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Update on Oxalate Crystal Disease

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Abstract

Oxalate arthropathy is a rare cause of arthritis characterized by deposition of calcium oxalate crystals within synovial fluid. This condition typically occurs in patients with underlying primary or secondary hyperoxaluria. Primary hyperoxaluria constitutes a group of genetic disorders resulting in endogenous overproduction of oxalate, whereas secondary hyperoxaluria results from gastrointestinal disorders associated with fat malabsorption and increased absorption of dietary oxalate. In both conditions oxalate crystals can deposit in the kidney leading to renal failure. Since oxalate is primarily renally eliminated, it accumulates throughout the body in renal failure, a state termed oxalosis. Affected organs can include bones, joints, heart, eyes and skin. Since patients can present with renal failure and oxalosis before the underlying diagnosis of hyperoxaluria has been made, it is important to consider hyperoxaluria in patients who present with unexplained soft tissue crystal deposition. The best treatment of oxalosis is prevention. If patients present with advanced disease, treatment of oxalate arthritis consists of symptom management and control of the underlying disease process.

Keywords

Oxalate crystal disease; Calcium oxalate; Crystalline arthropathy; Enteric hyperoxaluria; Oxalosis; Primary hyperoxaluria; Secondary hyperoxaluria; Diagnosis; Treatment

Introduction

Oxalate arthritis is an uncommon cause of arthropathy, typically seen in patients with hyperoxaluria. Oxalate ($C_2O_4^{2-}$) is an organic compound that can be generated endogenously via metabolism, or incorporated exogenously via the diet. Endogenous overproduction occurs in genetic disorders referred to as the primary hyperoxalurias (PH). A variety of gastrointestinal diseases associated with fat malabsorption result in secondary hyperabsorption of oxalate from the gut. Occasionally, oral intake of foods very high in oxalate or intake of precursors of oxalate may result in a substantial oxalate load. Regardless

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of its source, oxalate cannot be metabolized and must be excreted in the urine. Over time, excessive urinary oxalate can damage the kidneys leading to reduced renal excretion. Once the glomerular filtration rate declines to less than 30–40 ml/min/1.73m^2, renal excretion cannot fully eliminate the oxalate load and plasma levels increase rapidly [1]. When the plasma calcium oxalate supersaturation level exceeds the point of spontaneous crystallization, calcium oxalate begins to deposit throughout the body, a condition called oxalosis [1].

In patients with oxalosis, calcium oxalate crystals may deposit within the synovial space causing arthritis. Oxalate arthritis is often difficult to distinguish from other causes of crystalline arthritis, and identification of calcium oxalate crystals within the synovial fluid is required for diagnosis. Importantly, patients can present with renal failure and oxalosis before a diagnosis of hyperoxaluria has been made. Therefore, it is important to consider hyperoxaluria in patients who present with unexplained soft tissue crystal deposition, including crystalline arthritis. The purpose of this article is to review the pathophysiology, manifestations and treatment of oxalate disorders, with a focus on oxalate arthritis.

Primary Hyperoxaluria

The primary hyperoxalurias are a group of rare autosomal recessive, inherited diseases with an estimated prevalence of less than 3 in one million and an incidence of 0.15×10^6/year [2]. Three types of PH have been characterized (PH1, PH2, PH3). In all three types, glyoxylate is aberrantly metabolized into oxalate. A remaining subgroup of patients exists that appear to have a genetic cause of hyperoxaluria that cannot be classified into one of the 3 known types.

PH1 is the most common form of PH and accounts for 70–80% of all cases [1]. It is caused by mutations in the *AGXT* gene that encodes the liver-specific peroxisomal enzyme alanine/glyoxylate aminotransferase (AGT). The AGT protein is responsible for converting glyoxylate into glycine within liver peroxisomes. Over 100 disease-causing mutations in *AGXT* have been reported [1]. PH1 is the most severe form of the disease, and typically manifests in childhood with recurrent kidney stones and nephrocalcinosis. ESRD often develops by age 40–50 years but can occur at any age, including infancy [3].

Primary hyperoxaluria type 2 (PH2) is less common than PH1 and accounts for approximately 10% of cases. It is caused by mutations in the *GRHPR* gene leading to dysfunction of the enzyme glyoxylate/hydroxypyruvate reductase (GR/HPR), another enzyme that metabolizes glyoxalate. In the setting of decreased enzyme activity, glyoxylate is aberrantly converted into oxalate. Unlike AGT, GR/HPR is not limited to the liver and is expressed throughout the body. Patients with PH2 tend to have lower urinary oxalate levels and better renal outcomes than patients with PH1 [4].

The enzyme pathway involved in PH3 has been elucidated only recently. PH3 is caused by mutations in the *HOGA1* gene that reduce function of the mitochondrial enzyme 4-hydroxy-2-oxoglutarate aldolase (HOGA1) [5]. It is known that the HOGA1 protein is involved in hydroxyproline metabolism, but exactly how these mutations result in hyperoxaluria is not completely clear. Altered conversion of hydroxyproline to glyoxylate that in turn leads to overproduction of oxalate has been suggested [6, 7]. Patients with PH3 appear to be less likely to develop end-stage renal disease than patients with the other two types of PH [3].

Secondary hyperoxaluria

Secondary hyperoxaluria results from increased intestinal absorption of dietary oxalate, also referred to as enteric hyperoxaluria. Foods rich in oxalate include spinach, rhubarb, sweet potatoes and peanuts. Normally, oxalate within food is complexed with calcium rendering it difficult to absorb. In states of fat malabsorption, however, free fats in the colonic lumen bind calcium (saponification), thereby increasing the amount of free oxalate available for absorption [8–10]. Free fats and possibly bile acids may also increase colonic oxalate permeability [11]. In patients with fat malabsorption and an intact colon, oxalate absorption can increase dramatically from the normal level of 5–10% to over 30% [12]. Enteric hyperoxaluria is associated with a diverse number of conditions that cause fat malabsorption, including inflammatory bowel disease [13], celiac disease [14], short bowel syndrome, chronic pancreatitis [15], biliary cirrhosis [16] and bariatric surgery [10, 17, 18]. Forms of malabsorptive bariatric surgery including Roux-en-Y gastric bypass and jejunoileal bypass are associated with enteric hyperoxaluria [19], but not restrictive procedures such as gastric banding [20]. Rates of hyperoxaluria following malabsorptive gastric bypass procedures are estimated to be 20–29% [21, 22]. The hyperoxaluria can be severe and can result in kidney failure. In selected older case reports, oxalate nephropathy stabilized or improved after reversal of jejunoileal bypass surgery [23, 24]. Oxalate hyperabsorption can also result from medications such as orlistat that interfere with fat absorption from the gastrointestinal tract [25]. Although cases of hyperoxaluria associated with this medication are typically milder, acute kidney injury associated with calcium oxalate crystal deposition has been described [26]

In all cases of enteric hyperoxaluria, an intact colon is necessary for enteric hyperoxaluria to develop [12]. Colonic oxalate absorption is thought to be largely passive and paracellular [27]. Recently, however, it has been demonstrated that the apical SLC26A6 anion transporter can actively secrete oxalate, and that *SLC26A6* knockout animals become hyperoxaluric. This colonic secretory mechanism may be under hormonal influences [28, 29], although methods to manipulate it for therapeutic effect have not yet been discovered.

Ethylene glycol is hepatically-metabolized to oxalate, hence acute kidney injury is a well-known complication of ethylene glycol poisoning [30]. If cases are diagnosed early enough, fomeprazole can be administered to inhibit the conversion of ethylene glycol to oxalate by alcohol dehydrogenase [31]. Rarely, ingestion of large amounts of oxalate-rich foods such as rhubarb, star fruit or sorrel soup have been associated with acute kidney injury due to calcium oxalate crystal deposition [32, 33].

Cellular reactions to oxalate crystals

Cell culture experiments suggest that once adherent to cells, calcium oxalate crystals set into motion a cascade of responses that include crystal internalization [34, 35], changes in gene expression [36], cytoskeletal reorganization [34], and possibly cell proliferation [37]. Exposure of renal cells to calcium oxalate crystals stimulates expression of early response genes associated with mitogenesis and enhances expression of regulators of the extracellular matrix composition and specific growth factors which augment kidney fibroblast proliferation [37]. In addition, exposure of cultured renal cells to calcium oxalate crystals stimulates expression of the gene encoding osteopontin and release of this protein into the medium [38]. Importantly, many responses of cultured renal cells to calcium oxalate crystals replicate those initially reported in hyperoxaluric rats, including rapid adhesion of crystals to cells followed by internalization [34, 39–41]. Observations in renal tissue from hyperoxaluric subjects suggest similar processes occur in human kidneys *in vivo* [42].

Signs and symptoms

Patients with oxalate disorders display a variety of signs and symptoms. Oxalate is primarily eliminated via renal glomerular filtration. Given their direct role in oxalate excretion, the kidneys often sustain the most severe damage in states of oxalate excess. When increased quantities of oxalate are present in tubular fluid the anion can form insoluble complexes with calcium. Typically the supersaturation for calcium oxalate is not reached until the distal nephron, but in hyperoxaluric states crystallization can occur even in the proximal tubule. The resulting calcium oxalate crystals can damage tubular cells and also deposit within the renal parenchyma, pathologically referred to as nephrocalcinosis. Local inflammation and fibrosis can be the end result. Calcium oxalate crystals can also contribute to kidney stone formation and tubular obstruction. Patients with kidney stones frequently present with flank pain, hematuria or dysuria.

If renal function declines in patients with disorders of oxalate metabolism, calcium oxalate crystal deposition can occur within a variety of tissues (Table 1). Oxalate arthropathy, a rare cause of arthritis, is one manifestation of the resulting oxalosis [43]. Oxalate arthritis can be clinically indistinguishable from other crystal-induced arthropathies involving calcium phosphate, hydroxyapatite, calcium pyrophosphate dihydrate (CPPD) and monosodium urate. Oxalate arthritis may result from deposition of calcium oxalate crystals within bones, tendons, cartilage, and synovium. From these sites the crystals are thought to gain entry into the synovial fluid where they invoke an inflammatory response [44] causing joint effusions and arthralgias [45, 46]. Alternatively, supersaturation of calcium oxalate within the synovial fluid itself may lead to local crystal formation, especially when fluid is removed during dialysis, a phenomenon referred to as articular hyperconcentration [47]. In general, oxalate arthritis is symmetric and polyarticular. It can be acute or chronic. Typical joint involvement includes the proximal interphalangeal and metacarpophalangeal joints, knees, elbows and ankles [48]. X-rays of the joints in hyperoxaluria may reveal calcification around the joints and within tendon sheaths and soft tissue [45]. Chondrocalcinosis of the metacarpophalangeal and metatarsophalangeal joints may be seen [48]. Spinal stenosis caused by oxalate crystal deposition within the ligamentum flavum has also been reported. Oxalate deposition can also result in synovitis, tenosynovitis and bursitis [48].

Bone involvement in hyperoxaluria can manifest as diffuse bone pain. X-ray imaging reveals fractures, pseudofractures [45], sclerosis, cystic bone changes, subperiosteal resorption adjacent to oxalate deposits [48, 49], dense metaphyseal bands [50] and increased bone density [51] (see Figure 1). Calcium oxalate has a tendency to crystallize in previously damaged joints, such as distal and proximal interphalangeal joints involved in osteoarthritis, thus presenting as soft tissue calcification about the degenerated joint [47]. Inflammation may mimic the findings of erosive osteoarthritis or an atypical diuretic-related gout. High-resolution computed tomography (CT) may reveal advanced skeletal age, decreased bone mineral density, and altered bone microarchitecture [49]. Bone biopsy demonstrates oxalate crystals with surrounding granulomas containing histiocytes and macrophages with associated fibrosis [52]. Patients with oxalosis and bone marrow involvement often develop anemia that is resistant to erythropoietin-stimulating agents [53, 54].

Patients with cardiac involvement may present with arrhythmias due to crystal deposition within the conduction system. They may also present with palpitations, syncope, dyspnea and rarely chest pain [55]. Cardiac imaging may reveal valvular abnormalities [56] and evidence of an infiltrative process with impaired right and left ejection fraction [55]. Skin manifestations in hyperoxaluria vary depending on whether the patient has primary or secondary hyperoxaluria. PH has been reported to cause cutaneous disease through deposition of oxalate within the vessels resulting in gangrene, livido reticularis and

acrocyanosis. Secondary hyperoxaluria typically causes a milder cutaneous disease via extravascular oxalate deposition. Papules and nodules on the face and digits can be observed [57]. Oxalate crystal deposition within the retina is often observed and can cause visual disturbances in both primary and secondary hyperoxaluria [58–60]. Deposition within nerves and muscles can cause painful myopathies and progressive polyradiculoneuropathy. Biopsies of peripheral nerves reveal crystal deposition within axons and epineural blood vessels with associated axon loss and demyelination [61–64]. Oxalosis may also involve teeth [65–67] and blood vessels of the heart and liver [68, 69].

Diagnosis

The diagnosis of oxalate arthritis requires arthrocentesis and synovial fluid analysis [45]. Examination of synovial fluid reveals clear or cloudy fluid with a low cell count and calcium oxalate crystals [48]. Calcium oxalate crystals occur in two forms: monohydrate and dihydrate. Calcium oxalate monohydrate crystals appear as irregular squares or rods which may be confused with calcium pyrophosphate (CPP) crystals [45]. In contrast, calcium oxalate dihydrate crystals have a classic envelope-like shape and are more common [47]. Both types of oxalate crystals exhibit variable positive birefringence under polarized light, similar to CPP. The crystals also stain positive with alizarin red, indicating the presence of calcium [45]. Crystals may be intracellular or extracellular [47]. Radiographic imaging is unable to distinguish oxalate arthritis from other forms of arthritis such as CPP deposition (CPPD) [45]. Both may show chondrocalcinosis of the metacarpophalangeal or metatarsophalangeal joints on x-ray or CT imaging [45]. Occasionally, patients on chronic hemodialysis may have calcium oxalate crystals identified within synovial fluid without clinical or radiographic evidence of arthritis [47]. These patients do not have oxalate arthritis.

Any patient with systemic oxalosis, including oxalate arthritis, should be evaluated for an underlying oxalate disorder. If renal function is preserved (GFR> 40 ml/min/1.73m^2) hyperoxaluria will be present, defined as a urinary oxalate level >0.5 mmol/1.73m^2 per 24 hr. Patients with PH and intact renal function have only mild increases in plasma oxalate levels. If renal function declines below 40 ml/min/1.73 m^2, however, plasma oxalate levels rise, urinary oxalate levels fall, and diagnosis can become more difficult [1]. In patients with chronic kidney disease (GFR <30ml/min/1.732m^2), plasma oxalate values up to 30 μM/L can be normal. However, higher values strongly suggest the diagnosis of PH [70].

In patients on dialysis the diagnosis of PH can be particularly challenging. Marked increases in plasma oxalate and/or increased plasma glycolate (PH1) or glycerate (PH2) can be helpful. Ultimately, the diagnosis of PH can be confirmed by genetic testing performed at specialized centers for common mutations involving *AGXT*, *GRHPR* and *HOGA1*. In cases where a high degree of clinical suspicion for PH exists, but genetic testing is unrevealing, a liver biopsy can be obtained to check AGT and GR/HPR enzymatic activities.

Secondary causes of hyperoxaluria should be considered in patients with gastrointestinal conditions associated with fat malabsorption. Examples include small intestinal resection, bariatric surgical procedures for obesity , chronic pancreatitis, and inflammatory bowel disease [71, 72–74]. Fecal fat determination remains the gold standard to document the presence of fat malabsorption.

Treatment

Symptomatic treatment of oxalate arthritis includes NSAIDs, colchicine and steroids. The use of these agents may be limited by side effects. NSAIDs should be avoided in patients with chronic kidney disease, including recipients of kidney transplants, because they may contribute to worsening renal function and hypertension. Side effects of colchicine include

cytopenias, gastrointestinal toxicity, neuropathy and myopathy. Colchicine should be used sparingly or completely avoided in patients with chronic kidney disease. In addition, colchicine may interact with immunosuppressants such as cyclosporine or tacrolimus. Therefore intraarticular or oral steroids may be the safest treatment for patients with oxalate arthritis [45]. Calcium oxalate crystals induce inflammation via the NLRP3-IL-1β pathway [75]. In the future, IL-1β inhibitor therapies may play a therapeutic role in calcium oxalate disease.

The best treatment for oxalosis is prevention. Therefore, therapy for oxalate arthritis should focus on the underlying disease process. In general, patients with these rare disorders will benefit from consultation with a specialist familiar with these disease processes. If renal function is preserved, a guiding principle is that patients with either primary or secondary hyperoxaluria benefit from efforts to decrease oxalate precipitation in body tissues or in the urine. Hyperoxaluria can be addressed with hydration and crystalline inhibitors (Table 2). Patients with hyperoxaluria should drink at least 3 L of fluid per day in order to reduce the incidence of oxalate supersaturation in the urine. In addition, use of crystallization inhibitors such as oral phosphorus and citrate salts should be considered.

Additional treatments for oxalate disorders depend on whether the underlying cause is primary or secondary. Patents with enteric hyperoxaluria benefit from adhering to a low-fat and low-oxalate diet. Patients with fat malabsorption are often prescribed calcium supplements with meals to promote binding of dietary oxalate and decreased intestinal absorption [19]. Patients with fat malabsorption secondary to pancreatic insufficiency should benefit from pancreatic enzyme supplementation [76]. Recent studies suggest a promising role of the phosphate binder lanthanum carbonate in cases of secondary hyperoxaluria [77]. Lanthanum carbonate has been shown to inhibit intestinal oxalate absorption and prevent nephrocalcinosis in animal models [77]. Another commonly used phosphate binder, sevelamer hydrochloride, is less effective at binding oxalate [78]. Studies involving the use of probiotics in patients with enteric hyperoxaluria have demonstrated mixed results [79, 80].

In contrast to patients with secondary hyperoxaluria, patients with PH benefit from targeted strategies to reduce endogenous oxalate production. PH1 patients should receive a trial of pyridoxine, or vitamin B6, supplementation. Pyridoxine serves as a cofactor for the deficient enzyme AGT. Pharmacologic doses of pyridoxine (5–9 mg/kg) have been shown to decrease urinary oxalate in approximately 30% of patients with PH1 [81, 82]. Patients with a specific genetic mutation [c.508G>A (G170R)] that results in mis-targeting of AGT to mitochondria instead of peroxisomes are most likely to respond to pyridoxine therapy [83, 84].

In patients with PH in whom the glomerular filtration rate falls to < 30 ml/min/m^2, renal excretion is unable to keep pace with daily oxalate production. Dialysis is needed to augment oxalate removal and limit the development of progressive oxalosis [85]. The use of high flux dialyzers and daily dialysis is often required to remove as much oxalate as possible. Peritoneal dialysis alone is usually insufficient [85]. The use of continuous hemodialysis may be warranted in cases of severe systemic oxalosis [3, 86, 87]. In all cases, careful monitoring of plasma oxalate levels and dialysis oxalate removal is crucial.

Given that oxalate removal with dialysis is incomplete and consequences of progressive systemic oxalosis are severe, the preferred treatment for patients with PH is transplantation. Ideally, kidney transplantation should be performed prior to the initiation of dialysis, in order minimize oxalosis. Patients with PH can receive either a kidney transplant alone, or a combined liver/kidney transplant. PH1 patients with complete pyridoxine responsiveness may do well with kidney transplantation alone [3, 88, 89] with strict maintenance of pyridoxine therapy posttransplant. The remaining patients with PH1 should receive combined liver/

kidney transplantation [90]. Liver transplantation successfully restores the hepatic enzyme deficiency and protects the renal allograft from the development of recurrent oxalate nephropathy. Following combined liver/kidney transplantation, renal allograft survival at three years has steadily improved over the past decade to 84% [43, 91, 92]. Even after a successful liver/kidney transplant, urinary oxalate excretion can remain elevated for months to years depending on the amount of oxalate that accumulated in the tissues prior to transplant. In contrast to PH1, the defective enzyme in PH2 is not liver-specific. To date there has been no confirmation that liver transplantation fully corrects GR/HPR enzyme deficiency in patients with PH2. In addition, the renal effects of PH2 are less severe than PH1. For these reasons, most PH2 patients receive a kidney transplant only [91].

New treatment strategies for hyperoxaluria are being evaluated. One active area of investigation focuses on the use of oral *Oxalobacter formigenes*, a Gram-negative, anaerobic intestinal bacteria that is often present in the human colon and is capable of oxalate degradation. Animal studies have suggested that endogenously generated oxalate can be eliminated in the intestinal tract via administration of this organism [27, 28, 93–95]. In humans, repeated antibiotic use can eliminate the bacteria from the intestine, and limited evidence suggests colonization correlates with urinary oxalate excretion [96]. Potentially, oral administration of *O. formigenes* could be a therapy for hyperoxaluria, particularly in patients whose endogenous microbiome lacksthe organism. However, animal studies [97] and small pilot studies in humans have shown mixed results [98, 99]. Gene transfer therapy [100] and the use of molecular chaperones to stabilize defective enzymes in PH are currently under investigation [101, 102]

Conclusions

Oxalate arthritis is a rare cause of arthritis which is clinically indistinguishable from other crystalline arthropathies. Oxalate arthritis must be diagnosed by synovial fluid analysis and demonstration of oxalate crystals within the joint fluid. Patients with oxalate arthritis should be evaluated for underlying oxalate disorders, given that this type of arthropathy is only seen in the setting of systemic oxalosis. In the presence of preserved kidney function, a 24-hour urine collection to detect hyperoxaluria is most helpful. Once GFR falls below 40 ml/min/1.73m^2, however, the diagnosis of PH becomes more difficult and genetic testing may be necessary. Secondary hyperoxaluria should be considered in patients with clinical conditions that can cause fat malabsorption. Patients with either primary or secondary hyperoxaluria are prescribed a large fluid intake and inhibitors of urinary crystallization. Targeted therapies for PH include pyridoxine, kidney transplantation, and in select cases (PH1) combined liver/kidney transplantation. Specific treatment strategies for secondary hyperoxaluria include a low-oxalate diet and calcium supplementation with meals. Studies investigating the role of novel therapeutic agents in the treatment of hyperoxaluria are ongoing.

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References

1. Hoppe B, Beck BB, Milliner DS. The primary hyperoxalurias. Kidney international. 2009 Jun; 75(12):1264–1271. [PubMed: 19225556]

2. van Woerden CS, Groothoff JW, Wanders RJ, Davin JC, Wijburg FA. Primary hyperoxaluria type 1 in The Netherlands: prevalence and outcome. Nephrol Dial Transplant. 2003 Feb; 18(2):273–279. [PubMed: 12543880]

3. Hoppe B. An update on primary hyperoxaluria. Nat Rev Nephrol. 2012 Aug; 8(8):467–475. [PubMed: 22688746] An excellent review of primary hyperoxaluria.

4. Lieske JC, Monico CG, Holmes WS, Bergstralh EJ, Slezak JM, Rohlinger AL, et al. International registry for primary hyperoxaluria. Am J Nephrol. 2005 May-Jun;25(3):290–296. [PubMed: 15961949]

5. Belostotsky R, Seboun E, Idelson GH, Milliner DS, Becker-Cohen R, Rinat C, et al. Mutations in DHDPSL are responsible for primary hyperoxaluria type III. Am J Hum Genet. 2010 Sep 10; 87(3): 392–399. [PubMed: 20797690] Initial description of the genetic mutations responsible for primary hyperoxaluria type 3.

6. Monico CG, Rossetti S, Belostotsky R, Cogal AG, Herges RM, Seide BM, et al. Primary hyperoxaluria type III gene HOGA1 (formerly DHDPSL) as a possible risk factor for idiopathic calcium oxalate urolithiasis. Clin J Am Soc Nephrol. 2011 Sep; 6(9):2289–2295. [PubMed: 21896830] A study suggesting that genetic mutations involved in primary hyperoxaluria type 3 may also be a risk factor for idiopathic kidney stones.

7. Riedel TJ, Knight J, Murray MS, Milliner DS, Holmes RP, Lowther WT. 4-Hydroxy-2-oxoglutarate aldolase inactivity in primary hyperoxaluria type 3 and glyoxylate reductase inhibition. Biochim Biophys Acta. 2012 Oct; 1822(10):1544–1552. [PubMed: 22771891]

8. Cornelis T, Bammens B, Lerut E, Cosyn L, Goovaerts G, Westhovens R, et al. AA amyloidosis due to chronic oxalate arthritis and vasculitis in a patient with secondary oxalosis after jejunoileal bypass surgery. Nephrol Dial Transplant. 2008 Oct; 23(10):3362–3364. [PubMed: 18632590]

9. Dobbins JW, Binder HJ. Importance of the colon in enteric hyperoxaluria. N Engl J Med. 1977 Feb 10; 296(6):298–301. [PubMed: 831127]

10. Kumar R, Lieske JC, Collazo-Clavell ML, Sarr MG, Olson ER, Vrtiska TJ, et al. Fat malabsorption and increased intestinal oxalate absorption are common after Roux-en-Y gastric bypass surgery. Surgery. 2011 May; 149(5):654–661. [PubMed: 21295813] A study decribing the incidence of increased oxalate absorption following bariatric surgery.

11. Dobbins JW, Binder HJ. Effect of bile salts and fatty acids on the colonic absorption of oxalate. Gastroenterology. 1976 Jun; 70(6):1096–1100. [PubMed: 1269869]

12. Hylander E, Jarnum S, Jensen HJ, Thale M. Enteric hyperoxaluria: dependence on small intestinal resection, colectomy, and steatorrhoea in chronic inflammatory bowel disease. Scand J Gastroenterol. 1978; 13(5):577–588. [PubMed: 705253]

13. Hueppelshaeuser R, von Unruh GE, Habbig S, Beck BB, Buderus S, Hesse A, et al. Enteric hyperoxaluria, recurrent urolithiasis, and systemic oxalosis in patients with Crohn's disease. Pediatr Nephrol. 2012 Jul; 27(7):1103–1109. [PubMed: 22366809]

14. Ciacci C, Spagnuolo G, Tortora R, Bucci C, Franzese D, Zingone F, et al. Urinary stone disease in adults with celiac disease: prevalence, incidence and urinary determinants. J Urol. 2008 Sep; 180(3):974–979. [PubMed: 18639267]

15. Cartery C, Faguer S, Karras A, Cointault O, Buscail L, Modesto A, et al. Oxalate nephropathy associated with chronic pancreatitis. Clin J Am Soc Nephrol. 2011 Aug; 6(8):1895–1902. [PubMed: 21737848]

16. Rahman N, Hitchcock R. Case report of paediatric oxalate urolithiasis and a review of enteric hyperoxaluria. J Pediatr Urol. 2010 Apr; 6(2):112–116. [PubMed: 19664961] A review of enteric hyperoxaluria in children.

17. Nasr SH, D'Agati VD, Said SM, Stokes MB, Largoza MV, Radhakrishnan J, et al. Oxalate nephropathy complicating Roux-en-Y Gastric Bypass: an underrecognized cause of irreversible renal failure. Clin J Am Soc Nephrol. 2008 Nov; 3(6):1676–1683. [PubMed: 18701613]

18. Sinha MK, Collazo-Clavell ML, Rule A, Milliner DS, Nelson W, Sarr MG, et al. Hyperoxaluric nephrolithiasis is a complication of Roux-en-Y gastric bypass surgery. Kidney Int. 2007 Jul; 72(1): 100–107. [PubMed: 17377509]

19. Pang R, Linnes MP, O'Connor HM, Li X, Bergstralh E, Lieske JC. Controlled metabolic diet reduces calcium oxalate supersaturation but not oxalate excretion after bariatric surgery. Urology.

2012 Aug; 80(2):250–254. [PubMed: 22554593] A study outlining the limitations of a low-oxalate diet alone following bariatric surgery.

20. Penniston KL, Kaplon DM, Gould JC, Nakada SY. Gastric band placement for obesity is not associated with increased urinary risk of urolithiasis compared to bypass. J Urol. 2009 Nov; 182(5):2340–2346. [PubMed: 19762051]
21. Duffey BG, Pedro RN, Makhlouf A, Kriedberg C, Stessman M, Hinck B, et al. Roux-en-Y gastric bypass is associated with early increased risk factors for development of calcium oxalate nephrolithiasis. J Am Coll Surg. 2008 Jun; 206(3):1145–1153. [PubMed: 18501812]
22. Froeder L, Arasaki CH, Malheiros CA, Baxmann AC, Heilberg IP. Response to dietary oxalate after bariatric surgery. Clin J Am Soc Nephrol. 2012 Dec; 7(12):2033–2040. [PubMed: 23024163]
23. Ehlers SM, Posalaky Z, Strate RG, Quattlebaum FW. Acute reversible renal failure following jejunoileal bypass for morbid obesity: a clinical and pathological (EM) study of a case. Surgery. 1977; 82:629–634. [PubMed: 918850]
24. Verani R, Nasir M, Foley R. Granulomatous interstitial nephritis after a jejunoileal bypass: an ultrastructural and histochemical study. American journal of nephrology. 1989; 9(1):51–55. [PubMed: 2719063]
25. Sarica K, Akarsu E, Erturhan S, Yagci F, Aktaran S, Altay B. Evaluation of urinary oxalate levels in patients receiving gastrointestinal lipase inhibitor. Obesity (Silver Spring). 2008 Jul; 16(7): 1579–1584. [PubMed: 18451780]
26. Karamadoukis L, Shivashankar GH, Ludeman L, Williams AJ. An unusual complication of treatment with orlistat. Clinical nephrology. 2009 Apr; 71(4):430–432. [PubMed: 19356376]
27. Hatch M, Freel RW. Intestinal transport of an obdurate anion: oxalate. Urol Res. 2005 Feb; 33(1): 1–16. [PubMed: 15565438]
28. Hatch M, Cornelius J, Allison M, Sidhu H, Peck A, Freel RW. Oxalobacter sp. reduces urinary oxalate excretion by promoting enteric oxalate secretion. Kidney Int. 2006 Feb; 69(4):691–698. [PubMed: 16518326]
29. Hatch M, Freel RW, Vaziri ND. Regulatory aspects of oxalate secretion in enteric oxalate elimination. J Am Soc Nephrol. 1999 Nov; 10(Suppl 14):S324–S328. [PubMed: 10541256]
30. Jacobsen D, Hewlett TP, Webb R, Brown ST, Ordinario AT, McMartin KE. Ethylene glycol intoxication: evaluation of kinetics and crystalluria. The American journal of medicine. 1988 Jan; 84(1):145–152. [PubMed: 3337119]
31. Brent J, McMartin K, Phillips S, Burkhart KK, Donovan JW, Wells M, et al. Fomepizole for the treatment of ethylene glycol poisoning. Methylpyrazole for Toxic Alcohols Study Group. The New England journal of medicine. 1999 Mar 18; 340(11):832–838. [PubMed: 10080845]
32. Sanz P, Reig R. Clinical and pathological findings in fatal plant oxalosis. A review. The American journal of forensic medicine and pathology. 1992 Dec; 13(4):342–345. [PubMed: 1288268]
33. Barceloux DG. Rhubarb and oxalosis (Rheum species). Dis Mon. 2009 Jun; 55(6):403–411. [PubMed: 19446684]
34. Lieske JC, Swift HS, Martin T, Patterson B, Toback FG. Renal epithelial cells rapidly bind and internalize calcium oxalate monohydrate crystals. ProcNatlAcadSci, USA. 1994; 91:6987–6991.
35. Lieske JC, Toback FG. Regulation of renal epithelial cell endocytosis of calcium oxalate monohydrate crystals. AmJPhysiol. 1993; 264:F800–F807.
36. Hammes MS, Lieske JC, Pawar S, Spargo BH, Toback FG. Calcium oxalate monohydrate crystals stimulate gene expression in renal epithelial cells. Kidney Int. 1995; 48:501–509. [PubMed: 7564119]
37. Lieske JC, Walsh-Reitz MM, Toback FG. Calcium oxalate monohydrate crystals are endocytosed by renal epithelial cells and induce proliferation. AmJPhysiol. 1992; 262:F622–F630.
38. Lieske JC, Deganello S, Toback FG. Cell-crystal interactions and kidney stone formation. Nephron. 1999; 81(S1):S8–S17.
39. Khan SR, Finlayson B, Hackett RL. Scanning electron microscopy of calcium oxalate crystal formation in experimental nephrolithiasis. LabInvest. 1979; 41:504–510.
40. Dykstra MJ, Hackett RL. Ultrastructural events in early calcium oxalate crystal formation in rats. Kidney Int. 1979; 15:640–650. [PubMed: 459245]

41. Khan SR, Finlayson B, Hackett RL. Histologic study of the early events in oxalate induced intranephronic calculosis. InvestUrol. 1979; 17:199–202.
42. Lieske JC, Spargo BH, Toback FG. Endocytosis of calcium oxalate crystals and proliferation of renal tubular epithelial cells in a patient with type 1 primary hyperoxaluria. The Journal of urology. 1992 Nov; 148(5):1517–1519. [PubMed: 1433562]
43. Cochat P, Hulton SA, Acquaviva C, Danpure CJ, Daudon M, De Marchi M, et al. Primary hyperoxaluria Type 1: indications for screening and guidance for diagnosis and treatment. Nephrol Dial Transplant. 2012 May; 27(5):1729–1736. [PubMed: 22547750] *A review of methods used to diagnose primary hyperoxaluria*
44. Kohn NN, Hughes RE, Mc CD Jr. Faires JS. The significance of calcium phosphate crystals in the synovial fluid of arthritic patients: the “pseudogout syndrome”. II. Identification of crystals. Ann Intern Med. 1962 May.56:738–745. [PubMed: 14457846]
45. Sarraf P, Kay J, Reginato AM. Non-crystalline and crystalline rheumatic disorders in chronic kidney disease. Curr Rheumatol Rep. 2008 Jul; 10(3):235–248. [PubMed: 18638433]
46. Verbruggen LA, Bourgain C, Verbeelen D. Late presentation and microcrystalline arthropathy in primary hyperoxaluria. Clin Exp Rheumatol. 1989 Nov-Dec;7(6):631–633. [PubMed: 2612083]
47. Rosenthal A, Ryan LM, McCarty DJ. Arthritis associated with calcium oxalate crystals in an anephric patient treated with peritoneal dialysis. Jama. 1988 Sep 2; 260(9):1280–1282. [PubMed: 3404640]
48. Maldonado I, Prasad V, Reginato AJ. Oxalate crystal deposition disease. Curr Rheumatol Rep. 2002 Jun; 4(3):257–264. [PubMed: 12010612]
49. Bacchetta J, Fargue S, Boutroy S, Basmaison O, Vilayphiou N, Plotton I, et al. Bone metabolism in oxalosis: a single-center study using new imaging techniques and biomarkers. Pediatr Nephrol. 2010 Jun; 25(6):1081–1089. [PubMed: 20213134] A study of bone imaging and FGF23 levels in patients with primary hyperoxaluria.
50. El Hage S, Ghanem I, Baradhi A, Mourani C, Mallat S, Dagher F, et al. Skeletal features of primary hyperoxaluria type 1, revisited. J Child Orthop. 2008 Jun; 2(3):205–210. [PubMed: 19308578]
51. Behnke B, Kemper MJ, Kruse HP, Muller-Wiefel DE. Bone mineral density in children with primary hyperoxaluria type I. Nephrol Dial Transplant. 2001 Nov; 16(11):2236–2239. [PubMed: 11682674]
52. Aydin NE, Usta U. Oxalate deposition in tissues. Nephrol Dial Transplant. 2004 May; 19(5):1323–1324. [PubMed: 15102976]
53. Bakshi NA, Al-Zahrani H. Bone marrow oxalosis. Blood. 2012 Jul 5.120(1):8. [PubMed: 22953330]
54. Tapia G, Navarro JT, Navarro M. Leukoerythroblastic anemia due to oxalosis with extensive bone marrow involvement. Am J Hematol. 2008 Jun; 83(6):515–516. [PubMed: 17636470]
55. Mookadam F, Smith T, Jiamsripong P, Moustafa SE, Monico CG, Lieske JC, et al. Cardiac abnormalities in primary hyperoxaluria. Circ J. 2010 Nov; 74(11):2403–2409. [PubMed: 20921818]
56. Van Driessche L, Dhondt A, De Sutter J. Heart failure with mitral valve regurgitation due to primary hyperoxaluria type 1: case report with review of the literature. Acta Cardiol. 2007 Apr; 62(2):202–206. [PubMed: 17536611]
57. Blackmon JA, Jeffy BG, Malone JC, Knable AL Jr. Oxalosis involving the skin: case report and literature review. Arch Dermatol. 2011 Nov; 147(11):1302–1305. [PubMed: 21768445] A review of how oxalosis affects the skin.
58. Fielder AR, Garner A, Chambers TL. Ophthalmic manifestations of primary oxalosis. Br J Ophthalmol. 1980 Oct; 64(10):782–788. [PubMed: 7426550]
59. Munir WM, Sharma MC, Li T, Dealba F, Goldstein DA. Retinal oxalosis in primary hyperoxaluria type 1. Retina. 2004 Dec; 24(6):974–976. [PubMed: 15580002]
60. Small KW, Letson R, Scheinman J. Ocular findings in primary hyperoxaluria. Arch Ophthalmol. 1990 Jan; 108(1):89–93. [PubMed: 2297338]
61. Bilbao JM, Berry H, Marotta J, Ross RC. Peripheral neuropathy in oxalosis. A case report with electron microscopic observations. Can J Neurol Sci. 1976 Feb; 3(1):63–67. [PubMed: 175908]

62. Galloway G, Giuliani MJ, Burns DK, Lacomis D. Neuropathy associated with hyperoxaluria: improvement after combined renal and liver transplantations. Brain Pathol. 1998 Apr; 8(2):247–251. [PubMed: 9546283]
63. Hall BM, Walsh JC, Horvath JS, Lytton DG. Peripheral neuropathy complicating primary hyperoxaluria. J Neurol Sci. 1976 Oct; 29(2–4):343–349. [PubMed: 185338]
64. Moorhead PJ, Cooper DJ, Timperley WR. Progressive peripheral neuropathy in patient with primary hyperoxaluria. Br Med J. 1975 May 10; 2(5966):312–313. [PubMed: 48397]
65. Mitsimponas KT, Wehrhan T, Falk S, Wehrhan F, Neukam FW, Schlegel KA. Oral findings associated with primary hyperoxaluria type I. J Craniomaxillofac Surg. 2012 Dec; 40(8):e301–e306. [PubMed: 22417769]
66. Panis V, Tosios KI, Gagari E, Griffin TJ, Damoulis PD. Severe periodontitis in a patient with hyperoxaluria and oxalosis: a case report and review of the literature. J Periodontol. 2010 Oct; 81(10):1497–1504. [PubMed: 20528695]
67. Rinksma AJ, Oosterhuis JW, Wolvius EB, van der Wal KG. Oral manifestations of oxalosis: a case report and review of the literature. J Oral Maxillofac Surg. 2008 Sep; 66(9):1953–1956. [PubMed: 18718408]
68. Fishbein GA, Micheletti RG, Currier JS, Singer E, Fishbein MC. Atherosclerotic oxalosis in coronary arteries. Cardiovasc Pathol. 2008 Mar-Apr;17(2):117–123. [PubMed: 18329558]
69. Tanriover B, Mejia A, Foster SV, Mubarak A. Primary hyperoxaluria involving the liver and hepatic artery: images of an aggressive disease. Kidney Int. 2010 Apr.77(7):651. [PubMed: 20224594]
70. Milliner DS, Eickholt JT, Bergstralh E, Wilson DM, Smith LH. Results of long-term treatment with orthophosphate and pyridoxine in patients with primary hyperoxaluria. New Engl J Med. 1994; 331:1553–1558. [PubMed: 7969325]
71. Sinha MK, Collazo-Clavell ML, Rule A, Milliner DS, Nelson W, Sarr MG, et al. Hyperoxaluric nephrolithiasis is a complication of Roux-en-Y gastric bypass surgery. Kidney Int. 2007 Jul; 72(1): 100–107. [PubMed: 17377509]
72. Mandell I, Krauss E, Millan JC. Oxalate-induced acute renal failure in Crohn's Disease. AmJMed. 1980; 69:628–632.
73. Earnest DL, Johnson G, Williams HE, Admirand WH. Hyperoxaluria in patients with ileal resection: an abnormality in dietary oxalate absorption. Gastroenterology. 1974 Jun; 66(6):1114–1122. [PubMed: 4829118]
74. Andersson H, Bosaeus I. Hyperoxaluria in malabsorptive states. Urol Int. 1981; 36(1):1–9. [PubMed: 7020204]
75. Mulay SR, Kulkarni OP, Rupanagudi KV, Migliorini A, Darisipudi MN, Vilaysane A, et al. Calcium oxalate crystals induce renal inflammation by NLRP3-mediated IL-1beta secretion. J Clin Invest. 2013 Jan 2; 123(1):236–246. [PubMed: 23221343] *A study demonstrating how calcium oxalate crystals induce IL-1β secretion*
76. Rankin AC, Walsh SB, Summers SA, Owen MP, Mansell MA. Acute oxalate nephropathy causing late renal transplant dysfunction due to enteric hyperoxaluria. Am J Transplant. 2008 Aug; 8(8): 1755–1758. [PubMed: 18557738]
77. Robijn S, Vervaet BA, Hoppe B, D'Haese PC, Verhulst A. Lanthanum carbonate inhibits intestinal oxalate absorption and prevents nephrocalcinosis after oxalate loading in rats. J Urol. 2012 Dec 7.
78. Lieske JC, Regnier C, Dillon JJ. Use of sevelamer hydrochloride as an oxalate binder. J Urol. 2008 Apr; 179(4):1407–1410. [PubMed: 18289565]
79. Lieske JC, Goldfarb DS, De Simone C, Regnier C. Use of a probiotic to decrease enteric hyperoxaluria. Kidney Int. 2005 Sep; 68(3):1244–1249. [PubMed: 16105057]
80. Lieske JC, Tremaine WJ, De Simone C, O'Connor HM, Li X, Bergstralh EJ, et al. Diet, but not oral probiotics, effectively reduces urinary oxalate excretion and calcium oxalate supersaturation. Kidney Int. 2010 Dec; 78(11):1178–1185. [PubMed: 20736987] A study investigating the role of diet and priobiotics on urinary oxalate excretion in patients with hyperoxaluria.
81. Gibbs DA, Watts RW. The action of pyridoxine in primary hyperoxaluria. Clin Sci. 1970 Feb; 38(2):277–286. [PubMed: 5416155]

82. Watts RW, Veall N, Purkiss P, Mansell MA, Haywood EF. The effect of pyridoxine on oxalate dynamics in three cases of primary hyperoxaluria (with glycollic aciduria). Clin Sci. 1985 Jul; 69(1):87–90. [PubMed: 4064559]
83. Fargue S, Lewin J, Rumsby G, Danpure CJ. Four of the most common mutations in primary hyperoxaluria type 1 unmask the cryptic mitochondrial targeting sequence of alanine:glyoxylate aminotransferase encoded by the polymorphic minor allele. J Biol Chem. 2012 Dec 10. A study showing how specific mutations result in mistargeting of the the peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT) to mitochondria in primary hyperoxaluria
84. Monico CG, Rossetti S, Olson JB, Milliner DS. Pyridoxine effect in type I primary hyperoxaluria is associated with the most common mutant allele. Kidney Int. 2005 May; 67(5):1704–1709. [PubMed: 15840016]
85. Illies F, Bonzel KE, Wingen AM, Latta K, Hoyer PF. Clearance and removal of oxalate in children on intensified dialysis for primary hyperoxaluria type 1. Kidney international. 2006 Nov; 70(9): 1642–1648. [PubMed: 16955107]
86. Franssen CF. Oxalate clearance by haemodialysis--a comparison of seven dialysers. Nephrol Dial Transplant. 2005 Sep; 20(9):1916–1921. [PubMed: 15998647]
87. Hoppe B, Graf D, Offner G, Latta K, Byrd DJ, Michalk D, et al. Oxalate elimination via hemodialysis or peritoneal dialysis in children with chronic renal failure. Pediatr Nephrol. 1996 Aug; 10(4):488–492. [PubMed: 8865249]
88. Hoppe B, Langman CB. A United States survey on diagnosis, treatment, and outcome of primary hyperoxaluria. Pediatr Nephrol. 2003 Oct; 18(10):986–991. [PubMed: 12920626]
89. Hoppe B, Latta K, von Schnakenburg C, Kemper MJ. Primary hyperoxaluria--the German experience. Am J Nephrol. 2005 May-Jun;25(3):276–281. [PubMed: 15961947]
90. Cochat P, Fargue S, Harambat J. Primary hyperoxaluria type 1: strategy for organ transplantation. Curr Opin Organ Transplant. 2010 Oct; 15(5):590–593. [PubMed: 20733487] An overview of transplant options for patients with primary hyeroxaluria.
91. Bergstralh EJ, Monico CG, Lieske JC, Herges RM, Langman CB, Hoppe B, et al. Transplantation outcomes in primary hyperoxaluria. Am J Transplant. 2010 Nov; 10(11):2493–2501. [PubMed: 20849551] A study examining the outcome of transplantation in patients with primary hyperoxaluria over the past decade.
92. Monico CG, Milliner DS. Combined liver-kidney and kidney-alone transplantation in primary hyperoxaluria. Liver Transpl. 2001 Nov; 7(11):954–963. [PubMed: 11699031]
93. Allison MJ, Dawson KA, Mayberry WR, Foss JG. Oxalobacter formigenes gen. nov., sp. nov.: oxalate-degrading anaerobes that inhabit the gastrointestinal tract. Arch Microbiol. 1985 Feb; 141(1):1–7. [PubMed: 3994481]
94. Grujic D, Salido EC, Shenoy BC, Langman CB, McGrath ME, Patel RJ, et al. Hyperoxaluria is reduced and nephrocalcinosis prevented with an oxalate-degrading enzyme in mice with hyperoxaluria. American journal of nephrology. 2009; 29(2):86–93. [PubMed: 18698135]
95. Hatch M, Gjymishka A, Salido EC, Allison MJ, Freel RW. Enteric oxalate elimination is induced and oxalate is normalized in a mouse model of primary hyperoxaluria following intestinal colonization with Oxalobacter. American journal of physiology Gastrointestinal and liver physiology. 2011 Mar; 300(3):G461–G469. [PubMed: 21163900] Examination of the beneficial effect of Oxalobacter in mice with primary hyperoxaluria.
96. Sidhu H, Schmidt ME, Cornelius JG, Thamilselvan S, Khan SR, Hesse A, et al. Direct correlation between hyperoxaluria/oxalate stone disease and the absence of the gastrointestinal tract-dwelling bacterium Oxalobacter formigenes: possible prevention by gut recolonization or enzyme replacement therapy. J Am Soc Nephrol. 1999 Nov; 10(Suppl 14):S334–S340. [PubMed: 10541258]
97. Hatch M, Freel RW. Renal and intestinal handling of oxalate following oxalate loading in rats. Am J Nephrol. 2003 Jan-Feb;23(1):18–26. [PubMed: 12373077]
98. Hoppe B, Beck B, Gatter N, von Unruh G, Tischer A, Hesse A, et al. Oxalobacter formigenes: a potential tool for the treatment of primary hyperoxaluria type 1. Kidney Int. 2006 Oct; 70(7): 1305–1311. [PubMed: 16850020]

99. Hoppe B, Groothoff JW, Hulton SA, Cochat P, Niaudet P, Kemper MJ, et al. Efficacy and safety of Oxalobacter formigenes to reduce urinary oxalate in primary hyperoxaluria. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2011 Nov; 26(11):3609–3615. Lack of effect of Oxalobacter on urinary oxalate excretion in patients with primary hyperoxaluria.

100. Salido E, Rodriguez-Pena M, Santana A, Beattie SG, Petry H, Torres A. Phenotypic correction of a mouse model for primary hyperoxaluria with adeno-associated virus gene transfer. Mol Ther. 2011 May; 19(5):870–875. [PubMed: 21119625] A study describing the successful treatment of hyperoxaluria in mice using gene transfer.

101. Hopper ED, Pittman AM, Fitzgerald MC, Tucker CL. In vivo and in vitro examination of stability of primary hyperoxaluria-associated human alanine:glyoxylate aminotransferase. J Biol Chem. 2008 Nov 7; 283(45):30493–30502. [PubMed: 18782763]

102. Lumb MJ, Birdsey GM, Danpure CJ. Correction of an enzyme trafficking defect in hereditary kidney stone disease in vitro. Biochem J. 2003 Aug 15; 374(Pt 1):79–87. [PubMed: 12737622]

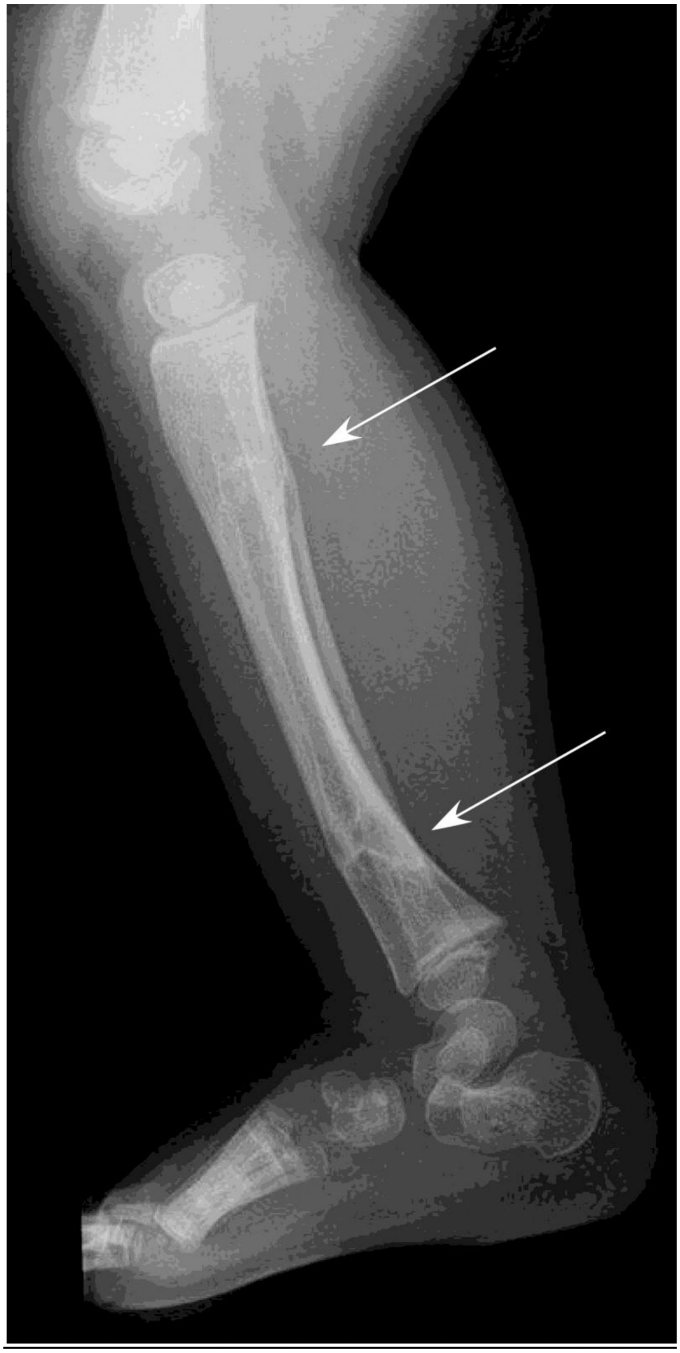

Figure 1. Oxalate osteopathy

Fracture deformities of both the proximal and distal tibia and fibula (arrows) in a 23-month-old girl with end stage renal failure secondary to type 1 PH.

Table 1

Systemic manifestations of oxalate disorders

Organ	Manifestations
Joints	• Arthritis • Chondrocalcinosis of the metacarpophalangeal and metatarsophalangeal joints • Spinal stenosis • Synovitis • Tenosynovitis • Bursitis
Kidneys	• Acute tubular necrosis • Interstitial fibrosis • Nephrocalcinosis • Kidney stones
Heart	• Arrhythmias • Diastolic dysfunction • Valvular abnormalities • Impaired ejection fraction • Infiltrative process
Skin	• Livido reticularis • Acrocyanosis • Papules and nodules on face and digits • Non-healing ulcers
Eyes	• Retinal oxalate deposition
Nerve and muscle	• Axon loss and demyelination • Myopathies • Polyradiculoneuropathies
Teeth	• Peridontitis • Jaw bone and root resorption • Dental mobility
Bone marrow	• Erythropoietin stimulating agent resistant anemia
Bones	• Fractures • Pseudofractures • Sclerosis • Cystic bone changes • Dense metaphyseal bands • Increased bone density

Table 2

Treatment of hyperoxaluria

Treatment	Type of hyperoxaluria
Fluid intake > 3 L per day	All types, when renal function is preserved
Urinary crystal inhibitors • Citrate • Phosphorus • Magnesium	PH with preserved renal function
Calcium supplementation with meals	Secondary hyperoxaluria due to fat malabsorption
Lanthanum supplementation	Possibly effective in secondary hyperoxaluria
Low-fat, low-oxalate diet	Secondary hyperoxaluria
Intensive hemodialysis	All types
Combined liver kidney transplantation	Type 1 PH
Kidney transplantation alone	Patients with type I PH and complete pyridoxine responsiveness Type 2 PH