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After studying the article by Dannon et al., you should be able to:

- Screen patients for pathological gambling and offer appropriate treatment to those who warrant the diagnosis.

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This pretest is designed to facilitate your study of the material.

- 1. Most pathological gamblers suffer from other psychiatric disorders, notably mood, anxiety, personality, and substance use disorders.**
 - a. True
 - b. False

Pretest answer and Posttest on page 391.

Pathological Gambling: A Review of Phenomenological Models and Treatment Modalities for an Underrecognized Psychiatric Disorder

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Pathological gambling (PG) is a prevalent and highly disabling impulse-control disorder. Two dominant phenomenological models for PG have been presented in the literature. According to one model, PG is included as an obsessive-compulsive spectrum disorder, while according to the second model, PG represents a form of nonpharmacologic addiction. In this article, we present an expanded conceptualization of the phenomenology of PG. On the basis of our clinical research experience and a review of data in the field, we propose 3 subtypes of pathological gamblers: the “impulsive” subtype, the “obsessive-compulsive” subtype, and the “addictive” subtype. We also review the current pharmacologic and nonpharmacologic treatment strategies for PG. A further aim of this article is to encourage awareness of the importance of improved screening procedures for the early detection of PG.

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Pathological gambling (PG) is classified in the DSM-IV as a disorder of impulse control with the essential feature being recurrent and maladaptive gambling behavior.¹ In the *International Classification of Diseases* of the World Health Organization, PG is coded under the heading of Habit and Impulse Disorders together with kleptomania, pyromania, and trichotillomania.² Impulse-control disorders are characterized by an overwhelming urge to perform a harmful act. Pathological gambling is a chronic, progressive, male-dominated disorder that has a prevalence of 1.0% to 3.4% among U.S. adults.³ Individuals with PG engage in persistent and recurrent maladaptive patterns of gambling behavior. Typically, the patient’s life becomes dominated by gambling behavior, leading to overwhelming financial burdens, an inability to maintain a career, and the eventual disintegration of family relationships. The enormous personal and social consequences of this disorder include a high rate of suicide attempts, increased rates of legal problems, and criminal behavior.⁴ Recent data have shown that PG that is comorbid with substance abuse confers an increased risk of health problems on the substance abuser^{5,6} and is associated with increased treatment resistance of the substance abuse.⁷

Epidemiologic studies have suggested that PG may be a familial disorder with a genetic component. Results of a twin study by Shah et al.⁸ showed evidence of genetic transmission in men. Furthermore, Black and colleagues,⁹ in a controlled study, showed that the first-degree relatives of pathological gamblers had significantly increased rates of PG as well as significantly increased rates of substance abuse. Data from this family study also suggested that PG coaggregates with antisocial personality disorder.⁹

Pathological gambling appears to be associated with other psychiatric disorders, most notably mood disorders, anxiety disorders, personality disorders, other impulse-control disorders, and alcohol and other substance abuse and dependence.^{10–12} Given the prominence of psychiatric comorbidity in PG, the current standard of care is to modify the choice of pharmacologic treatment according to the comorbid psychiatric conditions.^{13,14} We note that PG has been demonstrated to be highly prevalent in a

cohort of hospitalized psychiatric patients,¹⁵ suggesting an association with severe psychiatric disorders. Interestingly, recent epidemiologic data have confirmed clinical observations that pathological gamblers do not tend to seek out treatment for gambling behavior.¹⁶ Indeed, most PG patients are referred for psychiatric treatment due to a comorbid psychiatric or somatic disorder,⁵ and so the clinician must actively screen for the presence of pathological gambling behavior.

Hollander and Wong¹⁷ suggested that impulsive disorders such as PG are associated with strong compulsive and impulsive features, and, hence, PG can be viewed as an “impulsive” subtype of the “obsessive-compulsive (OC) spectrum” disorders.

Recently, investigators have looked at the role of impulsivity in both disorders of substance abuse and PG. Chambers and Potenza¹⁸ propose that the common trait of impulsivity might underlie PG, commonly comorbid psychiatric disorders, and related aspects of adolescent behavior. They postulate that immaturity of the frontal cortical and subcortical monoaminergic systems during adolescent neurodevelopment is a predisposing factor for adolescent impulsive behavior. It is of interest that lesions in the ventromedial prefrontal cortex can result in faulty decision-making based on the need for immediate as opposed to delayed gratification.¹⁹ Several theoretical models of addiction have suggested that addiction might be related to abnormality in the activity of the prefrontal cortex system that is necessary for inhibiting the immediate reward and excitement seeking behavior.^{20,21}

Over the past 7 years, we have conducted a number of clinical research protocols in our cohort of Israeli pathological gamblers. Our protocols included case-controlled family studies,^{22,23} blind-rater medication studies,^{24–26} neurocognitive studies (reference 27 and S. Kertzman, M.D.; K.L.; A. Aizer, M.D.; et al., unpublished data), and gender comparison studies.²⁸ Based on our research experience, we have seen that PG tends to be a heterogeneous disorder in which patients differ with respect to type and intensity of gambling behavior, psychiatric comorbidity, family history, age at onset, and gender. Based on the results of our clinical research experience and a review of data in the field (as discussed above), we propose that pathological gamblers may be classified according to 1 of 3 subtypes: (1) the “impulsive” subtype, (2) the “obsessive-compulsive” (OC) subtype, and (3) the “addictive” subtype. We will discuss these subtypes in terms of demographic characteristics, psychiatric comorbidity, and possible etiopathology.

THEORETICAL SUBTYPES

First, we propose that the impulsive subtype of PG comprises primarily young adult men who have high levels of risk-taking behavior and lack the ability to plan

ahead. Those with impulsive PG tend to have an increased severity of symptoms compared to other subtypes and tend to lose large sums of money at one sitting. Commonly comorbid psychiatric conditions include attention deficit disorder (ADD) and alcohol and other substance abuse and dependence, as well as other impulse-control disorders.²⁹ First-degree relatives tend to have high rates of gambling and addiction problems.³⁰ Neuropsychological studies of subjects with PG^{31,32} have demonstrated that these individuals have deficits in the frontal lobe/reward system, and we hypothesize that impairment of executive function may play an important role in the impulsive subtype of pathological gambler. These patients may respond best to medications such as bupropion^{33,34} or mood stabilizers,³⁴ which are thought to target impulsive behavior.

In the OC subtype of PG, we propose that there is a preponderance of female patients who tend to have the onset of symptoms in mid-life. These patients may develop pathological gambling behavior in response to a perceived psychological trauma such as divorce or the “empty nest syndrome.” We note that preliminary studies show that there may be gender differences among pathological gamblers. For example, a recent comparison study between male and female gamblers showed higher rates of depression and more maladaptive coping styles in the female versus the male PG patients.²⁸ Similarly, in a gender comparison study, Blanco et al.³⁵ showed that subclinical gambling behavior may be more common in women than in men and is associated with increased rates of lifetime mood and anxiety disorders. Blanco et al. also demonstrated that women reported the onset of gambling behavior as a way to cope with depressed mood. In a gender comparison study of adolescent gamblers, Desai et al.³⁶ reported that girls had significantly higher rates of dysphoria and depression. Commonly comorbid psychiatric disorders for the OC subtype of PG may include affective and anxiety disorders.¹⁷ According to Blaszczynski,³⁷ PG and obsessive-compulsive disorder tend to overlap in a treatment population, and heavy gamblers reported more hoarding symptoms and compulsive buying than light gamblers. In our experience, the primarily female pathological gamblers of the OC subtype tend to prefer slot machines and lottery and scratch tickets, while male patients tend to prefer playing cards, blackjack, poker, and sporting bets. Given the accumulated evidence regarding the high comorbidity of depressive and anxiety disorders in female gamblers,^{22,23,28} we suggest that these patients may be preferentially responsive to antidepressive agents such as the selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs). Psychotherapy addressing stress resolution and coping mechanisms may be particularly helpful in the group of women gamblers.

It is our opinion that the addictive PG subtype represents the largest subgroup of pathological gamblers and

is associated with a moderate severity of pathological gambling. Like the obsessive-compulsive subtype, this group tends to gamble small amounts of money at a time in a repetitive and compulsive fashion. The addictive subtype is distinguished from the OC subtype by a larger ratio of male patients and higher rates of comorbid alcohol abuse and dependence.²² The association between PG and substance abuse in males is well documented in the literature.^{38,39} In a comorbidity study of male and female gamblers,²⁸ our group demonstrated that male patients suffered from high rates of comorbid substance abuse and alcohol abuse. In contrast, the women in our sample had higher rates of obsessive-compulsive disorder, panic disorder, and generalized anxiety disorder. We note that comorbid substance abuse was also seen in the women pathological gamblers, but at lower rates compared with the men's cohort. Comorbid eating disorders were seen in our female patients but not in their male counterparts. Notably, comorbid depression was seen in both groups but was higher in the women. In a cross-sectional study, Goudriaan et al.⁴⁰ showed that pathological gamblers and abstinent alcoholics had similar patterns of deficits in executive functioning (such as impaired decision-making and feedback processing) and suggested a common neurocognitive etiology. We propose that the addictive subtype pathological gambler may respond well to opioid antagonists that target the frontal lobe reward system.

TREATMENT STRATEGIES

Psychological Interventions

Cognitive-behavioral therapy (CBT) currently represents the dominant psychological approach in the treatment of PG. Several outcome studies have shown CBT to be effective in the treatment of PG.⁴¹⁻⁴³ Models of CBT for PG have been drawn, in part, from experience in the field of addiction. Multiple studies have supported the theory that cognitive distortions or irrational beliefs pertaining to addictive behavior may operate at automatic levels.⁴⁴ Examples of cognitive distortion in the field of PG include magnification of gambling skills, superstitious beliefs, and selective memory,⁴⁵ as well as gambling-related cognitions such as "I feel lucky today" or "I know I can win."⁴⁷ The CBT model most often used for impulse-control disorders consists of 4 components: (1) cognitive restructuring to correct irrational and dysfunctional beliefs that precede impulsive behavior, (2) problem-solving skills aimed at generating alternative responses to stress, (3) social skills training, and (4) relapse prevention in which the patient is taught to identify and avoid high-risk situations.⁴⁶

Dynamic and psychoanalytic psychotherapy may also have a role in the treatment of PG. A recent study by Kausch et al.⁴⁷ showed that pathological gamblers have high rates of childhood trauma (including sexual and

physical trauma). Psychoanalytic theories provide insight into the sadomasochistic personality functioning and deeper object relational issues that may lie behind the gambling behavior.⁴⁸ Alternatively, recent data regarding neurocognitive deficits in pathological gamblers show that neuropsychological treatments could target deficits in executive function.⁴⁰

Pharmacologic Interventions

Emerging data in the field show that PG may be responsive to a range of psychopharmacologic agents including SSRIs, mood stabilizers, opioid antagonists, and the psychostimulant bupropion. We note that there is also preliminary evidence that combination pharmacotherapy has a role in the treatment of impulse-control disorders (S. Kertzman, M.D.; K.L.; A. Aizer, M.D.; et al., unpublished data).

To date, there have been 5 double-blind trials of SSRIs for the treatment of PG. Hollander et al.,⁴⁹ in a 16-week double-blind, crossover study, reported the superior effect of fluvoxamine (40.6% improvement on the pathological gambling modification of the Clinical Global Impressions scale [PG-CGI]) compared with placebo (16.6%). However, in a 6-month, double-blind, placebo-controlled study (N = 34), Blanco et al.⁵⁰ found that fluvoxamine treatment did not result in statistically significant improvement as measured by reduction in money and time spent gambling. Kim et al.,⁵¹ in an 8-week, double-blind trial (N = 41), found a significantly greater improvement (using patient-rated PG-CGI and clinician-rated PG-CGI) in the paroxetine group as compared with placebo. Grant et al.⁵² conducted a 16-week, multicenter, randomized, controlled study of paroxetine versus placebo in the treatment of PG (N = 76) and found no significant statistical superiority of paroxetine compared to placebo. Similarly, in a double-blind study, Saiz-Ruiz et al.⁵³ found that sertraline was not superior to placebo for the treatment of PG. Grant and Potenza,⁵⁴ in an open-label pilot study, reported that escitalopram treatment was associated with improvement in gambling and anxiety symptoms in patients with comorbid PG and anxiety. Pallanti et al.,⁵⁵ in a prospective, open-label trial, demonstrated that nefazadone, a novel SSRI that is a specific 5-HT₂ antagonist, was effective in reducing gambling urges and gambling behavior. This is of interest because there is evidence that 5-HT₂ receptors may play a role in disorders of impulsive aggression.⁵⁶ While showing mixed success overall, previous SSRI studies have had limitations including low numbers of women subjects, high dropout rates, and variability in the magnitude of the placebo response observed in different trials.

Pallanti et al.³⁴ describe a connection between the clinical features of PG and bipolar disorder. They discuss characteristics common to both disorders, such as impulsive risk-taking behavior, mood swings, poor judgment,

and grandiose thinking. In support of this theory, they present findings of a single-blind, 14-week trial (N = 42) that demonstrate the efficacy of lithium carbonate and valproate monotherapy in the treatment of PG. Hollander et al.,⁵⁷ in a double-blind study, showed that PG patients with comorbid bipolar spectrum disorder had a positive response to lithium in terms of gambling severity and impulsivity scales.

Topiramate is a newer anticonvulsant that is effective in the treatment of grand mal and partial seizures in epilepsy in children and adults and also effective in the treatment of Lennox-Gastaut disorder. The mechanism of action of topiramate includes both GABAergic and ant glutamatergic mechanisms. In a preliminary study, our group reported the possible usefulness of topiramate for the treatment of PG.²⁴

Naltrexone, an opioid antagonist that works on the reward system, has been shown to be effective for the treatment of alcohol and substance abuse^{58,59} and recently has been studied in the treatment of impulse-control disorders. Kim and colleagues,⁶⁰ in a double-blind study (N = 83), showed that naltrexone treatment significantly reduced the average intensity of gambling urges, gambling thoughts, and gambling behavior. In another double-blind study, Grant et al.,⁶¹ in a multicenter investigation, showed the efficacy of low-dose (25 mg/day) nalmefene in the treatment of PG. We note that treatment with naltrexone may be limited by the risk of hepatotoxicity, especially at higher doses. Kim et al.⁶² designed a study to address the issue of hepatotoxicity and reported that prolonged use of high-dose oral naltrexone (150 mg/day) appears to be safe in otherwise healthy patients if over-the-counter analgesic use is restricted.

Bupropion sustained release is a selective reuptake inhibitor of dopamine and norepinephrine and has been found to reduce nicotine withdrawal symptoms and the urge to smoke.⁶³ Bupropion has a chemical structure similar to the psychostimulants and indirectly stimulates the acetylcholine, hydroxytryptamine, and γ -aminobutyric acid receptors, as well as endorphins. Black³³ postulated that psychostimulants may be useful in the treatment of PG because of the overlap with ADD in terms of comorbidity, attentional deficits, and impulsivity. Black designed a small pilot study to test this hypothesis and found that bupropion treatment was associated with an increased ability to resist gambling urges. Our group reported the effectiveness of bupropion in a randomized drug comparison study (bupropion vs. naltrexone) and in a group of treatment-resistant pathological gamblers.²⁵

CONCLUSIONS

Our experience supports current evidence that PG may represent a heterogeneous disorder with different subtypes. Studies of psychiatric comorbidity, family studies, demographic information, and psychological profiles (i.e., atten-

tional deficits and impulsivity) are useful in building models of PG subtypes. An increased understanding of patient subtypes can potentially allow clinicians to use specific therapeutic strategies for specific subtypes of patients. Consistent with recommendations by Dell'Osso et al.,¹⁴ we propose that subtyping of pathological gamblers may have implications for pharmacologic treatment recommendations. For example, impulsive subtype patients may respond best to bupropion or mood stabilizers, which appear to target impulsivity. The obsessive-compulsive subtype may respond best to SSRIs or SNRIs, which may target related depressive and anxious symptoms as well as compulsive behavior. In addictive subtype patients, it would be logical to use opioid antagonists such as naltrexone or nalmefene as first-line agents.

Building a model of patient subtypes in PG may also have prognostic implications. Traditionally, PG has been thought of as a chronic disorder, but a recent epidemiologic study showed that the clinical course may be characterized as one of natural recovery.¹⁶ We propose that individuals with the impulsive and OC subtypes may be more likely to have remission of symptoms because these subtypes may be associated with lower rates of comorbid substance abuse. It is well accepted that comorbid substance abuse and PG leads to increased treatment resistance for both conditions, and therefore the addictive subtype pathological gambler will likely have a more chronic course if not treated aggressively.

We believe that a knowledge of risk factors for PG and knowledge of commonly comorbid psychiatric conditions may enable the psychiatrist to more effectively screen for this disorder. For example, given the high comorbidity between PG and alcohol abuse, it would be reasonable to screen all alcoholic patients for the presence of comorbid gambling behavior. Other potential risk factors for PG include living in a "disadvantaged" neighborhood and living in close proximity to gambling opportunities.⁶⁴ Clearly, early identification and treatment of PG are important in order to prevent the potentially devastating social, occupational, financial, medical, and legal consequences of this disorder. We suggest that future studies address the question of how to serve a broader patient population, and we hope that future treatment research can lead to expert consensus and treatment guidelines for pathological gambling.

Drug names: bupropion (Wellbutrin, Zyban, and others), escitalopram (Lexapro and others), lithium (Eskalith, Lithobid, and others), nalmefene (Revex), naltrexone (ReVia and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft and others), topiramate (Topamax and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, bupropion, escitalopram, lithium, nalmefene, naltrexone, paroxetine, sertraline, topiramate, fluvoxamine, and valproate are not approved by the U.S. Food and Drug Administration for the treatment of pathological gambling.

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Answer to Pretest: 1. a

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- 1. Compared with male pathological gamblers, female pathological gamblers tend to have higher rates of comorbid:**
 - a. Schizophrenia
 - b. Alcohol abuse
 - c. Attention deficit disorder
 - d. Depression
- 2. All of the following are true about the addictive subtype of pathological gambling *except*:**
 - a. Associated with high rates of comorbid substance abuse
 - b. May respond well to opioid antagonist pharmacotherapy
 - c. Associated with high rates of comorbid obsessive-compulsive disorder
 - d. Composed predominantly of males
- 3. The cognitive-behavioral therapy model most often used for pathological gambling treatment consists of all of the following components *except*:**
 - a. Cognitive restructuring to correct irrational and dysfunctional beliefs that precede impulsive behavior
 - b. Problem-solving skills aimed at generating alternative responses to stress
 - c. Talk with patients' family in order to solve patients' financial problems
 - d. Relapse prevention in which the patient is taught to identify and avoid high-risk situations
- 4. The addictive subtype pathological gambler may be more likely to have a chronic course of illness due to:**
 - a. Nonresponse to pharmacotherapy
 - b. Comorbid depression
 - c. Comorbid substance abuse
 - d. Comorbid trichotillomania
- 5. All of the following are true *except*:**
 - a. The pathological gambler will frequently be self-referred for treatment
 - b. The physician must play a proactive role in early detection of pathological gambling
 - c. Pharmacotherapy of pathological gambling may be chosen, in part, according to the dominant comorbid diagnosis
 - d. The authors recommend screening all patients with alcohol abuse for the presence of comorbid pathological gambling



REGISTRATION FORM

Circle the one correct answer for each question.

- 1. a b c d 4. a b c d
- 2. a b c d 5. a b c d
- 3. a b c d

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 - A. Enabled me to screen patients for pathological gambling and offer appropriate treatment to those who warrant the diagnosis. Yes No
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