

Metabolic Acidosis

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Common case presentation

A 68-year-old man with a history of muscle-invasive bladder cancer treated by radical cystectomy and urinary diversion 6 years ago presents to your office complaining of weakness, fatigue, and weight loss.

I. Receiving the phone call and initial thoughts

a. What are the patient's vitals?

Weakness and fatigue should first prompt a consideration of infection and fluid status.

b. What was the patient's pathology, treatment, and disease status?

In a patient with advanced bladder cancer, disease recurrence should also be considered as a possibility.

c. What type of urinary diversion did the patient have?

Urinary diversions are associated with metabolic abnormalities. The typical pattern of metabolic abnormality seen is dependent on the segment of bowel used for urinary diversion and is typically more severe with continent vs. incontinent urinary diversions, as well as with the length of bowel resected. When ileum and colon are used, the typical pattern of electrolyte abnormality is hyperchloremic metabolic acidosis, with the possibility of hypokalemia. Less commonly, when jejunum is used, this can result in hyponatremic, hyperkalemic, hypochloremic metabolic acidosis. When stomach is used, this can result in a hypochloremic, metabolic alkalosis with the possibility of hypokalemia.¹

d. How is he emptying his urinary diversion?

If he has a continent urinary diversion, then there is a greater contact time between the urine and intestinal mucosa.

e. What is the patient's baseline and current renal function?

Patients with poor renal function are less capable of compensating for an increased acid load

and more likely to exhibit metabolic acidosis.²

f. **What is the patient's baseline liver function?**

Patients with poor liver function can experience sequelae of elevated ammonia levels.

g. **What medications is the patient taking?**

h. **How are the patient's bowel movements?**

Chronic diarrhea and steatorrhea can occur after urinary diversion.

II. Differential Diagnosis

- a. **Metabolic Acidosis:** Most urinary diversions can lead to electrolyte abnormalities. The most common bowel segments used are ileum and colon are generally lead to a hyperchloremic, hypokalemic, metabolic acidosis
- b. **Hypokalemia:** Signs of hypokalemia include fatigue, constipation, weakness, muscle spasms
- c. **Renal Failure:** Following urinary diversion, patients have multiple sources of developing renal failure including age, utero-enteric anastomosis stricture, recurrent infections, nephrolithiasis, and reabsorption of creatinine through the intestinal epithelium (pseudoazotemia)
- d. **Urinary tract infection:** Common occurrence following urinary diversion
- e. **Hyperammonemic encephalopathy:** In urinary diversions, ammonia is re-absorbed through the bowel wall. Patients with normal liver function can typically deal with the increased ammonia load, however infections with urea-splitting bacteria, urinary tract obstruction, and poor liver function can lead to hyperammonemic encephalopathy and even coma³
- f. **Chronic Diarrhea:** Following urinary diversion, patients may experience chologenic (bile acid) diarrhea due to loss of bile acids. Normally, the ileum will resorb most conjugated bile acids, however resection of longer segments can produce a malabsorption of bile acids and these enter the colon with resultant loss of bile acids, water, and sodium.⁴ Depletion of bile acids can also result in malabsorption of fatty acids and the development of steatorrhea
- g. **Disease recurrence:** Metastatic disease can produce the constitutional symptoms the patient is complaining of

III. Evaluation

a. **Physical Exam – Key Points**

- i. **Vital signs:** Fever, tachycardia, or hypotension can be signs of infection
- ii. **Neurologic Exam:** Peripheral neuropathy can be caused by vitamin B12 deficiency. Mental status changes and altered sensorium should prompt concern for hyperammonemic encephalopathy
- iii. **Musculoskeletal** Muscle spasms can be a sign of hypokalemia
- iv. **Abdomen**
 - 1. Costovertebral tenderness may be an indicator of pyelonephritis or obstructive uropathy causing hydronephrosis
 - 2. Suprapubic discomfort may be an indication of neobladder infection or retention.

Discomfort over the site of an ileal conduit or continent cutaneous pouch may be an indication of 'pouchitis' or retained urine. Although it would be uncommon this far out, abdominal pain could be an indicator of rupture of the urinary reservoir

3. If an ileal conduit, the stoma should be examined for stenosis as this may result in urinary retention/stasis and for para-stomal hernia

b. Laboratory Data

i. Serum electrolytes

1. **Serum creatinine:** will allow for a calculation of glomerular filtration rate and estimation of current renal function. Following urinary diversion, patients have multiple reasons for elevations in creatinine and renal failure is associated with a higher risk of other electrolyte abnormalities and pH imbalance
2. **Serum chloride:** Commonly elevated in ileal or colonic urinary diversions. There are no specific symptoms of hyperchloremia although the causes do have symptoms. This finding should prompt concern for a metabolic acidosis
3. **Serum bicarbonate level:** When venous bicarbonate level is < 21 mmol/L, this is consistent with a metabolic acidosis
4. **Serum calcium:** Depletion of body calcium stores can occur with acidosis
5. **Complete blood count:** Leukocytosis can be an indicator of infection

ii. Arterial Blood Gas: This can be considered if the diagnosis is unclear

1. **pH:** Indicates acid/base balance and will determine if there is adequate respiratory compensation.
2. **Base deficit:** A base deficit/excess of ± 2 mEq/L is considered normal. A base excess indicates metabolic alkalosis, while a base deficit indicates a metabolic acidosis.

iii. Liver function tests: Poor liver function predisposes towards elevated serum ammonia levels.

iv. Serum ammonia: Ammonium dissociates into ammonia and hydrogen. Urinary ammonia is absorbed through the colon or ileal wall resulting in an acidosis. This can be exacerbated in the setting of infection with urea-splitting bacteria.

v. Serum vitamin B12: Levels below 180 ng/L may cause megaloblastic anemia and peripheral neuropathy. Levels of 1250-400 ng/L are considered borderline.

vi. Urine culture: If there are clinical concerns for infection. Urea-splitting bacteria can cause elevated ammonia levels.

c. Radiologic studies:

i. Renal bladder ultrasound: This is useful for determining if there concern for obstruction of the urinary tracts.

ii. Cross-sectional abdominal and pelvic imaging: This is useful for determining if there concern for obstruction of the urinary tracts, concern for rupture of the urinary reservoir, stone formation (in reservoir or within the kidneys or ureters), or recurrence of malignancy.

IV. Management

a. Initial management/problem to solve

- i. **Consider drainage of the urinary diversion:** If the electrolyte abnormality or acid/base imbalance is severe, placing a catheter to drain the urinary diversion will minimize urine-intestinal mucosal contact time.

ii. Treatment of electrolyte or acid/base abnormality

1. Acidosis

- a. The most common pH abnormality seen in ileal and colonic urinary diversions is metabolic acidosis. Correcting the acidosis may cause significant hypokalemia due to the fact that as serum pH rises, potassium will move into the intracellular space
- b. Typical regimens include oral sodium bicarbonate (1-2g TID), sodium citrate (1-3g QID), or potassium citrate. Other options include nicotinic acid (500mg – 2g daily, extended release)⁵, chlorpromazine (25-50mg qid)⁶

2. Vitamin B12 Deficiency

- a. Acute vitamin B12 deficiency should be treated with intramuscular injection of cyanocobalamin 1000 µg. Other options include high-dose oral treatment⁷

3. Diarrhea

- a. Treatment of chologenic (bile acid) diarrhea relies on principle of reducing of bile acids in the colon. This is accomplished by cholestyramine, a bile salt binding resin.⁸ Typical dose of cholestyramine is 4gm BID and gradually increased to 8gm BID. Complications of long-term usage of bile acid binders include risk of fat-soluble vitamin deficiency. Patients with persistent diarrhea can also benefit from gut mobility inhibitors such as loperamide (4mg-16mg daily). Fluid restriction is not advised due to risk of dehydration. Increased dietary fiber is advised⁹

4. Treatment of stones

- a. The formation of calculi within urinary reservoirs is a well-known complication. Factors contributing to this include urinary stasis, chronic metabolic acidosis, urinary infections (especially with urea splitting organisms), mucus production, stone formation on foreign bodies (i.e staples), and hyperoxaluria. Stones can be treated via open approach or endoscopic techniques with care taken to avoid injury to the sphincter, urethra, and without over distending the urinary diversion

b. Long-term management

- i. Consider operation to convert continent urinary diversion to incontinent
- ii. Ensure adequate drainage of a continent urinary diversion. Patient should empty pouch more frequently if experiencing metabolic abnormalities or recurrent urinary infections

- iii. **Alkali maintenance therapy:** to correct acidosis
- iv. **Vitamin B12 maintenance therapy:** If vitamin B12 levels have decreased, oral, intravenous, or intramuscular supplementation is advised. Oral vitamin B12 may be less effective due to malabsorption¹⁰
- v. **Calcium supplementation:** To bind oxalate in the setting of recurrent stone formers and offset the bone loss associated with metabolic acidosis
 - 1. See Core Curriculum section **Medical Stone Disease Management**
 - 2. See Core Curriculum section **Medical Stone Disease Pathology & Evaluation**
- vi. **High-fiber diet:** to slow intestinal transit time
- vii. **Bile-acid binders or gastrointestinal motility inhibitors:** to treat chologenic diarrhea

c. **Potential complications**

- i. **Renal failure:** Urinary diversion is a risk factor for deterioration of renal function for multiple reasons included stenosis, recurrent infections, urolithiasis. The deterioration of renal function is associated with exacerbation of associated electrolyte abnormalities
- ii. **Bone density loss:** Chronic acidosis leads to a decrease in bone mineral density which can lead to osteomalacia and osteoporosis (or rickets in children). There are several proposed mechanisms. Bone carbonate and phosphate acts as a buffer for chronic acidosis, releasing calcium into the circulation.¹¹ Chronic acidosis leads to increased intestinal absorption of sulfate, which inhibits renal reabsorption of calcium,¹² inhibits production of vitamin D, and also activates osteoclasts which then promote further bone resorption¹³
- iii. **Growth retardation:** This may be a concern in children with intestinal urinary diversion¹⁴
- iv. **Vitamin B12 deficiency:** The only source of vitamin B12 (cobalamin) in humans is dietary. Parietal cells in the stomach secrete intrinsic factor, which binds to dietary vitamin B12. This vitamin B12-intrinsic factor complex is absorbed in the ileum.¹⁵ Even in the setting of severe malabsorption of vitamin B12, there are typically large stores of vitamin B12 in the liver which prevent symptoms of vitamin B12 deficiency for years. Most cases of vitamin B12 deficiency are asymptomatic¹⁶; however, symptoms include megaloblastic macrocytic anemia and funicular myelosis (degeneration of the spinal cord white matter). Serum vitamin B12 levels should be checked annually following urinary diversion.¹⁷ Risk of vitamin B12 deficiency are higher with longer ileal resections (as would be used for continent urinary diversions),¹⁸ radiotherapy¹⁹, age²⁰, and use of proton pump inhibitors²¹
- v. **Fat malabsorption**
- vi. **Chronic diarrhea**

Table 1. Common Metabolic Abnormalities of Urinary Diversion with Ileum or Colon

Metabolic Disturbance	Notes	Management
Metabolic Acidosis	Decrease in bone mineral density, fatigue, altered temperature regulation, failure to thrive. Rapid shallow breathing, confusion in severe cases.	Correction of hyperchloremic metabolic acidosis with hydration and oral sodium bicarbonate (preferred), sodium citrate, nicotinic acid, chlorpromazine
Hypokalemia	Fatigue, constipation, weakness, muscle spasms	Replace potassium
Renal failure	May be related to anatomic obstruction, severe dehydration, poor emptying, chronic reflux, recurrent infection	Ensure proper emptying of diversion, consider catheterization of neobladder or conversion to non-continent diversion if conservative measures fail.
Diarrhea	Frequent, loose stools – may be associated bile acid malabsorption, loss of ileocecal valve, shortened intestinal transit time	High fiber diet, Consider bile salt binding resin such as cholestyramine or intestinal mobility inhibitors such as loperamid, Consider check levels of fat soluble vitamins (A, D, E, K).
Vitamin B12 deficiency	megaloblastic macrocytic anemia, neuropathy	Check annually, vitamin B12 supplementation intramuscularly or high-dose oral treatment

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Calcium oxalate stones	Nephrolithiasis, Infections, urinary tract obstruction	Calcium supplementation to bind oxalate in recurrent stone formers
Hyperammonemic encephalopathy	Mental disturbances, confusion, lethargy, vomiting, coma	Treat for possible urea-splitting bacteria, place catheter to minimize reabsorption of ammonia through bowel wall

Key Takeaways

- Urinary diversion can lead to metabolic abnormalities. Ileum or colon is mostly commonly used for urinary diversion and this can lead to hyperchloremic, hypokalemic metabolic acidosis. These can be exacerbated by continent diversion or poor renal function.
- Common complications of urinary diversion include metabolic acidosis, hypokalemia, diarrhea, vitamin B12 deficiency, calcium oxalate stones, and metabolic encephalopathy.
- Metabolic acidosis is typically treated with sodium bicarbonate (1-2g TID).

Extra Resources

AUA Update Series: Fluid, Electrolyte and Acid-Base Abnormalities in Urological Practice.²²

Videos

Metabolic Acidosis

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