

> THE PATIENT

Non-symptomatic
26-year-old man

> SIGNS & SYMPTOMS

- Elevated levels of AST, ALT, and CPK
- No family history of liver disease

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*The authors reported no
potential conflict of interest
relevant to this article.*

> THE CASE

A 26-year-old healthy male veteran with bipolar disorder and post-traumatic stress disorder was referred for a gastroenterology consultation after a routine laboratory evaluation revealed elevated levels of aspartate aminotransferase (AST), 1040 IU/L (normal range, 10-40 IU/L), and alanine aminotransferase (ALT), 334 IU/L (normal range, 7-56 IU/L). He had been taking divalproex and ziprasidone for the previous 2 years, during which time liver test results had been normal.

■ **The patient reported no symptoms** in the course of a detailed history. He had no family history of liver disease, drank alcohol infrequently, and didn't use tobacco. He hadn't received any blood transfusions and didn't have tattoos.

The patient indicated that he had recently returned from military deployment and that a week before his laboratory tests, he'd resumed weight training. To boost his workout, he'd begun taking a nutritional supplement supplied by a friend. Further questioning revealed that the supplement was MuscleMeds' Code Red, which contains 1,3-dimethylamylamine (DMAA). He denied using any other dietary supplements.

■ **The physical examination was unremarkable** and additional lab work was unrevealing. Lab results included normal levels of ceruloplasmin, alpha-1 antitrypsin, ferritin, iron, and transferrin. Viral hepatitis serologies revealed immunity to the hepatitis A and B virus. The patient tested negative for Epstein-Barr virus, cytomegalovirus, herpes simplex virus, human immunodeficiency virus, antinuclear antibody, anti-smooth muscle antibody, and antimitochondrial antibody. A toxicology screen was remarkable for cannabinoids. The remainder of the basic metabolic panel and complete blood count were within normal limits.

THE DIAGNOSIS

The patient's AST and ALT levels prompted measurement of creatine phosphokinase (CPK), which was elevated at 34,270 IU/L (normal range, 22-198 IU/L). We diagnosed rhabdomyolysis in this patient, which can be associated with elevated levels of AST and ALT. When we contacted the patient about the diagnosis, he reported no muscle aches or pains, or other symptoms.

We instructed the patient to increase his fluid intake and refrain from further use of Code Red. Repeat liver tests one month after the initial consultation revealed significant improvement in AST (29 IU/L) and ALT (68 IU/L), as well as a decline in CPK to 743 IU/L.

DISCUSSION

Much debate has surrounded the safety and use of DMAA, also known as methylhexamine or Geranamine, in dietary supplements such as Code Red. Eli Lilly and Company developed

and patented DMAA in the 1940s, then trademarked it under the name Forthane as an inhaled nasal decongestant in 1971.¹⁻³ United States Food and Drug Administration (FDA) approval for Forthane was withdrawn in 1983 at Lilly's request.⁴ DMAA was reintroduced as a dietary supplement more than a decade ago after the FDA, in 2004, banned supplements containing ephedrine alkaloids, which have effects similar to DMAA.⁵

DMAA has been used to increase muscle mass, promote weight loss, and improve physical performance; it's also been used as a recreational drug.⁶⁻⁸ Several case reports have described poor outcomes in patients who consumed DMAA products. In 2012, the deaths of 2 military personnel who used DMAA prompted the FDA to warn manufacturers of DMAA-containing supplements to stop production, but such supplements remain easily available in the United States.⁶

DMAA's validity as a dietary supplement is controversial. The claim that DMAA is naturally present in geraniums hasn't been verified, leading some to question whether an inaccurate description of DMAA as a natural substance was employed to justify its use as a nutritional supplement.⁹ No published evidence exists to establish DMAA as a dietary ingredient.^{10,11}

A long list of potential adverse effects

DMAA is an indirect sympathomimetic with vasoconstricting and cardiovascular effects.¹² Animal studies have shown effects similar to ephedrine and amphetamines.¹²⁻¹⁵ Marsh and colleagues reported that a single oral dose of 3 mg/kg in a human (210 mg/70 kg) moderately increases heart rate and blood pressure and can lead to confusion and concentration problems.¹⁶

Oral intake of DMAA affects the lungs at doses above 4 to 15 mg, the heart after 50 to 75 mg, and blood pressure after 100 mg.¹⁷ Because of the drug's long half-life—24 hours based on urinary excretion rates—Venhuis and Kaste reported that there is a risk from repeated doses within 24 to 36 hours that can lead to steadily stronger pharmacologic effects.¹⁷

The use of DMAA has been cited in 5 cases of hemorrhagic stroke, a case of acute heart failure, and the deaths of 2 military personnel who experienced asystole during aerobic exercise.^{7,8,18-20} These individuals ranged in age from 22 to 41 years.

Initial symptoms included severe headaches, palpitations, dizziness, twitching of extremities, nausea, vomiting, confusion, agitation, and chest pain. The 2 military personnel suffered leg cramps and dyspnea followed by loss of consciousness. Several individuals were hypertensive on presentation to the emergency department with blood pressures as high as 240/120 mm Hg.

THE TAKEAWAY

Our patient presented with transaminitis and was found to have rhabdomyolysis after using DMAA. A few case reports have associated rhabdomyolysis with elevated liver function tests.^{21,22} We suspect that DMAA use, which has been linked to adverse effects such as hypertension, tachycardia, and muscle aches, may also cause leakage of muscle enzymes and the development of rhabdomyolysis.

Although a single instance can't prove causation, this case may illustrate additional adverse effects of DMAA beyond the already long list of risks, including hypertension, seizures, cerebral hemorrhage, arrhythmias, myocardial infarction, cardiomyopathy, and death.^{7,8,18-20,23} It's important for physicians to recognize that their patients may be using dietary supplements to increase strength, energy, or weight loss and to be aware of the potential adverse effects. **JFP**

> Supplements containing DMAA are still readily available, despite a 2012 FDA warning to discontinue production.

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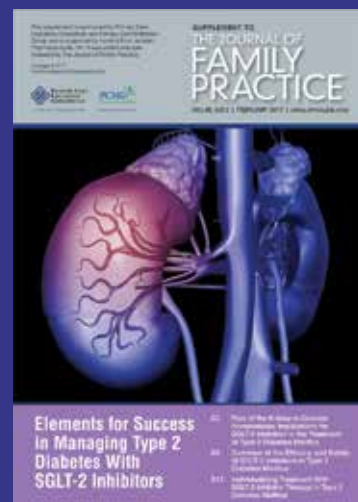
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This supplement is sponsored by Primary Care Education Consortium and Primary Care Metabolic Group and is supported by funding from Janssen Pharmaceuticals, Inc.