

Patient Management Exercise

FOR PSYCHOPHARMACOLOGY

B. Harrison Levine, M.D., M.P.H.
Ronald C. Albucher, M.D.

This exercise is designed to test your comprehension of material presented in this issue of *FOCUS* as well as your ability to evaluate, diagnose, and manage clinical problems. Answer the questions below, to the best of your ability, on the basis of the information provided, making your decisions as you would with a real-life patient.

Questions are presented at “decision points” that follow a section that gives information about the case. One or more choices may be correct for each question; make your choices on the basis of your clinical knowledge and the history provided. Read all of the options for each question before making any selections.

You are given points on a graded scale for the best possible answer(s), and points are deducted for answers that would result in a poor outcome or delay your arriving at the right answer. Answers that have little or no impact receive zero points. On questions that focus on differential diagnoses, bonus points are awarded if you select the most likely diagnosis as your first choice. At the end of the exercise you will add up your points to obtain a total score.

VIGNETTE

You are an adult psychiatrist in private practice. A patient was referred to you by the local psychiatric emergency services for outpatient follow-up. He presented to the psychiatric emergency services six days earlier for feelings of worthlessness, helplessness, mild but persistent suicidal ideation without intention or plan, poor sleep with both initial and middle insomnia, waking 3–4 times per night. He says he has had insomnia since he was a teenager. He normally works out 6 times per week but has not been able to go to the gym for the past two months due to lack of energy and desire. He does not enjoy movies because he can't focus and says he typically would have gone to the

theater once or twice per week. He is quite anxious, stating “my OCD is out of control.” He tells you he has not lost or gained significant weight. After stabilization in the emergency room he contracted for safety and an appointment was set up for him to see you.

He arrives early for his appointment, dressed appropriately, well groomed, with good hygiene. You notice as he enters your office that he keeps his gaze fixed either to the floor or to you, but does not seem to notice his surroundings. He is friendly but does not offer his hand when you offer yours. He takes out a piece of tissue from the box beside the chair you offer and wipes the seat quickly before sitting down. He keeps his gaze fixed to yours.

You begin the interview. He is a 31-year-old single Asian-American male, currently unemployed, who moved back to your town approximately three months earlier to live with his father. He tells you he moved home to his father's house because he was having trouble while living with his mother in Korea. She and his father divorced when the patient was 17 years old. His mother returned to Korea while his father, who is Caucasian, remained at home. He has a twin brother with whom he has not

CME Disclosure

B. Harrison Levine, M.D., M.P.H., Department of Child and Adolescent Psychiatry, New York Presbyterian Hospital of Columbia and Cornell Universities.
No affiliations with commercial interests.

Ronald C. Albucher, M.D., Adjunct Clinical Assistant Professor of Psychiatry, University of Michigan Medical School.

No affiliation with commercial interests.

had any contact in nearly 10 years due to his brother's illness. "It's just impossible to deal with him," he tells you.

You ask what happened in Korea. He says he lived there for the past 1.5 years. He left Los Angeles, where he worked as a financial analyst for a major banking firm because he became addicted to injecting heroin and cocaine. He says he has been tested for HIV and hepatitis and is negative. He tells you he did share needles and purposely used dirty needles to try and die. He has many friends, some are highly educated professionals; they performed an intervention to get the patient to quit using drugs and get help. He went to an inpatient rehabilitation center in Los Angeles for 14 days and then left for Korea. He says he stayed clean from heroin and cocaine since then.

He remembers his mother thought he was a "fussy" baby. He remembers crying at the age of 5 years because his family lived in a house with a leaky faucet. He would cry when he heard the leaking faucet because he thought all of the world's water would drain away there unless it could be shut off. That's the first time he remembers checking faucets on a daily basis. At first he would do it before bedtime, but by the time he was in junior high school he was also checking door locks because he thought his family might be robbed. He remembers as a child twisting his neck in a circle when he saw a corner because he did not like sharp edges. He would make the circle with his eyes and tongue as well because it felt like smoothing out the edges and for a short while he would feel less anxious. But the feeling would inevitably return. When he sees words, especially when they are on a sign or posted on a bulletin board, he has to rearrange the letters into every conceivable pattern, then assigns numerical values for the letters and performs calculations multiplying each number by 2. If he does not do this in a particular order he has to start again.

He also started making grunting noises as a child and his parents took him to the pediatrician because they thought he had a respiratory illness. He has continued to make this sound until the present and he demonstrates for you. He says he also has to take a quick, deep guttural breath before pronouncing certain syllables in words. He sometimes can control these tics but he will have to let them loose later. "It's like squeezing the end of a garden hose," he explains. "Eventually, once I let go, it comes out in a torrent." He denies ever using foul language. He has uttered words like "pinball" or "simple", but has no explanation why these particular words. He tells you he started grunting and blurting out words before the age of 10. He moves his elbow in a circular motion, sticks out his tongue, and often touches any person standing

near to him on the shoulder unconsciously. He finds he can stop these involuntary movements with great concentration and distraction, but inevitably once he relaxes or stops whatever activity was helping him "hold back" the tics, he will have a "tic explosion." He has been exhibiting these tics since he was 7 or 8 years old, he says.

Sometimes, he tells you, he has a panic attack. They are typically unprovoked, "out-of-the-blue", lasting 10–15 minutes, during which he feels diaphoretic, has chest pain and palpitations, and gets a feeling of impending doom. "Sometimes I think I'm about to die, like I'm having a heart attack or losing my mind." He has had episodes when he was afraid to go into public places because he feared he would have a panic attack or otherwise lose control of himself and have no way to escape. "It's horrible and embarrassing," he tells you. "Sometimes I just stay at home rather than risk it. Other times, however, I manage to forget about it and go out." The attacks began when he was a young boy, before he started using alcohol or drugs.

He tells you that he used alcohol, cocaine, heroin, marijuana, ecstasy, LSD, and prescription narcotics to try and relax or stop the tics and checking behaviors when they took over his days and kept him from work. When he uses the drugs he doesn't feel high but is able to stop the behaviors. However, the drugs eventually became a problem; they are difficult to obtain and he ran the risk of getting fired from various jobs if he ever was caught. In between bouts of alcohol dependence he would switch to "my cocktail" of shooting up heroin, cocaine, and smoking marijuana, which he did for at least two and a half years at the longest.

His problem with alcohol began when he was 15, drinking on weekends with friends. This escalated rapidly until he was drinking daily as a junior and senior at a local private high school. He laughs when he tells you he was elected class president both years. He managed to excel in school academically, and participated in wrestling and tennis. His mother came to his events but his father did not; he felt he had no one to push him to be better. He was nationally ranked in both sports as a junior, but quit as a senior during his parents divorce. During his senior year, he drank, first on weekends, then during the week. He began to show up at wrestling practice drunk, was reprimanded, and quit. He says it takes more and more alcohol to get drunk and if he stops he begins to shake, become diaphoretic, feels his heart racing, and feels nausea.

He has tried several times to stop drinking on his own but only succeeded some of the times. Other times he required the assistance of an intervention by family and friends and rehabilitation.

He has been in rehabilitation twice, once when he was in high school, also after an intervention by friends and family. He managed to stay clean from alcohol for several years, but then would relapse. He bounced between alcohol and harder drugs, kicking one for the other. He smokes two packs of cigarettes per day. He began smoking at 18, smoking just one or two per day, but gradually increased over the years to two packs. He has tried to quit numerous times and continues despite knowing the damage cigarette smoking is doing to his body.

He was hospitalized twice for psychiatric reasons relating to suicide attempts. Both hospitalizations were after overdoses. On another occasion he was taken to the emergency room after cutting his wrists, but after he was stitched up he eloped. He reports multiple bouts of major depression since high school, with long periods of remission. He tells you the depressive symptoms were not related to alcohol or drug abuse, but he cannot say this for certain since he has been using alcohol and various substances for so much of his life. He believes the depressive symptoms are related to his inability to control his OCD and tics.

His current depressive symptoms have lasted at least one year, worsening for the past two to three months. He denies hearing voices or visual hallucinations, denies delusions of paranoia or persecution, but is concerned about how others perceive him. "I am acutely

aware of my problems, my tics, my drinking and drug use," he tells you plainly. "I did not get angry each time my family and friends held an intervention. In fact, I was relieved."

Since graduating from college with degrees in mechanical engineering and political science, he has held five different jobs. He was always very strong in mathematics. He did not pursue graduate school; he was hired as an engineer and financial analyst for between 1–2 years before he would quit and move away because his symptoms were becoming too difficult to hide or manage. He made money, invested it well, and moved to Korea to teach English, learn Korean and Japanese, and be close to his mother, and away from troubles at home.

He stayed clean and sober for the first 6 months, but then began drinking again. "All they have in Korea is alcohol," he tells you. "It's extremely strong, but I ended up drinking about a liter or more a day before I left." He got into an alcohol-fueled fight with a taxi driver and wound up in jail just before leaving the country. He tells you he often got into fights while drinking. He would pick fights with random men in clubs, and one time he did get in trouble with the law.

When you ask if he has a partner or love interest, his expression turns flat. Then he laughs. "No," he says. "The longest was about 1 month."

DECISION POINT A:

Given what you know from the above history, what is your differential diagnosis? +2 points are given for correct answers, -2 points for incorrect.

AXIS I:	
AXIS II:	

DECISION POINT B:

Which of the following most accurately describes the initial pharmacological treatment for Obsessive Compulsive Disorder?

- B1. ___ Olanzapine
- B2. ___ Clomipramine with Lithium augmentation
- B3. ___ Clomipramine
- B4. ___ Nortriptyline
- B5. ___ There is no effective pharmacological treatment for OCD. Only Behavioral Therapy is effective.

DECISION POINT C:

Tourette Syndrome has been shown to be comorbid with OCD in 27% of cases. Given that the tics of the patient's Tourette Syndrome and OCD are negatively impacting his ability to function socially and at work, what pharmacologic strategy or strategies would best control his symptoms?

- C1. ___ paroxetine
- C2. ___ paroxetine and haloperidol
- C3. ___ paroxetine and fluphenazine
- C4. ___ methylphenidate
- C5. ___ clonidine

DECISION POINT D:

Match the following medications used to treat alcoholism with their respective utility profiles:

Medication	Utility Profile
D1. Naltrexone	A. Protective against Wernicke's encephalopathy
D2. Acamprosate	B. Causes nausea when alcohol is consumed
D3. Nalmefene	C. Pure opioid receptor antagonist blunts pleasurable effects, reduces craving.
D4. Disulfuram	D. Thrice daily dosing, major side effect is diarrhea
D5. Thiamine	E. Pure opioid receptor antagonist blunts pleasurable effects, reduces craving, known for absence of dose-dependent liver toxicity and more effective binding to central opiate receptors.

DECISION POINT E:

Given this patient's presentation, what medication(s) would you choose to treat his Panic Disorder with Agoraphobia? Rank the following medications by the order you would use them. Write "O" if you would not use them:

- E1. ___ Clomipramine
- E2. ___ Phenzelzine
- E3. ___ Paroxetine
- E4. ___ Buspirone
- E5. ___ Clonazepam
- E6. ___ Alprazolam



DECISION POINT A:

AXIS I:	(+2) Major Depressive Disorder, Recurrent, Severe, Without Psychotic Symptoms; (+2) rule out Substance-Induced Mood Disorder; (+2) Obsessive Compulsive Disorder; (+2) Tourette Syndrome; (+2) Panic Disorder With Agoraphobia; (+2) Alcohol Dependence; (+2) Nicotine Dependence; (+2) Opiate Dependence in Sustained Full Remission; (+2) Cannabis Dependence in Sustained Full Remission; (+2) Cocaine Dependence in Sustained Full Remission; (+2) Polysubstance Dependence in Sustained Full Remission; (+2) Hallucinogen Abuse in Sustained Full Remission
AXIS II:	

Major Depressive Disorder, Recurrent, severe, without psychotic symptoms: The patient complains of multiple episodes of Major Depression with intervals greater than 2 months between them. He complains of both depressed mood and anhedonia, and neither is due to a medical condition. Additionally he complains of depressed mood most of the day, diminished interest in activities, insomnia, loss of energy, feelings of worthlessness, poor concentration, and recurrent suicidal ideation. It is possible that these symptoms could be related to his extensive alcohol and drug use, but from the limited history it is not clear enough to make a definitive diagnosis of Substance-Induced Mood Disorder. For that reason, a rule-out for the latter diagnosis is appropriate. He does not complain of psychotic symptoms.

Obsessive compulsive disorder: The patient complains of both obsessions and compulsions, including intrusive thoughts about cleanliness, sharp corners, the order of numbers. Many of these thoughts are seemingly arbitrary, not related to real-life problems. He attempts to avoid the thoughts about sharp edges and corners by averting his gaze when he comes into your office. He tells you about how he attempts to control the obsessive thoughts in certain social and occupational situations. He also has insight into the obsessive thoughts as products of his own mind. He compulsively washes, orders, checks, rearranges numbers, all to reduce the anxiety produced by the obsessive thoughts. He tells you these thoughts are “out of control” and recognizes these obsessions and compulsions have caused him to leave jobs over the years. They cause marked distress, interfering with his normal occupational and social functioning, and are not restricted to a certain concern.

While it is possible these behaviors and thoughts are exacerbated by alcohol and substances, he reported that the first obsessive thoughts began when he was 5 years old.

Tourette’s disorder: The patient had both multiple motor and one or more vocal tics that were present at some time during the illness. They occurred many times a day nearly every day or intermittently throughout a period of more than 1 year, and during this period there was never a tic-free period of more than 3 consecutive months. Onset was when the patient was 7 or 8 years old.

While it is possible that alcohol or substances may have exacerbated his symptoms, they occurred long before he began using.

Panic disorder with agoraphobia: The patient complains of recurrent, unexpected Panic Attacks that are followed by one month or more of persistent concern about having additional attacks, feeling like the patient is losing control, having a heart attack, or “losing my mind”, and a significant change in behavior related to the attacks. The patient also complains of avoiding situations which might provoke the panic and stays at home.

Alcohol dependence: The patient has been drinking since he was a teenager with several periods of sobriety, but he is currently dependent. He demonstrates a maladaptive pattern of use manifest by tolerance, withdrawal syndrome, using larger quantities of the alcohol to achieve the desired affect, persistent efforts to cut down or quit, and has dropped or quit activities, such as wrestling, due to the alcohol dependence. He was arrested for starting fights while intoxicated and knows his problems worsen with the use of alcohol.

Nicotine dependence: The patient started with 1–2 cigarettes per day and eventually smoked 2 packs per day. He has tried unsuccessfully to cut down, suggesting withdrawal effects, and knows it is dangerous to him physically.

Opiate dependence in sustained full remission: The patient has not met criteria for Dependence or Abuse during a period of 12 months or longer.

Cannabis dependence in sustained full remission: The patient has not met criteria for Dependence or Abuse during a period of 12 months or longer.

Cocaine dependence in sustained full remission: The patient has not met criteria for Dependence or Abuse during a period of 12 months or longer.

Hallucinogen abuse in sustained full remission: The patient abused LSD and Ecstasy to help him cope with his OCD symptoms. He used them recurrently when he knew they would cause him to get fired from jobs. However, he has not used them for more than 12 months.

Polysubstance Dependence in Sustained Full Remission: The patient did use at least three different groups of substances not including caffeine and nicotine and he says that he would shift from alcohol to these other substances, suggesting one was not predominant (his “cocktail”). Dependence criteria were met for the substances individually, however, not only as a group. Additionally, he was in sustained remission from most of the substances. Therefore, although he meets criteria for Polysubstance Dependence in Sustained Full Remission, it is also accurate in this case to list each substance and alcohol separately. This also helps the clinician to understand exactly what substance and alcohol problems the patient has or had.

–2 **Obsessive-Compulsive Personality Disorder:** This diagnosis is for patients who demonstrate a preoccupation with orderliness, perfectionism, and mental and interpersonal control, at the expense of flexibility, openness, and efficiency, beginning by early adulthood and present in a variety of contexts, as indicated by four of eight criteria. This patient has more clear-cut obsessions and compulsions that are less well described as a personality or characterological style and more of an anxiety disorder.

DECISION POINT B:

B1. –3 The question asks for the most common initial treatment option. Since approximately 40% of OCD patients do not respond to SSRIs, olanzapine, an atypical antipsychotic, may be used alone or as an augmentation strategy if a patient does not improve on an SSRI or clomipramine. Also since patients are typically on anti-obsessional medications for long periods of time, you would have concerns about

using danzapine initially given the risks of initiating a metabolic syndrome.

- B2. –2 This is a potent augmentation strategy especially for depression, however the question asks for the most common initial treatment option.
- B3. +5 The tricyclic antidepressant clomipramine is a potent serotonin reuptake inhibitor and the anti-OCD effect has been linked to this property. The neurotransmitter(s) correlated with OCD have not been conclusively identified, and it is likely there are more than one involved; the serotonin hypothesis still dominates the logic behind the treatment of OCD. The evidence of co-morbid depression with OCD supports the utility of a serotonin reuptake blockade, although given the poor response of norepinephrine to treating the OCD suggests it is more sensitive to the serotonin reuptake blockade. Additionally, treatment of the OCD takes 12–26 weeks for a response, compared to 3–6 weeks for the relief of depressive symptoms. A substantial role for the neurotransmitter dopamine is suggested by the relationship between OCD symptoms and certain neurological disorders that feature seemingly purposeless, complex, repetitive behaviors as found in OCD. Additionally, chronic motor tic symptoms featuring the dysfunction of dopamine in the basal ganglia such as Von Economo encephalitis, Tourette syndrome, and Sydenham chorea, suggest a substantial role for this neurotransmitter. Subsequently, many patients do not respond well with an SSRI monotherapy and a variety of augmentation strategies may be tried.
- B4. –3 There is no strong evidence that a norepinephrine reuptake blockade is effective in anti-OCD action. Trials using noradrenergic reuptake inhibitors such as nortriptyline or desipramine have little to no anti-OCD action.
- B5. –5 Behavioral therapy is the most common adjunct therapy to pharmacotherapy. However, it is as effective in the treatment of OCD in selected cases and is often employed before the use of pharmacotherapy. This question, however, asks specifically for the correct medication.

DECISION POINT C:

- C1. +3 Since 45 to 90% of Tourette Syndrome patients have a history of comorbid OCD, the use of an SSRI is a reasonable first choice.
- C2. +5 The use of an SSRI is appropriate for treating the OCD, while a dopamine receptor antagonist is effective at controlling tics. Traditionally, older antipsychotics such as fluphenazine and pimozide are employed for this purpose. These typicals have been shown to be more effective and better tolerated than haloperidol.
- C3. +5 See above.
- C4. -3 Although it was previously felt that a stimulant would cause or worsen tics, one study of 136 children with comorbid ADHD and Tourette Syndrome demonstrated a lessening of tic severity compared to placebo, a similar number of patients with worsening tics comparing methylphenidate, clonidine plus methylphenidate, and placebo (20, 26, and 22% respectively). However, using a stimulant in a patient whose only symptom is tics has not been demonstrated as effective.
- C5. +3 This medication is more effective with comorbid Tourette Syndrome and predominant behavioral, impulse control, and rage control symptoms. While this patient has experienced rage control episodes, has poor impulse control, his OCD is predominantly of the classic variety.

DECISION POINT D:

This question emphasizes the pharmacotherapies for the treatment of alcoholism. It is well-established that group, especially peer-group therapies, with or without medication is most effective.

- D1. +2 C Naltrexone is a pure opioid receptor antagonist that blunts the pleasurable effects of alcohol and reduces craving. The number of drinking days is reduced as is relapse. It is felt to improve resistance to thoughts about drinking. However, relapse after discontinuation of naltrexone is common. The most common side effects are headache, arthralgias, anxiety and sedation. Naltrexone can cause hepatocel-

lular injury and subsequently should not be given to patients with acute hepatitis or liver failure. Prior to initiating treatment, liver function tests should be performed.

- D2. +2 D Acamprosate decreases excitatory glutamergic neurotransmission during alcohol withdrawal and thus was approved for relapse prevention. Guidelines suggest starting acamprosate as soon as possible after abstinence with thrice daily dosing. Some suggest the thrice daily dosing is appealing to this population because they are psychologically used to regular maintenance of their alcohol dependence, thus increasing likelihood of compliance. The major side effect is diarrhea.
- D3 +2 E A newer opioid receptor antagonist that does not have dose-dependent liver toxicity as with Naltrexone, and more effective binding to central opiate receptors. It has not yet been approved for use for alcohol abuse by the FDA.
- D4 +2 B By inhibiting activity of acetaldehyde dehydrogenase (ALDH), the ingestion of alcohol causes increased plasma levels of acetaldehyde, leading to facial flushing, tachycardia, hypotension, dyspnea, nausea, vomiting, headache, blurred vision, vertigo, and anxiety within 15–30 minutes, lasting several hours. The inhibitory activity lasts for several days. Dangers associated with disulfiram include violent reactions to anything containing alcohol, such as cough syrups or sauces. It can cause hepatotoxicity, increases drug levels of phenytoin, isoniazid, and anticoagulants. It can cause hepatitis.
- D5 +2 A Thiamine is a cofactor for several key enzymes important in energy metabolism, including transketolase, alpha-ketoglutarate dehydrogenase, and pyruvate dehydrogenase. In alcoholics, thiamine deficiency is typically caused by inadequate dietary intake, reduced gastrointestinal absorption, decreased hepatic storage, and impaired utilization. The etiology of the thiamine-deficiency brain lesions is unclear, however studies have linked this deficiency with Wernicke's encephalopathy, described first in 1881 by Carle Wernicke, as mental confusion, ophthalmoplegia, and gait ataxia.

DECISION POINT E:

SSRIs, Tricyclics, Benzodiazepines, and MAO-Is have all been shown to be effective treatments for Panic Disorder when compared to placebo. The primary differences for choosing between them are related to their side effect profiles. SSRIs are first-line choices because of their safety and relatively low side effects when compared to the other choices. However, since they often cause symptoms of jitteriness, agitation, restlessness, headache, insomnia, gastrointestinal problems such as diarrhea or nausea, recommended starting doses are low followed by slow titration to the optimal effective dose. The response time is typically 4–6 weeks, and if there is no response by 8–12 weeks, another class could be tried.

Tricyclics are less expensive, but anticholinergic properties and sedation are often cited as reasons for trying an SSRI first. However, if a patient has had good experience with tricyclics, they may be used as a first line treatment. Imipramine and Clomipramine are the most well-studied of the group. Nortriptyline is better tolerated than the Imipramine and Clomipramine.

Benzodiazepines have been demonstrated to be effective for patients who are unable to tolerate or do not respond favorably to antidepressants. Using longer-life benzodiazepines such as Clonazepam are less likely to cause the rebound anxiety that is often experienced by using shorter half-life benzodiazepines. Because of the highly addictive nature of this class of medication, use in patients with comorbid substance or alcohol abuse is not advised. Combination treatment with an SSRI, slowly tapering the benzodiazepine as the SSRI becomes effective has shown to be effective.

MAOI's are considered as effective as the other medications mentioned, however they are infrequently used because of orthostatic hypotension, the tyramine-free diet restriction, numerous dangerous drug-drug interactions, and other intolerable side effects. EMSAM, a transdermal patch form of selegeline, was approved by the FDA in 2006 for use in the treatment of depression. By bypassing the gut, the need for a tyramine diet is not necessary. As of this writing there have not yet been any studies of the transdermal form of selegeline for panic disorder. Given the more favorable side effect profile, however, clinicians may choose such an MAO-I more readily.

Buspirone is used as an anxiolytic but has not been demonstrated to be effective in the treatment of Panic Disorder.

- E1. 2 +2
- E2. 3 +2
- E3. 1 +2
- E4. 0 +2
- E5. 2 +2
- E6. 2 +2

The reader should keep in mind that the above presentation is of an individual with numerous psychiatric diagnoses derived from unclear etiologies. In all likelihood such a patient would require a multidisciplinary approach to his many issues and a combination of medications which would likely require a fair measure of trial and error. For the purposes of this exercise, the reader should bear in mind there are also differences across the country regarding the treatment of dual diagnosis patients, differences in insurance formularies dictating the availability of some of these medications, differences in socio-economic status or access to adequate mental health care.

YOUR TOTAL		
Decision Point	Your Score	Ideal Best Score
A		24
B		5
C		16
D		10
E		12
Total		67



