Session 5: Neurology and General Psychiatry
Answer Explanations

Neurology

1. **Answer C:** *Blue discoloration of the skin.*
   Ezogabine administration can lead to a blue discoloration of the lips, nail beds, face, legs, sclera, and conjunctiva. This effect may be permanent. Agranulocytosis is seen with a number of antiepileptics, including carbamazepine and felbamate. Angioedema has been reported with pregabalin and gabapentin. Perianal itching is an adverse effect of fosphenytoin.
   <u>Reference</u>
   Shkolink G, Feuerman H, Didkovsky E, et al. Blue-gray mucocutaneous discoloration: a new adverse effect of ezogabine. JAMA Derm 2014;150:987-9.

2. **Answer A:** *A 37-year-old man from India.*
   Patients with the *HLA-A*3101* allele are at a 10-fold elevated risk of Stevens-Johnson syndrome. Testing is recommended for Asians, including Indians.
   <u>Reference</u>
   Bloch KM, Sills GJ, Pirmohamed M, Alfirevic A. Pharmacogenetics of antiepileptic drug-induced hypersensitivity. Pharmacogenomics 2014;115:857-68.

3. **Answer D:** *Dabigatran 150 mg twice daily.*
   The patient's $CHADS_2$ score is 3, so she needs oral anticoagulation.
   <u>Reference</u>
   Culebras A, Messe SR, Caturvedi S, et al. Summary of evidence-based guideline update: prevention of stroke in nonvalvular atrial fibrillation. Neurology 2014;82:716-24.

4. **Answer B:** *Add quetiapine.*
   Although reducing the dose of carbidopa/levodopa may be effective at reducing the hallucinations, she is on a low dose and experiences debilitating Parkinsonian symptoms when she is late with or misses a dose. Therefore, she is unlikely to be able to reduce the dose. Typical antipsychotics, risperidone, and olanzapine have been shown to worsen Parkinsonian symptoms. Quetiapine is the drug of choice in this situation.
   <u>Reference</u>
   Miyasaki JM, Shannon K, Voon V, et al. Practice parameter: evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2006;66:996-1002.

5. **Answer B:** *Metoprolol.*
   Frovatriptan should not be used prophylactically in this situation. It is occasionally used for short-term prophylaxis for menstrually associated migraine. Propranolol, topiramate, and valproic acid are all effective for migraine prevention; however, propranolol may also be helpful for his hypertension. He would require blood pressure monitoring to determine whether he needs to transition to propranolol alone or simply add it to lisinopril.

Reference
Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 2012;78:1337-45.

6. **Answer C:** *Immunize for varicella today and begin fingolimod in 1 month.*
   Fatal varicella infections have occurred in patients without immunity who were treated with fingolimod. The recommendation is to vaccinate and wait 1 month to initiate therapy.
   Reference
   Willis MA, Cohen JA. Fingolimod therapy for multiple sclerosis. Semin Neurol 2013;33:37-44.

General Psychiatry

7. **Answer D:** *Paroxetine.*
   All antidepressants are equally efficacious in treating symptoms of depression. Therefore, the antidepressant adverse effect profile should be matched to the patient's symptoms. Because this patient was admitted for a medication overdose, nortriptyline would be poor choice. It and other tricyclic antidepressants are fatal in overdose. Bupropion, which can cause insomnia and decrease in appetite, would not be the best fit for a patient with anorexia and early morning awakening. Between the two SSRIs, fluoxetine is more activating and may therefore be less optimal. Paroxetine can increase appetite and cause sedation. This makes it a good fit for this patient.
   References
   i. Lam RW, Kennedy SH, Grigoriadis S, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. III. Pharmacotherapy. J Affect Disord 2009;117:S26-43.
   ii. Working Group on Major Depressive Disorder. Practice Guideline for the Treatment of Patients with Major Depressive Disorder, 3rd ed. Arlington, VA: American Psychiatric Association, 2010. Available at: http://psychiatryonline.org/guidelines.aspx. Accessed April 30, 2014.

8. **Answer B:** *Divalproex***.**
   This patient is experiencing a mixed episode in which both manic (pressured speech, hyperactivity, and agitation) and depressive (depressed affect, negative self-image, and suicidal ideation) symptoms exist simultaneously. Divalproex has the best evidence for efficacy in treating mixed states. Lithium tends to be suboptimal in these cases, and evidence for carbamazepine is weak. Lamotrigine has some efficacy against manic symptoms but is more optimal for the treatment of the depressive phase of bipolar disorder type I.
   References
   i. Suppes T, Dennehy EB, Hirschfeld RM, et al. The Texas implementation of medication algorithms: update to the algorithms for treatment of bipolar I disorder. J Clin Psychiatry 2005;66:870-86.
   ii. Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD)

collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2013. Bipolar Disord 2013;15:1-44.

9. **Answer B:** *Clozapine.*
   Although this patient responded to haloperidol, she can be considered to have treatment-resistant schizophrenia, as defined by failure to respond to two or more antipsychotics, including both an FGA and an SGA. She additionally had symptoms of tardive dyskinesia (TD), chewing and eyebrow lifting, so she should be placed on an antipsychotic with minimal risk for causing or worsening her TD. Clozapine is reserved for treatment-resistant schizophrenia and is not associated with tardive dyskinesia. Quetiapine is associated with minimal tardive dyskinesia but is not a good choice in a treatment resistant patient. Aripiprazole is associated with akathisia and is also not indicated for treatment-resistant schizophrenia. Thioridazine is an FGA. As such, it could worsen her TD. She additionally has a history of resistance to other FGAs.
   Reference
   Buchanan RW, Kreyenbuhl J, Kelly DL, et al. The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophrenia Bull 2010;36:71-93.

10. **Answer D:** *Fluvoxamine.*
    Obsessive-compulsive disorder (OCD) responds best to an antidepressant with serotonergic activity. Both fluvoxamine and clomipramine are used to treat OCD, but because of its side effect profile, clomipramine is usually reserved for patients for whom therapy with SSRIs such as fluoxetine has failed. Desipramine has primarily noradrenergic activity. Although buspirone is sometimes used as an adjunct in treatment-resistant OCD, it is not used as monotherapy,
    Reference
    Bandelow B, Zohar J, Hollander E, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders: first revision. World J Biol Psychiatry 2008;9(4):248-312.

11. **Answer C:** *Suvorexant.*
    This patient has difficulties with both sleep latency and sleep maintenance. Suvorexant can both decrease sleep latency and improve sleep time. It is also the only agent listed that is indicated for this pattern of insomnia. Although the pharmacokinetic profile of doxepin also fits the patient’s insomnia pattern, it is indicated only for impaired sleep maintenance. In addition, the presence of anticholinergic side effects lends itself to a higher risk for hangover effect. Both ramelteon and zaleplon have rapid onsets of action. They are good choices for patients with delayed sleep onset but play no role in maintaining sleep.
    References
    i. Belsomra, suvorexant [package insert]. Whitehouse Station, NJ: Merck & Co., Inc., 2014.
    ii. Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med 2008;4:487-504.

12. **Answer B:** *Nicotine gum + patch.*
    K.P. was not previously using the nicotine lozenge correctly. It should be dissolved in the mouth, not chewed and swallowed. This probably caused the gastrointestinal symptoms he experienced. Because he smokes 2 packs per day, the 14-mg patch was probably not a high enough dose. He would probably benefit from a combination of patch and as-needed nicotine dosage form. The nasal spray is prescription only and probably as expensive as the inhaler. Both bupropion and varenicline lower the seizure threshold and should be avoided in this patient. Although depression is not a contraindication for varenicline therapy, the patient would need to be closely watched for increased risk of suicidal ideation even if he did not have seizure disorder.
    Reference
    FIore MC, Jaén CR, Baker TB, et al. Treating tobacco use and dependence: 2008 update—a clinical practice guideline. Rockville, MD: U.S. Department of Health and Human Services 2008.