

# Malnourished and psychotic, and found incompetent to stand trial

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Mr. N, age 48, is arrested for cocaine possession but is declared incompetent to stand trial. He has chronic mental illness and is homeless. How would you proceed with his care?



## How would you handle this case?

Answer the **challenge questions** throughout this article

### **CASE** Psychotic while in jail

Mr. N, age 48, has chronic mental illness and has been in and out of psychiatric hospitals for 30 years, with diagnoses of bipolar disorder, not otherwise specified, without psychotic features and schizophrenia. He often is delusional and disorganized and does not adhere to treatment. Since age 18, his psychiatric care has been sporadic; during his last admission 3 years ago, he refused treatment and left the hospital against medical advice. Mr. N is homeless and often eats out of a dumpster.

Recently, Mr. N was arrested for cocaine possession, for which he was held in custody. His mental status continued to deteriorate while in jail, where he was evaluated by a forensics examiner.

Mr. N was declared incompetent to stand trial and was transferred to a state psychiatric hospital.

In the hospital, the treatment team finds that Mr. N is disorganized and preoccupied with thoughts of not wanting to “lose control” to the physicians. He shows no evidence of suicidal or homicidal ideation or perceptual disturbance. Mr. N has difficulty grasping concepts, making plans, and following through with them. He has poor insight and impulse control and impaired judgment.

Mr. N’s past and present diagnoses include bipolar disorder without psychotic features, schizophrenia, obsessive-compulsive per-

sonality disorder, paranoid personality traits, borderline intelligence, cellulitis of both legs, and chronic venous stasis. Although he was arrested for cocaine possession, we are not able to obtain much information about his history of substance abuse because of his poor mental status.

### What could be causing Mr. N’s deteriorating mental status?

- substance withdrawal
- malnutrition
- worsening schizophrenia
- untreated infection due to cellulitis

### **HISTORY** Sporadic care

Mr. N can provide few details of his early life. He was adopted as a child. He spent time in juvenile detention center. He completed 10th grade but did not graduate from high school. Symptoms of mental illness emerged at age 18. His employment history is consistent with

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### Disclosures

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

### Clinical Point

In rare cases, vitamin B<sub>12</sub> deficiency presents with psychiatric symptoms such as depression, mania, psychosis, dementia, and catatonia

**Table 1**

### Mr. N's folate and vitamin B<sub>12</sub> levels

Date	Folate (ng/mL)	Vitamin B <sub>12</sub> (pg/mL)
June 2002	36.0	61
July 2003	11.1	170
August 2005	7.9	<100
December 2005	13.3	<100
June 2011	14.8	<50
November 2011	19.9	55
December 2011	N/A	379

chronic mental illness: His longest job, at a grocery store, lasted only 6 months. He has had multiple admissions to psychiatric hospitals. Over the years his treatment has included divalproex sodium, risperidone, paroxetine, chlorpromazine, thioridazine, amitriptyline, methylphenidate, and a multivitamin; however, he often is noncompliant with treatment and was not taking any medications when he arrived at the hospital.

### EVALUATION Possible deficiency

The treatment team discusses guardianship, but the public administrator's office provides little support because of Mr. N's refusal to stay in one place. He was evicted from his last apartment because of hoarding behavior, which created a fire hazard. He has been homeless most of his adult life, which might have significantly restricted his diet.

A routine laboratory workup—complete blood count, basic metabolic panel, liver function test, thyroid-stimulating hormone, and lipids—is ordered, revealing an absolute neutrophil count (ANC) in the low range at 1,200/ $\mu$ L (normal range, 1,500 to 8,000/ $\mu$ L). Mr. N is offered treatment with a long-acting IM injection of risperidone because of his history of noncompliance, but he refuses the

medication. Instead, he is started on oral risperidone, 2 mg/d.

The cellulitis of both lower limbs and chronic venous stasis are of concern; the medical team is consulted. Review of Mr. N's medical records from an affiliated hospital reveals a history of vitamin B<sub>12</sub> deficiency. Further tests show that the vitamin B<sub>12</sub> level is low at <50 pg/mL (normal range, 160 to 950 pg/mL). Pernicious anemia had been ruled out after Mr. N tested negative for antibodies to intrinsic factor (a glycoprotein secreted in the stomach that is necessary for absorption of vitamin B<sub>12</sub>). Suspicion is that vitamin B<sub>12</sub> deficiency is caused by Mr. N's restricted diet in the context of chronic homelessness.

### The authors' observations

A review of the literature on vitamin B<sub>12</sub> deficiency describes tingling or numbness, ataxia, and dementia; however, in rare cases, vitamin B<sub>12</sub> deficiency presents with psychiatric symptoms, such as depression, mania, psychosis, dementia, and catatonia.<sup>1-13</sup>

We suspected that Mr. N's vitamin B<sub>12</sub> deficiency could have been affecting his mental status; consequently, we ordered routine laboratory work-up that included a complete blood count with differential and peripheral smear, which showed macrocytic anemia and ovalocytes. We also tested his vitamin B<sub>12</sub> level, which was very low at 55 pg/mL. These results, combined with his previously recorded vitamin B<sub>12</sub> level (Table 1), suggested deficiency.

### TREATMENT Oral medication

Two months after starting risperidone, the medical team recommends IM vitamin B<sub>12</sub> as first-line treatment, but Mr. N refuses. We considered guardianship ex parte for involuntary administration of IM B<sub>12</sub> injection to prevent life-threatening consequences of a non-healing ulcer on his leg that was related to his cellulitis. Meanwhile, we reviewed the literature on vitamin B<sub>12</sub> therapy, including



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Table 2

### Postive effect of vitamin B<sub>12</sub> on Mr. N's red blood cell and neutrophil counts and hemoglobin level

Date	Red blood cell count (× 10 <sup>6</sup> /μL)	Absolute neutrophil count (/μL)	Hemoglobin (g/dL)
November 16, 2011	2.29	1,200	9.3
November 21, 2011	2.50	2,100	9.9
November 22, 2011	2.35	2,100	10.0
December 16, 2011	3.55	3,200	13.1

route, dosage, and outcome.<sup>14-23</sup> Mr. N agrees to oral vitamin B<sub>12</sub>, 1,000 μg/d,<sup>21</sup> and we no longer consider guardianship ex parte. Mr. N's vitamin B<sub>12</sub> level and clinical picture improve 1 month after oral vitamin B<sub>12</sub> is added to oral risperidone. His thought process is more organized, he is no longer paranoid, and he shows improved insight and judgement. ANC and neutrophil count improve as well (**Table 2**). Mr. N's ulcer begins to heal despite his non-compliance with wound care.

The forensic examiner sees Mr. N after 3 months of continued therapy. His thought pattern is more organized and he is able to comprehend the criminal charges against him and to work with his attorney. He is determined competent by the forensic examiner; in a court hearing, the judge finds Mr. N competent to stand trial.

#### The authors' observations

Based on our experience treating Mr. N, we think that it is important to establish an association between vitamin B<sub>12</sub> deficiency and psychosis. Vitamin B<sub>12</sub> deficiency is uncommon; however, serum levels do not need to be significantly low to produce severe neuropsychiatric morbidity, which has been reported with serum levels ≤457 pg/mL.<sup>2-5,24,25</sup> It is more frequent than the other organic causes of psychosis<sup>5,10,24</sup> and Mr. N's improvement further strengthened the correlation.

Parenteral vitamin B<sub>12</sub> therapy is the first-line treatment for a deficiency, but oral

or sublingual vitamin B<sub>12</sub> can be given to patients who are disabled, geriatric, or refuse parenteral administration.<sup>21</sup> Only approximately 1% of oral vitamin B<sub>12</sub> is absorbed in patients who do not have intrinsic factor. The daily requirement of vitamin B<sub>12</sub> is 1.0 to 2.5 μg/d; large oral dosages of 1,000 to 5,000 μg/d therefore seem to be effective in correcting deficiency, even in the presence of intrinsic factor deficiency.<sup>15,20,21</sup> Large oral dosages also benefit other hematological abnormalities, such as a low white blood cell count and neutropenia.

#### How vitamin B<sub>12</sub> deficiency affects neuropsychiatric illness

Vitamin B<sub>12</sub> is essential for methylation, a process crucial for the formation of neurotransmitters such as serotonin, dopamine, and epinephrine. A low level of vitamin B<sub>12</sub>

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#### Clinical Point

**Oral or sublingual vitamin B<sub>12</sub> can be given to patients who are disabled, geriatric, or refuse parenteral administration**

#### NEXT MONTH IN

#### CASES THAT TEST YOUR SKILLS

#### Psychotic after a rave

Mr. D, age 23, presents with new-onset psychosis and catatonia 10 days after taking 2C-B, a hallucinogenic drug. He has no personal or family history of psychiatric illness. How would you treat him?

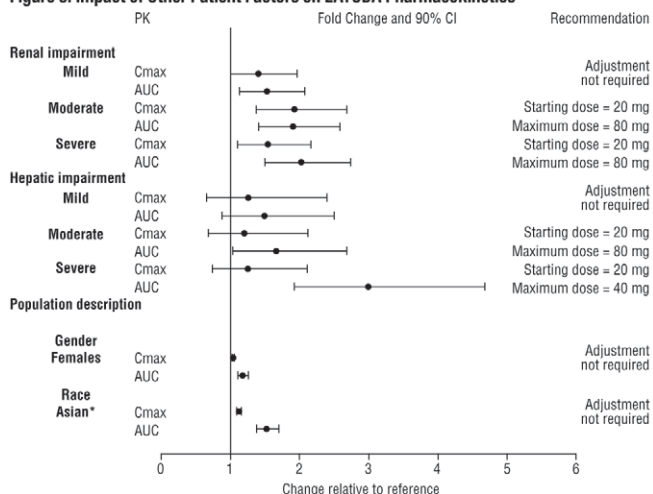
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## 8.6 Other Patient Factors

The effect of intrinsic patient factors on the pharmacokinetics of LATUDA is presented in Figure 3.

**Figure 3: Impact of Other Patient Factors on LATUDA Pharmacokinetics**



\*Compare to Caucasian

## 10 OVERDOSAGE

### 10.1 Human Experience

In premarketing clinical studies, accidental or intentional overdosage of LATUDA was identified in one patient who ingested an estimated 560 mg of LATUDA. This patient recovered without sequelae. This patient resumed LATUDA treatment for an additional two months.

### 10.2 Management of Overdosage

Consult a Certified Poison Control Center for up-to-date guidance and advice. There is no specific antidote to LATUDA, therefore, appropriate supportive measures should be instituted and close medical supervision and monitoring should continue until the patient recovers. Consider the possibility of multiple-drug overdose.

Cardiovascular monitoring should commence immediately, including continuous electrocardiographic monitoring for possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide, and quinidine carry a theoretical hazard of additive QT-prolonging effects when administered in patients with an acute overdose of LATUDA. Similarly, the alpha-blocking properties of bretylium might be additive to those of LATUDA, resulting in problematic hypotension.

Hypotension and circulatory collapse should be treated with appropriate measures. Epinephrine and dopamine should not be used, or other sympathomimetics with beta-agonist activity, since beta stimulation may worsen hypotension in the setting of LATUDA-induced alpha blockade. In case of severe extrapyramidal symptoms, anticholinergic medication should be administered.

Gastric lavage (after intubation if patient is unconscious) and administration of activated charcoal together with a laxative should be considered.

The possibility of obtundation, seizures, or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis.



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can interrupt methylation and cause accumulation of homocysteine and impaired metabolism of serotonin, dopamine, and epinephrine. Hyperhomocysteinemia can contribute to cerebral dysfunction by causing vascular injury.<sup>26</sup>

Vitamin B<sub>12</sub> also is involved in tetrahydrobiopterin synthesis in the brain, which is pivotal for synthesis of monoamine neurotransmitters. Vitamin B<sub>12</sub> deficiency can lead to accumulation of methyltetrahydrofolate, an excitatory neurotoxin. All of these can contribute to development of psychosis. Therefore, a defect in the methylation process could be responsible for the neuropsychiatric manifestations of vitamin B<sub>12</sub> deficiency.

## What did we learn from Mr. N?

In most people, vitamin B<sub>12</sub> levels are normal, however, we recommend that clinicians consider vitamin B<sub>12</sub> deficiency when a patient has new-onset or unresponsive psychosis,<sup>27</sup> particularly in a homeless person or one who has a restricted diet.<sup>28</sup> It is important to rule out vitamin B<sub>12</sub> deficiency in a patient with a low serum folate level because folic acid therapy could exacerbate neurologic manifestations of underlying vitamin B<sub>12</sub> deficiency and increase the risk of permanent nerve damage and cognitive decline.

We were intrigued to see improvement in Mr. N after we added vitamin B<sub>12</sub> to his ongoing treatment with an antipsychotic. We did not believe that vitamin B<sub>12</sub> supplementation was the sole reason his mental status improved enough to be found competent to stand trial, although we believe that initiating oral vitamin B<sub>12</sub> was beneficial for Mr. N.

Last, this case supports the need for research to further explore the role of vitamin B<sub>12</sub> in refractory psychosis, depression, and mania.

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## Related Resources

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### Drug Brand Names

Amitriptyline • Elavil	Methylphenidate • Ritalin
Chlorpromazine • Thorazine	Paroxetine • Paxil
Divalproex sodium • Depakote	Risperidone • Risperdal
	Thioridazine • Mellaril

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## Clinical Point

**A defect in the methylation process could be responsible for neuropsychiatric manifestations of vitamin B<sub>12</sub> deficiency**

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## Bottom Line

Vitamin B<sub>12</sub> deficiency can contribute to psychosis and other psychiatric disorders, especially in patients with a restricted diet, such as those who are homeless. Parenteral vitamin B<sub>12</sub> therapy is the first-line treatment, but oral supplementation can be used if the patient refuses therapy. Large oral dosages of 1,000 to 5,000 µg/d seem to be effective in correcting vitamin B<sub>12</sub> deficiency.