

A young man's 'trips' to heaven and hell

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Mr. F hears voices from Jesus and Satan. He has schizophrenia and is addicted to dextromethorphan in cold medications. Which problem is causing his auditory hallucinations?

CASE The man from Betelgeuse

Mr. F, age 33, has been hospitalized repeatedly for psychotic episodes after abuse of dextromethorphan in cold medications.

Approximately 1 week before presenting to us, Mr. F stormed out of his house after his father, with whom he lived, confronted him about spending his allowance on cold medications. He spent the week living on the streets, abusing dextromethorphan whenever he could get it.

One night, Mr. F approached a police officer at an accident scene and exclaimed, "Dude, I'm from the planet Betelgeuse." He appeared disorganized as police questioned him, and officers transported him to the county hospital's psychiatric emergency service.

At presentation, Mr. F is at times silly, irritable, and sleepy, and chants incantations during the intake interview. Alternately, he hears Jesus Christ and aliens from Betelgeuse telling him "everything is going to be cool" and voices of aliens threatening to abduct him.

We admit Mr. F to the inpatient psychiatric unit, start risperidone at 2 mg nightly, and titrate it to 6 mg nightly over 3 days, after which he is significantly more organized

with reduced auditory hallucinations. At discharge 6 days later, he still occasionally hears Jesus but has partial insight into his obsession with aliens and no paranoid delusions. We continue risperidone, 6 mg nightly, and refer him to an outpatient mental health program. He visits the clinic once but avoids the attending psychiatrist.

Five days later, Mr. F begins hallucinating at home and his father brings him back to the emergency psychiatry unit. At presentation, the patient claims to be an agent of Satan and waves his arms wildly while performing "black magic." He believes he is damned and that previous messages he thought came from Jesus and extraterrestrials were instead from the devil.

Mr. F's father reports that over the weekend his son ingested 6 boxes of cold medicine—each with 16 tablets containing 30 mg of dextromethorphan. Peeling skin on the lower part of Mr. F's forehead, the bridge of his nose, and under his eyes suggests chronic cold tablet abuse. We re-admit the patient after extended urine drug screen shows traces of chlorpheniramine.

What tests confirm recent cold medication abuse?

- urine drug screen
- extended urine drug screen
- blood testing

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The authors' observations

Routine urine drug screens based on radioimmunoassay detect many substances, but an extended or comprehensive urine drug screen based on gas chromatography-mass spectrometry is needed to detect dextromethorphan.¹ Tertiary hospitals and reference laboratories usually offer these tests.

An extended urine screen will not detect dextromethorphan 24 hours after use because the agent has a 3- to 11-hour half-life. The test can, however, detect other active cold preparation compounds with longer half-lives, such as chlorpheniramine.

If extended urine screening is not available, clinical findings discussed later in this article can confirm recent cold medication abuse. Blood testing can reveal dextromethorphan levels, but a 3- to 6-mL sample may be needed.

HISTORY 'Sick' at 16

Mr. F began abusing dextromethorphan at age 16, when friends would "turn him on" to 8-ounce bottles of cough syrup every other week. He later tried marijuana, cocaine, phencyclidine, methamphetamine, morphine, and LSD. Soon after graduating from high school, he stopped using substances and remained clean for several years.

At age 25, Mr. F suffered his first psychotic break, after which a psychiatrist diagnosed schizophrenia. Initial symptom control with antipsychotics helped him finish college.

Mr. F worked as a restaurant manager for about 4 months but found the job stressful and constantly argued with staff. He resumed abusing cough syrup to relieve his stress but soon became hooked on its dissociative and hallucinogenic effects. One night he ingested enough cough syrup to remain "high" until the next morning. He was hallucinating when he reported to work that day and was fired.

Since then, Mr. F's cold medication abuse has escalated from biweekly to almost daily at presentation. He switched to tablets because the syrup induced cold symptoms and he finds the "buzz" from the tablets easier to control.

He typically dresses in black (in keeping with his satanic obsessions) and wears a long black overcoat with several pockets, that allows him to carry boxes of cold capsules, books, and other items.

Mr. F's father has repeatedly tried to stop his son's cold tablet abuse by cutting off his allowance. Dextromethorphan-containing cold medications are inexpensive, however—a box of 16 30-mg tablets costs as little as \$1.50. Also, Mr. F often would get money for cold capsules by going to malls and participating in market research surveys.

In the past year, Mr. F was hospitalized 6 times after dextromethorphan-induced psychotic decompensations. He has been unemployed for more than 5 years, has not been in a serious romantic relationship since college, and depends on his father for financial support. He is not abusing other substances.

How prevalent is cold medication abuse among patients with schizophrenia?

- a) 50%
- b) 20%
- c) < 1%

The authors' observations

As many as 80% of patients with schizophrenia also have a substance abuse disorder.² Access to psychoactive substances, kindling associated with schizophrenia, and attempts to stop hallucinations with alcohol or illicit drugs may explain this high prevalence.² Also, genetic or phenotypic vulnerability in schizophrenia might alter the mesolimbic dopamine system that moderates reward.

Compared with patients with schizophrenia who are substance-free, comorbid substance abuse in schizophrenia increases:

- severity of psychotic symptoms

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Dependence risk with chronic dextromethorphan abuse

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Clinical Point

If extended urine drug screen does not detect dextromethorphan, check the sample for other active cold medication compounds

Clinical Point

Extreme somnolence followed by sleeplessness often follows recent cold medication abuse.

Box 1

How dextromethorphan works

How does dextromethorphan cause hallucinations and/or psychosis, and at what doses can these effects occur?

Dextromethorphan, a synthetic dextroisomer of codeine, exerts antitussigenic effects via the sigma opioid receptor but lacks other opioid activity.

In patients age ≥ 12 , dextromethorphan in cold medications is well tolerated at 60 to 120 mg/d in divided doses, with mostly benign adverse reactions such as drowsiness, dizziness, upset stomach, nervousness, and restlessness.⁷ Hallucinogenic effects surface at 160 to ≥ 300 mg and psychosis often occurs at >600 mg.⁸ Nonsuicidal use of 3,600 mg has been described.⁹

Hallucinogenic effects are caused by dextrophan, a metabolite of dextromethorphan resulting from degradation by the cytochrome P-450 2D6 isoenzyme. Dextrophan is serotonergic and blocks N-methyl-D-aspartate glutamate receptors.¹⁰

Patients who are extensive metabolizers of CYP-450 2D6 substrates show higher blood dextrophan and increased potential to abuse dextromethorphan for its dissociative and hallucinogenic effects.^{10,11}

- likelihood of emergency service use
- risk of suicide, illness, injury, hospitalization, or incarceration.³

Whereas alcohol, marijuana, and cocaine abuse are common in schizophrenia,² to our knowledge only 2 other cases of comorbid dextromethorphan dependence and schizophrenia have been reported.^{4,5}

Mr. F responded well to risperidone when he wasn't abusing cold tablets. After his last hospitalization, we referred him to a comprehensive outpatient program that could have addressed his cold medicine abuse and reintegrated him into the workplace. He avoided seeing the clinic psychiatrist, however, after promising his case manager that he would stop abusing dextromethorphan.

TREATMENT Back to Betelgeuse

Upon re-admission, we restart risperidone, 6 mg nightly. Mr. F shows extreme somnolence caused by massive cold capsule use and is minimally cooperative with the psychiatrist's follow-up interview. Over 36 hours, he awakens only for meals and medication and to use the bathroom. Once the somnolence passes, he cannot fall asleep at night.

Six days after admission, Mr. F is organized and hears voices mostly from Jesus with some demonic delusions. Extended urine drug screen taken 3 days after admission shows traces of chlorpheniramine but no dextromethorphan.

By day 7, Mr. F is nearly free of delusions and is discharged the next day. We continue risperidone, 6 mg nightly, to prevent the "voices," and add diphenhydramine, 50 mg nightly, to regulate his sleep. We arrange follow-up care at an outpatient clinic, but Mr. F again avoids the clinic psychiatrist.

The authors' observations

Mr. F's "robo" binge triggered a profound and prolonged psychotic decompensation.

Dextrophan—a pharmacologically active metabolite of dextromethorphan—might have disrupted cortical and subcortical glutamatergic neurotransmission,⁶ leading to florid psychosis and delayed recovery. Induction of the cytochrome P-450 2D6 isoenzyme, which metabolizes dextromethorphan, also could have prolonged Mr. F's psychosis (*Box 1*).⁷⁻¹¹

RELAPSE Return visits

Three weeks after discharge, Mr. F fights with police officers after they find him hallucinating in the streets. Police charge him with disorderly conduct and resisting arrest and bring him back to the psychiatric ER. We again resolve his auditory hallucinations with risperidone, 6 mg nightly. After 8 days we discharge him to police, who then transport him to jail and later release him on bail.

Six months later, Mr. F is hospitalized twice in 2 months after dextromethorphan-induced

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Box 2**Dextromethorphan: Fast facts****Street names**

CCC, triple C, DM, DXM, skittles, tuss, robo, poor man's PCP

Dosing forms

Liquid, capsules, liquid gelatin capsules, lozenge tablets, powder

Most commonly abused OTC preparations

Coricidin, Robitussin

decompensations. He recovers quickly both times but lacks insight into his mental illness and his “robo” problem.

The authors' observations

Dextromethorphan, known by many street names (**Box 2**), is contained in more than 100 OTC preparations, and is sold on the Internet in powder form.

Abuse of dextromethorphan-containing preparations is rising among teenagers and young adults. Nonmedical “robo” use led to 5,581 ER visits in the United States in 2004,¹² and California reported a 10-fold rise in dextromethorphan abuse among teenagers from 1999 to 2004.¹³ Numerous factors explain this increase:

- Most people do not know that dextromethorphan-laced medications are dangerous if misused.
- These preparations can be purchased at many stores or snatched from the medicine chest.
- Several Web sites describe how to “safely” abuse dextromethorphan.¹³

Further, some pediatricians, family physicians, emergency physicians, and psychiatrists do not suspect “robo” abuse, in part because ordinary urine drug screens do not detect dextromethorphan.

Medical consequences

Many dextromethorphan-laced preparations contain other active compounds—

such as pseudoephedrine, acetaminophen, chlorpheniramine, guaifenesin, or bromide—that can cause serious adverse effects at above-normal doses. Abuse of medications containing both chlorpheniramine and dextromethorphan leads to hallucinogenic euphoria and dissociation, followed by hours of intense somnolence.

Dextromethorphan can cause serotonin syndrome when taken with serotonergic drugs such as amphetamines, cocaine, monoamine oxidase inhibitors, or selective serotonin reuptake inhibitors. Symptoms include tachycardia, hypertension, diaphoresis, mydriasis, myoclonus, agitation, and seizures.

If you suspect cold medication abuse:

- a) look for psychiatric and physical signs/symptoms
- b) review patient history
- c) obtain collateral information
- d) all of the above

The authors' observations

Physical and psychiatric symptoms, patient history, and collateral information together can confirm dextromethorphan abuse in patients who present with mainly visual and tactile hallucinations. The signs are easy to miss in patients with schizophrenia because schizophrenia is believed to be causing the psychosis.

Psychiatric/physical symptoms. Psychiatric symptoms of “robo” intoxication include euphoria, altered time perception, disorientation, and tactile, visual and auditory hallucinations.⁷ Physical symptoms include excitation, nystagmus, tachycardia, hypertension, hyperthermia, vomiting, urinary retention, drowsiness, and rash. Extreme dextromethorphan withdrawal can cause dysphoria, insomnia, vomiting, diaphoresis, abdominal pain, and diarrhea.⁷

Psychiatric symptoms of intoxication with dextromethorphan or phencyclidine are similar, but phencyclidine-intoxicated patients typically present with fluctuating

Clinical Point

Dermatitis on the head, nose, or cheeks can signal chronic cold medication abuse

Related Resources

- U.S. Department of Justice, National Drug Intelligence Center. Intelligence bulletin: DXM (dextromethorphan). www.usdoj.gov/ndic/pubs11/11563/index.htm.
- Partnership for a Drug-Free America. Resource for parents. www.drugfree.org/Parent. Click on "Cough Medicine Abuse" under "Special Drug Reports."
- U.S. Food and Drug Administration. FDA warns against abuse of dextromethorphan (DXM). www.fda.gov, enter "dextromethorphan" in search field.

Drug Brand Names

Risperidone • Risperdal

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

behavior and motor symptoms including tremor, dystonic reactions, and catalepsy.

Also watch for dermatitis on the forehead, nose, or cheeks, which can result from chronic abuse of preparations containing dextromethorphan plus bromide or chlorpheniramine.

Patient history. Has the patient abused dextromethorphan before? If so, how often? When was he last treated for decompensation after cold medication abuse?

Also check for abuse of other substances, and ask teenage patients if their friends use cold preparations recreationally.

Collateral information. Ask family members to search the patient's room for supplies of cold medicine and for empty boxes and capsule cards, check the medicine chest regularly to see if cold medications are missing, and check the patient's jacket or coat pockets for cold tablets or cough syrup.

Treating 'robo' abuse

Convincing the patient and family that dextromethorphan abuse can cause severe harm is critical to promoting a positive outcome. Referral to a substance abuse rehabilitation program or 12-step group can help.

References

1. Cherkas JK, Friedman JH. Dextromethorphan-induced neurologic illness in a patient with negative toxicology findings. *Neurology* 2006; 66:1952-3.

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2. Westermeyer J. Comorbid schizophrenia and substance abuse: a review of epidemiology and course. *Am J Addict* 2006;15:345-55.
3. Winklbaur B, Ebner N, Sachs G, et al. Substance abuse in patients with schizophrenia. *Dialogues Clin Neurosci* 2006;8:37-43.
4. Orrell MW, Campbell PG. Dependence on dextromethorphan hydrobromide. *Br Med J* 1986;293:1242-3.
5. Iaboni RP, Aronowitz JS. Dextromethorphan abuse in a dually diagnosed patient. *J Nerv Ment Dis* 1995;183:341-2.
6. Krystal JH, D'Souza DC, Mathalon D, et al. NMDA receptor antagonist effects, cortical glutamatergic function, and schizophrenia: toward a paradigm shift in medication development. *Psychopharmacology (Berl)* 2003;169:215-33.
7. Wolfe TR, Caravati EM. Massive dextromethorphan ingestion and abuse. *Am J Emerg Med* 1995;13:174-6.
8. Cranston JW, Yoast R. Abuse of dextromethorphan. *Arch Fam Med* 1999;8:99-100.
9. Schadel M, Sellers EM. Psychosis with Vicks Formula 44-D abuse. *CMAJ* 1992;147:843-4.
10. Miller SC. Dextromethorphan psychosis, dependence and physical withdrawal. *Addict Biol* 2005;10:325-7.
11. Zawertailo LA, Kaplan HL, Busto UE, et al. Psychotropic effects of dextromethorphan are altered by the CYP2D6 polymorphism: a pilot study. *J Clin Psychopharmacol* 1998;18:332-7.
12. Ball JK, Albright V. Emergency department visits involving dextromethorphan. *Drug Abuse Warning Network Report* 2006;32:1-4.
13. Bryner JK, Wang UK, Hui JW, et al. Dextromethorphan abuse in adolescence: an increasing trend: 1999-2004. *Arch Pediatr Adolesc Med* 2006;160:1217-22.
14. Tuominen HJ, Tiihonen J, Wahlbeck K. Glutamatergic drugs for schizophrenia: a systematic review and meta-analysis. *Schizophr Res* 2005;72:225-34.
15. Andersen JD, Pouzet B. Spatial memory deficits induced by perinatal treatment of rats with PCP and reversal effect of D-serine. *Neuropsychopharmacology* 2004;29:1080-90.

Clinical Point

Important questions for teenage patients:

- Have you abused cold medications before?
- Do your friends take cold tablets to 'get high'?

Bottom Line

Suspect dextromethorphan abuse in patients who present after psychotic decompensation—especially if the patient has a psychotic illness and has been taking antipsychotics as prescribed. Excitation, drowsiness, rash, vomiting, and other physical symptoms can signal recent cold medication abuse. History of chronic misuse and collateral information can confirm the diagnosis.

Have a case from which other psychiatrists can learn?

Check your patient files for a case that teaches valuable lessons on dealing with clinical challenges, including:

- Sorting through differential diagnoses
- Getting patients to communicate clinical needs
- Catching often-missed diagnoses
- Avoiding interactions with other treatments
- Ensuring patient adherence
- Collaborating with other clinicians

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