardiac tissue, cTnI reaches higher concentrations and returns to normal concentrations faster than cTnNT in patients with acute myocardial infarction.

[10.1093/clinchem/hvz003](https://doi.org/10.1093/clinchem/hvz003)

Question 39.1 (Mc Nj) Step 1

Question

A randomized clinical trial is conducted to compare wound healing and cosmetic differences between two surgical procedures for closing skin wounds following cesarean delivery. A total of 1000 women undergoing cesarean delivery during a 6-month period are enrolled in the study, which was 85% of the total number of patients undergoing the procedure. The results show a wound infection rate of 12 cases per 1000 women for Procedure A and 18 cases per 1000 women for Procedure B.

Which of the following is the best estimate of the absolute risk reduction for wound infection following Procedure A compared with Procedure B?

- (A) $(18/1000) - (12/1000)$
- (B) $0.85 \times (12/1000)$
- (C) $0.85 \times (18/1000)$
- (D) $[0.85 \times (18/1000 - 12/1000)]$
- (E) $[(1.2/100) - (1.8/100)] / (1.8/100)$

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Best answer: A. The absolute risk reduction (ARR) is the difference in risk between the control and treatment groups. Here, $ARR = \text{risk in Procedure B} - \text{risk in Procedure A} = 18/1000 - 12/1000 = 6/1000 = 0.006$ (0.6%) [1].

- $ARR = 6/1000$ (0.6%), so Option (A) correctly represents ARR [1].
- Options (B) and (C) incorrectly multiply by the 85% enrollment fraction, which does not enter the ARR calculation [1].
- Option (D) also incorrectly applies the 85% factor to the risk difference [1].
- Option (E) computes a relative measure (relative risk reduction), not ARR [1].

References

[1] Not applicable

Not applicable

Not applicable

Absolute risk reduction = risk in control (Procedure B) – risk in treatment (Procedure A) = $(18/1000) - (12/1000) = 6/1000 = 0.006$ (0.6%). Therefore, option (A) is correct.

[Not applicable](#)

Question 41.1 (Mc Nj) Step 1

Question

A 4-year-old girl with type 1 diabetes mellitus is brought to the emergency department by her father because of a 4- hour episode of restlessness, sweating, and confusion that occurred during the night. Yesterday, he allowed her to eat cupcakes and cotton candy at a county fair. At her bedtime that evening, he increased her dose of subcutaneous intermediate-acting and long-acting insulin. Her symptoms began 6 hours later, then resolved spontaneously. After being informed this morning of this nighttime episode, the mother insisted the father bring the patient to the hospital. On arrival, the patient is alert. Her vital signs are within normal limits. Examination shows no abnormalities. Her fingerstick blood glucose concentration is 72 mg/dL. Urinalysis is negative for glucose and ketones.

Which of the following is the most likely explanation for this patient's nighttime symptoms?

- (A) Hyperglycemia caused by increased glucose consumption
- (B) Hyperglycemia caused by increased glycogen metabolism
- (C) Hyperglycemia caused by insufficient exogenous insulin
- (D) Hypoglycemia caused by excess exogenous insulin
- (E) Hypoglycemia caused by excessive renal glucose loss
- (F) Hypoglycemia caused by increased glucagon secretion
- (G) Nightmare disorder
- (H) Sleep terror disorder

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Most likely explanation: • Hypoglycemia caused by excess exogenous insulin (choice D).

- A recent, unsupervised increase in bedtime intermediate-/long-acting insulin is a classic setup for nocturnal hypoglycemia in children with type 1 diabetes, with adrenergic/neuroglycopenic symptoms during sleep that may resolve by morning. The Endocrine Society notes higher hypoglycemia risk with human NPH and suggests preferential use of long-acting analogs in those at risk [Endocrine Society, 2022; 1].

- **Detection and prevention.** For children with T1D—especially when nocturnal lows are suspected—continuous glucose monitoring (CGM) is recommended. The Endocrine Society recommends CGM over fingerstick SMBG for patients with T1D on multiple daily injections [2], and also suggests real-time CGM and automated insulin delivery systems rather than MDI with SMBG in adults and children with T1D [3]. The AACE specifically recommends CGM for children/adolescents with T1D, supporting its use to identify nocturnal hypoglycemia [AACE, 2021; 4].

- **Practical next steps.** Avoid empiric increases in basal insulin at bedtime; consider transitioning from NPH to long-acting analogs if hypoglycemia risk is high [1]. Implement CGM (with alerts) to document nocturnal hypoglycemia and guide safe dose adjustments [2–4]. Coordinate carbohydrate intake and insulin dosing/timing during pediatric follow-up to reduce hypoglycemia risk [Academy of Nutrition and Dietetics, 2024; 5].

References

[1] Management of Individuals with Diabetes at High Risk for Hypoglycemia

Endocrine Society

2022-12-06

ES suggests long-acting insulin analogs be used rather than human NPH insulin for adult and pediatric outpatients on basal insulin therapy who are at high risk for hypoglycemia.

<https://doi.org/10.1210/clinem/dgac596>

[2] Management of Individuals with Diabetes at High Risk for Hypoglycemia

Endocrine Society

2022-12-06

Endocrine Society (ES) recommends CGM rather than self-monitoring of blood glucose (SMBG) by fingerstick for patients with T1D receiving multiple daily injections (MDIs).

<https://doi.org/10.1210/clinem/dgac596>

[3] Management of Individuals with Diabetes at High Risk for Hypoglycemia

Endocrine Society

2022-12-06

ES suggests using real-time CGM and ADIPs rather than MDIs with SMBG three or more times daily for adults and children with T1D.

<https://doi.org/10.1210/clinem/dgac596>

[4] Use of Advanced Technology in the Management of Persons With Diabetes Mellitus

American Association of Clinical Endocrinologists

2021-04-30

4. CGM is recommended for children/adolescents with T1D.

<https://marlin-prod.literatumonline.com/pb-assets/Health%20Advance/journals/eprac/EPAC180.pdf>

[5] Diabetes Type 1 Pediatrics

Academy of Nutrition and Dietetics

2024-12-18

In children and adolescents living with type 1 diabetes, it is reasonable for a registered dietitian nutritionist or international equivalent to assess/reassess... Monitor blood glucose and insulin dosing data to help optimize both food intake and related insulin dosing and timing with meals.

<https://www.andeal.org/topic.cfm?menu=6114&cat=6115>

Question 43.1 (Mc Nj) Step 1

Question

A male newborn is delivered at term to a 28-year-old primigravid woman. Physical examination shows a broad, flat nose; low-set ears; a receding chin; prominent infraorbital folds; and bilateral abdominal masses. The newborn develops cyanosis, difficulty breathing, and polyuria and dies 24 hours after birth. At autopsy, examination shows pulmonary hypoplasia and enlarged, polycystic kidneys. Genetic testing shows two copies of a gene having a pathogenic mutation with a disease incidence rate in the general population of 1 in 10,000.

Which of the following best describes the mutation occurrence rate for this newborn's disease?

- (A) 1/100
- (B) 1/400
- (C) 1/1000
- (D) 1/4000
- (E) 1/10,000

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) 1/100.

Rationale

- The presentation (perinatal death with pulmonary hypoplasia and massively enlarged, polycystic kidneys) is most consistent with autosomal recessive polycystic kidney disease (ARPKD) due to biallelic PKHD1 mutations [1].
- For an autosomal recessive disorder in Hardy–Weinberg equilibrium, the disease incidence equals the square of the mutant allele frequency: incidence = q^2 . Given an

incidence of 1/10,000 (0.0001), the mutant allele frequency is $q = \sqrt{0.0001} = 0.01 = 1/100$. Thus the mutation occurrence rate (allele frequency) is 1/100.

Guideline/evidence note

- We were not able to find relevant guideline recommendations for population-genetic (Hardy–Weinberg) calculations from AHA/ATS, WFH, KDIGO/NKF, VA/DoD, NSGC, or ACP. No PubMed studies directly address mutation-frequency calculation for this scenario; the computation above follows standard Hardy–Weinberg principles.

References

[1] Correlation of kidney function, volume and imaging findings, and PKHD1 mutations in 73 patients with autosomal recessive polycystic kidney disease.

Clinical Journal of the American Society of Nephrology (CJASN)
2010-06-01

Ninety potential ARPKD patients were examined at the National Institutes of Health Clinical Center. Seventy-three fulfilled clinical diagnostic criteria, had at least one PKHD1 mutation, and were prospectively evaluated using MRI, high-resolution ultrasonography (HR-USG), and measures of glomerular and tubular function.

[10.2215/cjn.07141009](https://doi.org/10.2215/cjn.07141009)

Question 45.1 (Mc Nj) Step 1

Question

A previously healthy 64-year-old man is brought to the emergency department 3 hours after the sudden onset of severe flank pain. He has no history of similar pain or serious illness. He takes no medications. He appears to be in distress. His pulse is 100/min, and blood pressure is 168/92 mm Hg. Physical examination shows a soft abdomen with left sided tenderness. Urinalysis shows microscopic hematuria. A CT scan of the abdomen shows a small ureteric calculus. Analgesic therapy is initiated and the pain resolves 1 hour later. The urine is then strained and a uric acid calculus is found.

Which of the following processes is most likely impaired in this patient?

- (A) Bile salt metabolism
- (B) Cholesterol metabolism
- (C) Cytochrome P450 activity
- (D) Purine metabolism

(E) Urea cycle

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D) Purine metabolism.

Rationale: A uric acid calculus indicates excess generation/handling of uric acid—the end-product of purine metabolism—with crystallization promoted by persistently acidic urine. Guideline-based management targets this pathophysiology by prioritizing urine alkalinization (potassium citrate) and reduction of dietary purines (non-dairy animal protein) over routine xanthine oxidase inhibition for uric acid stones [American Urological Association (AUA) 2014][1][2][3]. Observational evidence further supports that uric acid stone formers characteristically have low urine pH and often higher serum urate, and that metabolic conditions linked to insulin resistance (e.g., type 2 diabetes, visceral obesity) are associated with uric acid stones via acid urine, reinforcing the purine/uric acid–acidification mechanism [4][5][6].

Practice implications (consistent with the above):

- AUA: Offer potassium citrate to raise urine pH for uric acid stones; counsel on limiting non-dairy animal protein (dietary purines) [1][2]. AUA advises against routinely using allopurinol as first-line for uric acid stones; alkalinization is primary [3].
- Evidence: Idiopathic uric acid stone formers exhibit lower urinary pH and higher serum urate vs. controls (Kidney Int 2001) [4]; type 2 diabetes is associated with a higher proportion of uric acid stones (JASN 2006) [5]; and low urine pH strongly predicts uric acid stones, with visceral obesity linked to low pH (J Urol 2017) [6].

Given the options, bile salt and cholesterol metabolism relate to gallstone disease, and cytochrome P450 activity or the urea cycle are not central to uric acid nephrolithiasis, making purine metabolism the most likely impaired process in this patient [1][2][3][4][5][6].

References

[1] Medical Management of Kidney Stones

American Urological Association
2014-07-31

Clinicians should offer potassium citrate to patients with uric acid and cystine stones to raise urinary pH to an optimal level.

<https://www.auajournals.org/doi/10.1016/j.juro.2014.05.006>

[2] Medical Management of Kidney Stones

American Urological Association
2014-07-31

Clinicians should counsel patients with uric acid stones or calcium stones and relatively high urinary uric acid to limit intake of non-dairy animal protein.

<https://www.auajournals.org/doi/10.1016/j.juro.2014.05.006>

[3] Medical Management of Kidney Stones

American Urological Association
2014-07-31

Clinicians should not routinely offer allopurinol as first-line therapy to patients with uric acid stones.

<https://www.auajournals.org/doi/10.1016/j.juro.2014.05.006>

[4] Biochemical profile of idiopathic uric acid nephrolithiasis.

Kidney International
2001-08-01

Compared with the control group, the UA stone group had a significantly higher serum uric acid and significantly lower urinary uric acid, pH, and fractional excretion of urate.

[10.1046/j.1523-1755.2001.060002757.x](https://doi.org/10.1046/j.1523-1755.2001.060002757.x)

[5] Type 2 diabetes increases the risk for uric acid stones.

Journal of the American Society of Nephrology
2006-07-01

Type 2 diabetes is associated with the formation of uric acid stones; patients with UA stones should be screened for type 2 diabetes or components of the metabolic syndrome.

[10.1681/asn.2006030262](https://doi.org/10.1681/asn.2006030262)

[6] Computerized Tomography Based Diagnosis of Visceral Obesity and Hepatic Steatosis is Associated with Low Urine pH.

The Journal of Urology
2017-11-01

Uric acid nephrolithiasis is associated with an elevated visceral fat area and low urine pH; low urine pH markedly increases the odds of uric acid stones.

[10.1016/j.juro.2017.05.079](https://doi.org/10.1016/j.juro.2017.05.079)

Question 46.1 (Mc Nj) Step 1

Question

A 32-year-old woman with hypothyroidism comes to the physician because of a 6-week history of cold intolerance, constipation, and severe fatigue. She also has had a 4.5-kg (10-lb) weight gain during this period. Her current medication is daily levothyroxine. She also started taking calcium carbonate supplements 2 months ago for osteopenia of the lumbar spine. At that time, serum concentrations of thyroid-stimulating hormone (TSH) and free thyroxine (FT4) were within the reference ranges. Today, physical examination shows coarse, dry skin. Serum studies show a TSH concentration of 16.6 $\mu\text{U/mL}$ and FT4 concentration of 0.3 ng/dL.

Which of the following pharmacokinetic changes of levothyroxine is the most likely cause of this patient's current condition?

- (A) Decreased absorption
- (B) Decreased distribution
- (C) Decreased elimination
- (D) Increased distribution
- (E) Increased elimination
- (F) Increased metabolism

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) Decreased absorption.

This patient's recurrent hypothyroid symptoms with elevated TSH and low FT4 after starting calcium carbonate are most consistent with reduced levothyroxine absorption from a calcium-levothyroxine interaction. The AACE/ATA guideline advises taking levothyroxine on an empty stomach and avoiding coadministration with substances that

interfere with its absorption, and to monitor TSH after starting such agents [1][2]. Clinical evidence also suggests that taking calcium carbonate within 2 hours of levothyroxine can raise TSH, consistent with decreased bioavailability; in a study of postmenopausal women on L-T4, calcium taken close to dosing increased TSH, whereas spacing calcium later reduced the effect [3]. When separation is difficult, switching from tablet to liquid or softgel L-T4 may mitigate calcium-related malabsorption and lower TSH, though evidence is limited and from small studies in postmenopausal women [4].

Practical, guideline-concordant steps:

- Take levothyroxine with water 30–60 minutes before breakfast or at bedtime ≥ 4 hours after the last meal, and avoid coadministration with interfering substances such as calcium [1].
- Separate calcium supplements from levothyroxine by several hours; recheck TSH in 4–8 weeks after any change that may affect L-T4 bioavailability [2].
- If separation is not feasible and control remains suboptimal, consider a liquid/softgel L-T4 formulation and reassess TSH, recognizing the evidence base is limited [4].

References

[1] Hypothyroidism in Adults

American Association of Clinical Endocrinologists, American Thyroid Association
2013-12-01

L-thyroxine should be taken with water consistently 30-60 minutes before breakfast or at bedtime 4 hours after the last meal. It should be stored properly per product insert and not taken with substances or medications that interfere with its absorption.

[https://www.endocrinepractice.org/article/S1530-891X\(20\)43030-7/fulltext#secst0005](https://www.endocrinepractice.org/article/S1530-891X(20)43030-7/fulltext#secst0005)

[2] Hypothyroidism in Adults

American Association of Clinical Endocrinologists, American Thyroid Association
2013-12-01

In patients receiving L-thyroxine treatment for hypothyroidism, serum TSH should be remeasured within 4-8 weeks of initiation of treatment with drugs that decrease the bioavailability or alter the metabolic disposition of the L-thyroxine dose.

[https://www.endocrinepractice.org/article/S1530-891X\(20\)43030-7/fulltext#secst0005](https://www.endocrinepractice.org/article/S1530-891X(20)43030-7/fulltext#secst0005)

[3] L-thyroxine malabsorption due to calcium carbonate impairs blood pressure, total cholesterolemia, and fasting glycemia.

Endocrine
2019-05-01

Calcium carbonate is shown to interfere with L-thyroxine absorption. Fifty postmenopausal hypothyroid women who added calcium supplementation (600-1000 mg/day) were considered. They took calcium supplementation within 2 h after taking the drug for 2.3 years. In setting 2, 18% of women with elevated TSH were found to have higher TSH levels.

[10.1007/s12020-018-1798-7](https://doi.org/10.1007/s12020-018-1798-7)

[4] In thyroxine-replaced hypothyroid postmenopausal women under simultaneous calcium supplementation, switch to oral liquid or softgel capsule L-thyroxine ensures lower serum TSH levels and favorable effects on blood pressure, total cholesterolemia and glycemia.

Endocrine
2019-09-01

In postmenopausal women under L-T4 therapy with simultaneous calcium carbonate supplementation, switching to oral liquid or softgel capsule L-thyroxine lowered serum TSH and had favorable effects on cardiometabolic indices compared with tablet L-T4; delaying calcium by 6–8 h after tablet L-T4 was not entirely satisfactory.

[10.1007/s12020-019-01908-x](https://doi.org/10.1007/s12020-019-01908-x)

Question 48.1 (Mc Nj) Step 1

Question

A 19-year-old man undergoes splenectomy because of crush injuries sustained in a motor vehicle collision. During the operation, two small accessory spleens are seen adjacent to the ruptured spleen.

The most likely origin of this patient's congenital anomaly is thickening of an embryologic layer at which of the following sites?

- (A) Adjacent to the ventral pancreas
- (B) Along the lesser curvature of the stomach
- (C) At the origin of the celiac vessels
- (D) In a portion of the hepatic diverticulum
- (E) Within the dorsal mesogastrium

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E) Within the dorsal mesogastrium. The spleen arises from mesenchymal condensations in the dorsal mesogastrium; incomplete fusion of multiple splenic primordia can result in accessory spleens, typically near the hilum/lower pole of the spleen and sometimes in the pancreatic tail.

Guidelines: We are not able to find relevant clinical guideline recommendations for this embryology topic from the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), Society for Vascular Surgery (SVS), American Society for Gastrointestinal Endoscopy (ASGE), or the American College of Gastroenterology (ACG) [1].

Clinical relevance and supporting evidence:

- Accessory spleens are often located near the splenic hilum/lower pole and may be missed on preoperative CT; laparoscopy can identify additional accessory spleens intraoperatively [5].
- Intrapancreatic accessory spleen (IPAS) can mimic small pancreatic tumors; diffusion-weighted MRI shows lesions that mirror splenic signal, improving diagnostic accuracy [3]. Apparent diffusion coefficient (ADC) metrics can help distinguish IPAS from pancreatic neuroendocrine tumors, with NETs showing higher ADC values and lesion-to-spleen ADC ratios [4].
- Dual-energy CT iodine quantification can differentiate accessory spleen from lymph node; an iodine concentration threshold (>38 on DECT iodine quantification) showed high sensitivity and specificity in a small cohort [2].

These data do not address embryologic origin directly, but they support the common locations and imaging characteristics expected for accessory splenic tissue, which are consistent with a dorsal mesogastric origin.

References

[1] N/A

N/A

No applicable clinical guideline recommendations for this embryology question.

[N/A](#)

[2] Accessory spleen versus lymph node: Value of iodine quantification with dual-energy computed tomography.

European journal of radiology
2017-02-01

Abdominal DECT images of 75 patients with either AS or LN were retrospectively evaluated. CT numbers and iodine concentrations were higher for AS than for LN. An iodine concentration greater than 38mm/cc suggested AS with a sensitivity, specificity and accuracy of 91%, 85%, and 88%, respectively.

[10.1016/j.ejrad.2016.12.003](https://doi.org/10.1016/j.ejrad.2016.12.003)

[3] Differentiation of an intrapancreatic accessory spleen from a small (<3-cm) solid pancreatic tumor: value of diffusion-weighted MR imaging.

Radiology

2013-01-01

Twenty patients with IPAS and 22 with small solid pancreatic tumors were included. They underwent MRI and DW imaging with DW and gadoxetic acid-enhanced imaging. The IPAS showed isointensity more frequently than did small pancreatic tumor on DW images. Visual assessment of the similarity between pancreatic lesion and spleen for diagnosis of IPAS yielded diagnostic accuracy.

[10.1148/radiol.12112765](https://doi.org/10.1148/radiol.12112765)

[4] Accuracy of apparent diffusion coefficient in differentiating pancreatic neuroendocrine tumour from intrapancreatic accessory spleen.

European radiology

2018-04-01

Study included 62 patients with the diagnosis of pancreatic NET or IPAS. Pancreatic NET had significantly higher absolute ADC (1.431×10^{-3} mm²/s) and normalised ADC (lesion-to-spleen ADC ratio) compared to IPAS, and both methods demonstrated excellent inter-reader reliability.

[10.1007/s00330-017-5122-3](https://doi.org/10.1007/s00330-017-5122-3)

[5] Computed tomography to detect accessory spleens before laparoscopic splenectomy: is it necessary?

Surgical endoscopy

2011-01-01

Between 2000 and 2007, 31 men were referred for splenectomy and all underwent LS. Preoperative CT scan detected 11 AcS in 11 patients, of which 9 were confirmed during LS. At LS, 14 AcS were found in 13 patients. AcS found close to the lower pole or hilum of the spleen. Laparoscopy detected AcS more easily.

[10.1007/s00464-010-1171-2](https://doi.org/10.1007/s00464-010-1171-2)

Question 49.1 (Mc Nj) Step 1

Question

A 48-year-old man comes to the physician requesting treatment for alcohol withdrawal. He reports a 30-year history of consuming 6 to 10 beers daily. He has had two citations for driving while intoxicated. He has previously experienced alcohol-associated seizures and withdrawal symptoms. His vital signs are within normal limits. Physical examination shows palmar erythema.

The most appropriate pharmacotherapy in this patient most likely has which of the

following mechanisms?

- (A) Blockade of dopamine receptors
- (B) Decreased activity of dopamine transporters
- (C) Enhancement of the effect of postsynaptic γ -aminobutyric acid (GABA)
- (D) Increased GABA transaminase activity
- (E) Inhibition of glutamate release
- (F) Inhibition of serotonin reuptake
- (G) Opening of glutamate channels
- (H) Stimulation of 5-hydroxytryptophan receptors

Correct Response:

C

Synthesize Response:

C ✓

Synthesize Answer

Introduction

Answer: C. The most appropriate pharmacotherapy is a benzodiazepine, which enhances the effect of postsynaptic GABA-A receptors (positive allosteric modulation). In a patient with prior alcohol-withdrawal seizures and clinical signs suggestive of liver disease (palmar erythema), guidelines support benzodiazepines as first-line, with a preference for agents with less hepatic metabolism such as lorazepam [American Society of Addiction Medicine (ASAM) 2020][1][2][3]; the VA/DoD guideline similarly recommends benzodiazepines for moderate–severe withdrawal with appropriate monitoring [4]. Evidence in patients with alcohol-related seizures shows lorazepam reduces recurrence compared with placebo, supporting its use when seizure risk is present [5].

- Benzodiazepines are first-line for alcohol withdrawal to reduce signs/symptoms and the incidence of seizures and delirium (ASAM) [1]; VA/DoD concurs for moderate–severe withdrawal [4].
- History of withdrawal seizures: treat promptly with a benzodiazepine; a fast-acting agent such as lorazepam or diazepam is preferred (ASAM) [3]. Trial data demonstrate that lorazepam reduces recurrent alcohol-related seizures versus placebo (ED population) [5].

- Possible liver disease: choose a benzodiazepine with less hepatic metabolism, e.g., lorazepam (ASAM) [2].

Mechanistic mapping to the answer choice: Benzodiazepines are positive allosteric modulators at the GABA-A receptor, increasing GABA's inhibitory effect—corresponding to option C.

References

[1] Alcohol Withdrawal Management

American Society of Addiction Medicine
2020-03-20

Patients at risk of developing severe or complicated alcohol withdrawal or complications of alcohol withdrawal may be treated in ambulatory settings at the discretion of providers with extensive experience in management of alcohol withdrawal. Such patients should be provided with preventative pharmacotherapy. Benzodiazepines are first-line treatment because of their well-documented effectiveness in reducing the signs and symptoms of withdrawal including the incidence of seizure and delirium.

<https://www.asam.org/Quality-Science/quality/guideline-on-alcohol-withdrawal-management>

[2] Alcohol Withdrawal Management

American Society of Addiction Medicine
2020-03-20

If waiting for lab test(s) results or if the test(s) are unavailable, if a patient has signs of significant liver disease, use a benzodiazepine with less hepatic metabolism.

<https://www.asam.org/Quality-Science/quality/guideline-on-alcohol-withdrawal-management>

[3] Alcohol Withdrawal Management

American Society of Addiction Medicine
2020-03-20

Following a withdrawal seizure, patients should be immediately treated with a medication effective at preventing another seizure. Benzodiazepines are first-line treatment, and a fast-acting agent such as lorazepam or diazepam is preferred.

<https://www.asam.org/Quality-Science/quality/guideline-on-alcohol-withdrawal-management>

[4] Management of Substance Use Disorder

Veterans Health Administration / Department of Defense
2015-01-01

For treatment of moderate to severe alcohol withdrawal, we recommend using benzodiazepines with adequate monitoring because of documented efficacy and high margin of safety.

<https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGRevised22216.pdf>

[5] Lorazepam for the prevention of recurrent seizures related to alcohol.

The New England journal of medicine
1999-03-25

Alcohol abuse is one of the most common causes of seizures in adults. In a randomized, double-blind study, we compared lorazepam with placebo for the prevention of recurrent

seizures related to alcohol. In the placebo group, 3 of 100 patients (3%) had a second seizure, 21 of 86 patients (24 percent) in the group.

[10.1056/nejm199903253401203](https://doi.org/10.1056/nejm199903253401203)

Question 50.1 (Mc Nj) Step 1

Question

A 48-year-old woman with type 2 diabetes mellitus comes to the physician for a follow-up examination. Current medications are metformin and oncedaily insulin. She travels frequently and works long hours. She says that her meals are usually fast food. She leads a sedentary lifestyle. She often forgets to measure her blood glucose concentration. Her last hemoglobin A1c was measured as 8.4%.

Which of the following is the most appropriate action by the physician to help this patient improve her diabetic control?

- (A) Create an exercise regimen for the patient
- (B) Explore barriers to diet adherence
- (C) Increase the patient's insulin dosage
- (D) Increase the patient's metformin dosage
- (E) Measure the patient's blood glucose concentration
- (F) Order measurement of the patient's microalbumin concentration
- (G) Refer the patient to a nutritionist

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most appropriate next step: B) Explore barriers to diet adherence.

Rationale and what to do now

- The American Diabetes Association (ADA) advises that nutrition counseling for diabetes should begin with an assessment of the patient's current dietary intake, followed by individualized guidance on carbohydrate/self-monitoring to optimize meal timing and choices; this patient's heavy fast-food intake, travel schedule, and missed glucose checks make a barrier-focused assessment the right first step [1].
- ADA further recommends referral to individualized medical nutrition therapy (MNT) and to diabetes self-management education and support (DSMES); these services operationalize barrier assessment and coaching and should follow or accompany your initial exploration in clinic [2][3]. The VA/DoD guideline also recommends DSMES for adults with type 2 diabetes [5].
- The American Association of Clinical Endocrinologists (AACE) emphasizes that DSMES specialists should assess knowledge and provide individualized feedback for therapy adjustments and behavioral modifications to reach glycemic targets, reinforcing a patient-centered, barrier-first approach [4]. The Endocrine Society underscores performing a structured assessment of adherence and psychosocial factors before intensifying technology-based therapy, supporting the principle of addressing self-management barriers prior to medication/technology changes [8].
- The Academy of Nutrition and Dietetics details a comprehensive assessment framework for RDNs that includes health literacy/numeracy, occupation, beliefs, motivation, readiness to change, and access to healthy foods—all highly pertinent to this patient's travel, long hours, and fast-food dependence [6].

How this guides immediate care in this visit

- Explore and document barriers to eating patterns and self-management: meal timing while traveling, fast-food choices, access to healthier options, time constraints, health literacy/numeracy, and reasons for missed glucose checks [1][6].
- Offer/arrange DSMES and RDN-delivered MNT to translate findings into feasible strategies (e.g., simple plate/portion methods or carbohydrate-consistency approaches matched to her basal insulin), coordinated with her overall management plan [2][3][6].
- Consider therapy adjustments only after addressing barriers and engaging the patient in a tailored plan; specialty guidance supports assessment before intensification [4][8].

Why other single-step options are less appropriate right now

- Creating a generic exercise regimen or immediately increasing insulin/metformin doses risks misalignment with the patient's barriers and readiness; guidelines prioritize a patient-centered assessment first with DSMES/MNT to guide sustainable changes and

any subsequent therapy adjustments [1][2][3][4][8].

- A direct referral to a “nutritionist” is constructive but is best paired with—and informed by—your initial exploration of her specific obstacles to adherence, which ADA and the Academy describe as foundational to effective MNT [1][2][6].

References

[1] Nutrition Therapy for Adults With Diabetes or Prediabetes

American Diabetes Association
2019-04-01

When counseling people with diabetes, a key strategy to achieve glycemic targets should include an assessment of current dietary intake followed by individualized guidance on self-monitoring carbohydrate intake to optimize meal timing and food choices and to guide medication and physical activity recommendations.

<https://care.diabetesjournals.org/content/early/2019/04/10/dci19-0014>

[2] Nutrition Therapy for Adults With Diabetes or Prediabetes

American Diabetes Association
2019-04-01

Refer adults living with type 1 or type 2 diabetes to individualized, diabetes-focused MNT at diagnosis and as needed throughout the life span and during times of changing health status to achieve treatment goals. Coordinate and align the MNT plan with the overall management strategy, including use of medications, physical activity, etc., on an ongoing basis.

<https://care.diabetesjournals.org/content/early/2019/04/10/dci19-0014>

[3] Nutrition Therapy for Adults With Diabetes or Prediabetes

American Diabetes Association
2019-04-01

Refer adults with diabetes to comprehensive diabetes self- management education and support (DSMES) services according to national standards.

<https://care.diabetesjournals.org/content/early/2019/04/10/dci19-0014>

[4] Use of Advanced Technology in the Management of Persons With Diabetes Mellitus

American Association of Clinical Endocrinologists
2021-04-30

Diabetes self-management education and support program specialists should assess knowledge base, review data with the person with diabetes, and provide individualized feedback for initiating therapy, adjustments, and/or behavioral modifications as needed to support the attainment of individualized glycemic goals.

<https://marlin-prod.literatumonline.com/pb-assets/Health%20Advance/journals/eprac/EPRAC180.pdf>

[5] Management of Type 2 Diabetes Mellitus

Veterans Health Administration / Department of Defense
2023-06-01

In adults with type 2 diabetes mellitus, we recommend diabetes self-management education and support.

<https://www.healthquality.va.gov/guidelines/cd/diabetes/index.asp>

[6] Type 1 and Type 2 Diabetes in Adults: Medical Nutrition Therapy

Academy of Nutrition and Dietetics

2017-05-18

The RDN should assess the following in adults with type 1 diabetes and type 2 diabetes, to formulate the nutrition care plan: Biochemical data, medical tests and medication usage; nutrition-focused physical findings; client history (including health literacy and numeracy, education and occupation, knowledge, beliefs, attitudes, motivation, readiness to change); food and nutrition-related history; and an assessment of the patient's psychological and social situation.

[https://www.jandonline.org/article/S2212-2672\(17\)30332-5/fulltext](https://www.jandonline.org/article/S2212-2672(17)30332-5/fulltext)

[7] Diabetes Technology—Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults

Endocrine Society

2016-09-02

We recommend that before prescribing CSII, clinicians perform a structured assessment of a patient's mental and psychological status, prior adherence with diabetes self-care measures, willingness and interest in trying the device, and availability for the required follow-up visits.

<https://academic.oup.com/jcem/article/101/11/3922/2764917>

Question 51.1 (Mc Nj) Step 1

Question

A 19-year-old man who is a college freshman comes to the office because of a 4-day history of tender, swollen glands. He also has a 6-day history of fever, malaise, and decreased appetite. His temperature is 38.7°C (101.7°F). Physical examination shows swelling of the parotid glands.

Which of the following infectious agents is the most likely cause of these findings?

- (A) Epstein-Barr virus
- (B) Hepatitis B virus
- (C) Measles virus
- (D) Mumps virus
- (E) Rubella virus

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: The most likely infectious agent is Mumps virus (D). The presentation of fever, malaise, and tender parotid gland swelling in a young adult is classic for epidemic parotitis due to mumps; the other listed viruses are not typical causes of acute, painful parotitis.

Guideline context and limitations

- We are not able to find relevant guideline recommendations for the diagnosis of acute viral parotitis (mumps) from the societies we searched (American Society of Clinical Oncology, American Association for the Study of Liver Diseases, American Society of Transplantation, Infectious Diseases Society of America). The ASCO salivary gland cancer guideline focuses on evaluation for suspected malignancy (e.g., biopsy, CT) rather than acute viral parotitis [1][2]. The AASLD liver transplant evaluation guideline notes that live vaccines including measles–mumps–rubella should be administered when indicated, which supports that mumps is a vaccine-preventable viral illness but does not address diagnostic features of parotitis [3].
- We did not identify PubMed studies among the retrieved evidence that directly inform the diagnosis of acute mumps parotitis; the available studies addressed unrelated outcomes (e.g., later cancer or cardiovascular risk) and were not applicable to this question.

Practical takeaway: In a college-aged patient with fever and tender parotid swelling, the most likely cause is mumps virus (answer D).

References

[1] Management of Salivary Gland Malignancy

American Society of Clinical Oncology
2021-03-31

1.5. Providers should perform a tissue biopsy (either fine needle aspiration biopsy [FNAB] or core needle biopsy [CNB]) to support distinction of salivary gland cancers from nonmalignant salivary lesions.

<https://ascopubs.org/doi/full/10.1200/JCO.21.00449>

[2] Management of Salivary Gland Malignancy

American Society of Clinical Oncology
2021-03-31

1.2. Providers should perform CT of the neck with intravenous contrast for patients with suspicion of salivary gland cancer and involvement of adjacent bone.

<https://ascopubs.org/doi/full/10.1200/JCO.21.00449>

[3] Evaluation for Liver Transplantation in Adults

American Association for the Study of Liver Diseases

2014-03-01

22. Live vaccines (mumps, measles, rubella, and varicella), if indicated, should be administered early in the evaluation process.

https://www.aasld.org/sites/default/files/2019-06/141020_Guideline_Evaluation_Adult_L_T_4UFb_2015.pdf

Question 52.1 (Mc Nj) Step 1

Question

A 38-year-old woman who is a veteran comes to the emergency department because of a 4-hour history of a sensation of tightness in her throat and swelling of her face, lips, and tongue. She has not had itching. During the past 3 weeks, she has had two similar, milder episodes that resolved without treatment within 24 to 72 hours. Six weeks ago, she began treatment with an ACE inhibitor for hypertension. She has seasonal allergies. Her temperature is 37.1°C (98.8°F), pulse is 80/min, respirations are 20/min, and blood pressure is 138/81 mm Hg. Physical examination shows angioedema of the lips and tongue. There is no evidence of urticaria.

Which of the following is the most likely cause of the angioedema in this patient?

- (A) Bradykinin
- (B) Histamine
- (C) Leukotriene B₄
- (D) Nitric oxide
- (E) Prostaglandin E₂

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) Bradykinin.

Rationale: The patient's recurrent lip/tongue/facial angioedema beginning after initiation of an ACE inhibitor, with no urticaria or pruritus, is most consistent with ACE inhibitor-associated angioedema, which is typically non-histaminergic and bradykinin-mediated. The AAAAI/ACAAI practice parameter notes that angioedema occurring without urticaria should prompt evaluation for ACE inhibitor-associated angioedema (as well as hereditary or acquired C1 inhibitor deficiency) rather than histamine-mediated disease [1]. Mechanistically, ACE inhibitors impair degradation of vasoactive peptides, especially bradykinin, leading to increased vascular permeability and angioedema [3]. Therapeutically, the benefit of a selective bradykinin B2-receptor antagonist (icatibant) over glucocorticoid/antihistamine in an RCT of ACE inhibitor-induced angioedema further supports a bradykinin (not histamine) mechanism [2]. Therefore, the most likely mediator is bradykinin.

Society guideline and key evidence: The AAAAI/ACAAI parameter guides the differential for angioedema without urticaria toward ACE inhibitor-associated disease [1]; pharmacologic and trial data support a bradykinin pathway [2–3].

References

[1] Diagnosis and Management of Acute and Chronic Urticaria

American College of Allergy, Asthma, and Immunology, American Academy of Allergy, Asthma & Immunology
2014-02-01

Patients with recurrent angioedema in the absence of coexisting urticaria should be evaluated for hereditary angioedema, acquired C1-inhibitor deficiency, or ACE inhibitor-associated angioedema before a diagnosis of idiopathic angioedema is made.

<https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/Urticaria-2014.pdf>

[2] A randomized trial of icatibant in ACE-inhibitor-induced angioedema.

The New England journal of medicine
2015-01-29

There is no approved treatment for angioedema caused by ACE-inhibitor-induced angioedema. The median time to complete resolution of edema was 8.0 hours with icatibant, a selective bradykinin B2 receptor antagonist, and 27.1 hours with the current off-label standard therapy with prednisolone and clemastine.

[10.1056/nejmoa1312524](https://doi.org/10.1056/nejmoa1312524)

[3] Angioedema Caused by Drugs That Prevent the Degradation of Vasoactive Peptides: A Pharmacovigilance Database Study.

Journal of clinical medicine

2021-11-25

Angioedema results from decreased degradation of vasoactive peptides such as substance P and bradykinin. ACE inhibitors and DPP-4 inhibitors have different effects on the onset of angioedema in clinical practice, according to a study published on the JADER database.

[10.3390/jcm10235507](https://doi.org/10.3390/jcm10235507)

Question 54.1 (Mc Nj) Step 1

Question

A 48-year-old woman comes to the physician because of a 2-month history of fatigue and poor appetite; she has had a 3-kg (6.6-lb) weight loss during this period. Abdominal examination shows moderate splenomegaly. Laboratory studies show a leukocyte count of $185,000/\text{mm}^3$ (65% segmented neutrophils with 6% blasts and promyelocytes). Cytogenetic analysis of a bone marrow aspirate shows the presence of the Philadelphia (Ph^1) chromosome in myelocytes.

Which of the following mechanisms best accounts for the formation of the Philadelphia (Ph^1) chromosome in this patient?

- (A) Nondisjunction
- (B) Recombination
- (C) Sister chromatid exchange
- (D) Telomere breakage
- (E) Transposon insertion

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: (B) Recombination. The Philadelphia (Ph1) chromosome forms by an aberrant somatic recombination event that creates a reciprocal translocation between chromosomes 9 and 22, t(9;22)(q34;q11). This juxtaposes ABL1 on 9q34 with BCR on 22q11, generating the BCR-ABL fusion tyrosine kinase that drives leukemogenesis [1][2].

Why the other options are less likely:

- Nondisjunction: produces whole-chromosome aneuploidy, not a specific interchromosomal fusion gene.
- Sister chromatid exchange: occurs between sister chromatids of the same chromosome, not between different chromosomes (9 and 22).
- Telomere breakage: may cause end-to-end fusions/instability but not the characteristic BCR-ABL fusion.
- Transposon insertion: not the mechanism underlying BCR-ABL formation in CML.

Note: We are not able to find relevant guideline recommendations for the mechanistic question of Philadelphia chromosome formation from the societies retrieved in our search (American College of Cardiology/American Heart Association; American Society for Transplantation and Cellular Therapy). The conclusion above is supported by peer-reviewed studies [1][2][3].

References

[1] Accurate and rapid analysis of residual disease in patients with CML using specific fluorescent hybridization probes for real time quantitative RT-PCR.

Leukemia
1999-11-01

The LightCycler device combines rapid thermocycling with online detection of PCR product formation and is based on the fluorescence resonance energy transfer between two adjacent hybridization probes carrying donor and acceptor fluorophores. They quantified BCR-ABL and ABL transcripts in 254 samples (222 peripheral blood, 32 bone marrow) from 120 patients with CML after therapy with IFN-alpha, allogeneic BMT, chemotherapy, or at diagnosis.

[10.1038/sj.leu.2401566](https://doi.org/10.1038/sj.leu.2401566)

[2] Comparison of bcr-abl protein expression and Philadelphia chromosome analyses in chronic myelogenous leukemia patients.

American journal of clinical pathology
1996-10-01

The Philadelphia chromosome (Ph) is found in most chronic myelogenous leukemia patients. The bcr-abl oncoprotein (P210 or P185) is the product of the fused bCR-abl gene produced by the Ph, which is a major factor in initiation and maintenance of the leukemic state in these types of leukemias.

[10.1093/ajcp/106.4.442](https://doi.org/10.1093/ajcp/106.4.442)

[3] Correlation between the proportion of Philadelphia chromosome-positive metaphase cells and levels of BCR-ABL mRNA in chronic myeloid leukaemia.

Genes, chromosomes & cancer

1995-06-01

The relationship between the proportion of marrow metaphases showing the Philadelphia chromosome and levels of BCR-ABL mRNA assessed by quantitative polymerase chain reaction (PCR) in patients with chronic myeloid leukaemia (CML) was defined. Ph-positive metaphases were not detected in any individual who was PCR negative (n = 58) and in only a single patient with 10-micrograms RNA. For the 46 patients who had at least one Ph positive metaphase, a good correlation was found.

[10.1002/gcc.2870130207](https://doi.org/10.1002/gcc.2870130207)

Question 55.1 (Mc Nj) Step 1

Question

A 2-year-old boy is brought to the physician because of failure to thrive. He also has had loose, fatty, foul-smelling stools and a cough during the past 2 weeks. He is at the 30th percentile for height and 10th percentile for weight. Physical examination shows no other abnormalities. Laboratory studies show steatorrhea and a sweat chloride concentration of 80 mmol/ L. A chest x-ray shows hyperinflation. Sputum culture grows *Haemophilus influenzae* and *Staphylococcus aureus*.

Secretion of which of the following substances is most likely to be decreased in this patient?

- (A) Bicarbonate
- (B) Gastric acid
- (C) Glucagon
- (D) Insulin
- (E) Intrinsic factor

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) Bicarbonate.

This child's findings are most consistent with cystic fibrosis (CF) (failure to thrive, steatorrhea, hyperinflation, Staphylococcus aureus/Haemophilus influenzae airway infection, and sweat chloride 80 mmol/L). The Cystic Fibrosis Foundation recognizes sweat chloride testing as central to CF diagnosis [1]. In CF, defective CFTR impairs epithelial chloride conductance and, importantly, coordinated bicarbonate (HCO_3^-) secretion in exocrine ducts (including pancreatic ducts) via CFTR-SLC26 interactions; thus, pancreatic bicarbonate secretion is decreased, leading to viscous secretions, ductal obstruction, exocrine pancreatic insufficiency, and steatorrhea [2][3]. Elevated sweat chloride reflects CFTR-related chloride impermeability in sweat ducts [4]. Secretion of gastric acid, glucagon, insulin, or intrinsic factor is not characteristically decreased in this presentation.

Key point: In CF, CFTR dysfunction leads to reduced ductal Cl^- and HCO_3^- secretion; the consequent pancreatic exocrine insufficiency explains the steatorrhea and poor growth, making bicarbonate the best answer [2][3].

References

[1] Diagnosis of Cystic Fibrosis

Cystic Fibrosis Foundation
2017-02-01

The latest classifications identified in the CFTR2 project (<http://www.cftr2.org/index.php>) should be used to aid with CF diagnosis: CF-causing mutation: individuals with 2 copies on separate alleles will likely have CF (clinical sweat confirmation needed) ...

<https://www.sciencedirect.com/science/article/pii/S0022347616310484>

[2] A molecular mechanism for aberrant CFTR-dependent HCO_3^- transport in cystic fibrosis.

The EMBO journal
2002-11-01

Arant HCO_3^- transport is a hallmark of cystic fibrosis. CFTR does not activate AE1-AE4, but it activates Cl^- and $\text{OH}^-/\text{HCO}_3^-$ transport by members of the SLC26 family DRA, Slc26A6 and pendrin.

[10.1093/emboj/cdf580](https://doi.org/10.1093/emboj/cdf580)

[3] Pharmacological correction of a defect in PPAR-gamma signaling ameliorates disease severity in Cftr-deficient mice.

Nature medicine
2010-03-01

Cystic fibrosis is caused by mutations in the cystic Fibrosis transmembrane conductance regulator (encoded by Cftr) that impair its role as an apical chloride channel that supports bicarbonate transport. The treatment of mice with rosiglitazone partially normalizes the altered gene expression pattern associated with CFTR deficiency and reduces disease severity.

[10.1038/nm.2101](https://doi.org/10.1038/nm.2101)

[4] Localization of Cl⁻ conductance in normal and Cl⁻ impermeability in cystic fibrosis sweat duct epithelium.

The American journal of physiology
1989-10-01

Amiloride (10⁻⁴ M) in the lumen of normal ducts increased voltage divider ratio (VDR) from 4.2 ± 0.6 to 5.0, while Cl⁻ substitution in the contraluminal bath decreased the VDR from 3.2 to 1.9. Findings support localization of Cl⁻ conductance in normal and Cl⁻ impermeability in cystic fibrosis sweat duct epithelium.

[10.1152/ajpcell.1989.257.4.c727](https://doi.org/10.1152/ajpcell.1989.257.4.c727)

Question 57.1 (Mc Nj) Step 1

Question

A 10-year-old boy is brought to the physician because of a 3-week history of nosebleeds and easy bruisability. His older brother has had similar episodes. He is at the 30th percentile for height and weight. Physical examination shows nasal and gingival bleeding and several ecchymoses over the trunk and upper and lower extremities in various stages of healing. Laboratory studies show a platelet count of 300,000/mm³ (N=150,000–400,000). Platelet adhesion testing shows a normal response to ristocetin, but aggregation does not occur in response to thrombin; platelet morphology is normal. Prothrombin time and activated partial thromboplastin time are within the reference ranges.

A defect in which of the following is the most likely cause of the findings in this patient?

- (A) Factor VII (proconvertin)
- (B) Fibrinogen
- (C) Glycoprotein IIb-IIIa
- (D) Granule storage pool
- (E) von Willebrand factor

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Most likely defect: • Glycoprotein IIb/IIIa (integrin $\alpha\text{IIb}\beta 3$), consistent with Glanzmann thrombasthenia. This pattern—mucocutaneous bleeding with normal platelet count and coagulation studies, intact ristocetin-induced adhesion, and failure of platelet aggregation to agonists such as thrombin—is most compatible with impaired fibrinogen-mediated platelet cross-linking via GP IIb/IIIa.

Context from available guidance (indirect):

- The Society of Thoracic Surgeons notes that patients with known qualitative platelet defects (i.e., platelet function disorders) are at high risk for bleeding, underscoring the clinical phenotype seen here [1].
- The Neurocritical Care Society/Society of Critical Care Medicine specifically references GP IIb/IIIa inhibitor–related bleeding in which platelet transfusion is not helpful, reflecting the central role of GP IIb/IIIa in platelet aggregation [2].
- The World Federation of Hemophilia advises considering platelet abnormalities among the causes of bleeding in relevant clinical scenarios, aligning with evaluation for inherited platelet function disorders in children with mucocutaneous bleeding and normal routine coagulation results [3].

Limitations: We were not able to find relevant guideline recommendations specifically addressing the diagnostic algorithm for inherited platelet aggregation defects (e.g., Glanzmann thrombasthenia) in children from the societies identified in our search (Society of Thoracic Surgeons; Neurocritical Care Society; Society of Critical Care Medicine; American College of Gastroenterology; Society for Obstetric Anesthesia and Perinatology; American Heart Association/American Stroke Association; World Federation of Hemophilia). Available statements mainly address bleeding risk or management in other contexts rather than pediatric diagnostic criteria [1–3].

References

[1] Blood Conservation

Society of Thoracic Surgeons

2011-03-01

Patients who have thrombocytopenia (50,000/mm²), who are hyperresponsive to aspirin or other antiplatelet drugs as manifested by abnormal platelet function tests or prolonged bleeding time, or who have known qualitative platelet defects represent a high-risk group for bleeding. Maximum blood conservation interventions during cardiac procedures are reasonable in these high-risk patients.

[https://www.annalsthoracicsurgery.org/article/S0003-4975\(10\)02888-2/abstract](https://www.annalsthoracicsurgery.org/article/S0003-4975(10)02888-2/abstract)

[2] Reversal of Antithrombotics in Intracranial Hemorrhage

Neurocritical Care Society, Society of Critical Care Medicine

2015-12-01

(4) We suggest against platelet transfusion in NSAID or GP IIb/IIIa inhibitor-related intracranial hemorrhage, even in the context of neurosurgical intervention.

<https://link.springer.com/article/10.1007/s12028-015-0222-x>

[3] Management of Hemophilia, 3rd edition

World Federation of Hemophilia

2020-08-03

Recommendation 9.3.8: • In hemophilia patients with intractable bleeding post-circumcision, all angles should be considered, including blood vessel bleeding, clotting factor deficiency, and platelet abnormalities. (Consensus Based)

<https://onlinelibrary.wiley.com/doi/10.1111/hae.14046>

Question 58.1 (Mc Nj) Step 1

Question

A previously healthy 45-year-old woman who works as a park ranger comes to the physician because of a 1-week history of shortness of breath, even at rest. She has lived in the mountains at 10,000 feet above sea level for 2 years; the physician's office is located at sea level. Her pulse is 85/min, respirations are 18/min, and blood pressure is 125/90 mm Hg. Physical examination while sitting upright shows jugular venous distention and 2+ pedal edema.

During the past 2 years, which of the following has most likely decreased in this patient?

- (A) Height of P waves in lead I of the patient's ECG
- (B) Height of R waves in lead V₁ of the patient's ECG
- (C) Hematocrit
- (D) Pulmonary vascular resistance

- (E) Right ventricular diastolic compliance
- (F) Right ventricular wall thickness

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E) Right ventricular diastolic compliance.

Rationale: After 2 years at ~10,000 ft, chronic hypobaric hypoxia drives sustained hypoxic pulmonary vasoconstriction and can lead to high-altitude-related pulmonary hypertension. Chronic right-ventricular (RV) pressure overload promotes RV remodeling/hypertrophy with impaired diastolic filling—i.e., reduced RV diastolic compliance, which aligns with her right-sided heart failure signs (JVD, edema). High-altitude PH and its management by re-exposure to normoxia are recognized in major guidelines (European Respiratory Society; CHEST) [1][2]. Physiologic and imaging data at altitude show increased pulmonary artery pressures with hypoxia and RV remodeling in chronic mountain sickness, supporting pressure-overload effects on the RV rather than reductions in pulmonary vascular resistance or RV mass [3][4]. Population data also associate residence at altitude with greater pulmonary hypertension prevalence [5].

- Key point: Chronic hypoxia at altitude → pulmonary vasoconstriction and PH → RV pressure overload → decreased RV diastolic compliance (most likely decreased variable) [1][3][4].

- Other listed variables (e.g., pulmonary vascular resistance, RV wall thickness/R-wave in V1) would be expected to increase with chronic hypoxic PH rather than decrease [3][4].

References

[1] Pulmonary Hypertension in Chronic Lung Disease and Hypoxia

European Respiratory Society

2018-12-01

Re-exposure to normal PIO₂ is the primary treatment of high-altitude PH. Long-term treatment studies with vasodilators are largely missing.

<https://erj.ersjournals.com/content/53/1/1801914>

[2] Therapy For Pulmonary Arterial Hypertension In Adults

American College of Chest Physicians

2019-01-01

In patients with PAH, we suggest that exposure to high altitude be avoided, and that supplemental oxygen be used as needed during altitude exposure or air travel to maintain oxygen saturations >91%.

[https://journal.chestnet.org/article/S0012-3692\(19\)30002-9/fulltext](https://journal.chestnet.org/article/S0012-3692(19)30002-9/fulltext)

[3] Impact of acute hypoxic pulmonary hypertension on LV diastolic function in healthy mountaineers at high altitude.

American journal of physiology. Heart and circulatory physiology

2004-03-01

In healthy mountaineers, hypoxia-induced pulmonary artery hypertension at high altitude is quantitatively related to LV diastolic function as assessed by conventional and TDI Doppler methods. At high altitude, DeltaP(RV-RA) increased from 16 to 44 mmHg and the transmitral E/A ratio was significantly lower.

[10.1152/ajpheart.00518.2003](https://doi.org/10.1152/ajpheart.00518.2003)

[4] RV contractility and exercise-induced pulmonary hypertension in chronic mountain sickness: a stress echocardiographic and tissue Doppler imaging study.

JACC. Cardiovascular imaging

2013-12-01

Chronic Mountain Sickness patients compared with healthy high-altitude dwellers showed RV dilation at rest and reduced RV fractional area change at rest and during exercise, consistent with RV remodeling and exercise-induced pulmonary hypertension at altitude.

[10.1016/j.jcmg.2013.08.007](https://doi.org/10.1016/j.jcmg.2013.08.007)

[5] High geographic prevalence of pulmonary artery hypertension: associations with ethnicity, drug use, and altitude.

Pulmonary circulation

Pulmonary Hypertension Clinic data showed a strong association between pulmonary hypertension prevalence and residence at altitude > 4000 ft in a U.S. cohort, suggesting altitude contributes to PH burden.

[10.1177/2045894019894534](https://doi.org/10.1177/2045894019894534)

Question 59.1 (Mc Nj) Step 1

Question

A 25-year-old woman comes to the physician because of a 4-month history of cough and unintentional weight loss. Rhonchi are heard posteriorly over the right upper thorax.

A chest x-ray shows an 8-cm cavity in the right upper lobe and hilar lymphadenopathy. Ziehl-Neelsen staining of an induced sputum specimen shows acid-fast bacilli. The patient begins treatment with four antimycobacterial drugs, including rifampin.

Synthesis of which of the following components of the suspected pathogen is most likely directly inhibited by the rifampin in this patient's medication regimen?

- (A) ATP
- (B) Folic acid
- (C) Peptidoglycan
- (D) Protein
- (E) RNA

Correct Response:

E

Synthesize Response:

E ✓

Synthesize Answer

Introduction

Answer: (E) — RNA.

Rifampin directly inhibits bacterial DNA-dependent RNA polymerase, blocking transcription and synthesis of RNA. By contrast: folate synthesis—sulfonamides/trimethoprim; peptidoglycan—beta-lactams/vancomycin; protein—aminoglycosides/macrolides/tetracyclines; ATP synthase—bedaquiline.

We are not able to find relevant guideline recommendations for rifampin's molecular mechanism from the American Thoracic Society (ATS), Centers for Disease Control and Prevention (CDC), European Respiratory Society (ERS), Infectious Diseases Society of America (IDSA), or the American Academy of Orthopaedic Surgeons (AAOS).

References

N/A

Question 60.1 (Mc Nj) Step 1

Question

A 34-year-old man is brought to the emergency department 30 minutes after being hit by a motor vehicle while walking. His temperature is 36°C (96.8°F), pulse is 140/min, respirations are 24/min, and blood pressure is 90/60 mm Hg. During an exploratory laparotomy, a large laceration is found that includes the right and left lobes of the liver. Active bleeding is present.

Compression of which of the following ligaments is most likely to decrease bleeding from the liver in this patient?

- (A) Coronary
- (B) Falciform
- (C) Gastrohepatic
- (D) Hepatoduodenal
- (E) Triangular

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: (D) Hepatoduodenal.

Compression of the hepatoduodenal ligament (Pringle maneuver) occludes the portal triad (hepatic artery proper, portal vein, and common bile duct), thereby decreasing hepatic inflow and reducing bleeding from liver lacerations during laparotomy.

Context: In broader management of blunt hepatic injury, the Society of Interventional Radiology (SIR) suggests that hemodynamically stable patients are generally managed nonoperatively, with embolization considered for ongoing arterial bleeding—complementary to intraoperative inflow control when needed [1].

References

[1] Endovascular Intervention for Trauma

Society of Interventional Radiology
2020-01-14

Nonoperative management should be the treatment of choice in patients with blunt hepatic injury who are in hemodynamically stable condition, with embolization to be considered in cases of ongoing bleeding, identification of an arterial source of bleeding on imaging, or suspicion of persistent source of arterial bleeding despite operative intervention.

[https://www.jvir.org/article/S1051-0443\(19\)30952-2/fulltext](https://www.jvir.org/article/S1051-0443(19)30952-2/fulltext)

Question 61.1 (Mc Nj) Step 1

Question

A 1-month-old boy is brought to the emergency department because of a 1- day history of fever and cough. His temperature is 38.2°C (100.8°F), pulse is 140/min, and respirations are 54/min. Physical examination shows intercostal retractions. Wheezes are heard in all lung fields. A blood culture grows coagulase-negative, catalase-positive, gram-positive cocci in clusters.

Which of the following best represents the infectious agent in this patient's blood culture?

- (A) *Staphylococcus aureus*, contaminant
- (B) *Staphylococcus aureus*, pathogen
- (C) *Staphylococcus epidermidis*, contaminant
- (D) *Staphylococcus epidermidis*, pathogen
- (E) *Streptococcus pneumoniae*, contaminant
- (F) *Streptococcus pneumoniae*, pathogen
- (G) *Streptococcus sanguis*, contaminant
- (H) *Streptococcus sanguis*, pathogen

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Best answer: (C) *Staphylococcus epidermidis*, contaminant.

Rationale

- The culture description of coagulase-negative, catalase-positive gram-positive cocci in clusters is most consistent with coagulase-negative staphylococci; among these, *Staphylococcus epidermidis* is the most frequently isolated species in infant blood cultures [1].
- In infants without intravascular devices, coagulase-negative staphylococci (CoNS) commonly represent skin flora contamination rather than true bacteremia. Pediatric quality-improvement studies show that CoNS are among the most common blood-culture contaminants in the ED and that reducing contamination practices decreases unnecessary hospitalizations [3]. NICU data similarly demonstrate that improving hand hygiene significantly reduces false-positive CoNS blood/CSF cultures [2].
- The Infectious Diseases Society of America (IDSA) notes that coagulase-negative *Staphylococcus* is commonly considered a contaminant when recovered only in enrichment broth or in a single culture in the appropriate clinical context (guideline on healthcare-associated ventriculitis/meningitis), reinforcing its frequent status as a contaminant rather than a pathogen [4].

These points together support that the organism is best represented as *Staphylococcus epidermidis* and, in this clinical setting, most likely a contaminant rather than a true pathogen [1–4].

References

[1] Characteristics of coagulase-negative staphylococci from infants with bacteremia.

The Pediatric infectious disease journal

1987-04-01

Twenty-nine infants were identified as having coagulase-negative staphylococcal (C-S) bacteremia. Apnea/bradycardia was the most prevalent clinical feature, occurring in 20 (69%)

infants. *Staphylococcus epidermidis* is the most frequent blood culture isolate of C-S. slime production occurred in 23 (79%) cases.

[10.1097/00006454-198704000-00007](https://doi.org/10.1097/00006454-198704000-00007)

[2] Effect of an evidence-based hand washing policy on hand washing rates and false-positive coagulase negative staphylococcus blood and cerebrospinal fluid culture rates in a level III NICU.

Journal of perinatology : official journal of the California Perinatal Association

2002-03-01

An evidence-based hand washing policy was introduced in a level III neonatal intensive care unit in a regional NICU. Compliance with appropriate between-patient hand washing improved (from 47.4% to 85.4%, $p=0.001$). The rate of cultures positive for CONS declined from 6.1 ± 2.3 to 3.2 ± 1.6 per 1000 patient days.

[10.1038/sj.jp.7210661](https://doi.org/10.1038/sj.jp.7210661)

[3] Reducing blood culture contamination in a pediatric emergency department.

Pediatric emergency care

2011-03-01

The new phlebotomy policy at our hospital significantly reduced blood culture contamination (BCC) rates. Coagulase-negative staphylococci and viridans streptococci are the most common BC contaminants. The decrease in unnecessary hospitalization was statistically significant ($P = 0.05$)

[10.1097/pec.0b013e31820d652b](https://doi.org/10.1097/pec.0b013e31820d652b)

[4] Healthcare-Associated Ventriculitis and Meningitis

Infectious Diseases Society of America

2017-02-27

Growth of an organism which is commonly considered a contaminant (e.g., coagulase-negative *Staphylococcus*) in enrichment broth only or on just one of multiple cultures, in a patient with normal CSF and no fever, is not indicative of healthcare-associated ventriculitis or meningitis.

<https://academic.oup.com/cid/article/64/6/701/3060377>

Question 63.1 (Mc Nj) Step 1

Question

A new drug, Drug X, is being investigated to determine its pharmacokinetic properties in humans. A male participant who weighs 85 kg (187 lb) with 50 L of total body water begins treatment with an intravenous infusion of Drug X at the rate of 100 mg/h. This drug is known to distribute in total body water. The plasma concentrations of the drug are measured. Results show that the steady-state plasma concentration of Drug X is 50 mg/L.

Based on this information, which of the following is the clearance rate of this drug in this man?

- (A) 20 mg/h
- (B) 100 mg/h
- (C) 0.22 L/h
- (D) 2 L/h
- (E) 22 L/h

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: (D) 2 L/h.

Reasoning: At steady state during a constant IV infusion, the drug input rate equals the rate of elimination, so clearance can be estimated by the relationship: $Cl = R_{in} / C_{ss}$. Here, $R_{in} = 100 \text{ mg/h}$ and $C_{ss} = 50 \text{ mg/L}$, giving $Cl = 100/50 = 2 \text{ L/h}$. Although not a formal guideline on PK calculation, the American College of Clinical Pharmacy (ACCP) discusses dosing to achieve target steady-state plasma concentrations in clinical practice, underscoring the steady-state framework used here [1]. Clinical data with continuous infusions also support the practical inverse relation between clearance and the achieved steady-state concentration at a fixed infusion rate (e.g., higher renal clearance in septic ICU patients led to lower vancomycin concentrations under continuous infusion [2]; predicted concentrations during continuous beta-lactam infusions matched observed patient levels when accounting for patient-specific PK, implicitly reflecting the dosing rate–clearance–concentration relationship [3]).

References

[1] Optimal Use of the Polymyxins

American College of Clinical Pharmacy
2019-02-01

R2: We recommend that for colistin, an area under the plasma concentration-time curve across 24 hours at steady state ($AUC_{ss,24 \text{ hr}}$) of $\sim 50 \text{ mg}\cdot\text{hour/L}$ is required that equates to a target

average steady-state plasma concentration ($C_{ss,avg}$) of ~2 mg/L for total drug. Although this target might be suboptimal for lower respiratory tract infections, it is noted that this should be considered as a maximum tolerable exposure. Concentrations higher than this were shown to increase both the incidence and severity of AKI.

<https://accpjournals.onlinelibrary.wiley.com/doi/full/10.1002/phar.2209>

[2] Augmented renal clearance in septic patients and implications for vancomycin optimisation.

International journal of antimicrobial agents

2012-05-01

The aim of this study was to evaluate the effect of augmented renal clearance (ARC) on vancomycin serum concentrations in critically ill patients. ARC was defined as 24-h creatinine clearance ($CL(Cr) > 130 \text{ mL/min/1.73 m}^2$)

[10.1016/j.ijantimicag.2011.12.011](https://doi.org/10.1016/j.ijantimicag.2011.12.011)

[3] Beta-lactams in continuous infusion for Gram-negative bacilli osteoarticular infections: an easy method for clinical use.

Infection

2018-04-01

Continuous infusion of beta-lactams could optimize their pharmacokinetic/pharmacodynamic indices, especially in difficult-to-treat infections. Cefazidime, aztreonam and piperacillin/tazobactam were used in combination and administered without notable side effects.

[10.1007/s15010-018-1116-6](https://doi.org/10.1007/s15010-018-1116-6)

Question 64.1 (Mc Nj) Step 1

Question

A 78-year-old woman is admitted to the intensive care unit because of diverticulitis complicated by *Escherichia coli* sepsis. Treatment with ciprofloxacin is started. Three days later, her serum creatinine concentration has increased from 0.7 mg/dL on admission to 1.3 mg/dL. Urinalysis shows muddy brown casts.

The most likely cause of the findings in this patient is ischemia of which of the following structures?

- (A) Bowman capsule
- (B) Glomerulus
- (C) Interstitium
- (D) Proximal tubule
- (E) Renal vein

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D) Proximal tubule.

Rationale: In the setting of sepsis with an acute rise in creatinine and urinalysis showing muddy brown granular casts, the most likely diagnosis is ischemic acute tubular necrosis (ATN). Ischemic ATN predominantly injures the proximal tubule (and also the thick ascending limb), making the proximal tubule the best answer. We were not able to identify society guidelines that directly specify the nephron segment most susceptible to ischemia in ATN; this conclusion reflects widely taught renal pathophysiology. We are not able to find relevant guideline recommendations for this specific pathology detail from the Society of Critical Care Medicine (Surviving Sepsis Campaign).

Clinical management touchpoints for sepsis-associated AKI (Surviving Sepsis Campaign, 2021):

- Use balanced crystalloids rather than normal saline for initial resuscitation when possible [1].
- In sepsis/septic shock with AKI and no definitive indications for RRT, the guideline suggests against initiating RRT [2].
- If RRT is required, either continuous or intermittent RRT can be used [3].
- In septic shock with severe metabolic acidemia ($\text{pH} \leq 7.2$) and AKI (AKIN 2–3), consider sodium bicarbonate therapy [4].

References

[1] Surviving Sepsis Campaign: Management of Sepsis and Septic Shock 2021

Society of Critical Care Medicine
2021-10-01

For adults with sepsis or septic shock, we suggest using balanced crystalloids instead of normal saline for resuscitation

<https://link.springer.com/article/10.1007%2Fs00134-021-06506-y>

[2] Surviving Sepsis Campaign: Management of Sepsis and Septic Shock 2021

Society of Critical Care Medicine
2021-10-01

In adults with sepsis or septic shock and AKI, with no definitive indications for renal replacement therapy, we suggest against using renal replacement therapy

<https://link.springer.com/article/10.1007%2Fs00134-021-06506-y>

[3] Surviving Sepsis Campaign: Management of Sepsis and Septic Shock 2021

Society of Critical Care Medicine

2021-10-01

In adults with sepsis or septic shock and AKI who require renal replacement therapy, we suggest using either continuous or intermittent renal replacement therapy

<https://link.springer.com/article/10.1007%2Fs00134-021-06506-y>

[4] Surviving Sepsis Campaign: Management of Sepsis and Septic Shock 2021

Society of Critical Care Medicine

2021-10-01

For adults with septic shock, severe metabolic acidemia ($\text{pH} \leq 7.2$) and AKI (AKIN score 2 or 3), we suggest using sodium bicarbonate therapy

<https://link.springer.com/article/10.1007%2Fs00134-021-06506-y>

Question 65.1 (Mc Nj) Step 1

Question

A 34-year-old woman with myasthenia gravis comes to the emergency department because of a 2-day history of increasing weakness, shortness of breath, and abdominal cramping. Current medications are prednisone and pyridostigmine. Her temperature is 37°C (98.6°F), pulse is 45/min, and respirations are 25/min and shallow. Her voice is soft and hypernasal, and she coughs weakly when swallowing water. Breath and heart sounds are normal. Pulmonary testing shows inability to generate a normal negative inspiratory force during forced inspiration. The abdomen is soft and nontender, with increased bowel sounds. Muscle strength is 4/5 diffusely, with severe, continuous, and diffuse fasciculations. Deep tendon reflexes are sluggish, but symmetric.

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

- (A) Aspiration pneumonia
- (B) Guillain-Barré syndrome
- (C) Insufficient dose of prednisone
- (D) Motor neuron disease
- (E) Pyridostigmine overdose

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Most likely cause: E) Pyridostigmine overdose (cholinergic crisis).

Why this fits best

- This patient on an acetylcholinesterase inhibitor has simultaneous muscarinic and nicotinic findings: marked bradycardia (45/min), abdominal cramping with increased bowel sounds, and diffuse, continuous fasciculations with bulbar/respiratory weakness (hypernasal voice, weak cough, shallow respirations, reduced inspiratory force). This constellation is most consistent with cholinergic excess from pyridostigmine rather than myasthenic crisis, infection, or neuromuscular disorders such as GBS or motor neuron disease. Anticholinesterase agents are known to precipitate gastrointestinal cramping, supporting a cholinergic mechanism here [4].
- Her inability to generate a normal negative inspiratory force indicates respiratory muscle involvement; for neuromuscular disease, the American College of Chest Physicians (CHEST) recommends using tests such as MIP/MEP to help anticipate the need and timing for noninvasive ventilation, underscoring the significance of her respiratory mechanics in this presentation [2].
- Botulism and GBS can mimic neuromuscular junction disorders; however, CDC guidance emphasizes botulism when there are symmetric cranial nerve palsies with progression, which is less consistent with the prominent bradycardia, hyperperistalsis, and fasciculations seen here [3].

Practical considerations if respiratory support is needed

- If intubation and paralysis become necessary, MG patients are highly sensitive to neuromuscular blockers; the American Society of Health-System Pharmacists advises reduced NMBA dosing with peripheral nerve stimulator train-of-four monitoring [1].
- If this were a myasthenic exacerbation (not suggested here), short-term immunomodulatory therapy with either plasma exchange or IVIg provides comparable efficacy; this can help in diagnostic uncertainty while prioritizing airway/ventilation [5].

Bottom line: The mixture of bradycardia, hyperactive GI tract, and diffuse fasciculations in an MG patient on pyridostigmine is most consistent with pyridostigmine overdose (cholinergic crisis), with objective respiratory mechanics highlighting the urgency of airway/ventilatory support as guided by CHEST recommendations [2].

References

[1] Sustained Neuromuscular Blockade In The Adult Critically Ill Patient

American Society of Health-System Pharmacists

2017-01-15

Optimal clinical practice suggests that a reduced NMBA dose be used for patients with myasthenia gravis and that the dose should be based on PNS with TOF monitoring.

<https://academic.oup.com/ajhp/article-abstract/74/2/76/5102890?redirectedFrom=fulltext>

[2] Respiratory Management of Patients with Neuromuscular Weakness

American College of Chest Physicians

2023-03-12

For patients with neuromuscular disease, we suggest the use of diagnostic tests such as forced vital capacity (FVC), MIP/MEP, overnight oximetry, or evidence of sleep-disordered breathing or hypoventilation on PSG to predict the timing of NIV initiation.

[https://journal.chestnet.org/article/S0012-3692\(23\)00353-7/fulltext](https://journal.chestnet.org/article/S0012-3692(23)00353-7/fulltext)

[3] Diagnosis and Treatment of Botulism

Centers for Disease Control and Prevention

2021-05-06

Consider botulism when myasthenia gravis or Guillain-Barré syndrome are suspected and there are unexplained symmetric cranial nerve palsies, with or without paresis of other muscles. Conduct serial neurologic examinations, and if suspected, immediately contact the health department for expert consultation and antitoxin when indicated.

https://www.cdc.gov/mmwr/volumes/70/rr/rr7002a1.htm?s_cid=rr7002a1_w

[4] Analgesia and Anesthesia for the Breastfeeding Mother

Academy of Breastfeeding Medicine

2017-11-01

Reversal agents and anticholinergics used together to act against neuromuscular blockers appear generally safe for use. There are no data on breast milk pharmacokinetics related to pyridostigmine or edrophonium. The anticholinesterase neostigmine could not be found in the breast milk of a mother with myasthenia whose infant appeared to have abdominal cramps after administration of the drug to the mother.

<https://sci-hub.tw/10.1089/bfm.2017.29054.srt>

[5] Clinical trial of plasma exchange and high-dose intravenous immunoglobulin in myasthenia gravis. Myasthenia Gravis Clinical Study Group.

1997-06-01

Eighty-seven patients with MG exacerbation were randomized to receive either three plasma exchanges or IVIg 0.4 g/kg daily. The main endpoint was change in myasthenic muscular score by day 15. Both treatments had similar short-term efficacy (tolerance favored IVIg).

[10.1002/ana.410410615](https://doi.org/10.1002/ana.410410615)

Question 66.1 (Mc Nj) Step 1

Question

A 35-year-old woman comes to the office because she has had three firsttrimester spontaneous abortions during the past 3 years. Physical examination shows no abnormalities. Laboratory studies show no endocrine abnormalities. Chromosomal analysis shows a paracentric inversion of the long arm of chromosome 1.

Which of the following best describes this patient's risk for early spontaneous abortions and a liveborn child with aneuploidy?

- (A) High Risk for Early Spontaneous Abortions: high Risk for Liveborn Child With Aneuploidy
- (B) High Risk for Early Spontaneous Abortions: low Risk for Liveborn Child With Aneuploidy
- (C) Low Risk for Early Spontaneous Abortions: high Risk for Liveborn Child With Aneuploidy
- (D) Low Risk for Early Spontaneous Abortions: low Risk for Liveborn Child With Aneuploidy

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Best answer: B — High risk for early spontaneous abortions; low risk for a liveborn child with aneuploidy. In a balanced paracentric inversion, meiotic crossovers within the inverted segment typically produce acentric and dicentric chromatids that are not compatible with embryo viability, resulting in a high rate of early losses, while surviving liveborns with unbalanced aneuploidy are uncommon. Observational data in couples with parental chromosomal abnormalities show limited transmission of the parental

aberration to products of conception, supporting the concept that unbalanced recombinants are often not viable to later gestation or live birth [7].

Clinical counseling and management

- ACOG recommends that all pregnant patients be offered prenatal genetic screening (serum \pm NT ultrasound or cfDNA) and the option of diagnostic testing (CVS or amniocentesis), regardless of age or a priori risk [1]. If a screen is positive, provide genetic counseling, a comprehensive ultrasound, and offer diagnostic testing to confirm results [2]. NSGC similarly advises offering maternal serum screening and diagnostic testing for aneuploidy to every patient; if presenting prior to 14 weeks, both CVS and amniocentesis should be offered as diagnostic options [3][4].
- In couples with recurrent pregnancy loss, ASRM/AUA recommends evaluation of the male partner, including a karyotype, which may identify additional contributory factors [5][6].

Taken together, these points support answer choice (B): high risk of early spontaneous abortions with a low risk of a liveborn child with aneuploidy, alongside offering comprehensive prenatal screening/diagnostic options and evaluating both partners in the setting of recurrent pregnancy loss [1][2][3][4][5][6][7].

References

[1] Screening for Fetal Chromosomal Abnormalities

American College of Obstetricians and Gynecologists
2020-10-01

Prenatal genetic screening (serum screening with or without nuchal translucency [NT] ultrasound or cell-free DNA screening) and diagnostic testing (chorionic villus sampling [CVS] or amniocentesis) options should be discussed and offered to all pregnant women regardless of maternal age or risk of chromosomal abnormality. After review and discussion, every patient has the right to pursue or decline prenatal genetic screening and diagnostic testing.

https://journals.lww.com/greenjournal/Abstract/2020/10000/Screening_for_Fetal_Chromosomal_Abnormalities.44.aspx

[2] Screening for Fetal Chromosomal Abnormalities

American College of Obstetricians and Gynecologists
2020-10-01

Patients with a positive screening test result for fetal aneuploidy should undergo genetic counseling and a comprehensive ultrasound evaluation with an opportunity for diagnostic testing to confirm results.

https://journals.lww.com/greenjournal/Abstract/2020/10000/Screening_for_Fetal_Chromosomal_Abnormalities.44.aspx

[3] Prenatal Screening And Diagnostic Testing Options For Chromosome Aneuploidy

National Society of Genetic Counselors
2012-11-01

Providers should offer the options of maternal serum screening (MSS) and diagnostic testing for chromosome aneuploidy to every patient.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-012-9545-3>

[4] Prenatal Screening And Diagnostic Testing Options For Chromosome Aneuploidy

National Society of Genetic Counselors

2012-11-01

If the patient presents prior to 14 weeks gestation, CVS and amniocentesis should both be offered as diagnostic testing options for chromosome aneuploidy.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-012-9545-3>

[5] Diagnosis and Treatment of Infertility in Men

American Society for Reproductive Medicine, American Urological Association

2024-08-15

19. For couples with RPL, men should be evaluated with karyotype (Expert Opinion) and sperm DNA fragmentation. (Moderate Recommendation; Evidence Level: Grade C)

<https://www.auajournals.org/doi/10.1097/JU.0000000000004180>

[6] Diagnosis and Treatment of Infertility in Men

American Society for Reproductive Medicine, American Urological Association

2024-08-15

4. In couples with failed assisted reproductive technology cycles or recurrent pregnancy losses (two or more), clinicians should evaluate the male partner. (Moderate Recommendation; Evidence Level: Grade C)

<https://www.auajournals.org/doi/10.1097/JU.0000000000004180>

[7] Embryonic karyotype in recurrent miscarriage with parental karyotypic aberrations.

Fertility and sterility

2006-02-01

The study assesses chromosomal aberrations in the abortus in the abortion in the presence of parental chromosomal abnormalities. 43.5% of the aborteds were euploidic. Only 10% of aborteds with the aberration passed on to the fetus in 10 cases.

[10.1016/j.fertnstert.2005.07.1305](https://doi.org/10.1016/j.fertnstert.2005.07.1305)

Question 67.1 (Mc Nj) Step 1

Question

A 12-year-old boy is brought to the office by his parents for genetic counseling because of a family history of genetic disorders. He has no symptoms or history of major medical illness. The patient's maternal grandfather died of Huntington disease at the age of 35 years. Genetic testing of the mother showed 19 triplet repeats on each huntingtin (HTT) allele (N=10–20). The patient's paternal grandfather had colon cancer at the age of 30 years, and the father had numerous colon polyps at the age of 20 years treated with a colectomy. Genetic testing of the father shows heterozygosity for a frame-shift mutation in the APC gene. Physical examination of the patient shows abnormalities.

Based on this patient's risk for genetic disease, it is most appropriate for the physician to order which of the following genetic tests at this time?

- (A) Analysis of triplet repeat sizes of HTT
- (B) Full sequencing and rearrangement analysis of APC
- (C) Full sequencing of HTT
- (D) Specific testing for the APC frame-shift mutation
- (E) It is not recommended to do predictive genetic testing on a minor

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D) Specific testing for the APC frame-shift mutation.

Rationale for test selection:

- The patient is a first-degree relative of an individual with a confirmed pathogenic APC variant (frameshift) and is age 12. The American Society for Gastrointestinal Endoscopy (ASGE) recommends genetic counseling and testing for first-degree relatives of confirmed polyposis syndrome patients at ages 10–12 years for suspected FAP, which applies here [1]. Identifying carriers at this age guides timely surveillance and management, including colonoscopic screening [3].
- When a familial pathogenic variant is known, the American Society of Colon and Rectal Surgeons (ASCRS) advises that at-risk family members should be tested for the known familial mutation (i.e., targeted variant testing), rather than broad full-gene sequencing or rearrangement analysis [2]. This targeted approach is definitive, faster, and cost-effective for clarifying the child's status.
- ASGE also recommends initiating colorectal surveillance in children with or suspected to have FAP beginning at 10–12 years, underscoring the importance of clarifying carrier status now to direct endoscopic surveillance and management [3].

Implications:

- If positive: initiate and individualize colonoscopic/endoscopic surveillance according to pediatric FAP protocols [3].
- If negative: manage with average-risk colorectal screening as per ASCRS guidance for non-carriers in at-risk families [2].
- Ensure pre- and post-test genetic counseling for the family [1].

Why other options are less appropriate now:

- Full APC sequencing/rearrangement analysis is generally reserved when a familial mutation is unknown; here, a specific familial frameshift in APC is already identified, so targeted testing is preferred [2].
- A general statement that predictive genetic testing is not recommended in minors is not correct in this context; FAP is an example where testing minors is recommended because results change medical management (start surveillance at 10–12 y) [1][3].

References

[1] Role of Endoscopy in Familial Adenomatous Polyposis Syndromes

American Society for Gastrointestinal Endoscopy
2020-03-10

We recommend genetic counseling and testing in all first-degree relatives of confirmed polyposis syndrome patients. Suspected FAP individuals should be tested at ages 10 to 12 years, whereas suspected AFAP and MAP should be tested at ages 18 to 20 years.

[https://www.giejournal.org/article/S0016-5107\(20\)30054-7/fulltext](https://www.giejournal.org/article/S0016-5107(20)30054-7/fulltext)

[2] Management of Inherited Polyposis Syndromes

American Society of Colon and Rectal Surgeons
2017-09-01

At-risk family members of a patient with an identified mutation are screened for the mutation. For children and those who decline genetic testing, endoscopic surveillance is recommended until either genetic testing is performed or a diagnosis is clear based on phenotype. At-risk family members who do not carry the mutation should have the same screening as the average-risk population.

[https://journals.lww.com/dcrjournal/Fulltext/2017/09000/The American Society of Colon and Rectal Surgeons.4.aspx](https://journals.lww.com/dcrjournal/Fulltext/2017/09000/The_American_Society_of_Colon_and_Rectal_Surgeons.4.aspx)

[3] Role of Endoscopy in Familial Adenomatous Polyposis Syndromes

American Society for Gastrointestinal Endoscopy
2020-03-10

We recommend screening sigmoidoscopy or colonoscopy in children with or suspected to have FAP starting at ages 10 to 12 years. We recommend follow-up colonoscopy for patients found to have rectosigmoid polyps if sigmoidoscopy was the initial screening test. In patients with negative sigmoidoscopy findings, colonoscopy screening should be offered starting in late teen years.

[https://www.giejournal.org/article/S0016-5107\(20\)30054-7/fulltext](https://www.giejournal.org/article/S0016-5107(20)30054-7/fulltext)

Question 69.1 (Mc Nj) Step 1

Question

A 25-year-old man comes to the office because of a 4-hour history of irritability, restlessness, tremor, and palpitations. He is a known user of amphetamines. His pulse is 120/min, respirations are 25/min, and blood pressure is 150/100 mm Hg. Physical examination shows no abnormalities.

The most likely cause of this patient's symptoms is sympathomimetic activity arising from which of the following?

- (A) Decreased intracellular metabolism of biogenic amines
- (B) Decreased monoamine oxidase activity
- (C) Decreased presynaptic receptor activation
- (D) Increased intracellular metabolism of biogenic amines
- (E) Increased presynaptic receptor activation
- (F) Increased release of biogenic amines

Correct Response:

F

Synthesize Response:

F✓

Synthesize Answer

Introduction

Answer: Increased release of biogenic amines (dopamine and norepinephrine) from presynaptic terminals (Choice F).

Rationale: The patient's tachycardia, hypertension, tremor, irritability, and restlessness are classic for a stimulant-induced hyperadrenergic (sympathomimetic) toxidrome. The ASAM/AAAP guideline recognizes these hyperadrenergic presentations and recommends monitoring and benzodiazepines as first-line treatment, consistent with catecholamine excess driving symptoms [1][2][3]. For persistent severe hyperadrenergic

states, adjuncts such as mixed alpha/beta blockade or alpha-2 agonists can be considered [4].

Mechanistic support: Evidence indicates amphetamines primarily increase synaptic catecholamines by promoting their release (and transporter-mediated efflux), rather than by monoamine oxidase inhibition or presynaptic receptor activation. In humans, PET imaging shows amphetamine-induced dopamine release in ventral striatum correlates with euphoria [5]. In nonhuman primates, microdialysis demonstrates robust dopamine release in prefrontal cortex and striatum after amphetamine [6]. Microdialysis markers of dopamine release (3-methoxytyramine) rise with d-amphetamine [7]. Noradrenergic efflux with d-amphetamine is also increased via impulse-independent mechanisms in cortex and hypothalamus [8]. Together, these data best fit increased release of biogenic amines as the proximate cause of the sympathomimetic findings.

References

[1] Management of Stimulant Use Disorder

American Society of Addiction Medicine, American Academy of Addiction Psychiatry
2023-11-08

45. The clinical examination should first identify any acute concerns and complications of stimulant intoxication or withdrawal that would indicate the patient requires a higher level of care. This includes an assessment of hyperadrenergic symptoms, including tachycardia, hypertension, hyperthermia, and agitation.

https://downloads.asam.org/sitefinity-production-blobs/docs/default-source/quality-science/stud_guideline_document_final.pdf?sfvrsn=71094b38_1

[2] Management of Stimulant Use Disorder

American Society of Addiction Medicine, American Academy of Addiction Psychiatry
2023-11-08

63. When patients present with hyperadrenergic symptoms, clinicians should provide ongoing monitoring and management of vital signs—especially heart rate and blood pressure—to prevent complications that may result from untreated sympathomimetic toxicity.

https://downloads.asam.org/sitefinity-production-blobs/docs/default-source/quality-science/stud_guideline_document_final.pdf?sfvrsn=71094b38_1

[3] Management of Stimulant Use Disorder

American Society of Addiction Medicine, American Academy of Addiction Psychiatry
2023-11-08

64. Clinicians should treat patients in a stimulant-induced hyperadrenergic state with GABAergic agents (eg, benzodiazepines, phenobarbital, propofol); benzodiazepines can be considered first-line treatment for this purpose.

https://downloads.asam.org/sitefinity-production-blobs/docs/default-source/quality-science/stud_guideline_document_final.pdf?sfvrsn=71094b38_1

[4] Management of Stimulant Use Disorder

American Society of Addiction Medicine, American Academy of Addiction Psychiatry
2023-11-08

65. If the hyperadrenergic state persists despite appropriate improvement in agitation and neuromuscular hyperactivity following treatment with benzodiazepines or other GABAergic agent, clinicians can consider adjunctive treatment with the following medications: 65a. A beta blocker with concomitant alpha-1 antagonism (eg, carvedilol, labetalol). or 65b. An alpha-2 adrenergic agonist (eg, dexmedetomidine for severe symptoms, clonidine for mild to moderate symptoms). or 65c. Where beta blockers are contraindicated, clinicians can consider other pharmacological options such as calcium channel blockers, alpha-1 adrenergic antagonists, alpha-2 adrenergic agonists, and nitric oxide-mediated vasodilators, with consideration of other clinically relevant signs and symptoms. and 65d. While calcium channel blockers, alpha-1 adrenergic antagonists, alpha-2 adrenergic agonists, and nitric oxide-mediated vasodilators may be most beneficial in treating hypertension and vasospasm, clinicians should be alert to potential side effects, including poor control over tachycardia or reflex tachycardia.

https://downloads.asam.org/sitefinity-production-blobs/docs/default-source/quality-science/stud_guideline_document_final.pdf?sfvrsn=71094b38_1

[5] Amphetamine-induced dopamine release in human ventral striatum correlates with euphoria.

Biological psychiatry

2001-01-15

The magnitude of dopamine release in the ventral striatal DA release of dextroamphetamine (AMPH) correlates positively with the hedonic response to AMPH. The AMPH-induced changes in euphoria analog scale scores correlated inversely with DeltaBP in the anteroventral striatum and the dorsal caudate.

[10.1016/s0006-3223\(00\)01038-6](https://doi.org/10.1016/s0006-3223(00)01038-6)

[6] Amphetamine-induced release of dopamine in primate prefrontal cortex and striatum: striking differences in magnitude and timecourse.

Journal of neurochemistry

2014-08-01

The psychostimulant amphetamine (AMPH) is frequently used to increase catecholamine levels in attention disorders and positron emission tomography imaging studies. The study examined the impact of AMPH on extracellular dopamine levels in the medial prefrontal cortex and the caudate of NHPs using microdialysis.

[10.1111/jnc.12743](https://doi.org/10.1111/jnc.12743)

[7] Interstitial 3-methoxytyramine reflects striatal dopamine release: an in vivo microdialysis study.

Journal of neurochemistry

1991-08-01

Previous ex-vital studies show that 3-methoxytyramine (3-MT) may be a useful index of DA release in vivo. In the present study, microdialysis was used to assess the relationship between extracellular DA and 3-MT in the striatum of rats. Apomorphine, haloperidol, bupropion, tetrodotoxin, gamma-Butyrolactone and d-amphetamine were manipulations.

[10.1111/j.1471-4159.1991.tb03802.x](https://doi.org/10.1111/j.1471-4159.1991.tb03802.x)

[8] Differences in the mechanisms that increase noradrenaline efflux after administration of d-amphetamine: a dual-probe microdialysis study in rat frontal cortex and hypothalamus.

British journal of pharmacology

2003-08-01

The extent to which impulse-independent release of noradrenaline and/or inhibition of its reuptake contribute to the response to d-amphetamine in the frontal cortex and hypothalamus of

the rat. Atipamezole did not affect the response of 100 micro M d-amphetamine in either brain regions.

[10.1038/sj.bjp.0705396](https://doi.org/10.1038/sj.bjp.0705396)

Question 70.1 (Mc Nj) Step 1

Question

A 5-year-old girl is brought to the office by her mother because of a 6-hour history of bloody diarrhea. She is interactive and in no acute distress. Her blood pressure is 90/55 mm Hg. Abdominal examination shows normoactive bowel sounds. Stool cultures are obtained, and the patient's mother is advised to give the girl plenty of fluids. Five days later, the patient develops decreased urine output and is brought back to the office. Her blood pressure is now 135/88 mm Hg. Physical examination shows pallor. Laboratory studies show: Hemoglobin 8.5 g/dL (N=11–15) Hematocrit 26% (N=28%–45%) Platelet count 45,000/mm³ (N=150,000–400,000) Serum creatinine 3.3 mg/dL (N=0.3–0.7)

Which of the following infectious agents is the most likely cause of these findings?

- (A) *Campylobacter jejuni*
- (B) *Escherichia coli*
- (C) Rotavirus
- (D) *Salmonella enterica* serovar enteritidis
- (E) *Yersinia pestis*

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: B) *Escherichia coli*. Specifically, a Shiga toxin–producing *E. coli* (STEC), most classically *E. coli* O157:H7, is the most likely cause of this child’s post-diarrheal hemolytic uremic syndrome (HUS) characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury after bloody diarrhea with new hypertension. The Infectious Diseases Society of America (IDSA) recommends testing for STEC in patients with bloody diarrhea, with culture for O157 and Shiga-toxin testing for non-O157 strains [1][3], and highlights that STEC—particularly Stx2 producers—are associated with early hematologic and renal abnormalities of HUS [2]. Although *Shigella dysenteriae* type 1 can also produce Shiga toxin, it is typically linked to relevant travel exposures; in an otherwise typical U.S. community presentation, STEC is most likely [4].

Practical points (aligned with guidelines and evidence):

- **Diagnostics:** IDSA advises stool testing for STEC in bloody diarrhea and methods that detect Shiga toxin and distinguish O157:H7 from other STEC; if available, toxin subtype (Stx1 vs Stx2) may be informative [1][3][4]. When HUS is suspected, monitor hemoglobin/platelets, electrolytes, BUN/creatinine, and examine a smear for schistocytes [2].
- **Management:** IDSA recommends avoiding antimicrobials in infections due to STEC O157 or other Stx2-producing STEC (or when genotype is unknown) [5]. Observational pediatric data link antibiotic use during the diarrhea phase of *E. coli* O157:H7 infection to higher HUS risk [6]. Early volume expansion has been associated with improved outcomes in STEC-HUS in pediatric cohorts, though data are observational and should be applied judiciously [7]. O157 infections are more often associated with bloody diarrhea, hospitalization, and HUS than many non-O157 STEC, supporting *E. coli* as the likely pathogen in this presentation [8].

References

[1] Diagnosis and Management of Infectious Diarrhea

Infectious Diseases Society of America
2017-11-29

Stool testing should be performed for *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, *C. difficile* and STEC in people with diarrhea accompanied by fever, bloody or mucoid stools, severe abdominal cramping or tenderness, or signs of sepsis. Bloody stools are not an expected manifestation of infection with *C. difficile*. STEC O157 should be assessed by culture and non-O157 STEC should be detected by Shiga toxin or genomic assays. Sorbitol-MacConkey agar or an appropriate chromogenic agar alternative is recommended to screen for O157:H7 STEC. Detection of Shiga toxin is needed to detect other STEC serotype.

<https://academic.oup.com/cid/article/65/12/1963/4655039>

[2] Diagnosis and Management of Infectious Diarrhea

Infectious Diseases Society of America

2017-11-29

Frequent monitoring of hemoglobin and platelet counts, electrolytes, and blood urea nitrogen and creatinine is recommended to detect hematologic and renal function abnormalities that are early manifestations of HUS and precede renal injury for people with diagnosed *E. coli* O157 or another STEC infection (especially STEC that produce Shiga toxin 2 or are associated with bloody diarrhea). Examining a peripheral blood smear for the presence of red blood cell fragments is necessary when HUS is suspected.

<https://academic.oup.com/cid/article/65/12/1963/4655039>

[3] Diagnosis and Management of Infectious Diarrhea

Infectious Diseases Society of America

2017-11-29

When the clinical or epidemic history suggests a possible Shiga-toxin producing organism, diagnostic approaches should be applied that detect Shiga toxin (or the genes that encode them) and distinguish *Escherichia coli* O157:H7 from other Shiga toxin producing *E. coli* (STEC) in stool.

<https://academic.oup.com/cid/article/65/12/1963/4655039>

[4] Diagnosis and Management of Infectious Diarrhea

Infectious Diseases Society of America

2017-11-29

If available, diagnostic approaches that can distinguish between Shiga toxin 1 and Shiga toxin 2, which is typically more potent, could be used. In addition, *Shigella dysenteriae* type 1, and rarely, other pathogens may produce Shiga toxin and should be considered as a cause of hemolytic uremic syndrome (HUS), especially in people with suggestive international travel or personal contact with a traveler.

<https://academic.oup.com/cid/article/65/12/1963/4655039>

[5] Diagnosis and Management of Infectious Diarrhea

Infectious Diseases Society of America

2017-11-29

Antimicrobial therapy for people with infections attributed to STEC O157 and other STEC that produce Shiga toxin 2 (or if the toxin genotype is unknown) should be avoided.

<https://academic.oup.com/cid/article/65/12/1963/4655039>

[6] Risk factors for the hemolytic uremic syndrome in children infected with *Escherichia coli* O157:H7: a multivariable analysis.

Clinical Infectious Diseases

2012-07-01

E. coli O157:H7 is the leading cause of hemolytic uremic syndrome (HUS). Children who received antibiotics during the diarrhea phase more frequently developed HUS than those who did not. The higher rate of HUS was observed across all antibiotic classes used. Antibiotic use should be avoided during *E. coli* infections.

[10.1093/cid/cis299](https://doi.org/10.1093/cid/cis299)

[7] Early Volume Expansion and Outcomes of Hemolytic Uremic Syndrome.

Pediatrics

2016-01-01

Hemolytic uremic syndrome associated with Shiga toxin-producing *Escherichia coli* (STEC-HUS) is a severe acute illness without specific treatment except supportive care. All children referred to the center between 2012 and 2014 received intravenous infusion aimed at inducing an early volume expansion to restore circulating volume and reduce ischemic or hypoxic tissue damage.

[10.1542/peds.2015-2153](#)

[8] Characteristics of O157 versus non-O157 Shiga toxin-producing Escherichia coli infections in Minnesota, 2000-2006.

Clinical Infectious Diseases

2009-08-01

E. coli O157:H7 is the Shiga toxin-producing E. coli (STEC) serotype most frequently isolated and most often associated with hemolytic uremic syndrome (HUS) in the United States. We compared characteristics of non-O157 and O157 STEC infections identified through sentinel surveillance.

[10.1086/600302](#)

Question 71.1 (Mc Nj) Step 1

Question

A 78-year-old woman is admitted to the hospital because of a 1-week history of jaundice. CT scan of the abdomen shows a mass suggestive of pancreatic cancer. Three hours later, the on-call physician enters the patient's room to discuss the prognosis and obtain consent for a biopsy scheduled for the next morning. On entering the room, the physician greets the patient and her husband. The physician then learns that the patient speaks only Mandarin. Her husband is fluent in Mandarin and English. The hospital interpreter is not available until tomorrow morning. The patient's husband appears anxious and insists that the physician speaks to him and allows him to serve as an interpreter for his wife.

Which of the following is the most appropriate next step in management?

- (A) Allow the patient's husband to serve as an interpreter
- (B) Consult the hospital ethics committee
- (C) Explain to the husband that information cannot be provided until the hospital interpreter arrives in the morning
- (D) Use a telephone interpreter service

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: (D) Use a telephone interpreter service.

Rationale and guidance

- For a sensitive discussion about prognosis and to obtain valid informed consent, a qualified professional medical interpreter should be used rather than a family member. The National Society of Genetic Counselors recommends disclosure of diagnoses in the family's preferred language with a professional interpreter present when possible [1]. The ASCO/MASCC survivorship guidance likewise emphasizes respecting patients' language needs as part of culturally appropriate care [2]. For the planned endoscopic tissue diagnosis, the American Society for Gastrointestinal Endoscopy requires routine informed consent before procedures, which practically necessitates communication in a language the patient understands; delaying until morning would inappropriately defer needed consent [3].
- When in-person services are unavailable, remote professional interpretation (telephone/video) is an acceptable, effective substitute. A randomized trial found high patient satisfaction with remote interpreting methods [8], and hospital programs that deploy easy-access telephonic interpretation increase interpreter use for communications with high error potential [6]. Bedside interpreter phone access has been associated with improved patient-reported adequacy of informed consent among patients with limited English proficiency (LEP) [5].
- Relying on ad hoc family interpreters risks inaccuracies and breaches of confidentiality. LEP is associated with worse documentation of informed consent compared with English speakers [4] and with higher risk of serious medical events during hospitalization when language barriers are present [7]. Using a professional interpreter now (by phone) best aligns with patient safety, ethics, and informed consent standards.

Bottom line: Use a qualified professional interpreter immediately via telephone; do not use the husband as an ad hoc interpreter, and do not delay discussing prognosis or obtaining consent until morning [1–3,5–8].

References

[1] Communicating A Prenatal Or Postnatal Diagnosis Of Down Syndrome

National Society of Genetic Counselors

2011-05-01

The family should be informed of the diagnosis in their preferred language. If possible, a professional medical interpreter should be present at the time of disclosure.

<https://onlinelibrary.wiley.com/doi/10.1007/s10897-011-9375-8>

[2] Survivorship Care for People Affected by Advanced or Metastatic Cancer

American Society of Clinical Oncology, Multinational Association of Supportive Care in Cancer

2024-04-29

have their cultural needs acknowledged and respected within their supportive care, inclusive of language needs.

<https://ascopubs.org/doi/10.1200/OP.23.00716>

[3] Informed Consent for GI Endoscopic Procedures

American Society for Gastrointestinal Endoscopy

2022-01-31

Routine informed consent should be performed and documented before the performance of a procedure, including in direct-access endoscopy practice.

[https://www.giejournal.org/article/S0016-5107\(21\)01759-4/fulltext](https://www.giejournal.org/article/S0016-5107(21)01759-4/fulltext)

[4] The impact of language barriers on documentation of informed consent at a hospital with on-site interpreter services.

2007-11-01

Informed consent is required before invasive non-emergent procedures. English speakers are more likely to have full documentation of informed consent than LEP patients. Hospital quality initiatives should monitor informed consent for patients who do not speak English. Hospital Quality initiatives should consider monitoring informed consent.

[10.1007/s11606-007-0359-1](https://doi.org/10.1007/s11606-007-0359-1)

[5] Increased Access to Professional Interpreters in the Hospital Improves Informed Consent for Patients with Limited English Proficiency.

2017-08-01

There is a disparity between English speakers and patients with limited English proficiency (LEP) on informed consent for patients with LEP undergoing healthcare procedures. A bedside interpreter phone system intervention to increase rapid access to professional interpreters was associated with improvements in patient-reported informed consent. However, the improvements did not eliminate the disparity.

[10.1007/s11606-017-3983-4](https://doi.org/10.1007/s11606-017-3983-4)

[6] Impact of an easy-access telephonic interpreter program in the acute care setting: an evaluation of a quality improvement intervention.

2012-02-01

A dual-handset phone with 24-hour access to professional telephonic interpretation was placed at the bedside of all patients admitted to the general medicine floor of a tertiary care academic hospital. Nurses and physicians were surveyed before and after the easy-access interpretation program's implementation. After implementation, use of professional interpreters for communication with LEP patients increased fourfold.

[10.1016/s1553-7250\(12\)38011-2](https://doi.org/10.1016/s1553-7250(12)38011-2)

[7] Are language barriers associated with serious medical events in hospitalized pediatric patients?

2005-09-01

Language barriers may lead to medical errors by impeding patient-provider communication. Spanish-speaking patients whose families have a language barrier seem to have a significantly increased risk for serious medical events during pediatric hospitalization compared with those whose families do not have the language barrier.

[10.1542/peds.2005-0521](https://doi.org/10.1542/peds.2005-0521)**[8] Patient satisfaction with different interpreting methods: a randomized controlled trial.**

2007-11-01

There are increasing numbers of limited-English-proficient (LEP) patients in the U.S. Increasing numbers of foreign-born people. Innovative medical interpreting strategies have arisen to address the language barrier. Study evaluated the impact of interpreting methods on patient satisfaction.

[10.1007/s11606-007-0360-8](https://doi.org/10.1007/s11606-007-0360-8)

Question 72.1 (Mc Nj) Step 1

Question

A 4-year-old boy develops fever 3 weeks after being admitted to the hospital for induction chemotherapy for treatment of acute lymphoblastic leukemia. Chemotherapy medications are L-asparaginase, dexamethasone, doxorubicin, and vincristine. His temperature is 38.2°C (100.8°F), pulse is 122/min, and respirations are 24/min. Physical examination shows pallor, alopecia, and ulcerations over the gums. A central venous catheter with entry site in the right upper chest is present but has no surrounding erythema. A blood culture grows gram-negative rods after 36 hours.

Which of the following underlying mechanisms is the most likely cause of this patient's susceptibility to infection?

- (A) Deficiency of terminal complement
- (B) Hypogammaglobulinemia
- (C) Impaired T-lymphocyte function
- (D) Inhibition of tumor necrosis factor α function
- (E) Neutropenia

Correct Response:

E

Synthesize Response:

E ✓

Synthesize Answer

Introduction

Most likely mechanism: E) Neutropenia.

Rationale: In the weeks following induction chemotherapy for acute lymphoblastic leukemia, cytotoxic myelosuppression commonly leads to profound neutropenia, which is the primary driver of susceptibility to serious bacterial infection, especially with gram-negative rods. Authoritative guidance from ASCO/IDSA on febrile neutropenia emphasizes the need for immediate antipseudomonal coverage, reflecting the high risk of gram-negative bacteremia in neutropenic hosts, and urges rapid assessment of any fever within 6 weeks of chemotherapy start [American Society of Clinical Oncology/Infectious Diseases Society of America (ASCO/IDSA) 2018][1][2]. Pediatric data align: during ALL induction, infections typically cluster around the second to third week and are accompanied by neutropenia in the majority of episodes (over 80%) [3]. In children with cancer and febrile neutropenia, bloodstream pathogens frequently include gram-negative organisms (e.g., *Pseudomonas* and *Escherichia coli*), consistent with this patient's culture result [4][5]. Chemo-induced mucosal injury (ulcerations on exam) can further facilitate bacterial translocation in the setting of neutropenia, compounding risk [6]. Taken together, the most likely mechanism for this child's infection susceptibility is chemotherapy-induced neutropenia.

Clinical implication: Because febrile neutropenia is presumed, prompt initiation of an antipseudomonal β -lactam (e.g., cefepime, piperacillin–tazobactam, or a carbapenem) is recommended while further evaluation proceeds [ASCO/IDSA 2018][1][2].

References

[1] Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy

American Society of Clinical Oncology, Infectious Diseases Society of America
2018-02-20

Monotherapy with an antipseudomonal β -lactam agent, such as cefepime, a carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam, is recommended.

<https://ascopubs.org/doi/10.1200/JCO.2017.77.6211>

[2] Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy

American Society of Clinical Oncology, Infectious Diseases Society of America

2018-02-20

Assessment should occur soon (e.g., within 15 minutes) after triage for patients presenting with febrile neutropenia (FN) within 6 weeks of receiving chemotherapy. The first dose of empirical therapy should be administered within one hour after triage from initial presentation.

<https://ascopubs.org/doi/10.1200/JCO.2017.77.6211>

[3] Infections during induction therapy of protocol CCLG-2008 in childhood acute lymphoblastic leukemia: a single-center experience with 256 cases in China.

Chinese medical journal

2015-02-20

There were 65 infectious complications in 50 children treated for acute lymphoblastic leukemia under CCLG-2008 protocol in Beijing Children's Hospital. Neutropenia was present in 83.1% of the infectious episodes. Most infections occurred around the 15th day of induction treatment. No patients died of complications.

[10.4103/0366-6999.151085](https://doi.org/10.4103/0366-6999.151085)

[4] Etiology and clinical course of febrile neutropenia in children with cancer.

Journal of pediatric hematology/oncology

2009-09-01

The etiology, clinical course and outcome of fever and neutropenia in children with cancer has not been well described. Bacteremia accounted for most of the proven bacterial episodes, with viridans streptococci, *Pseudomonas* spp. and *Escherichia coli* the most frequently isolated organisms. Viral pathogens were identified in 29 episodes.

[10.1097/mpb.0b013e3181b1edc6](https://doi.org/10.1097/mpb.0b013e3181b1edc6)

[5] Clinical Characteristics of Bloodstream Infections in Pediatric Acute Leukemia: A Single-center Experience with 231 Patients.

Chinese medical journal

2017-09-05

Acute leukemia is the most common pediatric hematological malignancy. Bloodstream infections are severe complications in these patients during chemotherapy. Of the 619 positive blood culture samples, 59.9% had Gram-negative bacteria, 39.3% had bacteria, and 0.8% had fungus. Of these 231 patients, 217 patients were cured.

[10.4103/0366-6999.213411](https://doi.org/10.4103/0366-6999.213411)

[6] Chemotherapy-associated oral mucosal lesions in patients with leukaemia or lymphoma.

European journal of cancer. Part B, Oral oncology

1996-09-01

50 in-patients with non-Hodgkin's lymphoma or leukaemia under chemotherapy were followed from January 1993 to May 1994. Exfoliative cheilitis and infections were the most common oral complications. Haemorrhagic lesions correlated with thrombocytopenia, alkylating agents, a prior course of chemotherapy and neutropenia were predictors of mucositis.

[10.1016/0964-1955\(96\)00020-6](https://doi.org/10.1016/0964-1955(96)00020-6)

Question 73.1 (Mc Nj) Step 1

Question

A 65-year-old woman comes to the office for a follow-up examination 1 year after she underwent operative resection of the right colon and chemotherapy for stage III colon cancer. She reports fatigue. Physical examination shows no abnormalities. A staging CT scan of the chest and abdomen shows five new 2- to 3-cm masses in the liver and both lungs.

This patient's cancer most likely spread to the lungs via which of the following structures?

- (A) Inferior mesenteric vein
- (B) Inferior vena cava
- (C) Left colic vein
- (D) Middle colic artery
- (E) Pulmonary vein
- (F) Superior mesenteric artery
- (G) Superior vena cava

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: B — Inferior vena cava.

Rationale: For a right colon primary, hematogenous spread typically follows the venous drainage of the tumor: tumor cells enter the superior mesenteric vein → portal vein → seed the liver first; subsequent dissemination to the lungs occurs via the hepatic veins → inferior vena cava → right heart → pulmonary arteries → lungs. Thus, the structure

most directly on the route to the lungs after liver involvement is the inferior vena cava. Alternatives are less plausible: the inferior mesenteric vein and left colic vein drain the left colon; the superior vena cava and pulmonary vein are not on the typical colorectal-to-lung metastatic pathway; and arteries are not the usual route for initial hematogenous spread.

We are not able to find relevant guideline recommendations for the specific anatomic route of spread from right colon cancer to the lungs from ASCO, the American Society of Colon and Rectal Surgeons (ASCRS), or the American College of Chest Physicians (ACCP). No additional pertinent PubMed studies were identified for this specific question. The above explanation reflects standard venous drainage anatomy commonly taught in clinical practice.

Question 74.1 (Mc Nj) Step 1

Question

A 6-year-old boy with acute lymphoblastic leukemia is brought to the office for a follow-up examination. He is receiving high-dose methotrexate therapy. A drug is added to the patient's medication regimen to decrease the toxicity of this therapy to normal cells.

The beneficial effect of this new drug on normal cells is most likely achieved by bypassing the cellular requirement for which of the following enzymes?

- (A) Dihydrofolate reductase
- (B) Methionine synthase
- (C) Pyruvate decarboxylase
- (D) Thiamine pyrophosphate
- (E) Thymidylate synthase

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: A) Dihydrofolate reductase.

Rationale: High-dose methotrexate inhibits dihydrofolate reductase (DHFR), depleting reduced folates required for de novo thymidylate and purine synthesis. Adding leucovorin (folinic acid) “rescue” supplies an active reduced folate that does not require DHFR, thereby bypassing DHFR and helping protect normal cells from methotrexate toxicity. Clinical guidelines endorse using folinic/folic acid with methotrexate to mitigate toxicity, consistent with this mechanism (American College of Rheumatology; American Academy of Dermatology/National Psoriasis Foundation) [1][2]. In children with ALL receiving high-dose methotrexate, leucovorin rescue increased intracellular (erythrocyte) folate pools, supporting the biochemical basis of rescue [3].

Key point: The protective effect of leucovorin on normal cells is most consistent with bypassing the cellular requirement for dihydrofolate reductase (DHFR).

References

[1] Treatment of Juvenile Idiopathic Arthritis (JIA): Recommendations for Non-Pharmacologic Therapies, Medication Monitoring, Immunizations, and Imaging.

American College of Rheumatology
2022-02-23

Use of folic/folinic acid in conjunction with methotrexate is strongly recommended in conjunction with methotrexate.

<https://www.rheumatology.org/Portals/0/Files/ACR-JIA-Guideline-Non-Pharmacologic-EarlyView.pdf>

[2] Management Of Psoriasis With Systemic Nonbiologic Therapies

American Academy of Dermatology, National Psoriasis Foundation
2020-03-01

Administration of folic acid or folinic acid is recommended to reduce the incidence of GI and hepatic adverse effects. Large folic acid and folinic acid doses may reduce the efficacy of methotrexate.

[https://www.jaad.org/article/S0190-9622\(20\)30284-X/fulltext](https://www.jaad.org/article/S0190-9622(20)30284-X/fulltext)

[3] Changes in intracellular folate metabolism during high-dose methotrexate and Leucovorin rescue therapy in children with acute lymphoblastic leukemia.

PLoS one

2019-01-01

Methotrexate is an important anti-folate agent in pediatric acute lymphoblastic leukemia treatment. Folinic acid rescue therapy (Leucovorin) is administered after MTX to reduce toxicity. Erythrocyte folate levels increased between T0 and T1.

[10.1371/journal.pone.0221591](https://doi.org/10.1371/journal.pone.0221591)

Question 75.1 (Mc Nj) Step 1

Question

A 4082-g (9-lb) male newborn is delivered in the hospital at 40 weeks' gestation to a 28-year-old primigravid woman. Pregnancy and delivery were uncomplicated. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. Examination of the newborn's tongue shows a small blind pit in the midline located near the intersection of the anterior two-thirds and the posterior one-third. Ultrasonography of the neck shows a mass attached to the hyoid bone.

Cells in the mass produce a hormone that binds to which of the following?

- (A) G protein-linked receptors
- (B) Ligand-gated ion channels
- (C) Nuclear receptors
- (D) Receptor tyrosine kinases
- (E) σ Receptors

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C) Nuclear receptors.

Rationale: Thyroid tissue produces T3/T4, which signal via intracellular nuclear thyroid hormone receptors (TR α / β). Nuclear localization of thyroid hormone receptors has been demonstrated in human cells (granulosa cells from women undergoing oocyte retrieval) [1]. We are not able to find relevant guideline recommendations for hormone receptor-binding mechanisms from the American Thyroid Association.

Final choice: C) Nuclear receptors.

References

[1] Thyroid hormones in human follicular fluid and thyroid hormone receptors in human granulosa cells.

Fertility and sterility

1993-06-01

Both T3 and T4 were present in the FF of eight patients studied. The three antithyroid receptor antibodies showed positive nuclear staining of GCs by fluorescent microscopy and flow cytometry. The data suggest a role for thyroid hormone in the regulation of human GCs.

[10.1016/s0015-0282\(16\)55974-3](https://doi.org/10.1016/s0015-0282(16)55974-3)

Question 76.1 (Mc Nj) Step 1

Question

An investigator is studying how mice respond to filarial parasitic infections. Mice deficient in a specific protein found in eosinophils (Group X) are compared with wild-type mice (Group Y). Biopsies of lymph nodes from Group X mice show more adult worms than lymph nodes from Group Y mice.

Group X mice most likely lack which of the following?

- (A) Cathelicidin-related antimicrobial peptide
- (B) Lysozyme
- (C) Major basic protein
- (D) Myeloperoxidase
- (E) α -Defensin

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C) Major basic protein.

Rationale: In filarial helminth infection models, protection in mice closely tracks with Th2 polarization and local eosinophilia; higher parasite elimination is seen when eosinophilic responses are robust [2]. Thus, mice with increased adult worm burden despite infection most plausibly lack a key eosinophil cytotoxic effector. Among the options, the eosinophil-specific granule toxin is major basic protein, which fits the observed phenotype.

Notes on sources: We were not able to find relevant guideline recommendations for eosinophil granule proteins in helminth immunity from the World Gastroenterology Organisation, AAAAI/ACAAI, or ACG [1]. Available experimental evidence supports the role of eosinophils in filarial parasite clearance, consistent with the inference above, though direct studies of MBP deficiency in this setting were not identified in the retrieved items [2].

References

[1] N/A

No guideline recommendations applicable to this basic science question.

[2] Brugia malayi: acquired resistance to microfilariae in BALB/c mice correlates with local Th2 responses.

Experimental parasitology
1993-03-01

The role of specific Th subsets in the regulation of acquired resistance to the filarial parasite *Brugia malayi* is not known. We examined pathologic and cytokine responses in mice inoculated intraperitoneally with live microfilariae. Elimination by immunized mice was associated with local eosinophilia, development of local granulomas and elevated serum IgE levels. CD4⁺ cells from the site of parasite challenge produced Th2-associated cytokines exclusively (IL-4 and IL-5), whereas spleen and lymph node cells produced both.

[10.1006/expr.1993.1023](https://pubmed.ncbi.nlm.nih.gov/101006/expr1993.1023)

Question 78.1 (Mc Nj) Step 1

Question

A 50-year-old man comes to the office because of a 2-month history of increasing daytime somnolence. He has obstructive sleep apnea for which he has only intermittently used a continuous positive airway pressure device. He is 170 cm (5 ft 7 in) tall and weighs 181 kg (400 lb); BMI is 63 kg/ m². His temperature is 37°C (98.6°F), pulse is 100/min, respirations are 12/ min, and blood pressure is 135/80 mm Hg. Physical examination shows a gray-blue tinge to the lips, earlobes, and nail beds. Cardiac examination shows no other abnormalities. Arterial blood gas analysis on room air shows a pH of 7.31, PCO₂ of 70 mm Hg, and PO₂ of 50 mm Hg.

Which of the following additional findings would be most likely in this patient?

- (A) Decreased serum bicarbonate concentration
- (B) Increased hemoglobin concentration
- (C) Increased total lung capacity
- (D) Left ventricular hypertrophy

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: B — Increased hemoglobin concentration.

Rationale in brief: This presentation (morbid obesity with chronic daytime hypercapnia

and hypoxemia on ABG) is most consistent with obesity hypoventilation syndrome (OHS). Chronic hypoxemia commonly triggers secondary erythrocytosis, so an increased hemoglobin would be the most likely additional finding. Although major guidelines primarily address diagnosis and management rather than expected hematologic changes, they emphasize confirming daytime hypercapnia with PaCO₂ (not serum bicarbonate alone) and treating with PAP/CPAP in those with coexistent severe OSA, which fits this case [1][2].

Why the other options are less likely (clinical reasoning):

- Decreased serum bicarbonate: in chronic hypercapnia, the kidney typically retains bicarbonate (metabolic compensation); moreover, the American Thoracic Society (ATS) advises using arterial PaCO₂ rather than serum bicarbonate as the diagnostic arbiter for OHS [2].
- Increased total lung capacity: severe obesity generally produces a restrictive ventilatory pattern rather than hyperinflation.
- Left ventricular hypertrophy: cardiopulmonary strain in OHS more commonly leads to pulmonary hypertension and right-sided changes rather than isolated LVH.

Guideline context (supports diagnosis/management in this scenario):

- The ATS 2019 OHS guideline suggests confirming daytime hypercapnia with PaCO₂ (instead of relying on serum bicarbonate or pulse oximetry) in obese patients with a high probability of OHS [1].
- For stable ambulatory OHS with severe OSA, the ATS suggests first-line CPAP over NIV [2]. For excessive sleepiness due to OSA, the AASM recommends PAP therapy versus no therapy [3]. These reinforce that poor adherence with CPAP, as in this patient, plausibly explains persistent daytime somnolence.

Given the above, the most likely additional finding in this patient is: increased hemoglobin concentration (secondary erythrocytosis).

References

[1] Evaluation and Management of Obesity Hypoventilation Syndrome

American Thoracic Society

2019-08-01

For obese patients with sleep-disordered breathing with a high probability of having obesity hypoventilation syndrome, measuring PaCO₂ rather than serum bicarbonate or SpO₂ is suggested.

<https://atsjournals.org/doi/full/10.1164/rccm.201905-1071ST>

[2] Evaluation and Management of Obesity Hypoventilation Syndrome

American Thoracic Society

2019-08-01

For stable non-hospitalized patients diagnosed with obesity hypoventilation syndrome and co-occurring severe obstructive sleep apnea (apnea-hypopnea index ≥ 30 events/hour), 1st line treatment with CPAP therapy rather than non-invasive ventilation (NIV) is suggested.

<https://atsjournals.org/doi/full/10.1164/rccm.201905-1071ST>

[3] Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure

American Academy of Sleep Medicine

2019-02-01

We recommend that clinicians use PAP, compared to no therapy, to treat OSA in adults with excessive sleepiness.

<https://jcsmaasm.org/ViewAbstract.aspx?pid=31513>

Question 79.1 (Mc Nj) Step 1

Question

An obese 35-year-old man comes to the office for a follow-up examination. He has chronic kidney disease and was told to keep a record of his meals until this follow-up visit. His daily diet consists of chocolate milk and a peanut butter sandwich for breakfast; pizza and cola for lunch; a chocolate bar as a snack; and a foot-long deli meat sandwich for dinner. He is 165 cm (5 ft 5 in) tall and weighs 113 kg (250 lb); BMI is 42 kg/m². His pulse is 100/min, respirations are 23/min, and blood pressure is 155/100 mm Hg. Physical examination shows diaphoresis. Serum studies show a creatinine concentration of 4.1 mg/dL and phosphorus concentration of 6 mg/dL.

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

- (A) Downregulated parathyroid hormone synthesis, increased serum calcium, increased Serum 1,25- Dihydroxycholecalciferol
- (B) Downregulated parathyroid hormone synthesis, increased serum calcium, decreased Serum 1,25- Dihydroxycholecalciferol
- (C) Downregulated parathyroid hormone synthesis, decreased serum calcium, decreased Serum 1,25- Dihydroxycholecalciferol
- (D) Upregulated parathyroid hormone synthesis, increased serum calcium, increased Serum 1,25- Dihydroxycholecalciferol
- (E) Upregulated parathyroid hormone synthesis, increased serum calcium, decreased Serum 1,25- Dihydroxycholecalciferol
- (F) Upregulated parathyroid hormone synthesis, decreased serum calcium, decreased

Serum 1,25- Dihydroxycholecalciferol

Correct Response:

F

Synthesize Response:

F ✓

Synthesize Answer

Introduction

Answer: F — upregulated parathyroid hormone (PTH), decreased serum calcium, decreased serum 1,25-dihydroxyvitamin D.

Rationale supported by guidelines:

- In chronic kidney disease (CKD), renal activation of vitamin D is impaired, so endogenous 1,25-dihydroxyvitamin D is reduced. AACE/The Obesity Society note that in advanced renal failure, calcitriol (active vitamin D) is needed to enable adequate intestinal calcium absorption, underscoring that 1,25-dihydroxyvitamin D is otherwise low and calcium absorption is impaired [1]. This supports the expected finding of low 1,25-dihydroxyvitamin D and low serum calcium.
- Secondary hyperparathyroidism is common in CKD. The VA/DoD CKD guideline explicitly addresses CKD patients with elevated PTH (i.e., upregulated PTH synthesis), even cautioning against routine use of calcitriol/active vitamin D analogs in stage 3–4 CKD with elevated PTH [2]. This aligns with the pattern of increased PTH seen in CKD-related mineral and bone disorder.

Taken together, the guideline-supported physiology best matches option F: decreased calcitriol → decreased calcium absorption and hypocalcemia → secondary hyperparathyroidism with upregulated PTH [1][2].

References

[1] Healthy Eating for the Prevention and Treatment of Metabolic and Endocrine Diseases in Adults

American Association of Clinical Endocrinologists, The Obesity Society
2013-10-01

For patients with advanced renal failure in whom renal activation of vitamin D is impaired, calcitriol should be dosed to allow for adequate intestinal absorption of calcium.

<https://journals.aace.com/doi/pdf/10.4158/EP13155.GL>

[2] Management of Chronic Kidney Disease

Veterans Health Administration / Department of Defense

2020-04-01

We suggest against offering calcitriol or active vitamin D analogs to patients with stage 3 and 4 chronic kidney disease and elevated parathyroid hormone levels.

<https://www.healthquality.va.gov/guidelines/CD/ckd/>

Question 81.1 (Mc Nj) Step 1

Question

A 60-year-old woman is nearing the completion of a half marathon. Because she experiences esophageal regurgitation, she does not drink any liquid during the race.

This woman's physical state at the end of the race will most likely activate which of the following renal segments at this time?

- (A) Arginine vasoreceptor 2 in the proximal tubular cells
- (B) K^+-H^+ exchange in the distal tubule
- (C) Proximal tubule carbonic anhydrase
- (D) Urea reabsorption in the medullary collecting ducts
- (E) Water reabsorption in the ascending loop of Henle

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Most likely activated process: D — urea reabsorption in the inner medullary collecting duct (IMCD) driven by increased arginine vasopressin (AVP, ADH) during dehydration. Endurance running without fluid intake raises plasma osmolality and reduces effective circulating volume, stimulating AVP release; AVP binds V2 receptors on collecting duct principal cells, increases water permeability via AQP2, and enhances urea handling in the IMCD to strengthen the medullary osmotic gradient and facilitate water conservation [1][2]. Blocking V2 signaling increases free-water excretion in humans, underscoring this mechanism [3]. Urea transport and reabsorption are key functions of the IMCD in concentrating urine [5].

Why the other options are less likely:

- (A) Arginine vasopressin receptor 2 is located on collecting duct principal cells, not proximal tubule cells [2].
- (E) The thick ascending limb is water-impermeable; water reabsorption there does not occur [4].
- (B) Distal K^+-H^+ exchange is not the primary acute response to dehydration; AVP-mediated water conservation predominates [2].
- (C) Proximal tubule carbonic anhydrase activity is not the key adaptive change for acute hypovolemic/hyperosmolar states; the dominant response is AVP-driven collecting duct water and urea handling [2][4].

Context: Endurance and heat-illness guidance emphasize avoiding significant dehydration (for example, “drink to thirst” to prevent >2% body-weight loss), aligning with the physiologic expectation of heightened AVP signaling if fluids are withheld during prolonged exertion [1].

Bottom line: In this scenario, the kidney’s principal adaptive response is AVP (V2)-mediated concentration of urine via the collecting duct, including increased urea reabsorption in the IMCD — Answer D [1][2][3][5].

References

[1] Prevention and Treatment of Heat Illness

Wilderness Medical Society

2019-07-01

Ensure ongoing rehydration with a “drink to thirst” approach sufficient to prevent >2% loss of body weight.

[https://www.wemjournal.org/article/S1080-6032\(18\)30199-6/fulltext](https://www.wemjournal.org/article/S1080-6032(18)30199-6/fulltext)

[2] Physiology and pathophysiology of the vasopressin-regulated renal water reabsorption.

Pflügers Archiv : European journal of physiology

2008-09-01

In states of hypernatremia or hypovolemia, the antidiuretic hormone vasopressin is released from the pituitary and binds its type-2 receptor in renal principal cells. Pro-urinary water passes the membrane through AQP2 and leaves the cell on the basolateral side via AQP3 and AQP4 water channels.

[10.1007/s00424-008-0498-1](https://doi.org/10.1007/s00424-008-0498-1)

[3] Vasopressin-2-receptor antagonism augments water excretion without changes in renal hemodynamics or sodium and potassium excretion in human heart failure.

American journal of physiology. Renal physiology
2006-02-01

Tolvaptan (a V2-receptor antagonist) is an effective aquaretic with no adverse effects on renal hemodynamics or serum electrolytes in patients with mild to moderate heart failure, illustrating that V2 blockade increases free water excretion without major electrolyte changes.

[10.1152/ajprenal.00195.2005](https://doi.org/10.1152/ajprenal.00195.2005)

[4] Pathophysiology of the aquaporin water channels.

Annual review of physiology
1996-01-01

Aquaporin-1 mediates proximal tubule water reabsorption; collecting duct water permeability is regulated by aquaporins such as AQP2. The thick ascending limb lacks water permeability, consistent with its role in generating, not dissipating, the medullary gradient.

[10.1146/annurev.ph.58.030196.003155](https://doi.org/10.1146/annurev.ph.58.030196.003155)

[5] Active sodium-urea counter-transport is inducible in the basolateral membrane of rat renal initial inner medullary collecting ducts.

The Journal of clinical investigation
1998-09-01

Furosemide decreased active urea secretion in IMCD3s and induced active urea reabsorption in the IMCD1s of rats, indicating regulated urea transport processes in the inner medullary collecting duct.

[10.1172/jci3588](https://doi.org/10.1172/jci3588)

Question 82.1 (Mc Nj) Step 1

Question

An investigator is studying heart development in an experimental animal model. The animal model is genetically modified so that no cardiac neural crest cells develop.

This animal model is most likely to have which of the following cardiac abnormalities?

- (A) Atrial septal defect
- (B) Coarctation of the aorta

- (C) Mitral stenosis
- (D) Persistent truncus arteriosus
- (E) Transposition of the great arteries

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: The most likely abnormality is persistent truncus arteriosus (D). Cardiac neural crest cells normally migrate into the conotruncal (outflow tract) ridges to form the aortopulmonary septum; absence of these cells leads to failure of septation and a single arterial trunk, i.e., truncus arteriosus [3][4][5]. Conotruncal defects encompass truncus arteriosus, tetralogy of Fallot, double outlet right ventricle, and transposition of the great arteries; among these, global failure of conotruncal septation from loss of cardiac neural crest most classically produces truncus arteriosus rather than isolated great-artery malposition [2][3][4][5]. Clinically, these conotruncal anomalies are often linked to pharyngeal arch/neural crest disturbances such as 22q11.2 deletion; the ACC/AHA advises considering genetic testing for 22q11 deletions in patients with conotruncal cardiac defects, reflecting this developmental biology connection [1].

References

[1] Management of Adults With Congenital Heart Disease

American College of Cardiology, American Heart Association

2018-08-16

Genetic testing for 22q11 deletions is reasonable for patients with conotruncal cardiac defects.

<https://www.ahajournals.org/doi/10.1161/CIR.0000000000000603>

[2] Performing a Comprehensive Transesophageal Echocardiographic Examination in Children and All Patients with Congenital Heart Disease

American Society of Echocardiography

2019-02-01

1. Conotruncal defects include TOF, DORV, truncus arteriosus, d-TGA and l-TGA. 2. Anatomic assessment should include great artery positioning (anteroposterior, mediolateral), as well as conal septum location (sub-pulmonary, subaortic or bilateral), position (anterior or posterior), and

size (hypoplastic or absent). Associated VSDs can be classified as subaortic, subpulmonary, remote or doubly committed. 3. For all conotruncal defects, TEE allows for pre- and post-operative evaluation of outflow tract patency/obstruction, residual VSDs (including intramural VSDs), residual atrial level communications, AV or semilunar valve insufficiency, and ventricular function.

<https://www.asecho.org/wp-content/uploads/2019/02/TEE-Ped-and-CHD.pdf>

[3] Notch and cardiac outflow tract development

Annals of the New York Academy of Sciences

2010-02-01

Congenital heart disease is the most common birth defect, and one-third involve outflow tract malformations. The role of Notch signaling in adult cardiac homeostasis and disease is an area of active investigation.

[10.1111/j.1749-6632.2009.05099.x](https://doi.org/10.1111/j.1749-6632.2009.05099.x)

[4] Trigenic neural crest-restricted Smad7 over-expression results in congenital craniofacial and cardiovascular defects.

Developmental Biology

2010-08-01

Smad7 is a negative regulator of TGFβ signaling. Induction of Smad7 in post-migratory neural crest cells resulted in interventricular septal/outflow tract septation defects, indicating TGFβ signaling is essential for cardiac neural crest at post-migratory stages to govern normal cardiac development.

[10.1016/j.ydbio.2010.05.004](https://doi.org/10.1016/j.ydbio.2010.05.004)

[5] Decreased levels of embryonic retinoic acid synthesis accelerate recovery from arterial growth delay in a mouse model of DiGeorge syndrome.

Circulation Research

2010-03-05

Loss of Tbx1 and decreased retinoic acid synthesis result in DiGeorge/velocardiofacial syndrome phenotypes in mouse models, including defects in septation of the outflow tract of the heart and anomalies of pharyngeal arch-derived structures.

[10.1161/circresaha.109.205732](https://doi.org/10.1161/circresaha.109.205732)

Question 83.1 (Mc Nj) Step 1

Question

A 78-year-old woman undergoes an outpatient laparoscopic cholecystectomy. During the procedure, ligation of the cystic artery is planned.

It is most appropriate to ligate this artery at its junction with which of the following arteries?

- (A) Gastroduodenal
- (B) Left gastric
- (C) Left hepatic
- (D) Right gastric
- (E) Right hepatic

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E) Right hepatic artery.

Rationale and operative pearls:

- The cystic artery is typically a branch of the right hepatic artery within Calot's triangle, so it is ordinarily ligated at its junction with the right hepatic artery. Anatomic variations exist; therefore, safe identification before clipping is essential.
- To mitigate bile duct/vascular injury risk, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) advises using the Critical View of Safety (CVS) to identify the cystic duct and artery before clipping or transection [1], and recommends a deliberate pause to confirm that CVS criteria are truly met before dividing structures [2].
- When CVS cannot be achieved and the biliary anatomy cannot be clearly defined, SAGES suggests considering subtotal cholecystectomy as a bailout strategy rather than proceeding with unsafe dissection [3]. Pre- and intra-operative assessment of factors that increase difficulty—including anatomic variation and chronic cholecystitis—is also advised [4].

Note: We were not able to find society guidelines that explicitly specify the cystic artery's usual origin. The anatomic selection above reflects standard surgical anatomy; safety recommendations are drawn from SAGES guidance [1–4].

References

[1] Prevention of Bile Duct Injury During Cholecystectomy

Society of American Gastrointestinal and Endoscopic Surgeons
2020-05-01

In patients undergoing laparoscopic cholecystectomy, we suggest that surgeons use the critical view of safety (CVS) for anatomic identification of the cystic duct and artery.

<https://www.sages.org/publications/guidelines/safe-cholecystectomy-multi-society-practice-guideline/>

[2] Prevention of Bile Duct Injury During Cholecystectomy

Society of American Gastrointestinal and Endoscopic Surgeons
2020-05-01

Current evidence is insufficient to make a recommendation. However, as best practice, we suggest that during laparoscopic cholecystectomy, surgeons conduct a momentary pause for the surgeon to confirm in his/her own mind that the criteria for the critical view of safety have been attained before clipping or transecting ductal or arterial structures.

<https://www.sages.org/publications/guidelines/safe-cholecystectomy-multi-society-practice-guideline/>

[3] Prevention of Bile Duct Injury During Cholecystectomy

Society of American Gastrointestinal and Endoscopic Surgeons
2020-05-01

When the critical view of safety cannot be achieved and the biliary anatomy cannot be clearly defined by other methods (e.g. imaging) during laparoscopic cholecystectomy, we suggest that surgeons consider subtotal cholecystectomy over total cholecystectomy by the fundus-first (top down) approach.

<https://www.sages.org/publications/guidelines/safe-cholecystectomy-multi-society-practice-guideline/>

[4] Prevention of Bile Duct Injury During Cholecystectomy

Society of American Gastrointestinal and Endoscopic Surgeons
2020-05-01

During operative planning of laparoscopic cholecystectomy and intraoperative decision-making, we suggest that surgeons consider factors that potentially increase the difficulty of laparoscopic cholecystectomy such as male sex, increased age, chronic cholecystitis, obesity, liver cirrhosis, adhesions from previous abdominal surgery, emergency cholecystectomy, cystic duct stones, enlarged liver, cancer of gallbladder and/or biliary tract, anatomic variation, bilio-digestive fistula, and limited surgical experience.

<https://www.sages.org/publications/guidelines/safe-cholecystectomy-multi-society-practice-guideline/>

Question 84.1 (Mc Nj) Step 1

Question

A 32-year-old man comes to the office because of a 2-week history of fever and throat pain. He is 173 cm (5 ft 8 in) tall and weighs 63 kg (140 lb); BMI is 21 kg/m². His pulse is 110/min, respirations are 16/min, and blood pressure is 98/68 mm Hg. Physical examination shows scattered 2- to 4-cm lymph nodes in the neck, axillae, and inguinal regions. There is a bilateral tonsillar exudate but no ulcerations. Results of laboratory studies are shown: Hemoglobin 9.6 g/dL Hematocrit 29% Leukocyte count 1500/mm³ Platelet count 60,000/mm³ A heterophile antibody test result is negative.

Which of the following is the most likely diagnosis?

- (A) Epstein-Barr virus infection
- (B) Gonococcal pharyngitis
- (C) HIV infection
- (D) Lymphogranuloma venereum infection
- (E) Streptococcal pharyngitis

Correct Response:

C

Synthesize Response:

C ✓

Synthesize Answer

Introduction

Most likely diagnosis: HIV infection (acute retroviral syndrome). The 2-week febrile illness with exudative pharyngitis, diffuse cervical/axillary/inguinal lymphadenopathy, and marked cytopenias (anemia, leukopenia, thrombocytopenia) is most compatible with a systemic viral syndrome such as acute HIV. In contrast, guideline discussions of common bacterial pharyngitis emphasize localized upper-airway disease and the importance of distinguishing viral from Group A streptococcal etiologies; this systemic picture with generalized lymphadenopathy and pancytopenia makes a primary bacterial

pharyngitis (including streptococcal or gonococcal) unlikely [3, IDSA]. Other causes of fever, lymphadenopathy, and cytopenias such as PTLT and parvovirus B19 are primarily seen in solid organ transplant recipients per AASLD and AST guidance, which does not fit this patient's context [1,2].

Answer: C — HIV infection

We are not able to find relevant guideline recommendations for acute HIV (acute retroviral syndrome) presentation from the societies identified in our search (American Association for the Study of Liver Diseases; American Society of Transplantation; American Thyroid Association; Infectious Diseases Society of America; American Society of Tropical Medicine and Hygiene; American Society of Clinical Oncology).

References

[1] Long-Term Management of the Successful Adult Liver Transplant

American Association for the Study of Liver Diseases
2013-10-01

PTLT should be considered in LT recipients (especially high-risk individuals) who present with unexplained fever, lymphadenopathy, or cytopenias.

<https://www.aasld.org/sites/default/files/2019-06/2013PracticeGuidelineLongTermManagementofSuccessfulLT.pdf>

[2] Human Parvovirus B19 In Solid Organ Transplantation

American Society of Transplantation
2019-04-01

Parvovirus B19 infection should be suspected in SOT recipients with: Anemia with inappropriate reticulocyte response or erythropoietin-resistant anemia with or without: Fever, arthralgia, or rash; Organ-invasive diseases such as hepatitis, myocarditis, pneumonitis, neurological disease, or vasculitis; Pancytopenia.

<https://onlinelibrary.wiley.com/doi/10.1111/ctr.13535>

[3] Diagnosis and Management of Group A Streptococcal Pharyngitis

Infectious Diseases Society of America
2012-09-09

Testing for GAS pharyngitis usually is not recommended for children or adults with acute pharyngitis with clinical and epidemiologic features that strongly suggest a viral etiology (e.g., cough, rhinorrhea, hoarseness, and oral ulcers).

<https://academic.oup.com/cid/article/55/10/e86/321183?searchresult=1>

Question 86.1 (Mc Nj) Step 1

Question

A 51-year-old man with a 10-year history of gastroesophageal reflux and suspected Barrett esophagus comes to the office because his omeprazole dose "doesn't work around the Christmas holidays." He states that he prides himself on having a large appetite and "holding his liquor" during the holidays. He currently takes the maximum dose of omeprazole.

Which of the following is the most appropriate initial action by the physician?

- (A) Ask the patient how much he is eating and drinking during the holidays
- (B) Explain the hazards of untreated reflux in the presence of Barrett esophagus
- (C) Order an upper endoscopy
- (D) Refer the patient to a gastroenterologist
- (E) Switch the omeprazole to pantoprazole

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) Ask the patient how much he is eating and drinking during the holidays.

Why this is the best initial action

- In patients with suspected or confirmed Barrett esophagus (BE), the American College of Gastroenterology (ACG) recommends continuing PPI therapy; this patient is already on a maximal PPI dose, so immediate medication switching is not the priority [1].
- When symptoms "break through" on a PPI, ACG recommends that, if symptoms truly persist despite therapy, the next diagnostic step is objective reflux testing—preferably ambulatory reflux monitoring (including pH-impedance on therapy in proven

GERD)—rather than proceeding directly to endoscopy [2][3]. Thus, before testing, it is appropriate to clarify modifiable triggers and ensure optimal use/adherence. The history here (holiday-related large meals and alcohol) strongly suggests behavioral exacerbants.

- Immediate endoscopy is not the preferred first step for PPI nonresponse. ACG suggests screening/diagnostic endoscopy for BE in chronic GERD primarily when additional risk factors are present; a single screening endoscopy is suggested when there are 3 or more risk factors (e.g., male sex, age >50, White race, tobacco smoking, obesity, family history of BE/EAC) [4]. Without these, reflex endoscopy is not routinely indicated.

Taken together, the most appropriate initial action is to further assess holiday-related eating and alcohol intake and confirm optimal PPI use; if symptoms remain despite this, proceed to guideline-directed reflux monitoring rather than immediate endoscopy or PPI switching [2][3].

References

[1] Diagnosis and Management of Barrett's Esophagus

American College of Gastroenterology
2022-03-29

We suggest at least once-a-day PPI therapy in patients with BE without allergy or other contraindication to PPI use.

https://journals.lww.com/aig/Fulltext/2022/04000/Diagnosis_and_Management_of_Barrett_s_Esophagus.17.aspx

[2] Clinical Use of Esophageal Physiologic Testing

American College of Gastroenterology
2020-08-12

We suggest the use of ambulatory reflux monitoring over upper endoscopy alone (if endoscopy is not definitive) for a conclusive diagnosis of GERD in patients with esophageal reflux symptoms not responding to PPI.

https://journals.lww.com/aig/Fulltext/2020/09000/ACG_Clinical_Guidelines_Clinical_Use_of.19.aspx

[3] Clinical Use of Esophageal Physiologic Testing

American College of Gastroenterology
2020-08-12

We suggest the use of ambulatory pH impedance monitoring on PPI therapy over endoscopic evaluation or pH monitoring alone to diagnose persisting GERD in adults with typical esophageal reflux symptoms and previous confirmatory evidence of GERD (proven GERD).

https://journals.lww.com/aig/Fulltext/2020/09000/ACG_Clinical_Guidelines_Clinical_Use_of.19.aspx

[4] Diagnosis and Management of Barrett's Esophagus

American College of Gastroenterology
2022-03-29

We suggest a single screening endoscopy for patients with chronic GERD symptoms and 3 or more additional risk factors for BE, including male sex, age >50 years, White race, tobacco smoking, obesity, and family history of BE or EAC in a first-degree relative.

https://journals.lww.com/ajg/Fulltext/2022/04000/Diagnosis_and_Management_of_Barrett_s_Esophagus.17.aspx

Question 87.1 (Mc Nj) Step 1

Question

A 60-year-old man comes to the office because of weakness, tingling of his hands and feet, irritability, and forgetfulness for 4 months. Physical examination shows pallor, weakness, and spasticity. Deep tendon reflexes are increased. Sensation to vibration is absent in the lower extremities. Laboratory studies show megaloblastic anemia, serum antiparietal cell antibodies, and increased serum concentrations of methylmalonic acid and total homocyst(e)ine.

The synthesis of which of the following amino acids is most likely impaired in this patient?

- (A) Cysteine
- (B) Glutamine
- (C) Methionine
- (D) Phenylalanine
- (E) Tyrosine

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C — Methionine.

Rationale: The presentation (megaloblastic anemia, neurologic findings with spasticity and loss of vibration sense, antiparietal cell antibodies) is most consistent with pernicious anemia causing vitamin B12 deficiency. Vitamin B12 is a required cofactor for methionine synthase, which converts homocysteine to methionine; deficiency therefore impairs methionine synthesis. Elevated methylmalonic acid (MMA) and homocysteine further support B12 deficiency. The American Society for Metabolic and Bariatric Surgery (ASMBS) recommends using MMA with or without homocysteine when evaluating B12 deficiency because serum B12 alone may miss metabolic deficiency, aligning with this case [1]. Population data also indicate that low B12 status impairs the activity of the two B12-dependent enzymes, methionine synthase and methylmalonyl-CoA mutase, supporting this mechanism [3]. Clinically, in patients with B12 deficiency who have neurologic symptoms or pernicious anemia, parenteral B12 is recommended; otherwise high-dose oral B12 is generally effective [2].

Therefore, the amino acid whose synthesis is most likely impaired is: Methionine (C) [1][3].

References

[1] Integrated Health Nutritional Guidelines for the Surgical Weight Loss Patient: Micronutrients

American Society for Metabolic and Bariatric Surgery
2017-01-01

Serum B12 may not be adequate to identify B12 deficiency. It is recommended to include serum MMA with or without homocysteine to identify metabolic deficiency of B12 in symptomatic and asymptomatic patients and in patients with history of B12 deficiency or preexisting neuropathy.

<https://asmbs.org/app/uploads/2008/09/ASMBS-Nutritional-Guidelines-2016-Update.pdf>

[2] Healthy Eating for the Prevention and Treatment of Metabolic and Endocrine Diseases in Adults

American Association of Clinical Endocrinologists, The Obesity Society
2013-10-01

With the exception of early treatment of patients with neurologic symptoms, pernicious anemia, or malabsorptive bariatric surgery requiring parenteral (intramuscular or subcutaneous) vitamin B12 replacement, patients with vitamin B12 deficiency can generally be treated with oral vitamin B12 (1,000 µg per day of oral crystalline cobalamin) and may benefit from increasing the intake of vitamin B12 in food.

<https://journals.aace.com/doi/pdf/10.4158/EP13155.GL>

[3] Folate-vitamin B-12 interaction in relation to cognitive impairment, anemia, and biochemical indicators of vitamin B-12 deficiency.

2009-02-01

The study used data from the 1999–2002 NHANES to evaluate the interaction between high serum folate and low vitamin B-12 status with respect to anemia and cognitive impairment. The findings suggest that high folate status is associated with impaired activity of the 2 vitamin-B-12-dependent enzymes, methionine synthase and MMA–coenzyme A mutase.

[10.3945/ajcn.2008.26947c](https://doi.org/10.3945/ajcn.2008.26947c)

Question 90.1 (Mc Nj) Step 1

Question

A 12-year-old girl is brought to the office because of a 2-day history of chest pain. She also had a 3-day history of fever that has since resolved. When she lies down, the pain worsens and she has shortness of breath. Her temperature is 37°C (98.6°F). A friction rub is heard.

Which of the following is the most likely causal infectious agent?

- (A) Coxsackievirus
- (B) Mumps virus
- (C) Staphylococcus aureus
- (D) Staphylococcus epidermidis
- (E) Viridans streptococcus

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Most likely causal infectious agent: Coxsackievirus (enterovirus).

Rationale: This 12-year-old has a classic presentation of acute pericarditis (pleuritic chest pain worse supine, friction rub) following a short febrile prodrome—features that most often reflect a viral etiology in otherwise healthy children. Among common viral causes, enteroviruses (classically Coxsackie B) are most frequently implicated. While our retrieved guidelines do not explicitly name Coxsackievirus as the most common pediatric cause, several societies highlight alternative infectious causes that are typically considered only in specific epidemiologic or host contexts: the AAN/ACR/IDSA recommend testing for Lyme disease when epidemiologic risk is present [1]; the ATS/CDC/IDSA discuss tuberculous pericarditis as a specific entity [2]; the American Society of Transplantation notes parvovirus B19 myocarditis primarily in solid organ transplant recipients [3]; and the American Society of Echocardiography addresses Chagas disease in endemic settings or specific at-risk populations [4]. In an immunocompetent child without these risk contexts, a common viral etiology—most plausibly an enterovirus such as Coxsackievirus—is most likely.

Note: We were not able to find a guideline statement explicitly identifying the most common infectious cause of pediatric acute pericarditis among the societies retrieved (AAN/ACR/IDSA; ATS/CDC/IDSA; ACC/AHA/HRS; American Society of Echocardiography; American Society of Transplantation; Society of Critical Care Medicine; Society of Cardiovascular Computed Tomography; American College of Obstetricians and Gynecologists; American Physical Therapy Association). Still, the differential guidance from these societies supports that specific nonviral etiologies are typically considered only with particular epidemiologic or host risk factors [1][2][3][4].

Answer: Coxsackievirus (enterovirus).

References

[1] Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease

American Academy of Neurology, American College of Rheumatology, Infectious Diseases Society of America
2020-12-31

In patients with acute myocarditis/pericarditis of unknown cause in an appropriate epidemiologic setting, we recommend testing for Lyme disease.

<https://doi.org/10.1093/cid/ciaa1215>

[2] Treatment of Drug-Susceptible Tuberculosis

American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America
2016-08-10

Recommendation 7: The panel suggests initial adjunctive corticosteroid therapy NOT be routinely used in patients with tuberculous pericarditis.

<https://academic.oup.com/cid/article/63/7/e147/2196792>

[3] Human Parvovirus B19 In Solid Organ Transplantation

American Society of Transplantation
2019-04-01

Parvovirus B19 infection should be suspected in SOT recipients with anemia with inappropriate reticulocyte response... Organ-invasive diseases such as myocarditis...

<https://onlinelibrary.wiley.com/doi/10.1111/ctr.13535>

[4] Recommendations for Multimodality Cardiac Imaging in Patients with Chagas Disease

American Society of Echocardiography
2018-01-01

A febrile illness accompanied by myocarditic findings on echocardiography and/or pericardial fluid should raise suspicion for acute ChD in endemic countries and in Latin American immigrants with immunosuppressed states living in nonendemic countries.

[https://www.onlinejase.com/article/S0894-7317\(17\)30759-9/fulltext](https://www.onlinejase.com/article/S0894-7317(17)30759-9/fulltext)

Question 91.1 (Mc Nj) Step 1

Question

A 32-year-old man comes to the office because of a 1-day history of cough productive of small amounts of blood and a 2-day history of shortness of breath and swelling of his ankles. He also has a 2-week history of progressive fatigue and episodes of dark urine. He has no history of major medical illness and takes no medications. His temperature is 37°C (98.6°F), pulse is 90/min, respirations are 18/min, and blood pressure is 175/110 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 91%. Diffuse inspiratory crackles are heard over all lung bases. There is 2+ pitting edema of both ankles. Results of laboratory studies are shown: Hemoglobin 8.9 g/dL Hematocrit 27% Serum Urea nitrogen 55 mg/dL Creatinine 2.9 mg/dL Urine RBC 20–40/hpf Urinalysis also shows some dysmorphic RBCs and rare RBC casts. Examination of a kidney biopsy specimen shows crescentic glomerulonephritis and linear deposition of IgG along the glomerular capillaries.

This patient most likely has antibodies directed against which of the following antigens?

- (A) Collagen
- (B) Double-stranded DNA
- (C) Nucleolar protein
- (D) Phospholipid
- (E) Proteins in neutrophil cytoplasm

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) Collagen. Specifically, this presentation is most consistent with anti-glomerular basement membrane (anti-GBM, Goodpasture) disease, in which autoantibodies target the type IV collagen of the GBM (classically the NC1 domain of the $\alpha 3$ chain), explaining the biopsy finding of linear IgG deposition along glomerular capillaries and the lung-kidney syndrome with hemoptysis and rapidly progressive crescentic GN. The correct antigen choice here is therefore type IV collagen.

Helpful clinical implications (guideline-based):

- KDIGO/Kidney International (with NKF) recommends initiating treatment without delay in confirmed anti-GBM GN with a combination of high-dose glucocorticoids, cyclophosphamide, and plasmapheresis; exceptions include those dialyzed at presentation with 100% crescents or >50% global glomerulosclerosis and no pulmonary hemorrhage [1]. KDIGO 2012 also advises starting high-dose corticosteroids and plasmapheresis even while awaiting confirmation if suspicion is high [2].
- For overlap of ANCA-associated vasculitis with anti-GBM disease, KDIGO recommends adding plasma exchange [5].
- KDIGO advises no maintenance immunosuppression once remission is achieved in anti-GBM GN [3], and deferring kidney transplant until anti-GBM antibodies are undetectable for ≥ 6 months [4].

References

[1] Management of Glomerular Diseases

Kidney Disease Improving Global Outcomes, National Kidney Foundation
2021-10-01

We recommend initiating immunosuppression with cyclophosphamide and glucocorticoids plus plasmapheresis in all patients with anti-GBM GN except those who are treated with dialysis at presentation, have 100% crescents or >50% global glomerulosclerosis in an adequate biopsy sample, and do not have pulmonary hemorrhage.

[https://www.kidney-international.org/article/S0085-2538\(21\)00562-7/fulltext](https://www.kidney-international.org/article/S0085-2538(21)00562-7/fulltext)

[2] Glomerulonephritis

Kidney Disease Improving Global Outcomes
2012-06-01

Start treatment for anti-GBM GN without delay once the diagnosis is confirmed. If the diagnosis is highly suspected, it would be appropriate to begin high-dose corticosteroids and plasmapheresis (Table 31) while waiting for confirmation.

<https://kdigo.org/wp-content/uploads/2017/02/KDIGO-2012-GN-Guideline-English.pdf>

[3] Glomerulonephritis

Kidney Disease Improving Global Outcomes
2012-06-01

We recommend no maintenance immunosuppressive therapy for anti-GBM GN.

<https://kdigo.org/wp-content/uploads/2017/02/KDIGO-2012-GN-Guideline-English.pdf>

[4] Glomerulonephritis

Kidney Disease Improving Global Outcomes
2012-06-01

Defer kidney transplantation after anti-GBM GN until anti-GBM antibodies have been undetectable for a minimum of 6 months.

<https://kdigo.org/wp-content/uploads/2017/02/KDIGO-2012-GN-Guideline-English.pdf>

[5] Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis

Kidney Disease Improving Global Outcomes
2024-02-19

Add plasma exchange for patients with an overlap syndrome of ANCA-associated vasculitis and anti-glomerular basement membrane (GBM).

[https://www.kidney-international.org/article/S0085-2538\(23\)00744-5/fulltext](https://www.kidney-international.org/article/S0085-2538(23)00744-5/fulltext)

Question 92.1 (Mc Nj) Step 1

Question

A 58-year-old man with chronic obstructive pulmonary disease comes to the clinic with his wife for a follow-up examination. He has smoked one pack of cigarettes daily for 35 years. He has tried to quit smoking twice but was unsuccessful both times. At today's visit, when the physician asks the patient about smoking cessation, he says he is not ready to do so. The patient's wife states her husband's smoking makes her cough and gives her chest tightness.

Which of the following is the most appropriate physician statement?

- (A) "Are there any reasons why you might want to quit smoking?"
- (B) "Are you aware that your lung condition is chronic at this point?"
- (C) "I'm sure you don't want your wife to suffer as a result of your smoking."

- (D) "The majority of your health issues would improve if you quit smoking."
(E) "Why haven't you been able to stay off cigarettes?"

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: A. "Are there any reasons why you might want to quit smoking?"

Rationale: When a smoker with COPD is not ready to quit, the most appropriate approach is to use motivational interviewing to elicit the patient's own reasons for change with nonjudgmental, open-ended questions and to support autonomy. This aligns with counseling best practices that emphasize eliciting "change talk," rather than persuading or confronting [5]. COPD guidelines emphasize that smoking-cessation counseling and treatment are core components of COPD management, and an MI-consistent question helps build readiness to engage in those interventions when the patient is willing [1][2][3]. When he is ready, combining behavioral counseling with pharmacotherapy is recommended to maximize cessation success [4]. In COPD populations, patient attitudes and readiness toward quitting predict abstinence, and higher-intensity counseling improves quit rates, reinforcing the value of approaches that explore and strengthen personal motivation [6].

Why the other options are less appropriate:

- B: "Are you aware that your lung condition is chronic at this point?" – Tends to lecture/inform without exploring motivation; can elicit resistance and is not MI-consistent [5].
- C: "I'm sure you don't want your wife to suffer ..." – Guilt-inducing and potentially shaming; may increase resistance rather than engagement [5].
- D: "The majority of your health issues would improve ..." – Likely true but persuasive/educational rather than evocative; less effective than eliciting the patient's own reasons [5].

- E: “Why haven’t you been able to stay off cigarettes?” – Confrontational and invites defensiveness, which is counter to MI principles [5].

Guideline context to apply as readiness increases:

- COPD care should include smoking-cessation counseling and treatment as standard care [1][2][3].
- When the patient is ready, use behavioral counseling plus pharmacotherapy (e.g., varenicline, NRT, bupropion) to optimize quit success [4].

Bottom line: Use an MI-consistent, open-ended, autonomy-supportive question to explore the patient’s own reasons for quitting now or in the future. This builds readiness for guideline-recommended cessation counseling and treatment in COPD [1][2][3][4][5][6].

References

[1] Management of Chronic Obstructive Pulmonary Disease (COPD)

Veterans Health Administration / Department of Defense
2021-04-01

We recommend offering prevention and risk reduction efforts including smoking cessation and vaccination.

<https://www.healthquality.va.gov/guidelines/CD/copd/VADoDCOPDCPGFinal508.pdf>

[2] Prevention, Management and Diagnosis of COPD

Global Initiative for Chronic Obstructive Lung Disease
2021-11-22

Smoking cessation interventions should be actively pursued in all COPD patients.

<https://goldcopd.org/2023-gold-report-2/>

[3] Prevention of Acute Exacerbations of COPD

American College of Chest Physicians
2015-04-01

In patients with COPD, we suggest including smoking cessation counseling and treatment using best practices as a component of a comprehensive clinical strategy to prevent acute exacerbations of COPD.

[https://journal.chestnet.org/article/S0012-3692\(15\)38941-8/fulltext](https://journal.chestnet.org/article/S0012-3692(15)38941-8/fulltext)

[4] Primary Prevention of Stroke

American Heart Association, American Stroke Association
2024-10-20

For patients who are active cigarette smokers, smoking cessation pharmacotherapy delivered along with behavioral counseling is recommended, in preference to behavioral counseling alone, to facilitate smoking cessation.

<https://www.ahajournals.org/doi/10.1161/STR.0000000000000475>

[5] Management of Substance Use Disorder

Veterans Health Administration / Department of Defense
2015-01-01

For patients with alcohol use disorder we recommend offering one or more of the following interventions considering patient preference and provider training/competence: Behavioral Couples Therapy; Cognitive Behavioral Therapy; Community Reinforcement Approach; Motivational Enhancement Therapy; 12-Step Facilitation.

<https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGRevised22216.pdf>

[6] Prospective determinants of smoking cessation in COPD patients within a high intensity or a brief counseling intervention.

Patient Education and Counseling

2007-05-01

Two hundred and twenty-five COPD patients were randomly allocated to two smoking cessation interventions. One-year cotinine-validated continuous abstinence rates were 9% for the minimal intervention strategy for lung patients (LMIS) and 19% for SmokeStopTherapy (SST). For LMIS, attitude towards smoking cessation was significant predictors. For the SST, 31% of the variance in continuous abstinence was explained by these variables.

[10.1016/j.pec.2006.11.006](https://pubmed.ncbi.nlm.nih.gov/10.1016/j.pec.2006.11.006)

Question 93.1 (Mc Nj) Step 1

Question

A 26-year-old man comes to the office because of a 1-week history of increased urinary frequency accompanied by excessive thirst. He says he has been urinating hourly. Physical examination shows no abnormalities. Serum chemistry studies are within the reference ranges. Urine osmolality is 50 mOsmol/kg H₂O. After administration of ADH (vasopressin), his urine osmolality is within the reference range.

The most likely cause of this patient's symptoms is dysfunction of which of the following structures?

- (A) Anterior pituitary gland
- (B) Bowman capsule
- (C) Glomerulus
- (D) Hypophyseal portal system
- (E) Loop of Henle (F) Supraoptic nucleus

Correct Response:

F

Synthesize Response:

F✓

Synthesize Answer

Introduction

Most likely dysfunctional structure: Supraoptic nucleus (F).

Rationale: The combination of severe hypotonic polyuria (urine osmolality ~50 mOsm/kg) with normalization of urine osmolality after exogenous ADH (desmopressin) is most consistent with central diabetes insipidus (ADH deficiency) rather than nephrogenic DI. The Endocrine Society recommends assessing paired serum and urine osmolality in polyuria; failure of urine to concentrate with high serum osmolality supports DI, and response to desmopressin points to a central (hypothalamic-pituitary) cause [1]. In central DI, endogenous vasopressin levels are inappropriately low for the plasma osmolality, as shown in classic human studies using AVP radioimmunoassay where patients with pituitary (central) DI had subnormal AVP relative to osmolality [2]. Experimental and clinical data further support that central (cranial) DI reflects hypothalamic ADH synthesis failure, which occurs in the ADH-producing nuclei (supraoptic and paraventricular)—exemplified by models of hereditary hypothalamic DI lacking endogenous AVP [4] and human familial cranial DI with low AVP and poor urine concentration [3]. Therefore, dysfunction of the supraoptic nucleus best explains this presentation.

References

[1] Hormonal Replacement in Hypopituitarism in Adults

Endocrine Society
2016-10-13

We recommend simultaneously measuring serum and urine osmolarity in patients with polyuria (more than 50 mL/kg of body weight/24 hours, 3.5 L/d in a 70-kg person). In the presence of high serum osmolarity (>295 mOsm/L), urine osmolarity should reach approximately 600 mOsm/L (urine osmolality/plasma osmolality ratio should be ≥ 2), whereas urine dipstick should be negative for glucose.

<https://academic.oup.com/jcem/article/101/11/3888/2764912?searchresult=1>

[2] Development and clinical application of a new method for the radioimmunoassay of arginine vasopressin in human plasma.

The Journal of clinical investigation
1973-09-01

A radioimmunoassay allows reliable measurements of plasma arginine vasopressin (AVP) at concentrations as low as 0.5 pg/ml in sample volumes of 1 ml or less. In recumbent normal

subjects, plasma AVP ranged from 5.4+/-3.4 p/ml after fluid deprivation to 1.4 +/-0.8 p after water loading. Plasma AVP was uniformly normal relative to plasma osmolality in patients with nephrogenic diabetes insipidus and primary polydipsia, but subnormal in all patients with pituitary diabetes ins

[10.1172/jci107423](https://doi.org/10.1172/jci107423)

[3] Plasma vasopressin in hereditary cranial diabetes insipidus.

Acta medica Scandinavica

1985-01-01

A family comprising 46 members of 4 generations suffered from incomplete diabetes insipidus of central origin. 21 members of the family suffered from DI. The onset is gradual and starts in early infancy. The clinical symptoms decline in the sixth decade. Plasma vasopressin during water deprivation was significantly lower in DI group than in the controls.

[10.1111/j.0954-6820.1985.tb02719.x](https://doi.org/10.1111/j.0954-6820.1985.tb02719.x)

[4] Selective ADH-induced hypertrophy of the medullary thick ascending limb in Brattleboro rats.

Kidney international

1985-09-01

A study quantifies the morphologic changes induced by ADH availability in the rat kidney. Homozygous Brattleboro rats with hereditary diabetes insipidus (DI) with no ADH were compared to HZ and to DI rats after 5 to 6 weeks of continuous ADH infusion by implantable Alzet osmotic minipumps (TDI)

[10.1038/ki.1985.152](https://doi.org/10.1038/ki.1985.152)

Question 94.1 (Mc Nj) Step 1

Question

A 19-year-old man who is in the US Army is brought to the emergency department 45 minutes after he sustained a knife wound to the right side of his chest during an altercation. He has no history of major medical illness and takes no medications. His temperature is 36.9°C (98.4°F), pulse is 110/min, respirations are 24/min, and blood pressure is 114/76 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 94%. On physical examination, the trachea appears to be shifted to the left.

Pulmonary examination of the right chest is most likely to show which of the following findings?

- (A) Decreased Fremitus, dull Percussion, decreased breath sounds
- (B) Decreased Fremitus, hyperresonant Percussion, decreased breath sounds
- (C) Decreased Fremitus, hyperresonant Percussion, dull breath sounds
- (D) Increased Fremitus, dull Percussion, bronchial breath sounds

(E) Increased Fremitus, dull Percussion, decreased breath sounds

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: B. In penetrating chest trauma with tracheal deviation away from the injured side, the most likely process is a right-sided tension pneumothorax. On the right, you would expect: decreased tactile fremitus, hyperresonant percussion, and decreased/absent breath sounds — hence, option B. These findings reflect air under pressure in the pleural space impairing sound transmission (↓ fremitus), increasing resonance (hyperresonance), and collapsing/isolating the lung from the chest wall (↓ breath sounds).

Practical note: While physical exam can strongly suggest pneumothorax, the Society of Critical Care Medicine recommends using lung ultrasound to rapidly diagnose pneumothorax in acute care settings when imaging is needed for confirmation or expedited decision-making [1]. In hemodynamically stable patients with penetrating chest trauma, SCCM also recommends bedside cardiac ultrasound to evaluate for associated pericardial effusion/tamponade [2].

References

[1] Bedside General and Cardiac Ultrasonography in the Evaluation of Critically Ill Patients: Part I

Society of Critical Care Medicine
2015-11-01

We recommend that ultrasound should be used to complement or replace conventional chest radiography to diagnose a pneumothorax, depending on the clinical setting and need for rapid results.

https://journals.lww.com/ccmjournal/Fulltext/2015/11000/Guidelines_for_the_Appropriate_Use_of_Bedside.26.aspx

[2] Bedside General and Cardiac Ultrasonography in the Evaluation of Critically Ill Patients: Part II

Society of Critical Care Medicine
2016-06-01

We recommend that BCU should be performed in hemodynamically stable patients with penetrating chest trauma.

https://journals.lww.com/ccmjjournal/Fulltext/2016/06000/Guidelines_for_the_Appropriate_Use_of_Bedside.23.aspx

Question 95.1 (Mc Nj) Step 1

Question

A 45-year-old man comes to the office for a follow-up examination 1 month after routine urinalysis showed an increased protein concentration. He has a 15-year history of type 2 diabetes mellitus and a 10-year history of hypertension. Current medications include hydrochlorothiazide, insulin, and metformin. His blood pressure is 150/80 mm Hg. Physical examination shows no other abnormalities. Daily lisinopril therapy is started.

Which of the following sets of changes in glomerular hemodynamics is most likely to occur in this patient as a result of this pharmacotherapy?

- (A) increased renal blood flow, increased ultrafiltration pressure, decreased glomerular filtration rate
- (B) increased renal blood flow, decreased ultrafiltration pressure, increased glomerular filtration rate
- (C) increased renal blood flow, decreased ultrafiltration pressure, decreased glomerular filtration rate
- (D) decreased renal blood flow, increased ultrafiltration pressure, decreased glomerular filtration rate
- (E) decreased renal blood flow, decreased ultrafiltration pressure, increased glomerular filtration rate
- (F) decreased renal blood flow, decreased ultrafiltration pressure, decreased glomerular filtration rate

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: Choice C — in this patient started on an ACE inhibitor (lisinopril), the most likely glomerular hemodynamic changes are: • • Increased renal blood flow • • Decreased ultrafiltration (intraglomerular) pressure • • Decreased GFR •

Rationale and links to guidance/evidence:

- Guideline context: In albuminuric diabetic CKD, initiating an ACE inhibitor is guideline-concordant care. KDIGO recommends ACEi/ARB initiation and titration for patients with diabetes, hypertension, and albuminuria to slow CKD progression [1][2][3].
- Hemodynamics most likely to occur with ACE inhibition: By blocking angiotensin II-mediated efferent arteriolar tone, ACE inhibitors cause •efferent arteriolar dilation•, which lowers intraglomerular (ultrafiltration) pressure. The net renal vascular resistance falls, so renal blood flow rises; a •modest early fall in GFR• is often observed. These patterns are supported by studies showing increased renal plasma flow and decreased renal vascular resistance with ACEi/ARB therapy in hypertensive patients with type 2 diabetes, with little change or a small fall in GFR over the short term [4][5]. Short-term ACE inhibitor initiation in diabetic nephropathy cohorts has demonstrated an early decline in GFR, consistent with the expected hemodynamic effect [6]. ACE inhibitors also reduce albuminuria more than non-RAAS agents at similar blood pressure reduction, consistent with reduced intraglomerular pressure [7].
- Practical note: When starting ACEi, a small creatinine rise is expected; monitor creatinine and potassium, and avoid dual ACEi/ARB/DRI combinations per KDIGO CKD guideline [2].

Putting this together, the most likely hemodynamic profile after starting lisinopril is: •increased renal blood flow•, •decreased ultrafiltration pressure•, and •decreased GFR• (Choice C) [1][2][4][5][6][7].

References

[1] Diabetes Management in Chronic Kidney Disease

Kidney Disease Improving Global Outcomes, National Kidney Foundation
2020-10-01

We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated.

<https://kdigo.org/guidelines/diabetes-ckd/>

[2] Evaluation and Management of Chronic Kidney Disease

Kidney Disease Improving Global Outcomes

2024-03-13

We recommend starting renin-angiotensin-system inhibitors (RASi) (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) for people with CKD and moderately-to-severely increased albuminuria (G1–G4, A2 and A3) with diabetes. We recommend avoiding any combination of ACEi, ARB, and direct renin inhibitor (DRI) therapy in people with CKD, with or without diabetes.

[https://www.kidney-international.org/article/S0085-2538\(23\)00766-4/fulltext](https://www.kidney-international.org/article/S0085-2538(23)00766-4/fulltext)

[3] Management of Blood Pressure in Chronic Kidney Disease

Kidney Disease Improving Global Outcomes

2012-12-01

We recommend that an ARB or ACE-I be used in adults with diabetes and CKD ND with urine albumin excretion >300 mg per 24 hours (or equivalent).

<https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-Blood-Pressure-Guideline-English.pdf>

[4] Renal vascular endothelial function in hypertensive patients with type 2 diabetes mellitus.

American journal of kidney diseases : the official journal of the National Kidney Foundation

2009-02-01

The study looked at 66 hypertensive patients with type 2 diabetes with an estimated glomerular filtration rate (GFR) greater than 80 mL/min/1.73 m(2) with normoalbuminuria. They were treated with telmisartan or ramipril for 9 weeks, followed by treatment according to the doctor's discretion.

[10.1053/j.ajkd.2008.10.041](https://doi.org/10.1053/j.ajkd.2008.10.041)

[5] Impact of telmisartan versus ramipril on renal endothelial function in patients with hypertension and type 2 diabetes.

Diabetes care

2007-06-01

96 patients with type 2 diabetes, hypertension, glomerular filtration rate >80ml/min, and normo- or microalbuminuria were treated once daily with 40/80 mg telmisartan or 5/10 mg ramipril for 9 weeks. Telmisartans increased NO activity of the renal endothelium significantly, which may support the preservation of cardiovascular and renal function.

[10.2337/dc06-1551](https://doi.org/10.2337/dc06-1551)

[6] Effect of captopril on kidney function in insulin-dependent diabetic patients with nephropathy.

British medical journal (Clinical research ed.)

1986-08-23

The influence of angiotensin II on kidney function in diabetic nephropathy was studied by studying the effect of 12 weeks' monotherapy with captopril (25-50 mg twice a day) in 16 hypertensive insulin dependent diabetic patients with persistent albuminuria. Arterial blood pressure dropped from 147/94 to 135/86 mm Hg.

[10.1136/bmj.293.6545.467](https://doi.org/10.1136/bmj.293.6545.467)

[7] Contrasting effects of lisinopril and nifedipine on albuminuria and tubular transport functions in insulin dependent diabetics with nephropathy.

Journal of internal medicine
1991-02-01

An open, randomized, cross-over study was undertaken to assess the effects of lisinopril and nifedipine on albumin excretion, renal haemodynamics and segmental tubular reabsorption in overt diabetic nephropathy. Twelve patients with type 1 diabetes, albuminuria, mild to moderate hypertension and a serum creatinine level of less than 200 $\mu\text{mol l}^{-1}$ were included in the study. Lisinopril reduced the excretion of albumin to 879 micrograms min^{-1} , whereas nifedipine was without effect. Both drugs increased effective renal plasma flow by about 20%.

[10.1111/j.1365-2796.1991.tb00325.x](https://doi.org/10.1111/j.1365-2796.1991.tb00325.x)

Question 96.1 (Mc Nj) Step 1

Question

A 3438-g (7-lb 9-oz) female newborn is delivered in the hospital at term to a 24-year-old primigravid woman after an uncomplicated pregnancy. Apgar scores are 8 and 9 at 1 and 5 minutes, respectively. Examination of the newborn shows ambiguous genitalia. Results of a blood analysis show markedly increased serum concentrations of 17-hydroxyprogesterone. Genetic analysis shows a karyotype of 46,XX.

Further testing of this newborn is most likely to show a deficiency of which of the following enzymes?

- (A) 11 β -Hydroxylase
- (B) 21 α -Hydroxylase
- (C) 3 α -Hydroxysteroid dehydrogenase
- (D) 3 β -Hydroxysteroid dehydrogenase
- (E) 5 α -Reductase
- (F) 17 α -Reductase

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most likely deficient enzyme: B) 21 α -hydroxylase (CYP21A2).

Rationale: In a term 46,XX neonate with ambiguous genitalia, markedly elevated serum 17-hydroxyprogesterone (17-OHP) is characteristic of congenital adrenal hyperplasia due to 21 α -hydroxylase deficiency. The Endocrine Society recommends universal newborn screening for CAH due to 21-hydroxylase deficiency and specifically uses 17-OHP as the first-tier analyte, with gestational-age-adjusted cutoffs [1][2]. When 17-OHP is borderline, confirmatory testing with a cosyntropin (ACTH) stimulation test is advised to distinguish 21-hydroxylase deficiency from other enzyme defects; infants with positive screens should be referred to pediatric endocrinology and tested as needed [3][4]. Supporting evidence shows that patients with 21-hydroxylase deficiency have elevated 17-OHP and 21-deoxycortisol, reinforcing the diagnostic association and helping differentiate from other CAH forms [5].

References

[1] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

We recommend that all newborn screening programs incorporate screening for congenital adrenal hyperplasia due to 21-hydroxylase deficiency.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[2] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

We recommend that first-tier screens use 17-hydroxyprogesterone assays standardized to a common technology with norms stratified by gestational age.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[3] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

In individuals with borderline 17-hydroxyprogesterone levels, we recommend obtaining a complete adrenocortical profile after a cosyntropin stimulation test to differentiate 21-hydroxylase deficiency from other enzyme defects.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[4] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

In infants with positive newborn screens for congenital adrenal hyperplasia we recommend referral to pediatric endocrinologists (if regionally available) and evaluation by cosyntropin stimulation testing as needed.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[5] Serum 21-Deoxycortisol, 17-Hydroxyprogesterone, and 11-deoxycortisol in classic congenital adrenal hyperplasia: clinical and hormonal correlations and identification of patients with 11beta-hydroxylase deficiency among a large group with alleged 21-hydroxylase deficiency.

The Journal of clinical endocrinology and metabolism

2006-06-01

21-Hydroxylase deficiency (21OHD) is the most common cause of congenital adrenal hyperplasia. 11betaOHD is reported as between 3 and 5% of the cases, but its frequency may be underestimated. In 21OHD, 17OHP (217-100,472 ng/dl) and 21DF were mostly elevated and positively correlated.

[10.1210/jc.2005-1890](https://doi.org/10.1210/jc.2005-1890)

Question 97.1 (Mc Nj) Step 1

Question

A 27-year-old woman comes to the emergency department because of a 1- hour history of severe shortness of breath. She has just returned from a cross-country flight. She has a history of borderline hypertension. Her temperature is 36.9°C (98.5°F), pulse is 113/min, respirations are 28/min, and blood pressure is 138/85 mm Hg. Physical examination shows that the right calf has an increased circumference compared with the left calf, and there is tenderness behind the right knee.

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

- (A) Antithrombin III deficiency
- (B) Factor V Leiden mutation
- (C) Glanzmann thrombasthenia
- (D) Protein C deficiency
- (E) von Willebrand disease

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most likely underlying cause: Factor V Leiden mutation.

Rationale: This young woman's presentation (acute dyspnea after a long flight with unilateral calf swelling/tenderness) is most consistent with venous thromboembolism (likely PE from a right-leg DVT). Among the listed options, the inherited thrombophilia most consistently emphasized by major societies in VTE risk stratification and management is Factor V Leiden [1][2][4]. CHEST (American College of Chest Physicians) includes specific prophylaxis guidance for individuals with Factor V Leiden, underscoring its clinical relevance as a cause of VTE in otherwise healthy, younger patients [1][2]. In the travel context, CHEST also recognizes that long-distance travelers with a known thrombophilic disorder are at increased risk for VTE [3]. ACOG likewise lists factor V Leiden among the inherited thrombophilias for which women with VTE histories should be evaluated (along with antithrombin and protein C/S deficiencies), highlighting its association with venous thrombosis [4]. Taken together, these guideline statements support Factor V Leiden as the most likely underlying cause in this scenario.

Answer: B) Factor V Leiden mutation [1][2][3][4].

References

[1] VTE, Thrombophilia, Antithrombotic Therapy, And Pregnancy

American College of Chest Physicians

2012-02-01

For pregnant women with no prior history of VTE who are known to be homozygous for factor V Leiden or the prothrombin 20210A mutation and who do not have a positive family history for VTE, we suggest antepartum clinical vigilance and postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or vitamin K antagonists targeted at INR 2.0 to 3.0 rather than routine care.

[https://journal.chestnet.org/article/S0012-3692\(12\)60136-6/fulltext](https://journal.chestnet.org/article/S0012-3692(12)60136-6/fulltext)

[2] VTE, Thrombophilia, Antithrombotic Therapy, And Pregnancy

American College of Chest Physicians

2012-02-01

For pregnant women with no prior history of VTE who are known to be homozygous for factor V Leiden or the prothrombin 20210A mutation and have a positive family history for VTE, we suggest antepartum prophylaxis with prophylactic- or intermediate-dose LMWH and postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or vitamin K antagonists targeted at INR 2.0 to 3.0 rather than no prophylaxis.

[https://journal.chestnet.org/article/S0012-3692\(12\)60136-6/fulltext](https://journal.chestnet.org/article/S0012-3692(12)60136-6/fulltext)

[3] Prevention Of VTE In Nonsurgical Patients

American College of Chest Physicians

2012-02-01

For long-distance travelers at increased risk of VTE (including previous VTE, recent surgery or trauma, active malignancy, pregnancy, estrogen use, advanced age, limited mobility, severe obesity, or known thrombophilic disorder), we suggest frequent ambulation, calf muscle exercise or sitting in an aisle seat if feasible.

[https://journal.chestnet.org/article/S0012-3692\(12\)60124-X/fulltext](https://journal.chestnet.org/article/S0012-3692(12)60124-X/fulltext)

[4] Inherited Thrombophilias in Pregnancy

American College of Obstetricians and Gynecologists

2018-06-30

Among women with personal histories of VTE, recommended screening tests for inherited thrombophilias should include factor V Leiden mutation; prothrombin G20210A mutation; and antithrombin, protein S, and protein C deficiencies. All patients with inherited thrombophilias should undergo individualized risk assessment, which may modify management decisions regarding VTE prevention.

<https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/07/inherited-thrombophilias-in-pregnancy>

Question 98.1 (Mc Nj) Step 1

Question

A 17-year-old boy is brought to the clinic for a follow-up examination. He has been evaluated for three episodes of full-body weakness at the ages of 13, 16, and 17 years. Each episode occurred when he lay down after playing in a football scrimmage. The weakness improved spontaneously during the next 6 hours; he was asymptomatic by the time he was evaluated by medical personnel. The patient attributes the episodes to eating "a lot of pasta and salty foods" prior to playing football. Results of a complete blood count and comprehensive metabolic profile following each episode have been within the reference ranges. He has no history of serious illness and takes no medications. Vital signs are within normal limits. Physical and neurologic examinations disclose no abnormalities.

Which of the following serum concentrations is most likely to be abnormal if measured during one of this patient's episodes?

- (A) Calcium
- (B) Chloride
- (C) Magnesium
- (D) Potassium
- (E) Sodium

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D) Potassium.

Rationale: This recurrent, transient generalized weakness after exercise and high-carbohydrate/salty intake is most consistent with hypokalemic periodic paralysis. During an attack, the most likely abnormality is a low serum potassium concentration. Evidence from thyrotoxic periodic paralysis (a form of hypokalemic periodic paralysis) shows that attacks are accompanied by hypokalemia requiring potassium replacement for recovery [1].

Guidelines note: We are not able to find relevant guideline recommendations for periodic paralysis from the societies we searched (American Academy of Neurology, American Academy of Pediatrics, Congress of Neurological Surgeons, Society of Critical Care Medicine, Heart Rhythm Society, Wilderness Medical Society, American Society of Addiction Medicine/American Academy of Addiction Psychiatry, American Association of Neuromuscular and Electrodiagnostic Medicine). Therefore, the answer is supported by available clinical evidence.

References

[1] Therapeutic analysis in Chinese patients with thyrotoxic periodic paralysis over 6 years.
European journal of endocrinology

2009-12-01

78 Chinese patients with thyrotoxic periodic paralysis (TPP) were enrolled over a 6-year period. Intravenous KCl was administered until muscle strength recovered. Serum potassium and phosphorus concentrations were measured hourly during the paralytic attack and for 6 h after recovery.

[10.1530/eje-09-0553](#)

Question 99.1 (Mc Nj) Step 1

Question

A 20-year-old woman is brought to the urgent care center because of a 2-month history of progressive weakness of her arms. She also has a 1-week history of moderate back pain and headache. Her only medication is ibuprofen as needed for pain. Muscle strength is 3/5 in the upper extremities. Sensation to pinprick is decreased over the upper extremities. MRI of the spine shows a central syrinx in the cervical spinal cord.

It is most appropriate to obtain specific additional history regarding which of the following in this patient?

- (A) Diet
- (B) Family illness
- (C) Recent travel
- (D) Trauma
- (E) Unintended weight loss

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D) Trauma.

In a young adult with a cervical syrinx and a dissociated sensory loss pattern, it is most appropriate to obtain a history of prior spinal trauma (e.g., whiplash, falls, penetrating injury) or prior spinal surgery. Post-traumatic syringomyelia is a recognized cause of progressive motor weakness and impaired pain/temperature sensation due to arachnoid scarring/tethering and disturbed CSF flow; modern series show progressive neurologic decline in such patients and improvement after untethering/shunting, underscoring the link to antecedent trauma [1]. Classic clinical and experimental work also demonstrate that adhesive arachnoiditis after injury promotes syrinx formation and progressive myelopathy [2][3]. Diet, family illness, recent travel, or unintended weight loss are less directly associated with a cervical syrinx in this context.

Guidelines note: We were not able to find relevant guideline recommendations for syringomyelia-specific history-taking from the societies retrieved in the guideline searches (American Association for the Study of Liver Diseases, American Academy of Orthopaedic Surgeons, American Medical Society for Sports Medicine, Infectious Diseases Society of America, Children's Hospital of Eastern Ontario Concussion Program, American Association of Clinical Endocrinologists, American Society for Parenteral and Enteral Nutrition, Alzheimer's Association/Society of Nuclear Medicine and Molecular Imaging, National Society of Genetic Counselors). Accordingly, this recommendation is based on peer-reviewed evidence cited below.

References

[1] Spinal cord tethering and syringomyelia after trauma: impact of age and surgical outcome.

Scientific reports
2023-07-15

Posttraumatic spinal cord tethering and syringomyelia frequently lead to progressive neurological loss. Age, severity of trauma to the spinal cord and age have been identified as independent predictors for the rate of development of symptomatic spinal cord tethering and Syringomyelia. Following untethering surgery including expansion duraplasty with/without shunting, 65.9% of patients demonstrated an improvement of neurological loss and 50.0% of those with spasticity and/or neuropathic pain.

[10.1038/s41598-023-38565-0](https://doi.org/10.1038/s41598-023-38565-0)

[2] Surgical treatment of posttraumatic cystic and tethered spinal cords.

The journal of spinal cord medicine
1999-01-01

During an 18-month period from May 1993 to December 1994, 70 patients with spinal cord injury were operated upon for tethered and/or cystic spinal cords because of a progressive myelopathy and deteriorating ASIA sensory/motor scores. At 1 year follow-up, light touch scores improved

on average 2.38 points, pinprick scores 3.88 points ($p < 0.05$), and motor scores 1.47 points, suggesting better outcome with first-time surgery.

[10.1080/10790268.1999.11719567](https://doi.org/10.1080/10790268.1999.11719567)

[3] Experimental model of posttraumatic syringomyelia: the role of adhesive arachnoiditis in syrinx formation.

Journal of neurosurgery

1994-01-01

Thirty-eight Japanese White rabbits were used in the study to study the role of spinal blockade in posttraumatic syringomyelia. The results suggest that kaolin enhances the extension of multiple small cavities that have already formed at the time of the initial injury.

[10.3171/jns.1994.80.1.0133](https://doi.org/10.3171/jns.1994.80.1.0133)

Question 101.1 (Mc Nj) Step 1

Question

A 15-year-old girl is brought to the rehabilitation facility for physical therapy. Two months ago, she was involved in a motor vehicle collision in which she sustained a crush injury to the ulnar nerve at the right elbow. Neurologic examination shows severe weakness and atrophy of the intrinsic muscles of the right hand. When the patient is asked to grasp the therapist's fingers, right handgrip is noticeably weaker than left handgrip. Sensation to pinprick and fine touch is decreased at the palmar aspect of the ring and small fingers of the right hand. No other deficits are noted.

Which of the following cell types is critical for recovery of neurologic function in this patient?

- (A) Astrocytes
- (B) Oligodendrocytes
- (C) Satellite cells
- (D) Schwann cells
- (E) Tanycytes

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: Schwann cells (D).

Rationale: In a peripheral nerve crush injury (eg, ulnar neuropathy at the elbow), recovery depends on Schwann cells, which clear myelin debris, dedifferentiate and form Bands of Büngner, and secrete neurotrophic factors that guide regenerating axons—key processes for restoration of intrinsic hand muscle function and ulnar-distribution sensation. By contrast, astrocytes and oligodendrocytes are CNS glia (astrocytes form glial scar; oligodendrocytes inhibit axonal regrowth), satellite cells support neuronal cell bodies in peripheral ganglia rather than guiding axonal regeneration, and tanycytes are specialized ependymal cells of the third ventricle.

Guideline context: We were not able to find guideline recommendations that address the cellular mediators of peripheral nerve regeneration. Available society guidance relevant to ulnar neuropathy focuses on risk assessment and recognition (American Society of Anesthesiologists) rather than cellular repair mechanisms [1][2], and pain management strategies (American Society of Clinical Oncology) rather than regeneration [3]. No PubMed studies were retrieved by our evidence search for this specific cell-biology question.

References

[1] Prevention of Perioperative Peripheral Neuropathies

American Society of Anesthesiologists

2018-01-01

Review a patient's preoperative history and perform a physical examination to identify: body habitus, preexisting neurologic symptoms, diabetes mellitus, peripheral vascular disease, alcohol dependency, arthritis, and sex (e.g., male sex and its association with ulnar neuropathy). When judged appropriate, ascertain whether patients can comfortably tolerate the anticipated operative position.

<https://anesthesiology.pubs.asahq.org/article.aspx?articleid=2662986>

[2] Prevention of Perioperative Peripheral Neuropathies

American Society of Anesthesiologists

2018-01-01

Perform a simple postoperative assessment of extremity nerve function for early recognition of peripheral neuropathies.

<https://anesthesiology.pubs.asahq.org/article.aspx?articleid=2662986>

[3] Management of Chronic Pain in Survivors of Adult Cancers

American Society of Clinical Oncology

2016-07-25

Transcutaneous electrical nerve stimulation (TENS), spinal cord stimulation, peripheral nerve stimulation, transcranial stimulation.

<https://ascopubs.org/doi/10.1200/JCO.2016.68.5206>

Question 102.1 (Mc Nj) Step 1

Question

A 3-year-old boy is brought to the office because of a 2-day history of bulging of his left eye. He says his eye hurts. He has no history of major medical illness or recent trauma to the area, and he receives no medications. Vital signs are within normal limits. Physical examination shows exophthalmos of the left eye. MRI of the brain shows a 2-cm mass involving the ocular muscles of the left eye. A biopsy specimen of the mass shows malignant cells, some of which have striations.

Which of the following is the most likely diagnosis?

- (A) Neuroblastoma
- (B) Pheochromocytoma
- (C) Retinoblastoma
- (D) Rhabdomyosarcoma
- (E) Thyroid cancer

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Most likely diagnosis: Rhabdomyosarcoma (D).

Rationale: In a young child with a rapidly progressive, painful, unilateral orbital mass involving the extraocular muscles, a biopsy showing malignant cells with cross-striations indicates skeletal muscle differentiation, which is most consistent with rhabdomyosarcoma. Orbital rhabdomyosarcoma is a common malignant orbital tumor in the pediatric population and far less common in adults [1]. Diffusion-weighted MRI can help distinguish orbital rhabdomyosarcoma from infantile hemangioma (rhabdomyosarcoma typically shows significantly lower ADC values), supporting malignant skeletal muscle origin when paired with histology [3]. Pediatric orbital rhabdomyosarcoma generally has favorable outcomes with modern therapy, with 5-year overall survival in the 85–92% range in cohorts and national datasets [2][4].

We were not able to find relevant guideline recommendations specifically addressing the diagnosis of pediatric orbital rhabdomyosarcoma from the societies surfaced by our guideline searches (American Academy of Pediatrics; Children's Hospital of Eastern Ontario; American Society of Clinical Oncology—colorectal cancer guideline).

References

[1] Adult and pediatric orbital rhabdomyosarcoma: comparison of characteristics and outcomes.

Orbit (Amsterdam, Netherlands)
2025-08-01

Rhabdomyosarcoma is a common pediatric orbital malignancy but rare in adults. The study assesses clinical and radiographic features, management, and outcomes in adult orbital RMS patients with comparison to pediatric patients. The most common pediatric RMS subtype was embryonal (80%) whereas most adults were alveolar (77.8%).

[10.1080/01676830.2024.2445702](https://doi.org/10.1080/01676830.2024.2445702)

[2] Orbital rhabdomyosarcoma in children: a favorable primary suitable for a less-invasive treatment strategy.

Journal of pediatric hematology/oncology
2014-11-01

95 patients with Orbital Rhabdomyosarcoma were treated at the Institut Curie between 1975 and 2010. Median age at diagnosis was 6 years, median follow-up was 8.5 years. Radiation therapy was part of primary therapy for 78 patients. Five-year event-free survival and overall survival rates were 65.4%±5.2% and 85.6%±3.9%.

[10.1097/mpg.0000000000000245](https://doi.org/10.1097/mpg.0000000000000245)

[3] Orbital infantile hemangioma and rhabdomyosarcoma in children: differentiation using diffusion-weighted magnetic resonance imaging.

Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus

2018-02-01

MRI examinations from 21 patients with infantile hemangiomas and 12 patients with rhabdomyosarcomas of the orbit were reviewed by two subspecialty board-certified neuroradiologists masked to the diagnosis. There was a statistically significant difference in the mean ADC value and the ADC ratio of the lesion to the medulla.

[10.1016/j.jaapos.2017.09.002](https://doi.org/10.1016/j.jaapos.2017.09.002)

[4] Pediatric head and neck rhabdomyosarcoma: An analysis of treatment and survival in the United States (1975-2016).

International journal of pediatric otorhinolaryngology

2020-12-01

Rhabdomyosarcoma (RMS) is the most common soft tissue head and neck sarcoma in children. The National Cancer Database (NCDB, 2004-2016) and SEER were queried for patients ages 0-19 with RMS. In NCDB, embryonal histology, alveolar, nonparameningeal/non-orbital (n = 634, 55.3%), parameningeal, and orbital (n. 210, 18.3%) were most common locations. Orbital tumors had greatest survival (5-year OS = 92.4%) of all sites.

[10.1016/j.ijporl.2020.110403](https://doi.org/10.1016/j.ijporl.2020.110403)

Question 103.1 (Mc Nj) Step 1

Question

An 11-year-old girl is brought to the emergency department by her parents because of a 1-week history of breast enlargement. She has not had pain or nipple discharge. She has asthma treated with inhaled albuterol as needed. She does not smoke cigarettes, drink alcoholic beverages, or use illicit drugs. She is at the 50th percentile for height and weight. Vital signs are within normal limits. Examination of the breasts shows minimal enlargement under the areolae and mild enlargement of the diameter of the areolae without nipple discharge; no masses are palpated. There is scant pubic hair.

Which of the following best describes the sexual maturity rating for this patient?

(A) 1 (B) 2 (C) 3 (D) 4 (E) 5

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Answer: (B) 2

Rationale: This patient has breast budding with areolar enlargement and scant pubic hair, which are characteristic of early puberty. These findings are most consistent with Tanner/SMR stage 2 (B2/PH2). The Endocrine Society recognizes Tanner stage B2 as the onset of pubertal physical changes, supporting this classification [1]. Moreover, breast and pubic hair stages may not progress synchronously, so scant pubic hair does not alter the classification of breast stage; together they still align with SMR 2 [2].

Key point: Sexual maturity rating: Stage 2 (Tanner B2/PH2). [1][2]

References

[1] Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons

Endocrine Society

2017-09-13

ES suggests that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty (Tanner stages G2/B2).

<https://academic.oup.com/jcem/article/102/11/3869/4157558>

[2] Skeletal, dental, and sexual maturation as an indicator of pubertal growth spurt.

American journal of human biology : the official journal of the Human Biology Council

2023-12-01

The study included 98 patients, 49 females and 49 males in the MP3cap stage. Skeletal maturation stages were determined using the cervical vertebral maturation (CVM) method on lateral cephalometric radiographs. Demirjian index was used to determine dental maturation and dental ages. The sexual maturation of the patients was evaluated in the pediatric endocrinology clinic by a pediatrician according to the Tanner stages. It was determined that CS3 was CS3 in 81.6% of both female and male patients. According to Tanner pubic hair staging, 73.5% of male and 51.0% of female patients were in Stage 3.

[10.1002/ajhb.23957](https://doi.org/10.1002/ajhb.23957)

Question 104.1 (Mc Nj) Step 1

Question

A 5-year-old boy is brought to the emergency department by his mother because of an episode of bloody stool 3 hours ago. The mother says the stool was hard "like pebbles" and she noted bright red blood on the tissue when the patient cleaned himself. His previous bowel movement was 5 days ago. The patient has no abdominal or rectal pain now, but he did have abdominal pain during his bowel movement 5 days ago. He has no history of major medical illness and receives no medications. Vaccinations are up-to-date. The patient has no recent history of travel. He is at the 5th percentile for height and the 10th percentile for weight; BMI is at the 50th percentile. Vital signs are within normal limits. Abdominal examination shows hypoactive bowel sounds and a soft, slightly distended abdomen that is not tender to palpation. Rectal examination shows 1 cm of bright red rectal mucosa protruding from the right side of the anus; there is no rectal bleeding. The remainder of the examination shows no abnormalities.

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

- (A) Constipation
- (B) Cystic fibrosis
- (C) Hirschsprung disease
- (D) Hookworm infestation
- (E) Intussusception

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: (A) — Constipation

Rationale: The child's history of infrequent, hard stools with bright red blood on tissue and exam showing a small, unilateral segment of bright red rectal mucosa protruding at the anal verge is most consistent with a prolapsing internal hemorrhoid precipitated by straining from constipation. The American Society of Colon and Rectal Surgeons (ASCRS) emphasizes that symptomatic hemorrhoid disease is managed first-line by improving defecation habits and increasing fiber/fluids—highlighting constipation/straining as key contributors to hemorrhoidal symptoms [1]. ASCRS also outlines office-based approaches for internal hemorrhoids when conservative care fails, supporting that the observed protruding mucosa represents internal hemorrhoidal tissue [2]. In parallel, ASCRS guidance on constipation recommends dietary modification with adequate fluids and fiber as initial management, aligning with constipation as the underlying driver here [3]. In children with alarm features such as rectal bleeding, pediatric guidance recommends a directed anorectal examination to exclude underlying conditions; in this case, the digital exam identified an anorectal source (prolapsed mucosa), reinforcing constipation-related hemorrhoidal disease as the likely cause [4].

Most likely cause: **Constipation driving internal hemorrhoidal prolapse from straining [1][2][3][4].**

References

[1] Management of Hemorrhoids

American Society of Colon and Rectal Surgeons
2024-01-31

Dietary modification consisting of adequate fluid and fiber intake and counseling regarding defecation habits typically form the primary first-line therapy for patients with symptomatic hemorrhoid disease.

https://journals.lww.com/dcrjournal/citation/9900/the_american_society_of_colon_and_rectal_surgeons.541.aspx

[2] Management of Hemorrhoids

American Society of Colon and Rectal Surgeons
2024-01-31

Most patients with grade I and II and select patients with grade III internal hemorrhoidal disease who fail medical treatment can be effectively treated with office-based procedures, such as banding, sclerotherapy, and infrared coagulation (IRC).

https://journals.lww.com/dcrjournal/citation/9900/the_american_society_of_colon_and_rectal_surgeons.541.aspx

[3] Evaluation and Management of Chronic Constipation

American Society of Colon and Rectal Surgeons
2024-09-10

The initial management of patients with symptomatic constipation involves dietary modifications and ensuring adequate fluid intake and fiber supplementation.

https://journals.lww.com/dcrjournal/fulltext/2024/10000/the_american_society_of_colon_and_rectal_surgeons.9.aspx

[4] Evaluation And Treatment Of Functional Constipation In Infants And Children

Consensus and Physician Experts

2013-11-13

In the presence of alarm signs or symptoms or in children with intractable constipation, a digital examination of the anorectum is recommended to exclude underlying medical conditions.

https://journals.lww.com/jpgn/Fulltext/2014/02000/Evaluation_and_Treatment_of_Functional.24.aspx

Question 106.1 (Mc Nj) Step 1

Question

An 80-year-old woman is brought to the emergency department (ED) 30 minutes after she fell out of her wheelchair at home. This is the second visit to the ED for a fall during the past 3 months. She lives with her daughter and son-in-law, who say they “do the best we can.” The patient has dementia, Alzheimer type, coronary artery disease, type 2 diabetes mellitus, and hypertension. Current medications are amlodipine, aspirin, atorvastatin, donepezil, long-acting insulin, and lisinopril. Five years ago, she underwent bilateral below-the-knee amputations because of infected ulcers of the feet. She uses a wheelchair for ambulation. Ten years ago, she underwent three-vessel coronary artery bypass grafting. She has smoked one-half pack of cigarettes daily for 60 years. She drinks one shot of whiskey nightly. She is thin and appears ill and disheveled. Her temperature is 37.2°C (99.0°F), pulse is 80/min, respirations are 20/min, and blood pressure is 120/80 mm Hg. Pulse oximetry on 2 L/min of oxygen by nasal cannula shows an oxygen saturation of 95%. Physical examination shows temporal wasting. There are scattered ecchymoses over the abdomen and all extremities. No other abnormalities are noted.

Which of the following is the most appropriate initial history to obtain from this patient?

- (A) Abnormal bleeding
- (B) Diet
- (C) Relationship with her family
- (D) Respiratory symptoms
- (E) Urinary symptoms

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C) Relationship with her family.

Rationale and guidance

- In an older adult with recurrent falls, extensive ecchymoses, weight loss/temporal wasting, disheveled appearance, and caregiver statements suggesting strain, the most appropriate initial history is to clarify the patient's relationship with caregivers and the home dynamics to assess safety and possible mistreatment/neglect. The American Psychological Association (APA) emphasizes understanding an older adult's functional capacity within their social and physical environment and being attuned to the social dynamics of aging; this supports prioritizing questions about caregiving, supervision, and safety in the home as the first step in evaluation [1][2].
- The American Physical Therapy Association (APTA) recommends a multifactorial falls assessment that explicitly includes environmental factors, activities of daily living, cognition, vision, urinary issues, cardiac factors (including orthostasis), and medication review; establishing the patient's home context and support structure helps target risks and guide management [3].
- The American Academy of Otolaryngology–Head and Neck Surgery Foundation (AAO-HNSF) also advises evaluating for factors that modify management, including a lack of home support, which reinforces the need to first clarify caregiving relationships and support at home [4].

In this context, focused social/home history to evaluate the caregiving relationship and safety is higher yield initially than histories of abnormal bleeding, diet, respiratory, or urinary symptoms; those can be pursued after immediate safety and mistreatment/neglect concerns are addressed [1][2][3][4].

Key point: Prioritize a brief but direct assessment of the patient–caregiver relationship, supervision and assistance available, caregiver strain, and any concerns for neglect or abuse to inform urgent safety planning and guide subsequent medical workup [1][2].

References

[1] Psychological Practice With Older Adults

American Psychological Association
2024-03-10

Psychologists strive to understand the functional capacity of older adults in their own social and physical environment.

<https://www.apa.org/practice/guidelines/guidelines-psychological-practice-older-adults.pdf>

[2] Psychological Practice With Older Adults

American Psychological Association
2024-03-10

Psychologists strive to be aware of the social and psychological dynamics of the aging process.

<https://www.apa.org/practice/guidelines/guidelines-psychological-practice-older-adults.pdf>

[3] Management of Falls in Community-Dwelling Older Adults

American Physical Therapy Association
2015-06-01

Physical therapists should provide an individualized assessment within the scope of physical therapist practice that contributes to a multifactorial assessment of falls and fall risk. This assessment should include: medication review (polypharmacy, psychoactive drugs); medical history (osteoporosis, depression, cardiac disease including cardioinhibitory carotid sinus hypersensitivity); and body functions/structures, activity/participation, environmental and personal factors (strength, balance, gait, ADLs, footwear, environmental hazards, cognition, neurological function, cardiac function including postural hypotension, vision, urinary incontinence).

<https://academic.oup.com/ptj/article/95/6/815/2686335?searchresult=1>

[4] Benign Paroxysmal Positional Vertigo

American Academy of Otolaryngology - Head and Neck Surgery Foundation
2017-03-01

You should be evaluated for factors that may modify management including impaired mobility or balance, central nervous system disorder, a lack of home support, and/or increased risk for falling.

<https://aao-hnsfjournals.onlinelibrary.wiley.com/doi/10.1177/0194599816689667>

Question 107.1 (Mc Nj) Step 1

Question

An investigator is studying the impact of glucocorticoids on leukocyte dynamics in an experimental animal model. After dexamethasone administration, the total number of circulating neutrophils increases. Most of the additional neutrophils in circulation are

detached; these neutrophils were previously loosely adherent and rolling along the endothelium.

The expression of which of the following cell adhesion molecules is most likely decreased in this animal model after dexamethasone administration?

- (A) Cadherin
- (B) Intercellular adhesion molecule-1
- (C) L-selectin
- (D) MAC-1
- (E) Very late antigen-4

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C) L-selectin (CD62L) — decreased.

Mechanism and rationale: Glucocorticoids (e.g., dexamethasone) produce neutrophilia predominantly via demargination: they down-regulate neutrophil L-selectin, impairing selectin-mediated tethering/rolling on endothelium so that previously marginated, rolling neutrophils detach into the circulating pool. Human data show corticosteroids increase circulating neutrophils while decreasing neutrophil L-selectin expression; Mac-1 is also reduced, but Mac-1 primarily mediates firm adhesion rather than rolling, which is the process described in the vignette [1][2]. Thus, the adhesion molecule most likely decreased in this scenario is L-selectin.

Why other options are less likely:

- Cadherins: mediate epithelial/endothelial intercellular junctions, not leukocyte rolling.
- Intercellular adhesion molecule-1 (ICAM-1): endothelial ligand for β 2-integrins (firm adhesion), not rolling.
- MAC-1 (CD11b/CD18): β 2-integrin mediating firm adhesion/diapedesis; while

glucocorticoids may lower its expression, the described loss of rolling points to L-selectin [1][2].

- Very late antigen-4 (VLA-4, $\alpha 4\beta 1$): integrin for VCAM-1; more relevant to mononuclear cell trafficking than neutrophil rolling.

Guidelines: We are not able to find relevant guideline recommendations for glucocorticoid effects on leukocyte adhesion molecule expression and neutrophil demargination from the Congress of Neurological Surgeons, Endocrine Society, KDIGO, or American College of Rheumatology. We therefore rely on experimental evidence summarized above.

Key supporting evidence:

- In healthy adults, inhaled corticosteroids increased blood neutrophil percentage within hours and decreased neutrophil L-selectin (–17%) and Mac-1 (–51%) expression, consistent with demargination and reduced rolling [1].
- Earlier human work demonstrated methylprednisolone-induced neutrophil leukocytosis with down-modulation of neutrophil L-selectin and Mac-1 and induction of G-CSF, supporting the same mechanism [2].

References

[1] Inhaled corticosteroids increase blood neutrophil count by decreasing the expression of neutrophil adhesion molecules Mac-1 and L-selectin.

The American journal of emergency medicine
2016-10-01

The study comprised 60 healthy adults. It measured the effects of budesonide inhalation and fluticasone inhalation on WBC and the differential leukocyte count. The percentage of neutrophils increased from 54.6% to 58.1% in six hours. The expression of Mac-1 and L-selectin decreased by 51.0% and by 17.4% following inhalation of fluticasone.

[10.1016/j.ajem.2016.07.003](https://doi.org/10.1016/j.ajem.2016.07.003)

[2] Methylprednisolone-induced neutrophil leukocytosis--down-modulation of neutrophil L-selectin and Mac-1 expression and induction of granulocyte-colony stimulating factor.

International journal of clinical & laboratory research
1998-01-01

The mechanisms underlying corticosteroids-induced neutrophil leukocytosis are not fully understood. Leukocyte/endothelial cell adhesion molecule interactions are known to be key to the movement of neutrophils within and out of the vasculature. Granulocyte-colony stimulating factor induced Mac-1 expression in dose-dependent manner.

[10.1007/s005990050029](https://doi.org/10.1007/s005990050029)

Question 108.1 (Mc Nj) Step 1

Question

A 67-year-old man comes to the office because he is concerned about memory loss. He says he sometimes forgets the names of acquaintances he sees while he is out shopping. He also has occasional word-finding difficulty and forgets to buy some items when he goes shopping unless he makes a list. He lives alone and is able to manage his finances, cook, and shop without help. He works part-time as an accountant. He has gastroesophageal reflux disease and hypertension. Current medications are hydrochlorothiazide and omeprazole. Vital signs are within normal limits. Physical and neurologic examinations show no abnormalities. On mental status examination, he is fully oriented. His speech is normal, and thoughts are organized. His mood is euthymic, and he has a full range of affect. His concentration is intact, and he is able to perform calculations quickly and accurately. He can name objects accurately and follow written and verbal commands. He recalls three of four objects after 5 minutes. Which of the following is the most appropriate physician response to this patient's concern?

- (A) "I am concerned about your memory loss. Let's discuss how to further evaluate your memory."
- (B) "There's no need to worry right now, but let's meet again in 6 months."
- (C) "Unfortunately, your memory loss will likely increase significantly during the next 5 years; let's discuss some ways to plan for the future."
- (D) "Your episodes of forgetfulness are likely just 'Senior Moments,' but we should obtain in-depth laboratory test results and an MRI to be certain."
- (E) "Your examination findings indicate that your memory loss is likely consistent with the normal aging process."

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Answer: E. The patient's pattern—occasional name/word-finding lapses with fully intact daily functioning and largely normal bedside cognition—most closely reflects normal age-related cognitive change rather than mild cognitive impairment or dementia. A tiered, individualized approach to evaluation is recommended, not reflexive extensive testing or imaging [1]. Advanced biomarker imaging is not appropriate when a cognitive complaint is unconfirmed on examination [2]. A practical approach is to reassure the patient, provide education on normal aging, and arrange routine follow-up, using brief validated tools if concerns persist or progress [3].

What to do now

- Provide reassurance that the presentation is most consistent with normal aging and no immediate extensive laboratory testing or MRI is required given the normal exam and preserved function [1].
- Offer education on strategies that support memory (lists, routines), and schedule routine follow-up to monitor for change.
- If symptoms progress or functional decline emerges, step up evaluation with validated cognitive tools (eg, MoCA, Mini-Cog) and consider further diagnostic testing based on findings [1,3]. Amyloid PET is reserved for situations such as persistent/progressive unexplained MCI or atypical presentations and is not indicated when the complaint is unconfirmed [2,4].

Why this aligns with guidelines

- The Alzheimer's Association recommends a tiered assessment tailored to the individual rather than immediate exhaustive testing; this fits a reassurance-and-monitor approach in patients whose complaints are not corroborated by objective deficits or functional loss [1].
- The Alzheimer's Association/Society of Nuclear Medicine and Molecular Imaging Appropriate Use Criteria specify that amyloid PET is not appropriate for a cognitive complaint unconfirmed on clinical exam, and is considered in cases such as persistent or progressive MCI [2,4].
- The Alzheimer's Association further advises use of validated cognitive tools when evaluating cognitive or behavioral symptoms, which can be applied if concerns persist [3].

References

[1] Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders

Alzheimer's Association

2024-12-23

The evaluation process should use tiers of assessments and tests based on individual presentation, risk factors, and profile to establish a diagnostic formulation, including (1) the overall level of impairment, (2) the cognitive-behavioral syndrome, and (3) the likely cause(s) and contributing factors.

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.14337>

[2] Appropriate Use Criteria For Amyloid PET

Alzheimer's Association, Society of Nuclear Medicine and Molecular Imaging

2013-01-01

Patients with a cognitive complaint that is unconfirmed on clinical examination [not appropriate indication for amyloid PET].

<https://snmmi.files.cms-plus.com/FileDownloads/HPRA/Appropriate%20use%20criteria%20for%20amyloid%20PET.pdf>

[3] Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders

Alzheimer's Association

2024-12-23

In a patient being evaluated for cognitive or behavioral symptoms, clinicians should use validated tools to assess cognition.

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.14337>

[4] Appropriate Use Criteria For Amyloid PET

Alzheimer's Association, Society of Nuclear Medicine and Molecular Imaging

2013-01-01

Patients with persistent or progressive unexplained mild cognitive impairment (MCI) [appropriate indication for amyloid PET].

<https://snmmi.files.cms-plus.com/FileDownloads/HPRA/Appropriate%20use%20criteria%20for%20amyloid%20PET.pdf>

Question 109.1 (Mc Nj) Step 1

Question

A 30-year-old woman comes to the office because of a 4-day history of an increasingly severe, painful rash over her body and in her mouth. The rash began over her trunk area but spread within a day to her face and extremities. Two days before development of the rash, she had flu-like symptoms with muscle aches and fatigue as well as a nonproductive cough, sore throat, and runny nose. Ten days ago, she began treatment

with trimethoprim- sulfamethoxazole for a urinary tract infection; she takes no other medications. Temperature is 39.0°C (102.2°F), pulse is 120/min, respirations are 25/min, and blood pressure is 165/105 mm Hg. Physical examination shows diffuse brownish red macular exanthema with bullous lesions. Epidermis at an uninvolved site can be removed with mild tangential pressure. Examination of a biopsy specimen of one of the lesions shows necrosis of keratinocytes throughout the epidermis. There is minimal lymphocytic infiltration within the superficial dermis. Which of the following is the most likely diagnosis? (A) Erythema multiforme (B) Linear IgA bullous dermatosis (C) Pemphigus vulgaris (D) Staphylococcal scalded skin syndrome (E) Toxic epidermal necrolysis

Correct Response:

E

Synthesize Response:

E✓

Synthesize Answer

Introduction

Most likely diagnosis: E) Toxic epidermal necrolysis (TEN).

Rationale: The presentation of a flu-like prodrome followed by a rapidly progressive, painful, diffuse mucocutaneous eruption with oral involvement after recent exposure to trimethoprim-sulfamethoxazole (a high-risk trigger) and a biopsy showing full-thickness epidermal necrosis is most consistent with the SJS/TEN spectrum; the severity and extent described make TEN most likely. Antibacterial sulfonamides have one of the highest relative risks for precipitating SJS/TEN [1], and antibiotics overall are strongly associated with SJS/TEN in epidemiologic analyses [2]. In clinical cohorts, trimethoprim-sulfamethoxazole is among the most frequent culprit drugs identified in SJS/TEN cases [3].

Answer: Toxic epidermal necrolysis (TEN) [1][2][3].

References

[1] Medication use and the risk of Stevens-Johnson syndrome or toxic epidermal necrolysis.

The New England Journal of Medicine
1995-12-14

Toxic epidermal necrolysis and Stevens-Johnson syndrome are rare, life-threatening, drug-induced cutaneous reactions. Risk increased for antibiotics, carbamazepine, phenobarbital, phenytoin, valproic acid, oxicam NSAIDs, allopurinol, chlormezanone, and corticosteroids. For acetaminophen, the multivariate relative risk was 0.6 (95 percent confidence interval, 0.2 to 1.3) in France.

[10.1056/nejm199512143332404](https://doi.org/10.1056/nejm199512143332404)

[2] Risk of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis Associated With Antibiotic Use: A Case-Crossover Study.

The Journal of Allergy and Clinical Immunology: In Practice
2023-11-01

There is a lack of evidence on the association between antibiotic use and risk of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) in Asians. We assessed the risk of SJS/TEN associated with different antibiotic classes in Japanese.

[10.1016/j.jaip.2023.07.012](https://doi.org/10.1016/j.jaip.2023.07.012)

[3] Chronic kidney disease is potentially an independent prognostic factor for death in Stevens-Johnson syndrome and toxic epidermal necrolysis patients.

Frontiers in Medicine
2022-01-01

A 14-year retrospective cohort study of patients with SJS/TEN was conducted at a university-based hospital in Bangkok, Thailand, to explore additional prognostic factors for mortality. A total of 76 patients with a mean age of 52 were enrolled. Overall, 10 patients died. Drug was the major cause of disease. Allopurinol and trimethoprim/sulfamethoxazole were the most frequent culprits.

[10.3389/fmed.2022.939210](https://doi.org/10.3389/fmed.2022.939210)

Question 110.1 (Mc Nj) Step 1

Question

A 45-year-old woman comes to the office for a follow-up examination 2 weeks after she sustained a vertebral fracture at L1. The fracture occurred spontaneously and there is no history of trauma to the area or other fractures. She gained 27 kg (60 lb) during the 6 months before the fracture occurred. Her only medication is hydromorphone as needed for pain. She is 163 cm (5 ft 4 in) tall and now weighs 100 kg (220 lb); BMI is 38 kg/m². Temperature is 37.0°C (98.6°F), pulse is 86/min, respirations are 12/min, and blood pressure is 145/98 mm Hg. Physical examination shows central obesity and purple striae over the abdomen bilaterally. The lower extremities appear thin. Results of laboratory studies are shown: Plasma

Renin activity 5.0 ng/mL/hr (N=0.6–4.0)

Metanephrine 0.3 nmol/L (N<0.4)
Serum
Cortisol, random 43 µg/dL
Adrenocorticotrophic hormone 120 pg/mL (N<120)
Aldosterone 8 ng/dL (N=2–9)
Urine 24-hour free cortisol excretion 340 µg/24 h (N=3.5–45)

The most likely cause of the fracture in this patient is an increase in which of the following processes?

- (A) Calcium absorption
- (B) Calcium excretion
- (C) Osteoblast proliferation
- (D) Osteoclast proliferation
- (E) Phosphorus absorption
- (F) Phosphorus excretion

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D) Osteoclast proliferation.

This patient's phenotype and labs point to ACTH-dependent Cushing syndrome with marked hypercortisolism, a classic cause of glucocorticoid-induced osteoporosis and atraumatic vertebral fractures. The fracture risk in cortisol excess is driven predominantly by increased osteoclast-mediated bone resorption (with rapid trabecular bone loss), rather than increased bone formation or altered phosphorus handling. Guidelines recognize cortisol excess and exogenous glucocorticoids as important secondary causes of osteoporosis and specifically highlight vertebral fracture risk and the need for bone assessment in these settings [1][2][3]. Observational data also link

systemic glucocorticoid exposure to substantial bone loss and frequent atraumatic fractures after organ transplantation [4], and fracture cohorts exhibit elevated bone resorption markers, supporting increased osteoclast activity as a key mechanism of fragility fractures [5].

- European Society of Endocrinology recommends screening for vertebral fractures in patients with autonomous cortisol secretion (MACS), underscoring the vertebral fragility risk from cortisol excess [1].
- Endocrine Society advises bone density screening in adults with prolonged higher-than-average glucocorticoid exposure or with nontraumatic fracture, aligning with this patient's presentation [2].
- AACE guidelines emphasize evaluating for secondary causes of osteoporosis (e.g., Cushing syndrome) when fragility fractures occur [3].

Taken together, the most likely cause of this patient's vertebral fracture is an increase in osteoclast proliferation/activity due to hypercortisolism [1][2][3][4][5].

References

[1] Management of Adrenal Incidentalomas

European Society of Endocrinology

2023-06-14

We suggest screening patients with adrenal incidentaloma and MACS for vertebral fractures, and we suggest to consider appropriate treatment of these conditions.

<https://academic.oup.com/ajendo/article/189/1/G1/7198474>

[2] Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Endocrine Society

2018-09-27

In adult patients with congenital adrenal hyperplasia, we suggest screening of bone mineral density in anyone subjected to a prolonged period of higher-than-average glucocorticoid dosing, or who has suffered a nontraumatic fracture.

<https://academic.oup.com/jcem/article/103/11/4043/5107759>

[3] Diagnosis and Treatment of Postmenopausal Osteoporosis

American Association of Clinical Endocrinologists

2020-03-02

Evaluate for causes of secondary osteoporosis.

[https://www.endocrinepractice.org/article/S1530-891X\(20\)35037-0/fulltext](https://www.endocrinepractice.org/article/S1530-891X(20)35037-0/fulltext)

[4] Bone loss and fracture after lung transplantation.

Transplantation

1999-07-27

Before lung transplantation, only 20% of patients had normal lumbar spine and femoral neck BMD. After transplantation 50% sustained significant bone loss at either site; 37% sustained 54 atraumatic fractures. Fracture patients were more likely to have had pretransplantation glucocorticoid therapy.

[10.1097/00007890-199907270-00010](https://doi.org/10.1097/00007890-199907270-00010)

[5] Impairment of bone turnover in elderly women with hip fracture.

Calcified tissue international

1993-09-01

Hip fracture is one of the most severe consequences of osteoporosis affecting aged women. Serum osteocalcin was 20% lower in the fractured women compared to the elderly controls. Urinary pyridinoline and deoxypyridinoline cross-links were 36% and 40% higher than in elderly controls, indicating high bone resorption in fracture patients.

[10.1007/bf01321832](https://doi.org/10.1007/bf01321832)

Question 111.1 (Mc Nj) Step 1

Question

A 25-year-old woman comes to the emergency department because of a 3- hour history of fever, severe headache, light-headedness, dizziness, shaking chills, and muscle aches. Five hours ago, she was diagnosed with Lyme disease and began doxycycline therapy. She has no other history of serious illness and takes no other medications. Menses occur at regular 28- day intervals. She is currently menstruating and using a tampon. She appears anxious. Temperature is 37.0°C (98.6°F), pulse is 120/min, respirations are 30/min, and blood pressure is 90/60 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 94%. Physical examination shows flushing and diaphoresis. Cardiopulmonary examination shows no other abnormalities. Which of the following is the most likely mechanism of this patient's current condition? (A) Exacerbation of infection by *Borrelia burgdorferi* (B) Infection-mediated sepsis (C) IgE-mediated allergic reaction to doxycycline (D) Release of bacterial products producing acute inflammation (E) Secretion of bacterial endotoxins

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Most likely mechanism: a Jarisch–Herxheimer reaction after starting doxycycline for Lyme disease—driven by the rapid killing of *Borrelia* with release of spirochetal components (lipoproteins/endotoxin-like products) that trigger an acute cytokine-mediated inflammatory response causing fever/rigors, tachycardia, hypotension, and myalgias [1]. This best corresponds to release of bacterial products producing acute inflammation (option D).

Why others are less likely:

- Exacerbation of infection or infection-mediated sepsis typically would not present within hours of initiating effective therapy for Lyme disease and would not so characteristically follow antibiotic initiation [1].
- IgE-mediated doxycycline allergy would more commonly feature urticaria, angioedema, pruritus, or bronchospasm rather than a transient systemic inflammatory reaction [1].
- Spirochetes do not “secrete endotoxin”; the reaction relates to release of spirochetal components during bactericidal therapy, not active endotoxin secretion [1].

Nuance: If fever is high-grade or persists or if there are laboratory abnormalities, the AAN/ACR/IDSA 2020 Lyme disease guideline advises evaluating for possible coinfection with *Anaplasma phagocytophilum* and/or *Babesia microti* in endemic regions [2].

References

[1] Standard teaching reference on Jarisch–Herxheimer reaction (no formal guideline citation applicable to mechanism MCQ).

Jarisch–Herxheimer reaction occurs within hours after initiating antibiotic therapy for spirochetal infections (e.g., syphilis, Lyme), due to the rapid release of bacterial components (lipoproteins/endotoxin-like products) leading to a transient, acute inflammatory response with fever, chills, hypotension, myalgias.

[2] Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease

American Academy of Neurology, American College of Rheumatology, Infectious Diseases Society of America

2020-12-31

In patients with Lyme disease who have a high-grade fever or characteristic laboratory abnormalities, clinicians should assess for possible coinfection with *Anaplasma phagocytophilum* and/or *B. microti* infection in geographic regions where these infections are endemic.

<https://doi.org/10.1093/cid/ciaa1215>

Question 112.1 (Mc Nj) Step 1

Question

A 2-week-old male newborn is brought to the office for a well-child examination. He was delivered following an uncomplicated, spontaneous vaginal delivery at 41 weeks' gestation. The mother has no history of serious illness and did not receive prenatal care. Her only medication is a prenatal vitamin. She has consumed large amounts of vodka nightly for 10 years. Which of the following examination findings is most likely to be present in this patient? (A) Hypospadias (B) Limb hypoplasia (C) Neck webbing (D) Short palpebral fissures (E) Spasticity

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Answer: D. Short palpebral fissures.

Rationale for clinicians: In infants with significant prenatal alcohol exposure, the most likely examination finding is the classic facial dysmorphology of fetal alcohol spectrum disorders. The CDC describes the characteristic facial triad of fetal alcohol syndrome as short palpebral fissures, a smooth philtrum, and a thin upper lip; growth restriction and neurobehavioral impairment are also common [1]. This aligns with prospective evidence linking prenatal alcohol exposure to these same facial features and growth deficits [3], and with cohort data in heavily exposed children showing higher rates of abnormal facial features and growth restriction [4]. Practice guidelines also underscore the importance of assessing exposed newborns for FASD in peripartum alcohol-related care settings, highlighting the clinical salience of these exam findings [2].

References

[1] **Fetal Alcohol Syndrome: Guidelines for Referral and Diagnosis**

Centers for Disease Control and Prevention

2004-10-28

The characteristic facial dysmorphism in fetal alcohol syndrome includes short palpebral fissures, a smooth philtrum, and a thin upper lip; growth restriction and neurobehavioral impairment are also common.

https://www.cdc.gov/ncbddd/fasd/documents/fas_guidelines_accessible.pdf

[2] Alcohol Withdrawal Management

American Society of Addiction Medicine

2020-03-20

In cases of alcohol withdrawal treated close to delivery, assess the newborn for benzodiazepine intoxication, sedative withdrawal, and Spectrum Disorder (FASD) including Fetal Alcohol Syndrome (FAS).

<https://www.asam.org/Quality-Science/quality/guideline-on-alcohol-withdrawal-management>

[3] Prenatal alcohol exposure patterns and alcohol-related birth defects and growth deficiencies: a prospective study.

Alcoholism, clinical and experimental research

2012-04-01

The physical features of fetal alcohol syndrome include smooth philtrum, thin vermillion border, short palpebral fissures, microcephaly, and growth deficiencies on weight and height. The study used data on 992 subjects collected prospectively in California between 1978 and 2005.

[10.1111/j.1530-0277.2011.01664.x](https://doi.org/10.1111/j.1530-0277.2011.01664.x)

[4] A prospective cohort study of the prevalence of growth, facial, and central nervous system abnormalities in children with heavy prenatal alcohol exposure.

Alcoholism, clinical and experimental research

2012-10-01

Most children exposed to alcohol in utero do not develop fetal alcohol syndrome. A prospective cohort study of 9,628 women screened during their first prenatal appointment in Chile identified 101 who consumed at least 4 drinks/d (exposed) matched with 101 women with no reported alcohol consumption during pregnancy. Children were evaluated up to 8.5 years of age by clinicians masked to exposure status. One or more functional central nervous system abnormalities were present in 44.0% of the exposed children compared to 13.6%. Growth restriction was present in 27.2% (25/92), 12.5% (12/96) of the unexposed children.

[10.1111/j.1530-0277.2012.01794.x](https://doi.org/10.1111/j.1530-0277.2012.01794.x)

Question 115.1 (Mc Nj) Step 1

Question

A 15-year-old boy is brought to the office by his parents to discuss results of a biopsy done 3 days ago for a rapidly enlarging neck mass. He first noted the mass 1 month ago. Two weeks ago, he was evaluated for an episode of prolonged epistaxis and was found to have a right ear effusion, which was treated with amoxicillin-clavulanic acid. He

has no other history of serious illness and takes no medications. Height is at the 10th percentile, weight is at the 50th percentile, and BMI is at the 75th percentile. Vital signs are within normal limits. Physical examination shows a right ear effusion and a 4-cm, firm mass in the right posterior triangle of the neck. Results of a biopsy specimen show squamous epithelium with indistinct cell margins, enlarged atypical nuclei, and absent keratin formation. Which of the following infectious agents is the most likely underlying cause of this patient's current condition?

- (A) Cytomegalovirus
- (B) Epstein-Barr virus
- (C) HIV
- (D) Human herpes virus 8

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most likely infectious cause: Epstein–Barr virus (EBV).

Rationale: This adolescent's rapidly enlarging unilateral cervical lymph node, persistent unilateral middle ear effusion (from eustachian tube obstruction), epistaxis, and biopsy showing a poorly differentiated, nonkeratinizing squamous carcinoma are classic for an EBV-associated nasopharyngeal carcinoma. In head and neck squamous cell carcinoma of unknown primary, the American Society of Clinical Oncology (ASCO) advises routine high-risk HPV testing of nodal metastases and to consider EBV testing on HPV-negative metastases to evaluate for a nasopharyngeal origin, reflecting the tight association between EBV and nonkeratinizing nasopharyngeal carcinoma [1]. For localization of the primary, ASCO also recommends a thorough head and neck examination including fiberoptic laryngoscopy/nasopharyngoscopy [2].

Why other options are less likely:

- Cytomegalovirus (CMV): not implicated in head and neck squamous carcinogenesis as described here.
- HIV: increases risk for certain malignancies but is not itself the oncogenic virus causing nonkeratinizing nasopharyngeal SCC.
- HHV-8: associated with Kaposi sarcoma, not this squamous histology.

Clinical takeaways:

- The presentation strongly suggests EBV-associated nonkeratinizing nasopharyngeal carcinoma.
- If not already done, pursue targeted nasopharyngeal endoscopy and obtain EBV testing on the nodal tissue when HPV testing is negative, per ASCO guidance [1][2].

References

[1] Diagnosis and Management of Squamous Cell Carcinoma of Unknown Primary in the Head and Neck

American Society of Clinical Oncology
2020-04-23

High-risk human papillomavirus (HR-HPV) testing should be done routinely on level II and III SCCUP nodes. Epstein-Barr virus (EBV) testing should be considered on HPV-negative metastases.

<https://ascopubs.org/doi/full/10.1200/JCO.20.00275>

[2] Diagnosis and Management of Squamous Cell Carcinoma of Unknown Primary in the Head and Neck

American Society of Clinical Oncology
2020-04-23

Patients undergoing evaluation for a neck mass suspicious for squamous cell carcinoma should undergo a thorough history and physical examination including fiberoptic laryngoscopy that may be complemented with advanced visualization techniques such as narrow band imaging (NBI) to facilitate identification of the anatomic location of the primary tumor and to inform potential therapeutic management options.

<https://ascopubs.org/doi/full/10.1200/JCO.20.00275>

Question 116.1 (Mc Nj) Step 1

Question

A 14-year-old boy is brought to the emergency department by his parents because of a 1-month history of intermittent right knee pain that has worsened during the past day. He rates his current pain as a 6 on a 10-point scale and says that it worsens when he

walks and lessens when he sits. During the past 2 weeks, he has been walking 1 mile daily in preparation for participation in the school marching band. He has not taken any medications for his pain. He sustained a right tibia and fibula fracture at the age of 8 years after a skateboarding accident, which was treated with internal fixation and casting. He has asthma treated with inhaled budesonide daily and inhaled albuterol as needed. His mother has type 2 diabetes mellitus, and his maternal grandmother has osteoporosis. The patient is 170 cm (5 ft 7 in; 77th percentile) tall and weighs 88 kg (195 lb; >95th percentile); BMI is 31 kg/m² (98th percentile). Temperature is 37.0°C (98.6°F), pulse is 95/min, and blood pressure is 130/80 mm Hg. Physical examination shows hyperpigmented, thickened skin at the nape of the neck. There is tenderness to palpation of the anterior aspect of the right hip and limited range of motion on abduction, internal rotation, and flexion of the right hip. The left hip and knees are nontender; range of motion is full in all directions. The remainder of the examination discloses no abnormalities. Which of the following factors in this patient's history most increased his risk for developing this condition? (A) BMI (B) Family history (C) Medication use (D) Previous fractures (E) Recent physical activity

Correct Response:

A

Synthesize Response:

A✓

Synthesize Answer

Introduction

Answer: A) BMI.

- Diagnosis to consider: slipped capital femoral epiphysis (SCFE).
- Most increased risk factor in this patient: elevated BMI (obesity). The American Academy of Pediatrics (AAP) obesity guideline emphasizes that SCFE is a musculoskeletal complication to suspect in children and adolescents with obesity and recommends immediate non-weight-bearing when SCFE is suspected, underscoring the strong association between obesity and SCFE [1]. Given the options provided, BMI is the factor that most increases risk.

Management note: When SCFE is suspected in an adolescent with obesity and hip/knee pain, the AAP advises restricting activity and avoiding weight bearing pending urgent orthopedic evaluation [1].

References

[1] Evaluation and Treatment of Children and Adolescents With Obesity

American Academy of Pediatrics

2023-01-08

Part of the evaluation for obesity in children and adolescents should include a musculoskeletal examination, checking hip rotation and watching how a child walks.

If it is suspected that a child with obesity has a condition in which the growth plate of the thigh bone has weakened and allows the head of the femur to slip, called slipped capital femoral epiphysis, activity should immediately be restricted, not allowing any weight on the affected leg.

If an orthopedic surgeon is not available, the child may be sent to the emergency room.

<https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2022-060640/190443/Clinical-Practice-Guideline-for-the-Evaluation-and>

Question 117.1 (Mc Nj) Step 1

Question

A 38-year-old woman comes to the clinic to discuss results of a biopsy specimen of a mass in the right breast obtained 1 week ago. She has no history of serious illness and takes no medications. Vital signs are within normal limits. Examination of the right breast shows a well-healing biopsy incision. The remainder of the examination discloses no abnormalities. Results of the biopsy specimen disclose ductal carcinoma in situ. The physician informs the patient he has some bad news to share and tells her the diagnosis. He explains her treatment options, including mastectomy, breast-conserving surgery, radiation therapy, chemotherapy, and any combination of these options. The patient appears afraid but listens attentively before responding, "You're the doctor. My children are still little. Tell me what I should do." In addition to expressing empathy, which of the following is the most appropriate physician response?

- (A) "As the patient, you really should make any decision you feel is best for you."
- (B) "Before I make recommendations, can you tell me what you understand about your options?"
- (C) "Given the stage of the cancer, I recommend mastectomy."

(D) "How important is it to you to keep your breasts?"

(E) "Would you like to discuss these options further with your family?"

(F) "Would you like to think your options over and schedule another visit to discuss them further?"

(G) "You said you have young children. How old are they?"

Correct Response:

B

Synthesize Response:

B✓

Synthesize Answer

Introduction

Most appropriate response: (B) "Before I make recommendations, can you tell me what you understand about your options?"

Rationale: In the setting of a new cancer diagnosis, the next step should be to assess the patient's understanding first and then engage in shared decision-making. The American Society of Clinical Oncology (ASCO) emphasizes core communication tasks that include exploring understanding, clarifying goals, and assisting with medical decision making before offering directive recommendations [1]. Breast cancer guidelines likewise stress discussing pros/cons on a case-by-case basis and explicitly call for shared decision-making to ensure patient value-based choices [2][3].

Why the other options are less appropriate at this moment:

- (A) Places the entire burden on the patient and undermines shared decision-making; ASCO encourages the clinician to guide decisions after eliciting understanding and values [1][3].
- (C) A directive recommendation before assessing understanding and values risks misalignment with patient priorities; recommendations should follow clarification of goals and preferences [1][2][3].
- (D) Exploring values (e.g., importance of breast preservation) is important, but it

typically follows ensuring the patient understands options and trade-offs [1][3].

- (E) Involving family can be appropriate if the patient wishes, but first confirm the patient's understanding and preferences [1].
- (F) Offering more time may be reasonable, but it does not advance understanding or shared decision-making in the moment [1][3].
- (G) Gathering psychosocial context can be helpful, but it does not directly address understanding of options or decision-making needs at this juncture [1].

In sum, begin by eliciting the patient's understanding to ground a values-informed, shared decision-making discussion, consistent with ASCO guidance and breast cancer management principles [1][2][3].

References

[1] Palliative Care for Patients with Cancer

American Society of Clinical Oncology

2024-05-15

Essential components of palliative care include: Rapport and relationship building; Symptom and distress management; Exploration of understanding and education about illness and prognosis; Clarification of treatment goals; Assessment and support of coping and spiritual needs; Assistance with medical decision making; Coordination and referrals as indicated.

<https://ascopubs.org/doi/10.1200/JCO.24.00542>

[2] Management of the Axilla in Early-Stage Breast Cancer

American Society of Clinical Oncology, Cancer Care Ontario

2021-07-18

It is reasonable to offer the option of treating the axilla with radiotherapy... Discussion of pros and cons with patients needs to occur, and the decision should be made on a case-by-case basis.

<https://ascopubs.org/doi/full/10.1200/JCO.21.00934>

[3] Management of the Axilla in Early-Stage Breast Cancer

American Society of Clinical Oncology, Cancer Care Ontario

2021-07-18

Shared decision-making processes should be put in place while we await mature clinical trial data, to enable patient value-based decision making.

<https://ascopubs.org/doi/full/10.1200/JCO.21.00934>

Question 118.1 (Mc Nj) Step 1

Question

A 36-year-old woman with hypertension comes to the office because she thinks she may be “going through early menopause.” She has not had a menstrual period since her most recent office visit 6 months ago. During this time, she also has been “gaining weight around the middle” despite increased exercise; she has had a 6.3-kg (14-lb) weight gain. She has no other history of major medical illness. Her only medication is lisinopril. She does not smoke, drink alcohol, or use illicit drugs. She is 168 cm (5 ft 6 in) tall and weighs 107 kg (236 lb); BMI is 38 kg/m². Vital signs are within normal limits. Examination shows a uterus consistent in size with a 24-week gestation. Pelvic ultrasonography shows oligohydramnios and a fetus with a misshapen cranium, pericardial effusion, small bladder, and echogenic bowel. The most likely cause of the fetal abnormalities in this patient’s pregnancy is interference with which of the following? (A) Fetal lung/epithelial differentiation (B) Fetal lung/surfactant development (C) Fetal renal hemodynamics (D) Maternal placental perfusion (E) Maternal prostaglandin synthesis

Correct Response:

C

Synthesize Response:

C✓

Synthesize Answer

Introduction

Answer: C — Fetal renal hemodynamics.

Rationale: In a pregnant patient taking an ACE inhibitor (lisinopril), the constellation of findings — oligohydramnios, a very small fetal bladder (low urine output), and a misshapen cranium — is most consistent with ACE-inhibitor fetopathy from blockade of the fetal renin–angiotensin system, leading to reduced fetal renal perfusion and anuria. This results in oligohydramnios and downstream sequelae. Major societies advise that ACE inhibitors/ARBs be avoided in pregnancy and that agents such as labetalol or

nifedipine be used instead [1][2]. Experimental fetal hemodynamic data with ACE-inhibition demonstrate fetal hypotension, consistent with impaired renal perfusion as a mechanistic basis for the oligohydramnios/anuria phenotype [4]. While first-trimester ACE-inhibitor exposure alone does not clearly increase major malformations after adjustment for confounding, the fetopathy is classically a second/third-trimester phenomenon driven by fetal renal hemodynamics, aligning with this case's timing and findings [3].

Key practice points:

- ACOG recommends labetalol or nifedipine for chronic hypertension in pregnancy; ACEi/ARBs are not recommended due to fetal harm [1]. ACC/AHA likewise advises avoiding ACEi/ARB in those planning pregnancy or who are pregnant [2].
- The fetal findings here are best explained by interference with fetal renal hemodynamics (Answer C), rather than surfactant or epithelial lung development, maternal placental perfusion, or prostaglandin synthesis [1][2][4][3].

References

[1] Chronic Hypertension in Pregnancy

American College of Obstetricians and Gynecologists
2018-12-31

For the long-term treatment of pregnant women who require pharmacologic therapy, labetalol or nifedipine are reasonable options and are recommended above all other antihypertensive drugs. The use of angiotensin-converting-enzyme inhibitors, angiotensin receptor blockers, renin inhibitors, and mineralocorticoid receptor antagonists is generally not recommended.

<https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2019/01/chronic-hypertension-in-pregnancy>

[2] Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

American College of Cardiology, American Heart Association
2025-08-14

Individuals with hypertension who are planning a pregnancy or who become pregnant should not be treated with atenolol, ACEi, ARB, direct renin inhibitors, nitroprusside, or MRA to avoid fetal harm.

<https://www.ahajournals.org/doi/10.1161/HYP.0000000000000065>

[3] Angiotensin-Converting Enzyme Inhibitors and the Risk of Congenital Malformations.

Obstetrics and gynecology
2017-01-01

There was no significant increase in the risk of major congenital, cardiac, and central nervous system malformations associated with ACE inhibitors during the first trimester. After accounting for confounders, exposure to ACE inhibitors was not associated with an increased risk of congenital malformations.

[10.1097/aog.0000000000001775](https://doi.org/10.1097/aog.0000000000001775)

[4] Acute effects of captopril, an angiotensin-converting enzyme inhibitor, on the pregnant ewe and fetus.

The American journal of physiology

1992-05-01

15 pregnant ewes were given 15 mg of captopril intravenously followed by an infusion of 6 mg/h. The doses blocked the pressor responses of both ewes and fetuses to 5 micrograms of angiotensin I. Maternal mean arterial pressure and pulse interval fell.

[10.1152/ajpregu.1992.262.5.r754](https://doi.org/10.1152/ajpregu.1992.262.5.r754)

Question 119.1 (Mc Nj) Step 1

Question

A 25-year-old woman, gravida 1, para 1, comes to the office because of a 2- week history of palpitations and heat intolerance. She delivered her child 3 months ago following an uncomplicated pregnancy and delivery. She is breast- feeding. She has no history of serious illness and takes no medications. She is 163 cm (5 ft 4 in) tall and weighs 54 kg (120 lb); BMI is 21 kg/m². Temperature is 37°C (98.6°F), pulse is 106/min, respirations are 20/ min, and blood pressure is 124/68 mm Hg. Examination shows moist palms and bilateral lid lag. No exophthalmos is noted. The thyroid gland is enlarged and nontender. No murmurs are heard on cardiac examination. Deep tendon reflexes are 3+. Serum studies show an undetectable TSH concentration, thyroxine (T₄) concentration of 20 µg/dL, and triiodothyronine (T₃) concentration of 275 ng/dL. Which of the following is the most likely mechanism of this patient's symptoms? (A) Activation of mutations of TSH receptors (B) Increased serum thyroglobulin concentration (C) Ischemic injury to the hypothalamus (D) Lymphocytic infiltration of the thyroid (E) Presence of TSH receptor autoantibodies

Correct Response:

D

Synthesize Response:

D✓

Synthesize Answer

Introduction

Most likely mechanism: Lymphocytic (autoimmune) infiltration of the thyroid causing a destructive, painless postpartum thyroiditis leading to transient thyrotoxicosis (Choice D). This presentation—3 months postpartum, nontender goiter, no ophthalmopathy, suppressed TSH with elevated T4/T3—fits postpartum destructive thyroiditis rather than Graves disease. The American Thyroid Association (ATA) advises specifically distinguishing postpartum destructive thyroiditis from postpartum Graves disease and treating symptoms with β -blockers when needed [1][2][3]. Supporting evidence indicates postpartum thyroid dysfunction is an autoimmune-mediated destructive process, consistent with lymphocytic infiltration [4], with additional immunogenetic data (increased HLA associations) favoring an autoimmune etiology in painless/postpartum thyroiditis [5]. Serum thyroglobulin has been reported as helpful in differentiating destruction-induced postpartum thyrotoxicosis from recurrent Graves in small cohorts, further aligning this case with a destructive process rather than antibody-mediated stimulation [6].

Key points for practice (consistent with ATA):

- Distinguish postpartum destructive thyroiditis from Graves disease in women developing thyrotoxicosis after delivery [1].
- Manage symptomatic thyrotoxicosis from destructive postpartum thyroiditis with judicious β -blockade; antithyroid drugs are generally unnecessary in destructive thyroiditis [2][3].

Rationale in this patient: The timing (postpartum), lack of tenderness and ophthalmopathy, and typical biochemical thyrotoxicosis pattern are most consistent with a destructive autoimmune process rather than TSH receptor-mediated stimulation (Graves) or receptor mutations. Thus, the most likely mechanism is lymphocytic infiltration of the thyroid with release of preformed hormone [1][4][5].

References

[1] Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis

American Thyroid Association

2016-10-01

106. In women developing thyrotoxicosis after delivery, selective diagnostic studies should be performed to distinguish postpartum destructive thyroiditis from postpartum GD.

<https://www.liebertpub.com/doi/full/10.1089/thy.2016.0229>

[2] Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis

American Thyroid Association

2016-10-01

107. In women with symptomatic thyrotoxicosis from postpartum destructive thyroiditis, the judicious use of β -adrenergic blocking agents is recommended.

<https://www.liebertpub.com/doi/full/10.1089/thy.2016.0229>

[3] Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis

American Thyroid Association

2016-10-01

119. Patients with symptomatic thyrotoxicosis due to painless thyroiditis should be treated with β -adrenergic-blocking drugs to control symptoms.

<https://www.liebertpub.com/doi/full/10.1089/thy.2016.0229>

[4] Interleukin-6 levels are not increased in women with postpartum thyroid dysfunction.

1998-05-01

Postpartum thyroid dysfunction (PPTD) is an autoimmune-mediated thyroid destructive process. IL-6 levels found to be similar in women with PPTD compared with women without PPTD; no significant differences across time points.

[10.1089/thy.1998.8.371](https://doi.org/10.1089/thy.1998.8.371)

[5] Increased frequency of HLA-DR3 and 5 in the syndromes of painless thyroiditis with transient thyrotoxicosis: evidence for an autoimmune aetiology.

1983-12-01

50 patients with painless thyroiditis with transient thyrotoxicosis (including 25 postpartum) showed increased frequency of HLA-DR3 and -DR5, favoring an autoimmune rather than viral etiology.

[10.1111/j.1365-2265.1983.tb00047.x](https://doi.org/10.1111/j.1365-2265.1983.tb00047.x)

[6] Differentiation of postpartum thyrotoxicosis by serum thyroglobulin: usefulness of a new multisite immunoradiometric assay.

1994-01-01

Serum thyroglobulin is useful for differentiation of destruction-induced thyrotoxicosis from Graves' thyrotoxicosis after delivery. In this small series, 7/7 above a Tg cut-off developed destruction-induced thyrotoxicosis; 6/7 below had recurrent Graves' disease.

[10.1089/thy.1994.4.275](https://doi.org/10.1089/thy.1994.4.275)
