Clinical Manifestations and Diagnosis of Hyperoxaluria

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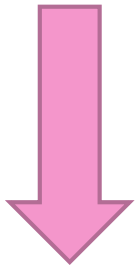
Primary Hyperoxaluria Type 1

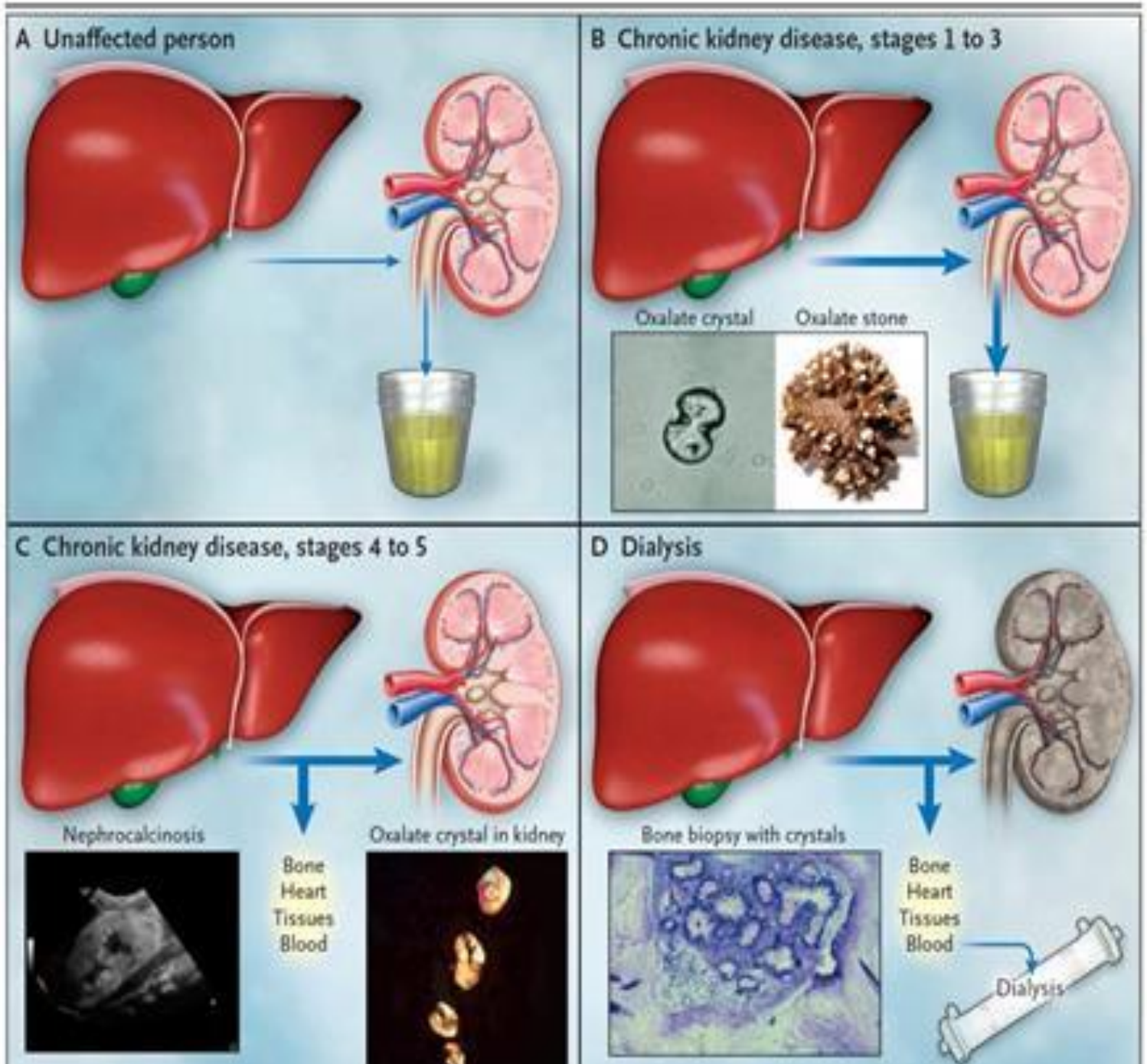
- Prevalence 1-3 cases per million population.
- Contributes to 1% of End stage Renal Disease (ESRD) in paediatric population
- More frequently seen where consanguineous marriages are practiced

Primary Hyperoxaluria Type 1

- Most severe type of Primary Hyperoxaluria
- Presents in childhood with failure to thrive
- Life threatening oxalosis.
- In adulthood , with presence of kidney stone.
- Recurrent nephrolithiasis and progressive nephrocalcinosis



- the majority of the patients reach ESRD during 3^{rd}-5^{th} decade of life



A. Oxalate excreted in urine

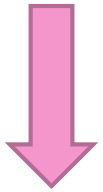
B. Increased load leads to crystaluria and oxalate stones

C and D. GFR < 30 ml/min/1.73 m^2

- Diffuse **nephrocalcinosis**
- **Oxalate crystals in proximal tubules**
- Because oxalate not adequately cleared, wind up in:
  - **Heart** (NICM)
  - **Bone** (accelerated bone maturity)
  - **Bone marrow** (leads to treatment resistant anemia)

SYSTEMIC OXALOSIS

Calcium oxalate salts are poorly soluble in body fluids.



Calcium oxalate deposits within renal tissue as nephrocalcinosis and also forms renal stones (nephrolithiasis).

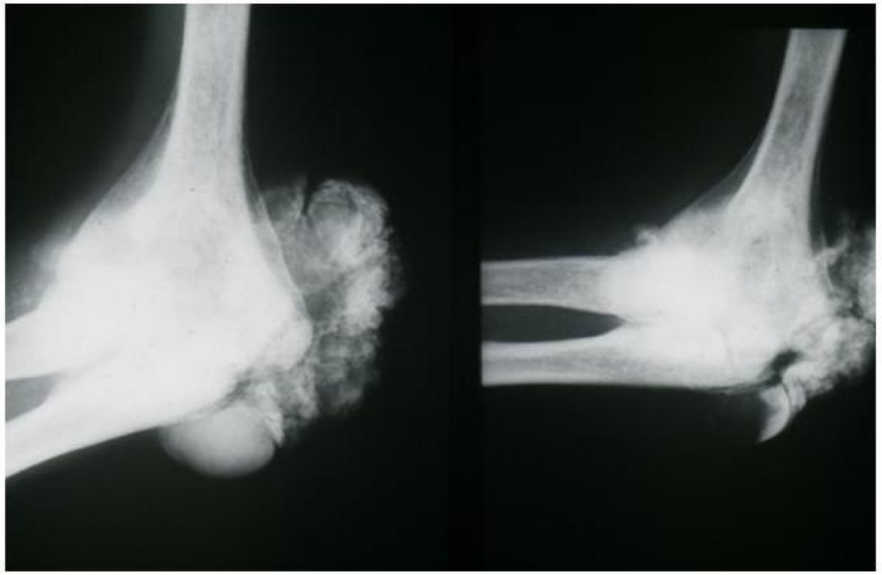
Progressive renal injury and inflammation and tubular obstruction

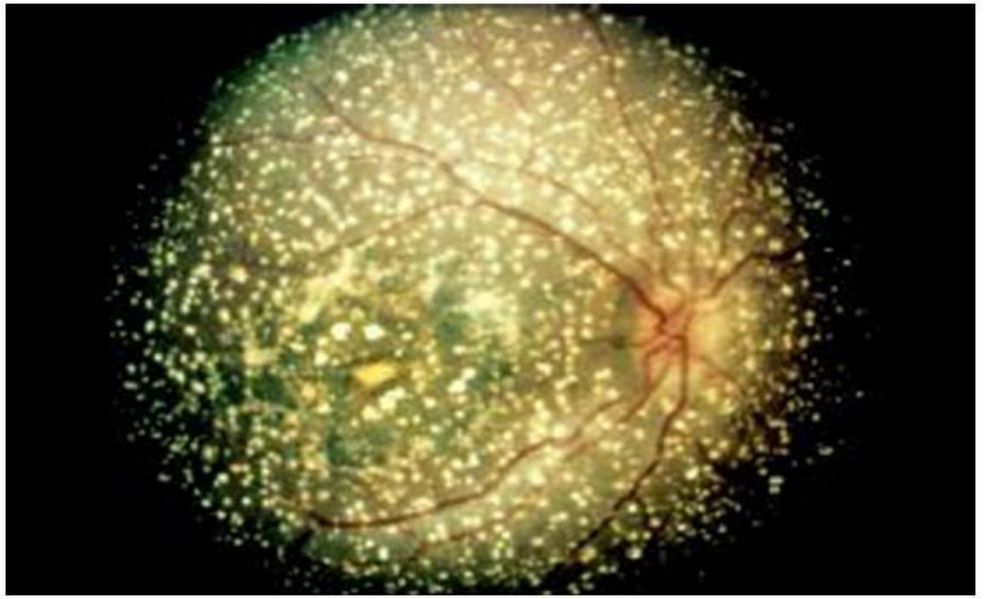
- interstitial fibrosis, declining renal function and eventually ESRD

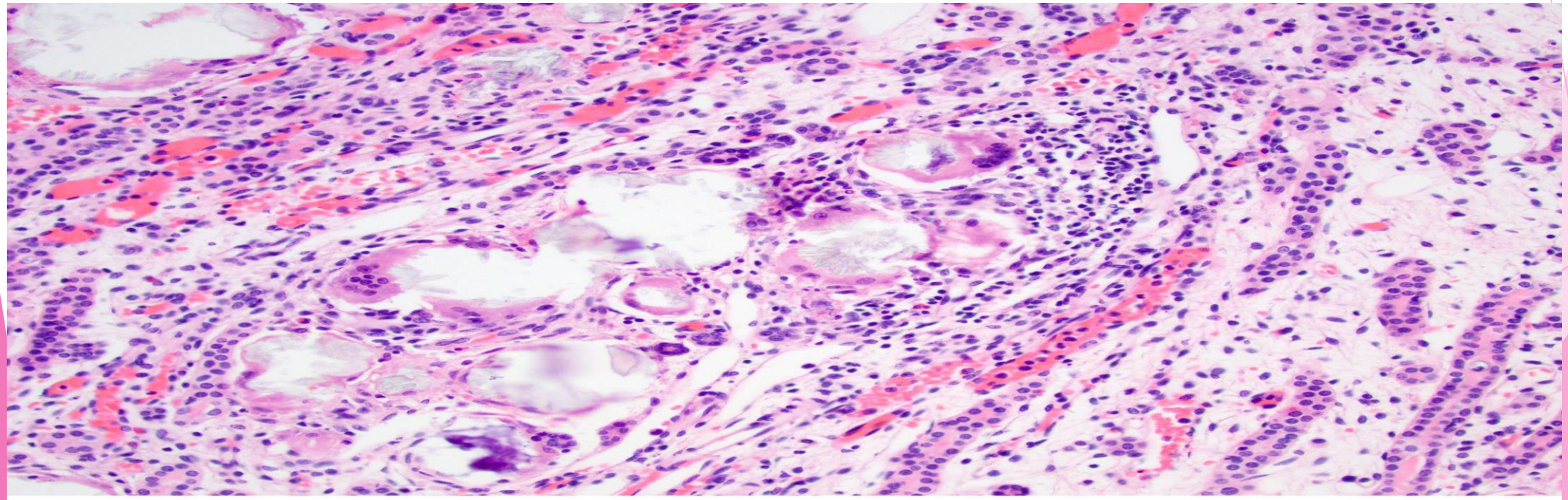
- When glomerular filtration rate (GFR) drops below 30-40 mL/min per 1.73 m^2

- Renal capacity to excrete calcium oxalate is significantly impaired

- calcium oxalate starts to deposit in extra renal tissues







Multinucleated giant cells engulfing calcium oxalate crystals; from a patient with type 1 primary hyperoxaluria

Primary Hypeoxaluria Type 2

- Less aggressive form of PH
- Better preservation of renal function
- Lower incidence of ESRD and less severe nephrocalcinosis.
- Lower oxalate excretion in PH2
- altered urine composition with reduced urinary levels of citrate and magnesium in PH1 compared to PH2

Primary Hyperoxaluria Type 3

- Recurrent nephrolithiasis in the early decades of life
- Increase in urinary calcium levels
- Genetic defects in the *HOGA1* gene
- More benign than other forms

Secondary Hyperoxaluria

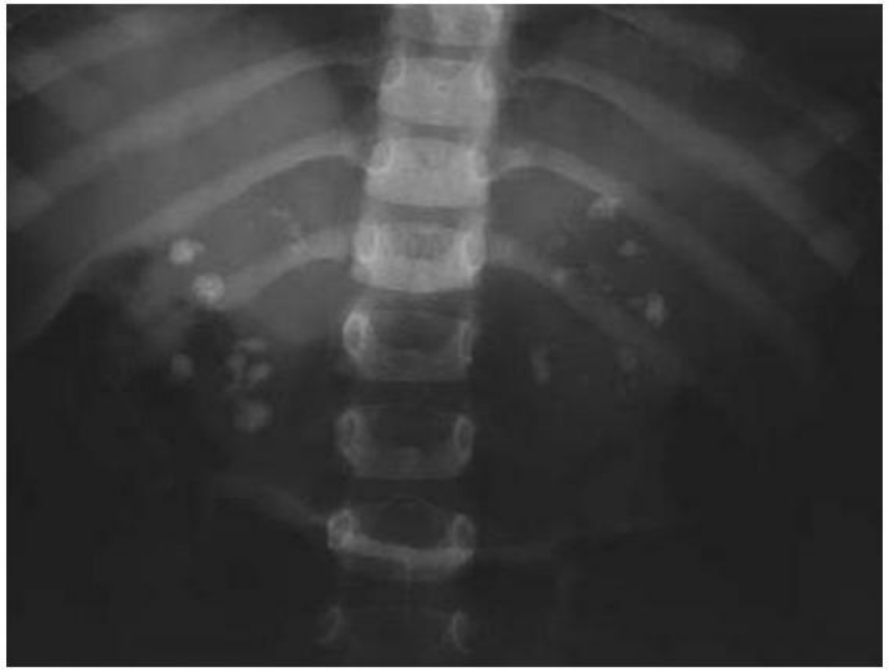
- Predisposition to developing recurrent calcium oxalate stones
- Leading to worsening renal damage and progression to ESRD.
- Systemic oxalosis is less common in secondary hyperoxaluria but reported in some severe cases of Crohn’s disease

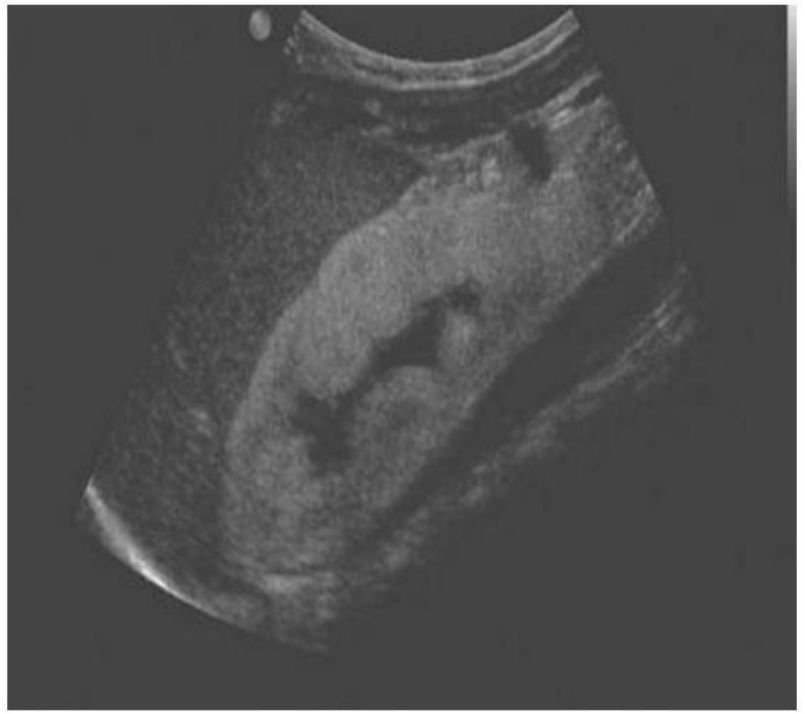
Screening

- All Children with first incidence of renal stone
- All adults with recurrent Calcium oxalate stones.
- PH Type 1 strongly considered in any patient with renal failure of unknown etiology, particularly when there is nephrocalcinosis
- Presence of monohydrate calcium oxalate crystals is also a strong pointer towards primary hyperoxaluria

Diagnosis

- Ultrasound or Xray KUB to confirm the presence of nephrocalcinosis and urolithiasis





- Stone analysis should be done
- Stones in PH are composed of monohydrate calcium oxalate (whewellite) which assume a dumbbell shaped form

- The initial biochemical tests include urinary oxalate excretion preferably measured in 24 h urine collection
- Oxaluria must be confirmed using two urine samples.

- Primary Hyperoxaluria is characterized by
- urinary oxalate excretion > 1.0 mmol/1.73 m^2 per 24 hours in majority
- Some cases may exceed 2.0 mmol/1.73 m^2/ 24 hours

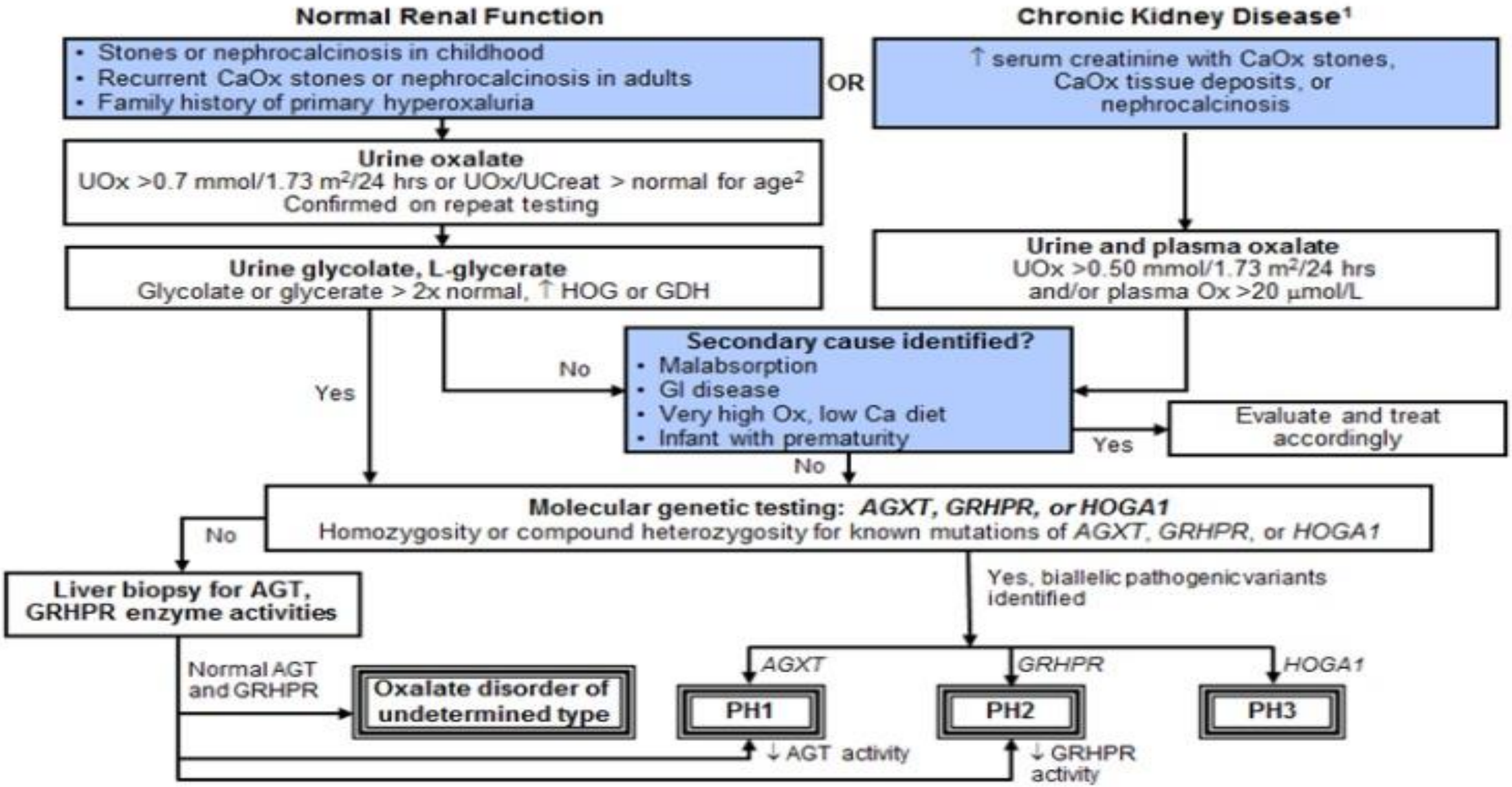
(Normal:< 0.45 mmol/1.73 m^2/ 24 hours)

- In patients with hyperoxaluria > 0.8 mmol/1.73 m^2 per 24 h, urinary glycolate and glycerate levels should be measured.
- Elevated urinary glycolate levels but normal glycolate levels do not exclude the diagnosis.
- Urinary glycerate levels are noted to be high in PH2 patients

- In Secondary Hyperoxaluria, stones are usually mixed (whewellite and weddellite) in contrast to PH.
- The excretion of urinary oxalate is increased in Secondary Hyperoxaluria and may be > 0.7 mmol/1.73 m^2 per 24 h but in some cases may exceed 1.0 mmol/1.73 m^2 per 24 hours.
- Other available diagnostic tests include use of PCR in stool samples to identify *oxalobacter formigenes*

- Increased intestinal oxalate absorption can be assessed by an absorption test using ($^{13}C2$) oxalate.
- This test can help identify hyperabsorbers who would benefit from dietary interventions focusing on lowering oxalate and increasing calcium in the diet.
- This diagnostic test also helps to differentiate between primary and secondary forms of hyperoxaluria

Diagnosis of Primary Hyperoxaluria



THANK YOU