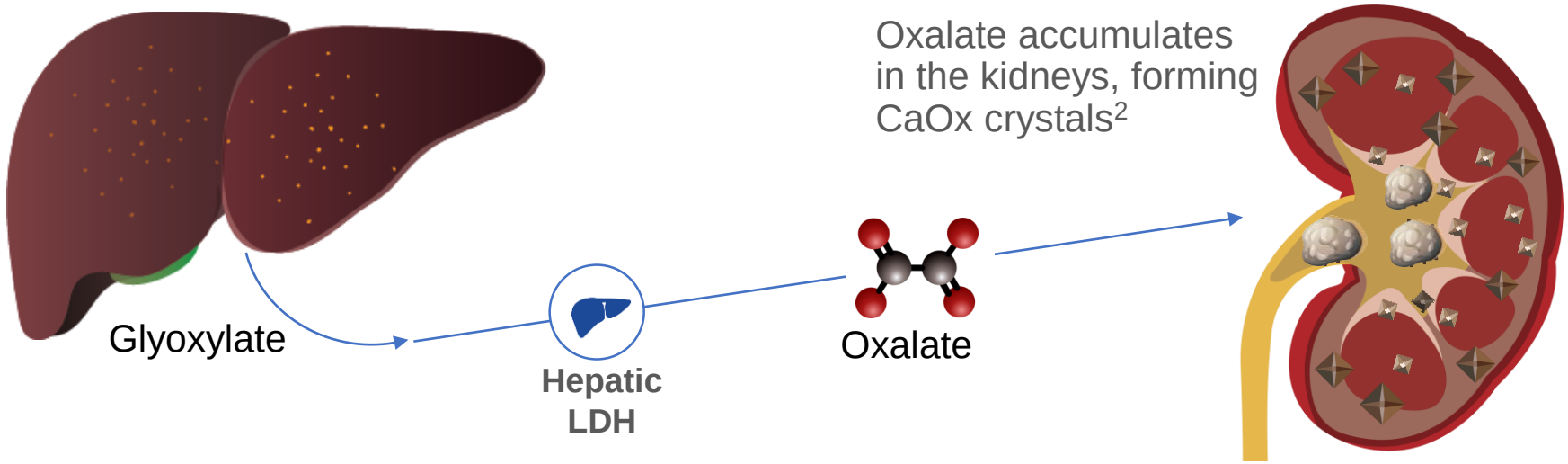
# PH is a family of rare genetic disorders causing hepatic oxalate overproduction that can result in life-threatening kidney damage[1]




## Liver enzyme deficiency

causes metabolic pathway dysregulation and the overproduction of glyoxylate. LDH catalyzes the final common step in this pathway, resulting in an overproduction of oxalate[1-4]

## Renal damage

is caused by CaOx crystals that form kidney and bladder stones and nephrocalcinosis, which results in progressive kidney deterioration, CKD, and systemic oxalosis[2,5]

Abbreviations: CaOx, calcium oxalate; CKD, chronic kidney disease; LDH, lactate dehydrogenase.

1. Cochat P, Rumsby G. *N Engl J Med*. 2013;369(7):649-658. 2. Lai C, et al. *Mol Ther.* 2018;26(8):1983-1995. 3. Belostotsky R, et al. *J Mol Med (Berl).* 2012;90(12):1497-1504.
4. Riedel TJ, et al. *Biochim Biophys Acta*. 2012;1822(10):1544-1552. 5. Hoppe B, Martin-Higueras C. *Curr Opin Pediatr.* 2020;32(2):273-283.

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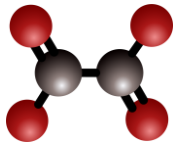
# Calcium oxalate crystals combine to form stones in PH

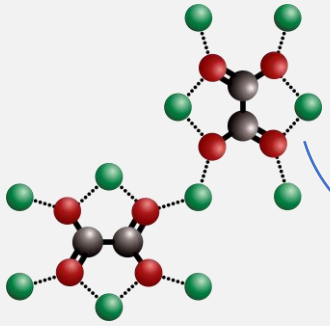
*Hyperoxaluria is a condition defined by increased urinary excretion of oxalate*[1]



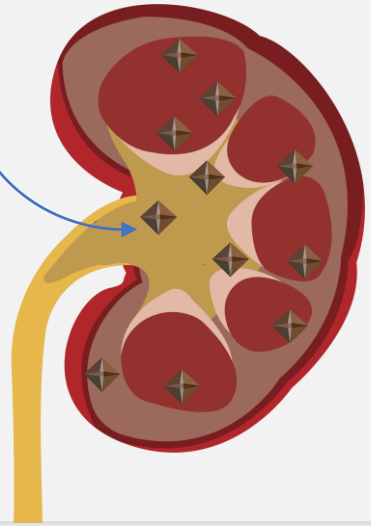
= carbon
= oxygen
= calcium

**Oxalate**[2] is a metabolic end product, which can also be ingested through food, that is of no known use to the body[1,3]

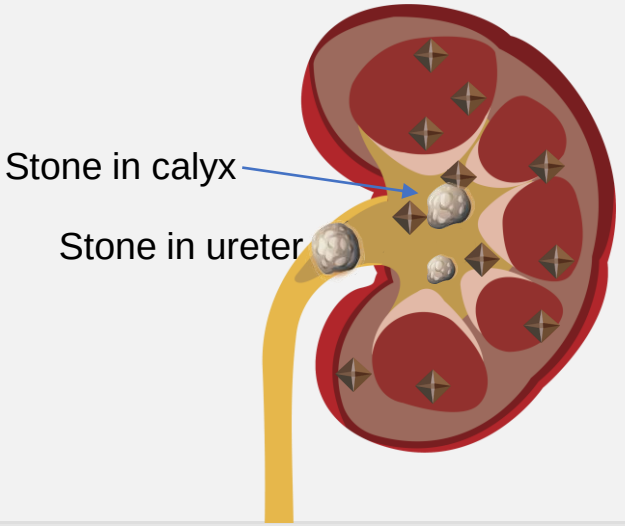
When too much oxalate accumulates in the kidneys, it binds with calcium to form **calcium oxalate** (CaOx) crystals[4,5]



CaOx crystal[6,7]



CaOx crystals aggregate to form **stones** in the kidneys and urinary tract, and also distribute throughout the kidney tissue, causing **nephrocalcinosis**[3]




= calcium oxalate crystal

= stone

1. Bhasin B, et al. *World J Nephrol.* 2015;4(2):235-244. 2. National Center for Biotechnology Information. PubChem Database. Oxalate, CID=71081. https://pubchem.ncbi.nlm.nih.gov/compound/71081. Accessed June 11, 2020. 3. Danpure CJ, Rumsby G. *Expert Rev Mol Med.* 2004;6(1):1-16. 4. Dindo M, et al. *Urolithiasis.* 2019;47(1):67-78. 5. Lai C, et al. *Mol Ther.* 2018;26(8):1983-1995. 6. Hochrein O, et al. *Z Anorg Allg Chem*. 2008;634(11):1826-1829. 7. National Center for Biotechnology Information. PubChem Database. Calcium oxalate, CID=33005. https://pubchem.ncbi.nlm.nih.gov/compound/33005. Accessed June 11, 2020.

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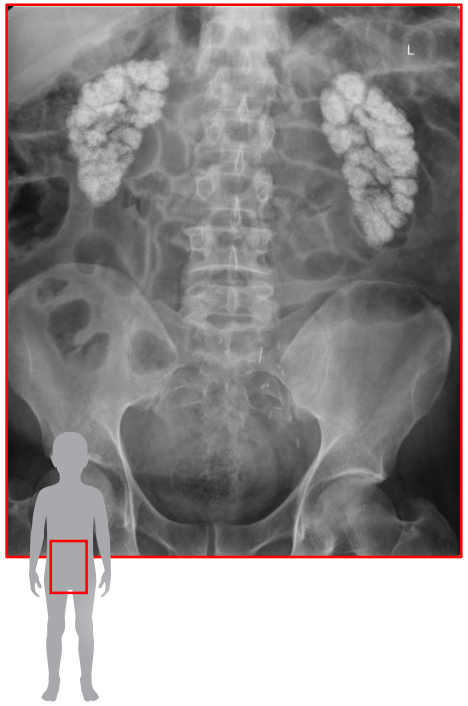
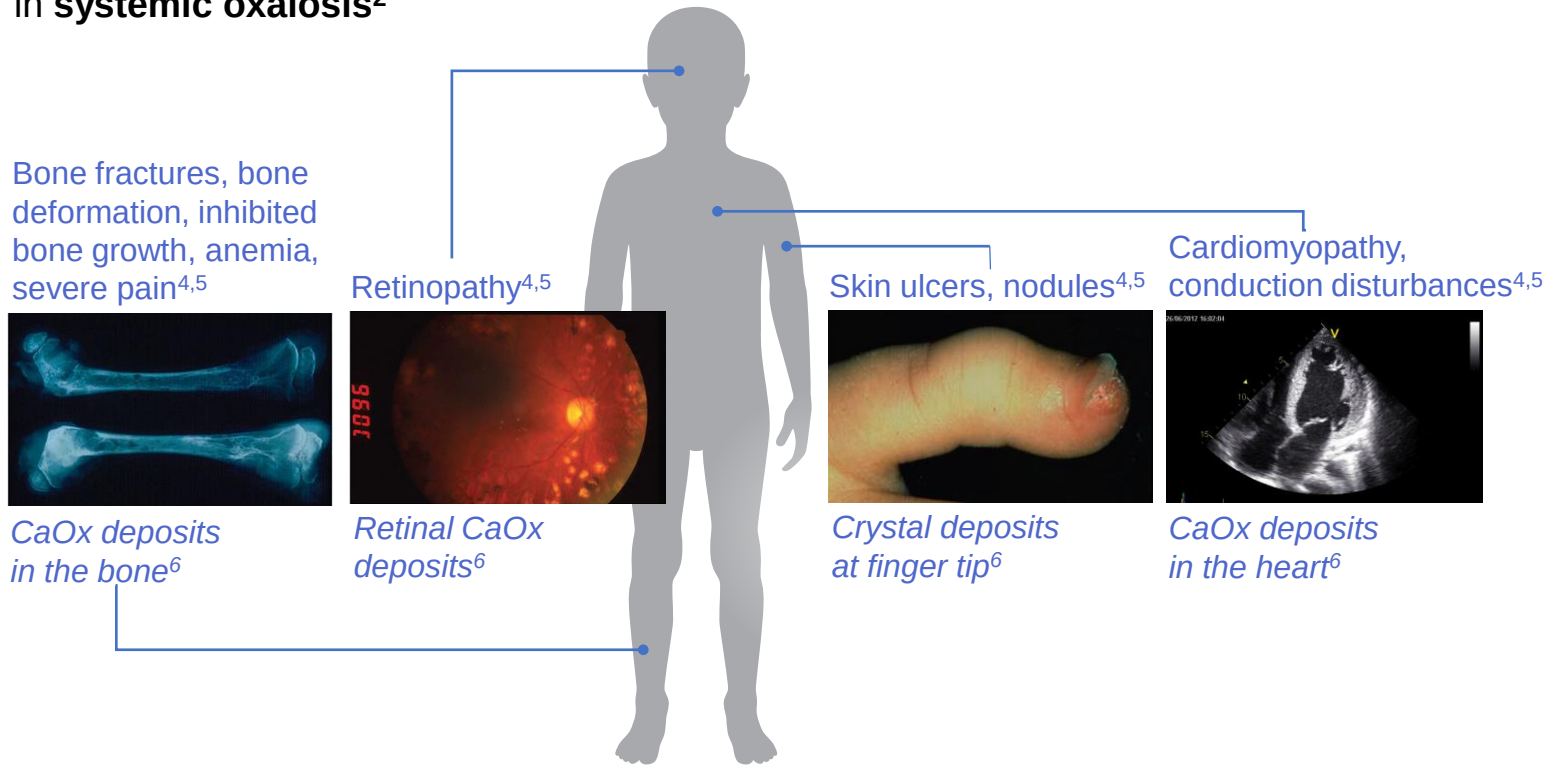
# As PH advances, progressive nephrocalcinosis and renal damage may lead to end-stage renal disease and systemic oxalosis

**1** Progressive calcification (**nephrocalcinosis**), inflammation, and interstitial fibrosis lead to **ESRD**[1,2,*]



**2** When glomerular filtration rate drops below 30-45 mL/min, oxalate is no longer adequately filtered by the kidneys, resulting in **systemic oxalosis**[2]

CaOx crystals are deposited in tissue throughout the body, especially the skeleton[3]




Abbreviations: CaOx, calcium oxalate; ESRD, end-stage renal disease.
*Case courtesy of Dr Ian Bickle, Radiopaedia.org, rID: 45927.

1. Lai C, et al. *Mol Ther.* 2018;26(8):1983-1995. 2. Harambat J, et al. *Int J Nephrol.* 2011;2011:864580. 3. Cochat P, Rumsby G. *N Engl J Med*. 2013;369(7):649-658.
4. Salido E, et al. *Biochim Biophys Acta.* 2012;1822(9):1453-1464. 5. Sas DJ, et al. *Urolithiasis.* 2019;47(1):79-89. 6. Hoppe B, et al. *Kidney Int.* 2009;75(12):1264-1271.

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