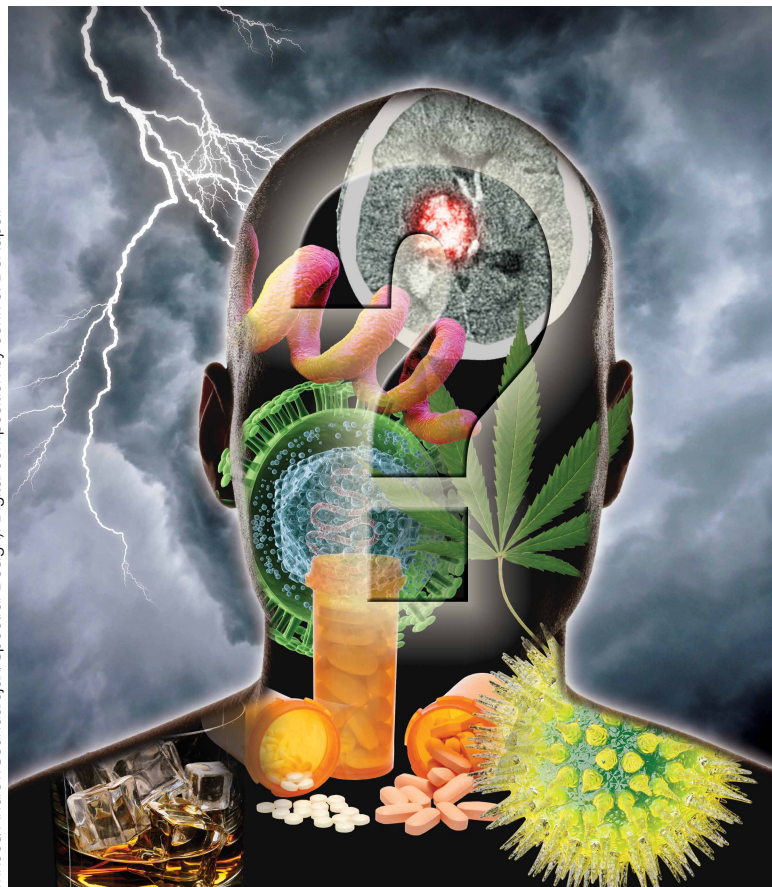


Medical Mimics of Psychiatric Conditions, Part 2

Steven R. Knight, MD; Martin R. Huecker, MD; Mary Nan S. Mallory, MD, MBA

In the conclusion of this review of medical mimics, the authors focus on psychiatric presentations associated with dementia, cancer, cardiac disease, nutritional deficiencies, endocrine disorders, or toxins.



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Although the emergency physician (EP) typically encounters common conditions such as chest pain, urinary tract infection, and gastroenteritis, many other clinical presentations can confound diagnosis of the true underlying condition. This may be the case with a patient who presents with apparent psychiatric symptoms that are actually masking an acute medical condition. For example, a patient who appears to be depressed may actually be exhibiting early signs of dementia. Likewise, a manic patient may not have a true underlying psychiatric disorder but rather rhabdomyolysis and hyperthermia from ingesting an illicit substance such as synthetic cathinones (“bath salts”).

Part 1 of this series reviewed psychiatric presentations caused by underlying infectious, pharmacological withdrawal, metabolic, autoimmune, traumatic, and central nervous system etiologies (*Emerg Med.* 2016;48[5]:202-211). Part 2 covers psychiatric presentations related to dementia, cancer, cardiac disease, nutritional deficiencies, endocrine disorders, or toxins (Table 1).

Dr Knight is an emergency medicine resident, University of Louisville School of Medicine, Kentucky. **Dr Huecker** is an assistant professor, department of emergency medicine, University of Louisville School of Medicine, Kentucky. **Dr Mallory** is a professor of emergency medicine at the University of Louisville School of Medicine, Kentucky.

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Case Scenarios

Case 1

A 62-year-old man with a history of hypertension, hyperlipidemia, and past alcohol abuse presented to the ED with reported mental status changes after he was pulled over by police for driving the wrong way down the highway. On presentation, the patient's vital signs were normal. When questioned, the patient was alert and fully oriented and believed the officers were mistaken about what was reported. He denied any recent illness and had a normal physical examination, including neurological examination.

A brief work-up was ordered and the patient passed the time by politely flirting with the nurses. When his wife arrived at the ED, she was relieved that her husband seemed to be all right. She confirmed that the patient had not consumed any alcohol in years. The patient, meanwhile, playfully minimized his wife's concern at his presence in the ED. A full toxicology screen, laboratory evaluation, and head computed tomography (CT) scan were ordered.

Case 2

A 48-year-old woman with a history of anxiety disorder, depression, and diabetes mellitus presented to the ED with a 2-hour history of chest pain. She stated that the pain had started toward the end of a heated argument with her son. The patient was escorted into the examination room by hospital security because she was still agitated and kept yelling at her son. On examination the patient was tachycardic (110 beats/minute), diaphoretic, and crying. During the examination, she asked the EP for a "Xanax"; her son further noted that this would help his mother's condition.

The patient repeatedly claimed she could not breathe and could not lie flat on the stretcher. After verbal de-escalation, she cooperated with the electrocardiography (ECG) technician and phlebotomist. Her ECG showed nonspecific ST changes with no prior study for comparison. While

glaring at her son, she maintained that she had constant chest pain.

Dementia

Alzheimer's Disease

Alzheimer's disease (AD), the most common cause of dementia, is a chronic neurodegenerative disease characterized by an insidiously progressive cognitive decline and loss of function. There is considerable apparent variability in the early signs of the disease, and recent literature has suggested that the manifestation of initial symptoms may be age-dependent. Younger patients tend to present with non-memory cognitive changes such as problem-solving difficulties, as well as personality changes and behavioral symptoms of depression, apathy, and withdrawal.¹

Lewy Body Dementia

Lewy body dementia (LBD) is a chronic neurodegenerative disease with a presentation that overlaps substantially with AD. However, LBD is associated with a significantly more rapid course than AD and presents more frequently with visual hallucinations or illusions due to specific visuospatial dysfunction.²

Frontotemporal Dementia

Frontotemporal dementia is a comparatively rare chronic neurodegenerative disease characterized by early-onset memory impairment with cognitive decline, as well as behavioral changes such as disinhibition, emotional blunting, and language difficulty. Initial presentations can also include atypical features such as paranoia or delusion, and misdiagnosis as a primary psychiatric problem is common.³

Cancer

Brain Tumor

Primary and metastatic brain tumors classically present with either focal neurological signs or less specific symptoms such as headaches, seizures, or syncope. Additionally, central nervous system (CNS) tumors

Table 1. Medical Etiologies Associated With Psychiatric Presentations

Etiology	Diagnosis	Psychiatric Presentation
Dementia	Alzheimer's disease ¹	Problem-solving difficulty, depression, apathy, withdrawal
	Lewy body dementia ²	Visual hallucinations, illusions
	Frontotemporal dementia ³	Disinhibition, emotional blunting, language difficulty, paranoia, delusions
Cancer	Brain tumor ⁴	Personality changes, depression, mania, panic attacks, auditory or visual hallucinations
	Paraneoplastic limbic encephalitis ⁵	Confusion, cognitive problems, behavioral changes, irritability, depression, psychosis, hallucinations
	Malignant meningitis ⁶	Depression, anxiety, disorientation, paranoia
	Pancreatic insulinoma ⁷	Irrational behavior, confusion, depression, anxiety
Cardiac Disease	Transient left ventricular apical ballooning syndrome ⁸	Dissociative amnesia
Nutritional Deficiencies	Wernicke/Korsakoff syndrome ^{9,10}	Mental status changes, ophthalmoplegia, ataxia
	Subacute combined degeneration ¹¹	Mood disorders, acute psychosis, psychotic depression, paranoid hallucinations
	Zinc/vitamin D deficiency ^{12,13}	Depressive disorders, bipolar disorder, episodic psychosis
Endocrine Disorders	Hypothyroidism ¹⁴	Mood disorders, cognitive impairment, exacerbation of underlying psychiatric disorders Myxedema madness: mania, psychosis, auditory or visual hallucinations
	Hyperthyroidism ¹⁵	Psychosis, catatonia, auditory hallucinations, delusional parasitosis, new-onset sleepwalking, dissociative disorder, suicide attempts
	Steroid dysregulation ^{16,17}	Cushing disease: major depression with psychotic features
		Adrenal insufficiency: severe psychotic disorder
		Chronic treatment: recurrent subacute mania Acute treatment: hallucinations, delusions
	Parathyroid dysregulation ¹⁸	Hyperparathyroidism: cognitive slowing, psychomotor slowing, memory impairment, depression Hypoparathyroidism: mood disorders
Pheochromocytoma ¹⁹	Nervousness, anxiety, panic attacks, depression	
Toxins (see also Table 2)	Gonadal hormone dysregulation ²⁰	Acute psychosis
	Synthetic cannabinoids ²²	New-onset psychosis, paranoid delusions, hallucinations, suicide ideation or attempt
	Synthetic cathinones ²³	Acute psychosis
Heavy metals ²⁴	Chronic: abnormal neurodevelopment, behavioral disturbances, and progression of neurodegenerative diseases	
	Acute: new-onset impaired emotional behavior	

can also initially present with primary psychiatric complaints (eg, personality changes, depression, mania, panic attacks, auditory or visual hallucinations). Patients with a brain neoplasm who are initially misdiagnosed with a primary psychiatric disorder face significant delays in proper diagnosis and treatment, leading to increased morbidity. To correctly diagnose the true cause as soon as possible, early imaging is recommended for patients who present with psychiatric symptoms that are abrupt in onset, atypical in presentation, resistant to conventional treatments, or associated with a change in headache pattern.⁴

Paraneoplastic Limbic Encephalitis

Paraneoplastic limbic encephalitis (PLE) is a rare neurological consequence of certain cancers. Although PLE most commonly occurs in patients with small cell lung cancer, the condition has also been reported (though less frequently) in cases of esophageal adenocarcinoma, ovarian teratoma, metastatic breast cancer, and germ cell testicular cancer.⁵ This disease overlaps substantially with anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis. Moreover, PLE can present initially with prominent neuropsychiatric symptoms such as confusion, cognitive problems, behavioral changes, irritability, depression, or frank psychosis with hallucinations. Paraneoplastic limbic encephalitis can occur early in the course of cancer—often before other systemic signs appear—and its significance is often only recognized in retrospect or postmortem. A higher index of suspicion for the disorder may lead to earlier detection of treatable cancers.

Malignant Meningitis

Malignant meningitis is the metastatic spread of a primary solid tumor to the leptomeninges. It can present as a wide variety of neuropsychiatric complaints, including depression, anxiety, disorientation, and paranoia. Diagnosis can often be

made through lumbar puncture. Malignant meningitis should be considered in the differential diagnosis of new psychiatric symptoms in a patient with a history of cancer—even in the absence of focal neurological deficits or meningeal signs.⁶

Pancreatic Insulinoma

Pancreatic insulinoma is a rare, potentially curable endocrine tumor that can present initially with vague psychiatric complaints such as irrational behavior, confusion, depression, or anxiety. In up to 64% of patients, insulinomas are misdiagnosed as primary neurological or psychiatric disease, which can delay potentially curative surgery—sometimes for years.⁷ The EP should suspect pancreatic insulinoma in any patient who presents with psychiatric symptoms and unexplained episodes of hypoglycemia.⁷

Cardiac Disease

Transient Left Ventricular

Apical Ballooning Syndrome

Transient left ventricular apical ballooning syndrome (TLVABS), first identified in Japan as Takotsubo syndrome, has more recently been recognized worldwide as overlapping with the classic broken heart syndrome. In postmenopausal women, TLVABS appears to follow a catecholamine surge triggered by extreme emotional stress, resulting in an acute coronary artery spasm. Researchers have hypothesized that there may be a link between TLVABS and dissociative amnesia, which is also thought to result from a catecholamine surge in response to emotional stress.⁸

Nutritional Deficiencies

Wernicke/Korsakoff Syndrome and Thiamine Deficiency

Wernicke encephalopathy and Korsakoff syndrome (WKS) represent a spectrum of neurodegenerative disorders caused by thiamine deficiency. The condition typically occurs in malnourished alcoholic patients, manifesting as a triad of mental

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status changes, ophthalmoplegia, and ataxia. Recent research has suggested that WKS is more common than previously thought, is not confined exclusively to alcoholic patients, is unlikely to present with the full classic triad, and is typically only diagnosed postmortem.⁹

Nonalcoholic WKS tends to occur in younger female patients with a wide array of conditions that affect nutrition (eg, gastrointestinal malignancy, bariatric surgery, hyperemesis gravidarum, anorexia nervosa).⁹ In a patient with chronic alcoholism, application of the Caine criteria (any two of the following findings: ophthalmoplegia, ataxia, even mild memory impairment or confusion without another cause, evidence of malnutrition) has been shown to be more sensitive and specific than the classic triad.¹⁰

Subacute Combined Degeneration

Patients with subacute combined degeneration and extrapyramidal symptoms due to B₁₂ (cobalamin) deficiency are well documented. However, patients with B₁₂ deficiency can also present with mood disorders, acute psychosis, psychotic depression, or paranoid hallucinations. The EP should always consider vitamin B₁₂ deficiency as an important, reversible cause of altered mental status—even in the absence of megaloblastic anemia—especially in patients with celiac disease or anorexia nervosa, and in teenagers and those who are vegans/vegetarians.¹¹

Zinc/Vitamin D Deficiency

Zinc and vitamin D deficiency are both highly prevalent in geriatric patients and have been associated with a range of psychiatric complaints, including depressive disorders, bipolar disorder, and psychotic episodes. Though the neurodevelopmental effects of long-term deficiency of these nutrients are well documented in pediatric patients, the role and relationship to acute psychiatric complaints in elderly patients remain unclear.^{12,13}

Endocrine Disorders

Hypothyroidism

Hypothyroidism is a commonly encountered endocrine disruption that classically presents with fatigue, cold insensitivity, weight gain, and thinning hair. Thyroid dysfunction can result in various neuropsychiatric presentations, including mood disorders, cognitive impairment, and exacerbation of underlying psychiatric disorders. Though rare, primary hypothyroidism can present as mania, psychosis, and auditory or visual hallucinations, a phenomenon termed “myxedema madness.” Myxedema madness typically occurs in older women, but has also been described in adolescents and as a postoperative complication of thyroidectomy.¹⁴

Hyperthyroidism

Hyperthyroidism classically presents with tachycardia, nervousness or anxiety, heat insensitivity, and weight loss despite increased appetite. Involvement of the CNS in thyrotoxicosis is rare, but when present, it is a significant predictor of mortality. Neuropsychiatric presentations of hyperthyroidism or thyroid storm vary widely, and have been reported to include psychosis, catatonia, auditory hallucinations, delusional parasitosis, new-onset sleepwalking, dissociative disorder, and suicide attempts.¹⁵

Steroid Dysregulation

Steroid dysregulation, either endogenous or iatrogenic in nature, has been reported to cause neuropsychiatric symptoms. Major depression with psychotic features can be an initial presentation of Cushing disease, especially in the presence of other systemic signs.¹⁶ Adrenal insufficiency has also been shown to cause severe psychotic disorder.¹⁷

Chronic treatment with exogenous corticosteroids can cause a recurrent steroid psychosis, primarily manifesting as subacute mania with psychotic features. Treatment of acute adrenal crisis can also cause

an acute steroid psychosis with hallucinations, delusions, and dangerous behavior.¹⁷

Parathyroid Dysregulation

Elevated calcium levels caused by primary hyperparathyroidism can present as cognitive slowing, reductions in psychomotor speed, memory impairment, and depression. While the disorder is most prevalent in older women, it has been reported in adolescents, and often remains undiagnosed in younger patients until end-organ damage occurs.¹⁸ Hypoparathyroidism has also been reported to cause mood disorders, which can occur with or without the classic symptoms of hypocalcemia (eg, tetany, seizures, dementia, and parkinsonism).¹⁸

Pheochromocytoma

Pheochromocytoma is a neuroendocrine tumor of the adrenal medulla that causes sympathetic hyperactivity by the release of large amounts of catecholamines. Pheochromocytoma is well-reported to present with nervousness, anxiety, panic attacks, or depression.¹⁹

Gonadal Hormone Dysregulation

Gonadal hormone dysregulation can be either congenital or acquired and is typically caused by a pituitary tumor or traumatic brain injury. Thought to be a result of dopaminergic hyperactivity, acute psychosis can develop in cases of hypogonadotropic hypogonadism, hypopituitarism, and/or hyperprolactinemia.²⁰ There is a high incidence of psychotic manifestations in hypogonadal disorders such as Klinefelter syndrome and Prader-Willi syndrome.

Toxins

Many toxins can cause altered mental status and psychiatric manifestations. The administration of these toxins can be iatrogenic, related to prescribed use, or overdose—whether accidental, recreational, or intentional (eg, suicide attempt). **Table 2** lists common drugs and toxins associated with psychiatric symptoms.²¹

Table 2. Selected Drugs and Toxins With Known Psychiatric Effects²¹

Prescription Medications:

- Amphetamines
- Anticholinergics
- Antidepressants
- Antihypertensives
- Antipsychotics
- Anxiolytics
- Cimetidine
- Digitalis
- Interferon
- Indomethacin
- Insulin
- Levodopa
- L-thyroxine
- Sedatives
- Steroids
- Sympathomimetics
- Xanthene derivatives

Illicit Substances:

- Alcohol
- Hallucinogens (lysergic acid diethylamide, phencyclidine, psilocybin)
- Marijuana
- Stimulants (methamphetamine, cocaine)
- Synthetics (“Spice,” “bath salts”)

Other Toxins:

- Caffeine
- Carbon dioxide
- Chloroacetophenone solvents
- Organophosphates

Synthetic Drugs

The use of numerous unregulated, synthetic analogues of popular recreational drugs has greatly increased over the last several years. Synthetic cannabinoids are available under a variety of names (eg, “Spice,” “K2”) and can cause prominent psychiatric symptoms, including new-onset psychosis, paranoid delusions, hallucinations, and suicide ideation or attempt. While most clinical symptoms are self-

limited and require only supportive care, more serious complications have been reported, including myocardial infarction, ischemic stroke, and acute kidney injury.²² Synthetic cathinones (bath salts) can also cause autonomic instability and prominent acute psychosis, sometimes creating a clinical picture indistinguishable from excited delirium syndrome.²³

Heavy Metals

Chronic toxicity of many heavy metals is implicated in abnormal neurodevelopment, behavioral disturbances, and progression of neurodegenerative diseases. Recent literature has also implicated acute metal overload in new-onset impaired emotional behavior, though the mechanism is not currently well understood.²⁴

Case Scenarios Continued

Case 1

[The 62-year-old man with altered mental status.]

The patient's laboratory evaluation and toxicology screen were negative, including a screen for alcohol. He remained jovial but otherwise in no distress. Since the noncontrast head CT scan showed a subtle asymmetry in the frontal lobes, a magnetic resonance imaging (MRI) study was recommended. The brain MRI showed a 5-cm mass in the right frontal lobe with surrounding edema, findings consistent with glioblastoma multiforme. A neurosurgeon was consulted, and the patient was admitted to the intensive care unit.

Case Scenarios Continued

Case 2

[The 48-year-old woman with chest pain.]

The patient received a dose of oral lorazepam, after which she began to feel less anxious, and her chest pain and shortness of breath also improved slightly. The repeat ECG showed worsening of the ST segment changes. The laboratory evalua-

tion was negative. The patient's son asked if he could take his mother home for what he felt was much needed rest. The EP, however, ordered a stat two-dimensional echocardiogram (ECHO) and repeat troponin level test. The repeat troponin test was positive, and the ECHO was remarkable for a decreased left ventricular ejection fraction of 15%, with apical ballooning. These findings were consistent with stress cardiomyopathy (Takotsubo syndrome). The patient was admitted to the cardiology service and given a beta blocker and an angiotensin-converting enzyme inhibitor.

After a normal coronary angiogram, the patient developed cardiogenic shock and was intubated. Seven days later, she was extubated and transferred to inpatient rehabilitation services where she also received an assessment and treatment for her underlying depression. Eight weeks post-diagnosis, the patient's ejection fraction had returned to 50%, and she was close to her baseline exercise tolerance.

References

1. Barnes J, Dickerson BC, Frost C, Jiskoot LC, Wolk D, van der Flier WM. Alzheimer's disease first symptoms are age dependent: Evidence from the NACC dataset. *Alzheimers Dement*. 2015;11(11):1349-1357.
2. Yoshizawa H, Vonsattel JP, Honig LS. Early neuropsychological discriminants for Lewy body disease: an autopsy series. *J Neurol Neurosurg Psychiatry*. 2013;84(12):1326-1330.
3. Iroka N, Jehangir W, Ji JL, Pattan V, Yousif A, Mishra AK. Paranoid personality masking an atypical case of frontotemporal dementia. *J Clin Med Res*. 2015;7(5):364-366.
4. Filley CM, Kleinschmidt-DeMasters BK. Neurobehavioral presentations of brain neoplasms. *West J Med*. 1995;163(1):19-25.
5. Said S, Cooper CJ, Reyna E, Alkhateeb H, Diaz J, Nahleh Z. Paraneoplastic limbic encephalitis, an uncommon presentation of a common cancer: Case report and discussion. *Am J Case Rep*. 2013;14:391-394.
6. Weitzner MA, Olofsson SM, Forman AD. Patients with malignant meningitis presenting with neuropsychiatric manifestations. *Cancer*. 1995;76(10):1804-1808.
7. Ding Y, Wang S, Liu J. Neuropsychiatric profiles of patients with insulinomas. *Eur Neurol*. 2010;63(1):48-51.
8. Toussi A, Bryk J, Alam A. Forgetting heart break: a fascinating case of transient left ventricular apical ballooning syndrome associated with dissociative amnesia. *Gen Hosp Psychiatry*. 2014;36(2):225-227.
9. Scalzo SJ, Bowden SC, Ambrose ML, Whelan G, Cook MJ. Wernicke-Korsakoff syndrome not related

- to alcohol use: a systematic review. *J Neurol Neurosurg Psychiatry*. 2015;86(12):1362-1368.
10. Isenberg-Grzeda E, Kutner HE, Nicolson SE. Wernicke-Korsakoff-syndrome: under-recognized and under-treated. *Psychosomatics*. 2012;53(6):507-516.
 11. Issac TC, Soundarya S, Christopher R, Chandra SR. Vitamin B12 deficiency: an important reversible comorbidity in neuropsychiatric manifestations. *Indian J Psychol Med*. 2015;37(1):26-29.
 12. Grønli O, Kvamme JM, Friberg O, Wynn R. Zinc deficiency is common in several psychiatric disorders. *PLoS One*. 2013;8(12):e82793.
 13. Grønli O, Kvamme JM, Jorde R, Wynn R. Vitamin D deficiency is common in psychogeriatric patients, independent of diagnosis. *BMC Psychiatry*. 2014;14:134.
 14. Heinrich TW, Grahm G. Hypothyroidism presenting as psychosis: myxedema madness revisited. *Prim Care Companion J Clin Psychiatry*. 2003;5(6):260-266.
 15. Swee du S, Chng CL, Lim A. Clinical characteristics and outcome of thyroid storm: a case series and review of neuropsychiatric derangements in thyrotoxicosis. *Endocr Pract*. 2015;21(2):182-189.
 16. Tang A, O'Sullivan AJ, Diamond T, Gerard A, Campbell P. Psychiatric symptoms as a clinical presentation of Cushing's syndrome. *Ann Gen Psychiatry*. 2013;12(1):23.
 17. Farah Jde L, Lauand CV, Chequi L, et al. Severe psychotic disorder as the main manifestation of adrenal insufficiency. *Case Rep Psychiatry*. 2015;2015:512430.
 18. Rice T, Azova S, Coffey BJ. Negative symptoms in a depressed teen? Primary hyperparathyroidism and its psychiatric manifestations. *J Child Adolesc Psychopharmacol*. 2015;25(8):653-655.
 19. Zardawi IM. Pheochromocytoma masquerading as anxiety and depression. *Am J Case Rep*. 2013;14:161-163.
 20. Kate S, Dhanwal DK, Kumar S, Bharti P. Acute psychosis as a presentation of hypopituitarism. *BMJ Case Rep*. 2013;2013.
 21. Abramowicz M. Drugs that may cause psychiatric symptoms. *Med Lett Drugs Ther*. 2008;50(1301-1302):100-103.
 22. Tait RJ, Caldicott D, Mountain D, Hill SL, Lenton S. A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment. *Clin Toxicol (Phila)*. 2016;54(1):1-13.
 23. Karch SB. Cathinone neurotoxicity ("The "3Ms"). *Curr Neuropharmacol*. 2015;13(1):21-25.
 24. Menon AV, Chang J, Kim J. Mechanisms of divalent metal toxicity in affective disorders. *Toxicology*. 2016;339:58-72.