A 49-year-old man presented to the emergency department with an eight-hour history of unsteady gait, impaired concentration, difficulty speaking and blurry vision, which had developed over the previous seven hours. During the preceding two days, he had been excessively thirsty and drank large amounts of water, cola and a “sports drink.” He had eaten a large portion of rice with dinner the evening before presentation. On the day he presented, he had woken in the morning feeling dizzy. As he was leaving for work, he had experienced difficulty using his keys and turning doorknobs.

The patient’s medical history included Crohn disease and two major small-bowel resections at 33 and 35 years of age that had left about one metre of small intestine. He had undergone an esophageal bougienage three weeks earlier for a stricture related to Crohn disease. After the bougienage, the patient had regained his ability to consume solids and dramatically increased his caloric intake to regain weight. His diet consisted mainly of fast food, candy bars and soft drinks.

The patient reported that he did not smoke, consume substantial amounts of alcohol or have any drug allergies. On a daily basis, he took prednisone 20 mg, loperamide 2–4 mg, vitamin B₁₂ and multivitamins. Except for the addition of prednisone for the Crohn-related stricture, his regimen of medications had not changed during the past year. He had experienced no changes in his usual Crohn symptoms.

On clinical examination, the patient was alert, oriented and not in distress. His vital signs were normal and he had no significant postural changes. Other than mild vertical and horizontal nystagmus, the results of cranial nerve testing were normal. The patient had truncal ataxia and notable dysmetria on finger-nose testing. He had an unsteady, wide-based gait and could not tolerate walking more than five steps. Rapid alternating movements and heel-shin tests were normal. His strength and reflexes, and the results of sensory testing, were normal. The rest of the clinical examination was unremarkable except for midline abdominal surgical scars.

Initial laboratory investigations are presented in Table 1 and include a serum carbon dioxide level of 10 mmol/L with an anion gap of 22 mEq/L. Complete blood count, creatinine, coagulation studies, liver enzymes and urinalysis were within normal limits. Arterial blood gas analysis showed a pH of 7.21, partial pressure of carbon dioxide (pCO₂) of 23, partial pressure of oxygen (pO₂) of 119 and HCO₃⁻ of 9. Serum lactate...
Eubacterium cient neutralization of gastric acid.4

tions of low luminal pH, which may be enhanced by insuffi-

metabolize carbohydrates before they are absorbed. Excess

and reductions in bowel motility can provide colonic bacteria

such as

they may serve as substrates for D-lactate-producing bacteria,

small intestine and thus pass undigested into the colon. There,

risk that some carbohydrates may not be absorbed by the

inflammation associated with excess bacteria, increase the

association between D-lactic acidosis and short-gut syn-

faster, easier to use and more sensitive than serologic assays.2,3

Measurement of D-lactate, however, is not available routinely

level greater than 3 mmol/L is diagnostic for this condition.1

serum assay showing a higher than normal D-lactate level. A

els when other causes have been excluded (Table 2).

Association with short-gut syndrome

Various mechanisms have been proposed to describe the

association between D-lactic acidosis and short-gut syn-

drobe. Decreased surface area of the small bowel, as well as

inflammation associated with excess bacteria, increase the

risk that some carbohydrates may not be absorbed by the

small intestine and thus pass undigested into the colon. There,

they may serve as substrates for D-lactate-producing bacteria,

such as Lactobacillus, Streptococcus, Bifidobacterium and

Eubacterium. Growth of these bacteria is favoured in condi-

tions of low luminal pH, which may be enhanced by insuffi-

cient neutralization of gastric acid.6

The anatomic lesions associated with bowel resections and

reductions in bowel motility can provide colonic bacteria

with an opportunity to migrate into the small intestine and

metabolize carbohydrates before they are absorbed. Excess

ingestion of carbohydrates, particularly those that are poorly

broken down or absorbed, can then lead to high levels of

colic D-lactic acid.5

High-fructose corn syrup has been added increasingly to

commercially available sweetened drinks over the past 40

years. Fructose that is joined with glucose in the form of a

sucrose disaccharide is well absorbed by glucose transporters.

However, because of a lack of fructose-specific intestinal trans-

porters, the absorption of fructose is limited when it is found in

mixtures with excess glucose. This limited absorption results in

elevated luminal sugar substrates for D-lactic acid production.6

Various dietary sources of D-lactate exist, including sour

milk, molasses, and certain fruits and vegetables. Clinical inves-
tigations into the efficiency with which D-lactate is metabolized

have been contradictory. Some studies have found that it is read-

ily metabolized to pyruvate by D-lactate dehydrogenase in the

liver and kidneys3 at a rate similar to the metabolism of

L-lactate.7 Other studies have shown that it is metabolized more

Discussion

Metabolic acidosis with an elevated anion gap has a limited
differential diagnosis (Box 1).1,4-6 The laboratory tests investi-
gating these typical causes were negative in our patient. D-
lactic acidosis is a much rarer cause of metabolic acidosis
with an elevated anion gap. Its presence is suggested by ele-
vation of the anion gap in patients with shortened small bow-
eels when other causes have been excluded (Table 2).

The presence of D-lactic acidosis can be confirmed by a
serum assay showing a higher than normal D-lactate level. A
level greater than 3 mmol/L is diagnostic for this condition.1
Measurement of D-lactate, however, is not available routinely
in most hospital laboratories. Urinary D-lactate assays may be
faster, easier to use and more sensitive than serologic assays.2,3

Box 1: Differential diagnoses for large and normal
anion gap metabolic acidoses1,4-6

Common causes of metabolic acidosis with a large anion gap

Production of endogenous acids:
• Ketoacidosis (e.g., associated with diabetes, alcoholism,
toxicity, starvation)
• Renal failure
• Lactic acidosis (e.g., caused by poor tissue oxygenation,
decreased renal clearance, toxins)

Ingestion of exogenous acids:
• Toxic alcohols (e.g. ethylene glycol and methanol)
• Acetylsalicylic acid
• Paraldehyde

Ingestion of other potential toxins:
• Phenformin
• Iron
• Isoniazid
• Acetaminophen

Common causes of metabolic acidosis with a normal anion gap

Gastrointestinal losses of bicarbonate:
• Diarrhea
• Pancreatic fistula
• High-volume drainage of gastrointestinal tube

Renal losses of bicarbonate:
• Proximal renal tubular acidosis
• Distal renal tubular acidosis
• Hypoaldosteronism

Ingestion of potential toxins:
• Toluene
• Carbonic anhydrase inhibitors
• Cholestyramine

Dilutional:
• Rapid infusion of intravenous fluids that do not contain
bicarbonate
slowly because of lower abundance of specific metabolizing enzymes for D-lactate and slower renal clearance.9

**Neurologic findings**

The clinical manifestations of D-lactic acidosis are listed in Box 24,10 and include altered mental status and cerebellar ataxia. The cause of these neurologic abnormalities is debated. A reduction in serum pH alone is insufficient to explain such manifestations, given that acidosis of comparable severity from other causes does not always result in this presentation. Various theories have been advanced, including suggestions that low pH may affect intraneural metabolism of L-lactate, which is the preferred substrate of nervous aerobic metabolism,11 or may inhibit central and peripheral neurotransmitter production.4,12 The accumulation of D-lactate in brain tissue because of naturally low levels of D-lactate dehydrogenase has also been hypothesized.11

These theories are not supported by a study showing that infusion of D-lactate into healthy volunteers to a serum concentration of 6 mmol/L did not cause neurologic symptoms.9 This finding suggests the presence of other mediators associated with D-lactate.15 However, infusing D-lactate into peripheral venous blood may not reproduce the clinical presentation associated with D-lactic acidosis because D-lactate absorbed from the colon passes through the portal circulation and into the liver before being released into the systemic circulation.

**Treatment**

Although treatment of D-lactic acidosis includes intravenous fluid resuscitation to promote renal excretion of D-lactic acid, no evidence exists to support this intervention in euvolemic patients.10 Poorly absorbed oral antibiotics (e.g., metronidazole, neomycin and vancomycin) are effective in reducing lev-

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**Table 2: Steps involved in determining the cause of metabolic acidosis**

| Step | In our patient |
|------|---------------|
| 1. **Calculate the anion gap** | Results of testing for arterial blood gas (pH = 7.21, pCO\(_2\) = 23 and HCO\(_3^-\) = 9) suggested a metabolic acidosis with respiratory compensation. Anion gap = Na\(^+\) – (Cl\(^-\) + HCO\(_3^-\)) = 139 – (107 + 9) = 23, which is consistent with metabolic acidosis with a large anion gap. |
| 2. **Determine whether the type of acidosis is mixed or non-anion gap** | Delta bicarbonate was 24 – 10 = 14. The delta anion gap was 12 ± 2 = 23 = -9 to -13. The difference in HCO\(_3^-\) from the expected value was 14. The difference in the anion gap from the expected value was -9 to -13. Because only a small discrepancy was observed, a pure large anion gap metabolic acidosis was diagnosed. |
| 3. **Determine whether the acidosis is caused by endogenous acids or ingestion of exogenous acids** | The osmolar gap was equal to (measured osmolality – calculated osmolality), or 292 – (2 \times 139 + 7.1 + 2.3) = 4.6, which was not large enough to consider methanol or ethylene glycol ingestion as a cause. Preliminary screening for the most common causes of a large anion gap metabolic acidosis showed a negative toxicology screen for salicylates and ethanol. Serum lactate, glucose, creatinine and ketones were also normal. Based on clinical suspicion, a serum D-lactate assay was eventually ordered, which was positive. |
Box 2: Clinical manifestations of D-lactic acidosis

Altered mental status
- Disorientation
- Decreased level of consciousness
- Irritability
- Coma
Cerebellar signs
- Ataxia
- Dysarthria
- Gait disturbance
- Impaired motor coordination
- Nystagmus
Weakness
Blurred vision
Psychosis

Prevention
Prevention of D-lactic acidosis begins with reduced consumption of substrates that promote the proliferation of acid-resistant colonic bacteria in patients with shortened small bowels. Therefore, a diet low in carbohydrates, including avoidance of sweetened beverages, is important. Immediate treatment with antibiotics when early symptoms (e.g., disorientation and dysarthria) are detected can avoid progression to the full spectrum of neurologic abnormalities.

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