



Brigham and Women's Hospital
Founding Member, Mass General Brigham

General Internal Medicine Board Review

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- Clinical focus: Internal Medicine
- Interests: Population Health, Career Development

No disclosures



Question 1

46 yo M presents for follow-up of hypertension. He takes lisinopril 40 mg, HCTZ 25 mg, and amlodipine 10 mg. He is compliant with his medications. BP is 152/92. What would be the best choice of an additional medication to control his BP?

- A. Aliskiren
- B. Spironolactone
- C. Doxazosin
- D. Bisoprolol
- E. Valsartan



Answer: B

Resistant hypertension

- Hypertension despite maximal dose of 3 anti-hypertensives of different classes, one of which is a diuretic.
- PATHWAY-2 study (2015): for patients with resistant hypertension (pts were on ACE/ARB, CCB and diuretic), spironolactone was most effective additional agent vs bisoprolol or doxazosin
- ACC/AHA 2017 hypertension guidelines: spironolactone (or eplerenone) is the preferred medication for resistant hypertension.
- Monitor for hyperkalemia if used with ACE/ARB.
- Consider evaluation for secondary causes of HTN.



Question 2

65 yo professor presents after a colleague found him wandering, unable to find his office. His wife reports several falls, 2 episodes where he thought he saw another person at the dinner table with them, and that he thrashes around violently in his sleep. Only 1 year ago he accepted a major prize for his research.

On exam he is orthostatic with slowed speech, and some limb rigidity. No tremor. He has marked difficulty with clock drawing. B12, TSH, RPR are nl. MRI shows cortical atrophy.



Question 2

Based on these findings, the most likely diagnosis is:

- A. Alzheimer's disease
- B. Parkinson's disease
- C. Lewy body dementia
- D. Multi-infarct dementia
- E. Normal pressure hydrocephalus



Answer: C

Lewy body dementia

- Typically shorter course than Alzheimers, often with rapid decline.
- Early deficits in visuospatial and executive functioning
- Core features in addition to dementia (need 2+ for dx)
 - Visual hallucinations - highly specific for Lewy body
 - Cognitive fluctuations with variable attention/alertness
 - REM sleep disorder: “acting out dreams”
 - Parkinsonism, especially bradykinesia and stiffness



Answer: C

Lewy body dementia

Other supportive features:

- Onset of dementia and Parkinsonian symptoms typically within 1 year of each other
- Postural instability ☐ frequent falls
- Apathy, depression, anxiety
- Autonomic dysfunction
- Extreme sensitivity to anti-psychotics (avoid!)

Imaging:

- MRI, advanced SPECT/PET techniques and EEG all have characteristic findings



Question 3

A 33-year-old female presents to establish care. Her medical history is significant for Hodgkin's lymphoma diagnosed at age 14 and treated with ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) plus chest irradiation. She has been free of disease since completion of therapy. She feels entirely well and has no complaints.



Question 3

Which of the following screening tests is indicated in this 31-year-old woman?

- A. Annual mammograms
- B. Annual breast MRIs
- C. Echocardiogram every other year
- D. Annual TSH
- E. All of the above



Answer: E

Pediatric cancer survivorship

General principles of pediatric cancer survivorship

- Childhood cancer survivors are at increased risk of treatment-related toxicities – both malignant and non-malignant
- Risk varies with treatment regimen
- Imperative to know specifics of treatment and manage accordingly
- **High index of suspicion for serious illness even in young patients**



Answer E

Hodgkin's lymphoma survivorship

- 18-fold increased risk of secondary malignancy
 - Risk of cancer: 26% at 30 years post tx; higher in women
 - 13% of female survivors will get breast cancer by age 40
 - Poorer treatment outcomes vs pts with *de novo* cancers
- Cardiovascular complications from mediastinal irradiation increase with anthracycline treatment
 - Accelerated atherosclerosis primary cause of death
 - Valvular disease, LV dysfunction, arrhythmias common
- Pulmonary complications in patient who received bleomycin +/- chest irradiation



Answer E

Hodgkin's lymphoma survivorship

- Thyroid dysfunction in as many as 30% of survivors
- Infertility/premature menopause
- Anxiety, posttraumatic stress symptoms, neuro-cognitive dysfunction
- Financial distress
- Un- or underemployment
- Therapy continues to advance immediate and long term outcomes



Answer E

Hodgkin's lymphoma survivorship

- Female patients with chest irradiation:
 - Mammograms AND breast MRI annually from age 25 or 8 years post treatment (whichever is latest)
- Chest irradiation + anthracycline treatment:
 - Echocardiogram/EKG at least q2yr
- Thyroid testing annually
- Pelvic or abdominal radiation (not this patient):
 - Colonoscopy at 30 or 5 yr post treatment
- Don't forget immunizations



Pediatric cancer survivorship

Clinical guidelines for follow up according to specific treatment regimens:

- Children's Oncology Group Long-Term Follow-up Guidelines– great resource
- www-survivorshipguidelines.org



Question 4

24 yo M presents for a routine exam. He feels entirely well and has no medical problems. He was born in China and emigrated to the US at age 4. His mother died at age 46 from liver cancer. No high-risk sexual behaviors.

Testing reveals the following:

- HBsAg: positive
- Anti-HBs: negative
- Anti-HBc: positive
- HBeAg: positive
- ALT/AST normal
- Viral load >100 million



Question 4

What is the best next step?

- A. No intervention; repeat testing in 3 months and consider treatment if ALT is elevated
- B. No intervention; repeat testing in 3 months and consider treatment if viral load does not decline
- C. Refer for liver biopsy
- D. Start entecavir



Answer: A

Chronic hepatitis B

Initial immune-tolerant phase:

- if hep B acquired at birth, lasts 20-30 years
- if hep B acquired as an adult, short or absent
- HBeAg positive, high viral load, normal ALT
- minimal inflammation or fibrosis
- typically asymptomatic
- highly infectious due to high viral load

Surveillance for progression

- ALT, viral load q3-6 months; HBeAg q6-12 months

Consider treatment if ALT persistently elevated



Chronic hepatitis B

PHASES OF CHRONIC HEP B INFECTION*					
	sAg present?	e-antigen present?	ALT	Viral load	Histologic findings
Immune tolerant	Yes	Yes	normal	Typically > 10 million IU/mL	Minimal inflammation No fibrosis
Immune active	Yes	Yes	Elevated	>20,000	Chronic hepatitis with moderate-severe necroinflammation +/- fibrosis
		No	Elevated	>2000	
Inactive carrier (immune control)	Yes	No (anti-HBe positive)	Normal	<2000	No necroinflammation Variable fibrosis
Resolved (infrequent)	No	No	Normal	undetectable	
Reactivation (spontaneous or due to immunosuppression)		No	Elevated	Increased over baseline	Inflammation

*Phases are not always sequential and patients may fall in indeterminate areas



Question 5

A 68-year-old male complains of urinary urgency, frequency and awakening 3 times a night to urinate small volumes. He denies hesitancy, terminal dribbling, weak stream, or straining to void. He has cut back on caffeine and alcohol with no improvement. On exam, his prostate is mildly enlarged, smooth and symmetrical. PVR is 20 ml. Urinalysis is unremarkable; PSA and renal function are normal.



Question 5

The best first choice of medication for him would be:

- A. Tamsulosin
- B. Solifenacin
- C. Finasteride
- D. Sildenafil
- E. Bladder botulinum toxin



Answer: B

Male lower urinary tract symptoms

- Not all LUTS are due to prostatic enlargement
- Common causes include:
 - Prostate: BPE (BPH), prostate cancer
 - Bladder: detrusor overactivity, bladder tumor, bladder neck obstruction
 - Other GU: urethral stricture, distal urethral stones
 - Neurogenic: CVA, PD, MS, spinal cord injury
 - Systemic: Obesity, DM, CVD, OSA, UTI
 - Meds: antidepressants, diuretics, caffeine



Answer: B

Male lower urinary tract symptoms

Lower urinary tract symptoms

- Bladder storage phase symptoms:
 - Urgency, frequency , nocturia, involuntary loss of urine
- Bladder outlet obstruction symptoms:
 - Hesitancy, incomplete emptying (elevated post void residual), weak stream, dribbling

This patient has an enlarged prostate but no symptoms of bladder obstruction and normal PVR

First choice for overactive bladder without bladder outlet obstruction is an anti-muscarinic



Question 6

Which of the following patients should be treated for latent TB infection?

- A. 58 yo M starting hemodialysis with PPD 10 mm
- B. 27 yo student from Uganda with PPD 5 mm
- C. 34 yo injection drug user with cough, weight loss
- D. 24 yo suburban teacher with PPD 10 mm
- E. 45 yo healthy spouse of patient with active pulmonary TB and negative PPD



Answer: A

Latent TB infection

- Infection without clinical evidence of active TB
- Approximately 13 million people in US have LTBI
 - Reactivation is most common cause of new TB in US
 - ~5% will reactivate within 2 years of infection
 - ~5% will reactivate at some point
- Goal: to screen those at high risk for reactivation:
 - Recent PPD conversion
 - HIV-positive
 - Immunosuppressed
 - Close contacts of patients with active TB
 - High risk medical conditions including:
 - DM, ESRD, substance abuse, head/neck or hematologic malignancy, malabsorption/intestinal bypass



Answer: A

Latent TB infection

- Who should be treated for LTBI?
- PPD 5 mm* is considered positive in:
 - HIV positive
 - Immunosuppressed
 - Close contacts of pts with active TB
 - Patients with an abnormal CXR suggesting healed TB
- PPD 10 mm:
 - IV drug users
 - Homeless or residents/employees of congregate housing
 - Healthcare workers including lab personnel
 - Patients with high-risk medical conditions
 - Recent arrivals from high incidence areas



*Ignore history of BCG vaccination when interpreting TST results

Answer: A

Latent TB infection

For this case:

- A. Hemodialysis patients are at high risk for reactivation and should be treated
- B. From TB endemic area: likely early exposure and lower risk of reactivation
- C. Symptoms of active pulmonary TB and should be tested with sputum AFB testing
- D. Low risk patients should not be tested but if they are, should not be treated unless PPD>15 mm
- E. This patient tested negative and does not need treatment now; however, they are at high risk of contracting TB and should be retested 8-10 weeks after last exposure



Question 7

45 yo F presents with persistently abnormal LFTs. She feels entirely well. History of early stage breast cancer 3 yrs prior, on tamoxifen and leuprolide. BP 122/74, BMI 21, exam normal.

Testing shows:

- AST 184, ALT 226, alk phos 130, bili normal
- Hep A,B,C negative
- ANA, AMA negative, ferritin 550, Tsat 28%
- Liver US: fatty liver



Question 7

What would you do next?

- A. Recommend weight loss of 5% body weight
- B. Prescribe steroids
- C. Prescribe N-acetylcysteine
- D. Discontinue medications
- E. Refer for liver biopsy



Answer: D

Drug induced liver injury

- Often overlooked cause of abnormal LFTs
- Onset ranges from days to a year; even if no longer taking the drug
- Risks typically idiosyncratic to specific drug
- Classification of injury helps guide evaluation:
 - Presence/absence of immune features such as fever, eosinophilia
 - Type of liver injury: hepatocellular vs cholestatic vs mixed



Answer: D

Drug induced liver injury

Evaluation:

- Complete H&P including all meds, OTC, supplements used in last year and timing relative to injury
- For hepatitis/mixed picture: viral serologies (+/- CMV, EBV), autoimmune serologies (ANA, AMA, ASMA), ultrasound
- For cholestatic picture: autoimmune serologies, imaging (ultrasound +/- cholangiography)

When to consider liver bx? If autoimmune, planning steroids, progression or failure to resolve after stopping culprit med



Answer: D

Drug induced liver injury

Pattern of LFTs/histology for liver injury from common drugs:

- Hepatocellular: APAP, ASA, allopurinol, NSAIDs, methotrexate, statins, valproic acid
- Cholestatic: amox/clav, sulfonamides, nitrofurantoin, anabolic steroids
- Autoimmune hepatitis: minocycline, TNF- α , nitrofurantoin
- **Steatohepatitis (this case): tamoxifen**, amiodarone, methotrexate, valproic acid
- Fibrosis: methotrexate



Drug-induced liver injury

Treatment:

- **Stop offending agent**
- Steroids for DILI with systemic hypersensitivity features or positive autoimmune serologies
- N-acetylcysteine: used in acetaminophen toxicity, may help in acute liver failure from other drugs
- Ursodeoxycholic acid: sometimes considered for DILI with cholestasis – but few data to support use

LiverTox website (<http://livertox.nlm.nih.gov>)



Question 8

A 45 yo transwoman (MTF) presents to discuss gender-affirming hormone therapy. At her recent annual exam she was found to be in good health, with negative STD testing. She has not had any prior medical or surgical treatments related to gender. Her father had prostate cancer. Though she is estranged from her biologic family, she has a close circle of friends whom she deems family. She does not smoke. No substance abuse. Mental health history is positive for gender dysphoria since her teens but no other major mental health diagnoses



Question 8

Which of the following is TRUE re: care of patients on MTF gender-affirming hormone therapy?

- A. Ethinyl estradiol is the preferred estrogen to suppress androgen secretion.
- B. Prostate cancer screening is no longer necessary in patients on hormone therapy > 1 yr, due to low circulating androgens.
- C. Breast development is only modest on estrogen therapy.
- D. Anti-androgens such as spironolactone are useful adjuncts to estrogen therapy to reduce male secondary sexual characteristics such as facial hair and deep voice.



Answer: C

- Ethinyl estrogen is contraindicated due to increased risk of VTE. All estrogen preparations increase risk; transdermal estradiol is lowest.
- The risk of prostate cancer in transwomen is lower than in cis-gender men, but prostate cancer screening should proceed according to same guidelines. However, PSA may be suppressed by estrogen therapy and **PSA levels >1** should prompt further evaluation.



Answer: C

- Breast growth is usually modest (\leq A cup); some pts only develop breast buds. Growth starts at 2-3 months and is complete by 2 years.
- Spironolactone is often used with estrogen therapy. It directly inhibits testosterone secretion and binding to the testosterone receptor; it may also exert an estrogenic effect of its own. It is useful to reduce male pattern facial hair, but it does not result in alterations in voice. Speech therapy may be beneficial for those wishing to change their voice.



Question 9

72 yo female with COPD (FEV1/FVC .6, FEV1 55% predicted) presents for follow up. She has had a good year with no exacerbations, but notes slowly progressive loss of exercise tolerance, finding it hard to keep up when walking with family due to breathlessness. Current medications include daily inhaled tiotropium and albuterol prn.



Question 9

For this patient classified as GOLD 2, STAR 1-2 what would be the best class of medications to add to her current regimen of daily tiotropium and prn albuterol

- A. Short acting muscarinic
- B. Long-acting beta agonist
- C. Theophylline
- D. Inhaled corticosteroid
- E. Phosphodiesterase-4 inhibitor



Answer: B

For GOLD 2B (more symptomatic/lower exacerbation risk) pts who are still symptomatic despite use of a single long-acting bronchodilator (LAMA or LABA):

Escalate to combination therapy with LAMA + LABA

- Increases FEV1
- Reduces symptoms vs. monotherapy
- Reduces exacerbations
- Inhaled steroids: increase risk of pneumonia (reserve use)

If insufficient response to LAMA + LABA

- Escalate to LAMA + LABA + ICS
- Consider checking eosinophil count (<100 likely no benefit, >300 likely benefit from ICS)



Answer: B

- Theophylline: modest bronchodilator effect and toxicity is an issue
- PDE-4 inhibitors: modest benefit, reserved for pts with frequent exacerbations despite maximal inhaled therapies



Question 10

A 45 yo woman presents to establish care. She moved to the area to care for her father who just died of metastatic prostate cancer at age 74. She worries that she will also get cancer. She has read about companies that do genetic testing and wants to know what you think. There is no other history of cancer in her family. What advice do you give her?



Question 10

- A. Advise against genetic testing as her family history of prostate cancer is not a problem for a woman
- B. Advise against genetic testing because her family history is not suggestive of a hereditary syndrome
- C. Advise against genetic testing because even if a pathologic variant is identified, there is nothing that can be done
- D. Suggest genetic testing and agree with direct-to-consumer testing as an inexpensive alternate to genetic counseling/testing
- E. Suggest genetic testing but recommend it be performed in consultation with a genetic counselor



Answer: E

Genetic testing/cancer risk

- BRCA gene mutations are associated with increased risk of breast, ovarian, pancreatic and high grade prostate cancers.
- Study of 692 men with metastatic prostate cancer
 - 11.8% had germline mutations in DNA repair genes
 - vs 4.6% men with localized prostate cancer
 - vs 2.7 % men without cancer
 - *BRCA2* (44%), *ATM*(13%), *CHEK2*(12%), and *BRCA1*(7%)
 - Mutation frequencies did not differ with FHx prostate cancer or age at diagnosis



Answer: E

Genetic testing/cancer risk

- NCCN 2020 guidelines include recommendations for genetic testing of anyone with a first degree relative with pancreatic or metastatic prostate cancer, regardless of age at diagnosis
- Continue to test anyone with first degree relative with ovarian cancer at any age
- See guidelines for specifics of testing for family history of breast cancer



Answer: E

Genetic testing/cancer risk

- Genetic testing is a multistep process that should include a genetic counselor, specialty physicians (genetics, oncology etc)
- Issues: insurance coverage, privacy, stigma, implications of results for patient and family, possibility of variants of unknown significance, need for appropriate referral for medical/surgical management
- Guidelines recommend testing only for conditions for which risk mitigation and/or treatment is available



Answer: E

Genetic testing/cancer risk

Direct to consumer genetic testing is inadequate for medical decision making

- Testing is often incomplete and can falsely reassure patients at risk
- False positive rates as high as 40% have been documented on independent testing
- Interpretation/counseling/management are not provided

Confirm any result of direct-to-consumer testing



Question 11

A 67 yo male presents for follow up after a spell of L arm weakness that lasted 30 minutes then resolved spontaneously. His medical history is significant for hypertension and hyperlipidemia. His neurologic exam is completely normal. MRI brain/MRA head and neck showed no infarct or hemodynamically significant stenosis. Echocardiogram was normal and a 7 day event monitor showed no arrhythmias.



Question 11

Which of the following is the best option for long-term secondary prevention of stroke in this patient who has had a TIA?

- A. Warfarin
- B. Ticlopidine
- C. ASA
- D. Prasugrel
- E. ASA + clopidogrel



Answer: C

Secondary prevention of stroke

Antiplatelet agents are useful for secondary prevention; current AHA/ASA guidelines recommend:

- ASA (low doses as effective as high doses)
- ASA + dipyridamole
- Clopidogrel
- On average, risk of stroke reduced by 22% with these agents

Long term use of ASA + clopidogrel led to an increased risk of bleeding with no reduction in vascular risk (MATCH trial)



Answer: C

Secondary prevention of stroke

- Warfarin should not be used in patients with a non-cardioembolic TIA/stroke
- Ticlopidine is effective for prevention but is associated with significant side effects (severe neutropenia, rash, diarrhea)
- Prasugrel – studies of prasugrel in ACS noted increased risk of intracranial bleeding especially in stroke patients and it is therefore not recommended
- Don't forget management of risk factors (lipids, DM, HTN etc)



Question 12

A 19-year-old female with a history of IUD placement 3 weeks ago presents with complaints of crampy lower abdominal pain and dyspareunia. She is afebrile and vital signs are normal. Her exam is notable for cervical friability and bilateral adnexal tenderness. Pregnancy test is negative.



Question 12 (con't.)

What treatment to you recommend?

- A. Ceftriaxone 250 mg IM + azithromycin 1 g
- B. Ciprofloxacin 500 mg bid x 7 days and metronidazole 500 mg tid x 7 days
- C. Ceftriaxone 500 mg IM + doxycycline 100 mg b.i.d. + metronidazole 500 mg b.i.d. x14 days
- D. Drug regimen in C plus removal of the IUD.



Answer: C

Pelvic inflammatory disease

- Ascending infection of the female upper genital tract
- Major cause of infertility and ectopic pregnancy
- Polymicrobial infection: *C. trachomatis* and *N. gonorrhoeae*, streptococci, gram-negatives, anaerobes, *M. genitalium*
- Presentation: lower abdominal or pelvic pain +/-
 - Dyspareunia, intermenstrual or post-coital bleeding
 - Vaginal discharge, dysuria also common
- **Treat if any one:** uterine, adnexal or cervical motion tenderness, **microbial testing is not needed.**



Answer: C

Pelvic inflammatory disease

- Treatment needs to cover common organisms
- Increasing resistance has led to updated recommendations in treating gonorrhea/chlamydial infections
- Gonorrhea: Current guidelines for treating gonorrhea: single 500 mg dose ceftriaxone (1 g if >300 lb)
- Chlamydia: Doxycycline favored over azithromycin if possible gonococcal co-infection
- Anaerobes: Improved long term outcomes in PID with addition of metronidazole (also covers trichomonas)
- **PID treatment (outpatient) incorporating above changes:** Ceftriaxone 500 mg IM + doxycycline 100 mg bid x 14 d + metronidazole 500 mg bid x14 d
- IUDs do not have to be removed unless no response in 48 hr



Question 13

44 yo male presents with pain/stiffness in his hands. He also notes some erectile dysfunction. He has recently been diagnosed with diabetes and is being evaluated for abnormal liver function tests. On exam he has bony enlargement of 2nd, 3rd MCPs but no synovitis. What test is most likely to be diagnostic?

- A. Anti-nuclear antibody
- B. Transferrin saturation
- C. Anti-cyclic citrullinated peptide antibody
- D. Rheumatoid factor
- E. No laboratory testing needed



Answer: B

Hemochromatosis

Iron overload as a result of mutations in *HFE* gene

Frequency: 1 in 200-500 people in US

Symptoms:

- Early: arthropathy, fatigue, impotence
- Late: diabetes, cirrhosis, cardiomyopathy

Polyarticular/symmetric arthritis is common

- Classic: bony enlargement of 2nd/3rd MCPs without synovitis
- Earlier than OA by decade or more

Screen: Fe/TIBC (>60% men, >50% women)

Positive screens should be followed up by genetic testing

