

# Rapid weight loss, irritability, and nausea after restarting ADHD treatment

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## How would you handle this case?

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Mr. L, age 58, reports being distracted and forgetful after stopping his ADHD medication. After restarting treatment, he experiences rapid weight loss and nausea. What is causing these symptoms?

### **CASE** Medication management

Mr. L, age 58, presents to the outpatient psychiatric clinic seeking treatment for attention-deficit/hyperactivity disorder (ADHD), which was first diagnosed 11 years ago. Since discontinuing his ADHD medication, lisdexamfetamine 60 mg/d, 8 months ago, he has not been completing tasks and has been distracted in his job as a limousine driver. Mr. L says that when he was taking the medication, "I could focus and prioritize." He reports that he has trouble retaining information and is easily distracted. He says he generally is organized with appointments and keeping track of things but is messy, forgetful, tardy, and impatient. Procrastination is an ongoing problem. He denies misplacing things or being impulsive. Mr. L reports that as a child he was frequently reprimanded for talking in class. He states, "I get in trouble even now for talking too much."

Mr. L is cooperative and polite, maintains good eye contact, and is alert. No psychomotor abnormalities are noted. His speech is spontaneous and coherent, with normal rate, rhythm, and volume. He reports that his mood is "all right," and denies suicidal or homicidal ideation. His insight is full, judgment is intact, and thought is linear and logical. Mr. L sleeps 5 hours at night and takes a nap during the day, but his energy varies.

His psychiatric history is negative for suicide attempts or hospitalizations. Mr. L denies a history of major depressive episodes, manic symptoms, hallucinations, or delusions. Anxiety history is negative for excessive worrying, obsessions and compulsions, and panic attacks. Mr. L has no family history of mental illness or substance abuse, and he denies any personal history of drug use. He stopped using tobacco 14 years ago. Mr. L says he drinks 3 caffeinated drinks a day and 2 glasses of wine once a week. Previous medications included lisdexamfetamine, dextroamphetamine/amphetamine, and bupropion. His medical history is notable for irritable bowel syndrome, gastroesophageal reflux disease, hyperlipidemia, hemorrhoids, recently treated *H. pylori*, eczema, and benign prostatic hyperplasia. He has no history of head trauma. He is currently taking omeprazole EC, 20 mg twice a day, tamsulosin, 0.4 mg at bedtime, aspirin, 81 mg/d, and cimetidine, 150 mg twice a day.

A review of systems is negative. Vital signs are unremarkable. A recent electrocardiogram (EKG) showed normal sinus rhythm.

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#### **Disclosure**

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Thyroid-stimulating hormone, comprehensive metabolic panel (CMP), lipids, iron, vitamin B<sub>12</sub>, folate, complete blood count (CBC), hemoglobin A<sub>1c</sub>, and urine analysis are normal, except for mildly elevated low-density lipoprotein. Testing for hepatitis C is negative.

The previous diagnosis of ADHD is confirmed, and Mr. L is started on methylphenidate extended-release (ER), 27 mg every morning. At 1-month follow-up, Mr. L demonstrates good tolerance to the medication, and reports that he feels the dose is appropriate; no changes are made. The following month, Mr. L reports that, although the medication still works well, he feels anxious, irritable, and agitated, and has palpitations. He reports feeling tired during the day, with a return of energy at night, resulting in difficulty sleeping. He also is experiencing nausea and headaches, and has lost 15 lb. Mr. L thinks that the symptoms, particularly the weight loss, are adverse effects from the methylphenidate ER and requests a lower dose. The methylphenidate ER dose is decreased to 18 mg/d.

**Which of the following are potential iatrogenic causes of agitation and irritability?**

- some asthma medications
- hypothyroid treatment
- antidepressants
- some migraine treatments

#### **The author's observations**

Anxiety, irritability, agitation, and palpitations can all be symptoms of stimulant medications.<sup>1,2</sup> There are numerous other iatrogenic causes, including steroid-based asthma treatments, thyroid medications, antidepressants in bipolar patients, and caffeine-based migraine treatments. Mr. L's theory that his 15-lb weight loss was the result of his methylphenidate ER dose being too high was a reasonable one. Often, medication doses need to be adjusted with weight changes. His

decrease in energy during the day could be explained by the methylphenidate ER controlling his hyperactive symptoms, which include high energy. At night, when the medication wears off, his hyperactivity symptoms could be returning, which would account for the increase in energy when he gets home from work. Although longer-acting stimulants tend to have a more benign adverse effects profile, they can cause insomnia if they are still in the patient's system at bedtime. Shorter-acting stimulants wear off quickly but can be advantageous for patients who want to target concentration during certain times of day, such as for school and homework.

#### **TREATMENT A surprising cause**

The next month, Mr. L presents to the emergency room complaining of jitteriness, headache, and tingling in his fingers, and is evaluated for suspected carbon monoxide (CO) poisoning. Three months earlier, he had noted the odor of exhaust fumes in the limousine he drives 7 days a week. He took it to the mechanic twice for evaluation, but no cause was found. Despite his concerns, he continued to drive the car until an older client, in frail health, suddenly became short of breath and developed chest pain shortly after entering his vehicle, on a day when the odor was particularly bad. Before that, a family of passengers had complained of headaches upon entering his vehicle. The third time he brought his car to be checked, the mechanic identified an exhaust system leak.

In the emergency room, work-up includes CMP, CBC, troponin, arterial blood gas (ABG), and carboxyhemoglobin (COHb) level. His CBC, CMP, and troponin levels are normal. ABG test shows low partial pressure of oxygen of 35 mm Hg (normal is 75 to 100 mm Hg) and low oxygen saturation of 71.8% (normal 92% to 98.5%). His anion gap was low at 4.7 mEq/L (normal 10 to 20 mEq/L). COHb level is significantly elevated at 5.0% (normal 0% to 1.5%) (*Table 1,*<sup>3-5</sup> *page 54*). He is diagnosed with CO poisoning and treated with oxygen by mask for

#### **Clinical Point**

**Mr. L's theory that his methylphenidate ER dose was too high was a reasonable one; often doses need to be adjusted with weight changes**

**Clinical Point**

Common symptoms of chronic, low-dose CO poisoning include headache, fatigue, dizziness, paresthesia, chest pain, and palpitations

**Table 1**  
**Typical COHb levels in various populations**

Population	COHb levels
Nonsmokers	<1%
Smokers	<1% to 9%
Pregnancy	<5%
Hemolytic anemia	<5%
Urban polluted areas	At least 1% higher than normal

COHb: carboxyhemoglobin  
 Source: References 3-5

**Table 2**  
**Adverse effects of stimulants and occult CO poisoning**

Stimulants	Occult CO poisoning
Nervousness	Fatigue
Headache	Headache
Irritability	Difficulty thinking
Dizziness	Dizziness
Nausea	Nausea
Insomnia	Insomnia
Palpitations	Heart pounding

CO: carbon monoxide  
 Source: References 1,2,8

2 hours. After treatment, repeat laboratory tests are normal.

**Which of the following tests would be most helpful in diagnosing CO poisoning?**

- a) ABG
- b) COHb
- c) urinalysis
- d) EKG

**The author's observations**

Although CO is odorless, it is a component of exhaust fumes; thus, an odor may be present in a vehicle with an exhaust system leak, but it is not that of the CO itself.<sup>6</sup> CO has an affinity for hemoglobin >200 times that of oxygen.<sup>7</sup> Sources of unintentional poisoning include motor vehicle exhausts, defective heating

systems, tobacco smoke, and urban pollution. Common symptoms of chronic, low-dose CO poisoning include headache, fatigue, dizziness, paresthesia, chest pain, palpitations, and visual disturbances (*Table 2*).<sup>1,2,8</sup>

Work-up for suspected CO poisoning includes ABG, COHb level, CBC, basic metabolic panel, EKG, cardiac enzymes, and chest radiography, as well as other laboratory tests as deemed appropriate. Treatment includes oxygen by mask for low-level poisoning.

High levels of poisoning may require hyperbaric oxygen, which should be considered for patients who are unconscious or have an abnormal score on the Carbon Monoxide Neuropsychological Screening Battery, COHb of >40%, signs of cardiac ischemia or arrhythmia, history of ischemic heart disease with COHb level >20%, recurrent symptoms for up to 3 weeks, or symptoms that have not resolved with normobaric oxygen after 4 to 6 hours.<sup>9</sup> Any pregnant woman with CO poisoning should receive hyperbaric therapy.<sup>10</sup>

**OUTCOME Lasting improvement**

Mr. L presents for follow-up in the psychiatric clinic 3 weeks after his emergency room visit. After his limousine was repaired, his symptoms resolved. He no longer experiences fatigue during the day with higher energy at night, palpitations, jitteriness, headache, or tingling. His concentration has improved, so he opts to stick with the 18-mg dose of methylphenidate ER rather than increase it to the initial dose. He places a CO detector in his vehicle, which proves to be a good decision when it gives him a warning that the exhaust leak had not been properly repaired.

**Which of the following symptoms of CO poisoning are also seen in some psychiatric disorders?**

- a) confusion
- b) fatigue
- c) behavioral changes
- d) memory loss

### The author's observations

Although the correct cause of Mr. L's symptoms was found incidentally, this case is an important reminder to always consider medical causes in the differential diagnosis. We are taught in medical school to look first for horses (more likely causes), not zebras (less likely causes), but sometimes zebras do occur. Be mindful that medical causes should be considered not only for symptoms of primary illnesses, but also for symptoms thought to be caused by adverse effects of medications. The differential diagnosis for Mr. L's symptoms (palpitations, agitation, anxiety, irritability, weight loss, fatigue, nausea, and headache) included metabolic and endocrine abnormalities (thyroid disease, pheochromocytoma, hypoglycemia); psychiatric conditions (panic, bipolar disorder, depression); substance abuse (caffeine, cocaine, amphetamines); immune disorders; cardiac disorders; malignancy; toxic exposure; infectious sources; and nutritional deficiencies. CO poisoning can cause many of these symptoms (*Table 2, page 54*).<sup>1,2,8</sup>

Intentional CO poisoning should be considered in an obtunded or unconscious patient with depression. Patients may consider CO poisoning a more peaceful way to complete suicide than shooting, cutting, or hanging. As for unintentional poisoning, clinical suspicion can be increased by time of year, occupation, locale, and smoking status. Winter months increase risk because of the high use of heating devices, cars warming up in the garage, closed fireplace flues, and vehicle tailpipes blocked by snow. As in

### Related Resources

- Varon J, Marik P. Carbon monoxide poisoning. *The Internet Journal of Emergency and Intensive Care Medicine*. 1997;11(2).
- Harper A, Croft-Baker J. Carbon monoxide poisoning: undetected by both patients and their doctors. *Age Ageing*. 2004;33(2):105-109.

#### Drug Brand Names

Acetylsalicylic acid • Aspirin	Lisdexamfetamine • Vyvanse
Bupropion • Wellbutrin	Methylphenidate ER • Concerta
Cimetidine • Tagamet	Omeprazole • Nexium
Dextroamphetamine/ amphetamine • Adderall	Tamsulosin • Flomax

Mr. L's case, occupation also may increase suspicion; drivers, mechanics, tollbooth operators, parking attendants, miners, and firefighters are all at increased risk for CO poisoning. Regarding locale, polluted urban environments as well as cold climates requiring heating sources cause higher risks for CO exposure. Rarely, excessive smoking can result in CO poisoning. The author once had a patient with schizophrenia who was admitted to the hospital with delirium. It was determined that he had CO poisoning from his 5-pack-a-day smoking habit.

Psychiatric patients often have the frustrating experience of their physical symptoms being attributed to psychiatric causes, which results in major medical issues being overlooked. We psychiatrists can fall into the same trap of overlooking medical illnesses, as indicated in this case, where Mr. L's CO poisoning initially was attributed to adverse effects of his psychiatric medication.

continued

### Clinical Point

**Intentional CO poisoning should be considered in an obtunded or unconscious patient with depression**

## Bottom Line

Adverse effects of psychiatric medications may have overlapping symptoms with some physical illnesses. Assiduous history taking, including possible occupational exposures, may be necessary to reveal carbon monoxide poisoning or other medical causes.

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### Clinical Point

Risk of unintentional CO poisoning can be increased by time of year, occupation, locale, and smoking status