

# Pediatric CKD-MBD: pathophysiology and management



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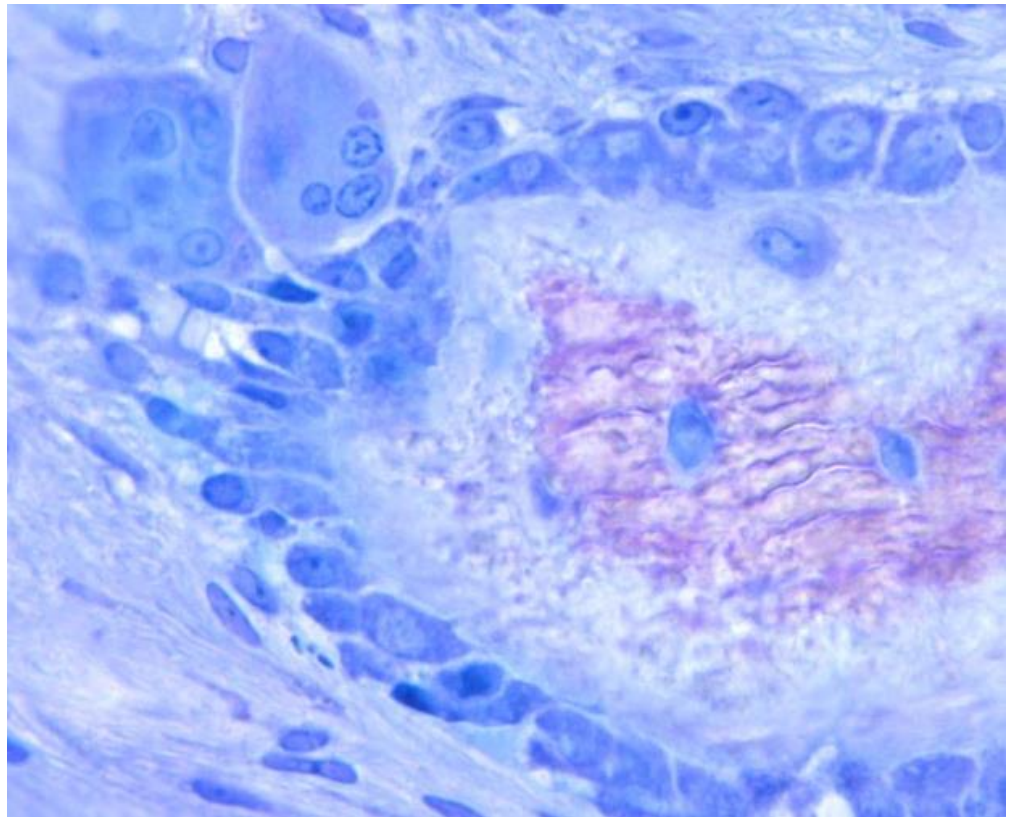
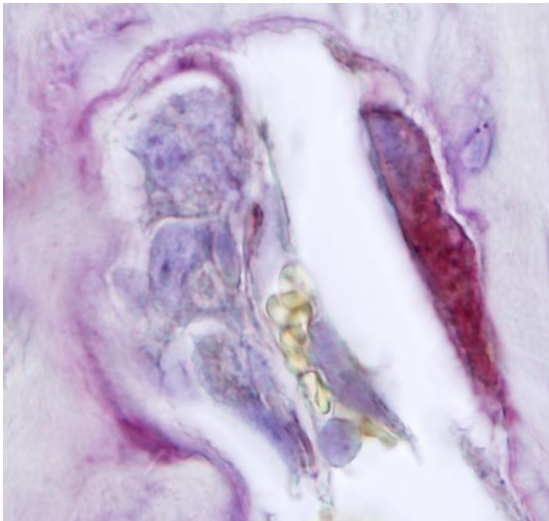
European  
Reference  
Network

for rare or low prevalence  
complex diseases

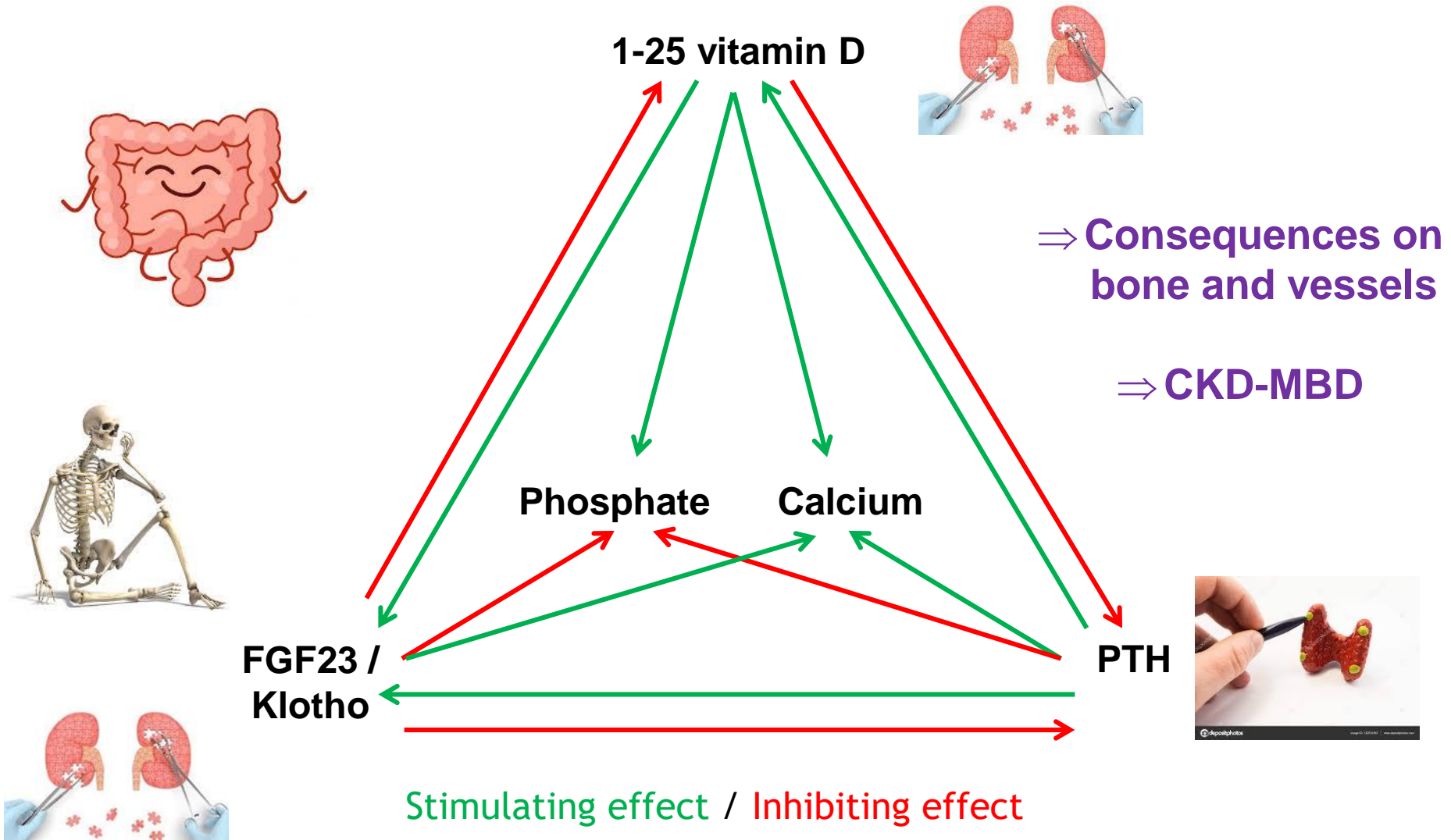
• **Network**  
Kidney Diseases (ERKNet)

• **Member**  
Hospices Civils de Lyon —  
France

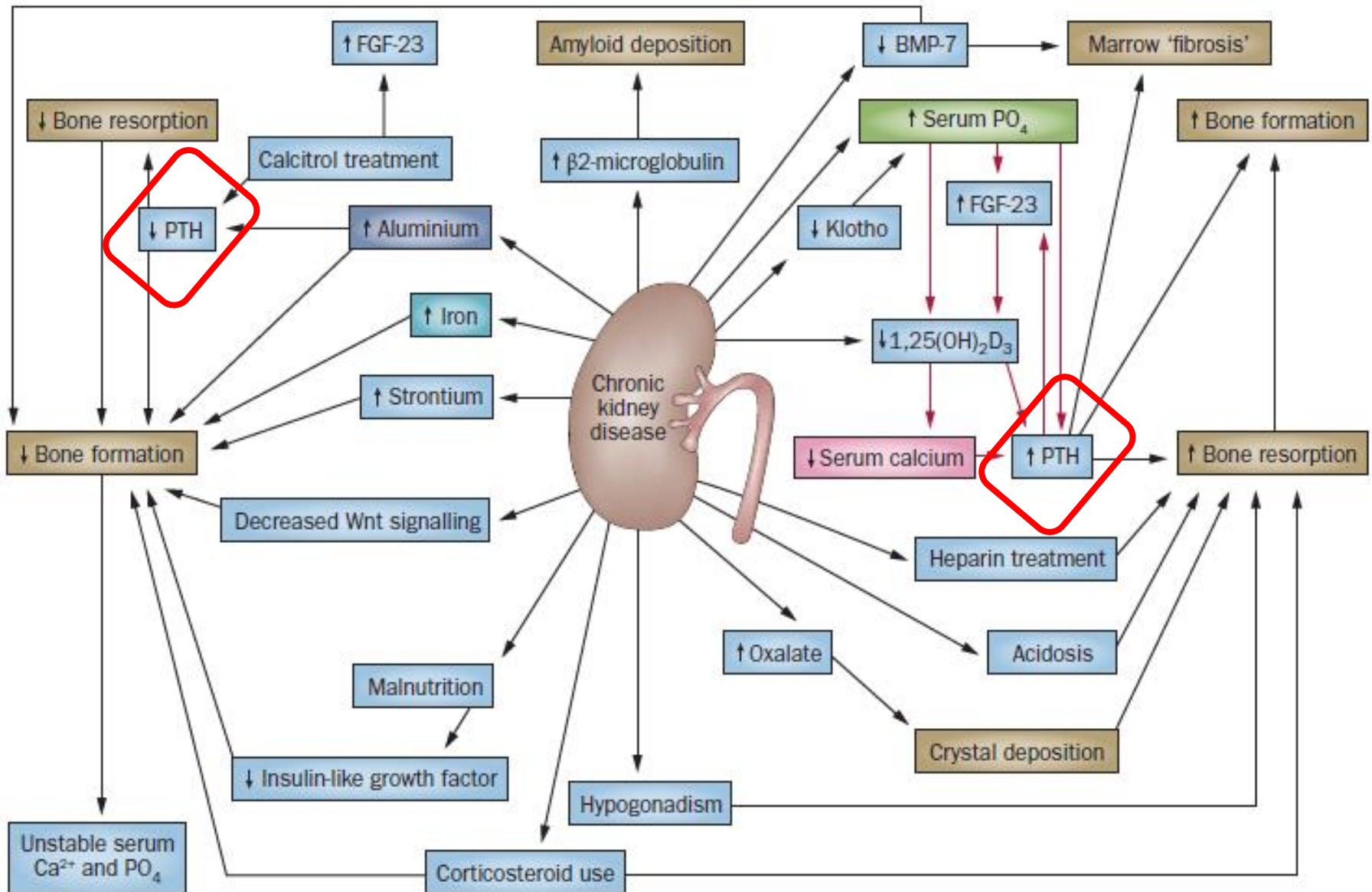
# Overview of pediatric CKD-MBD



# Overview of calcium and phosphate metabolism: everything is modified by CKD!



# The complex interplay between bone and kidney



# CKD-MBD

## *A systemic disease*

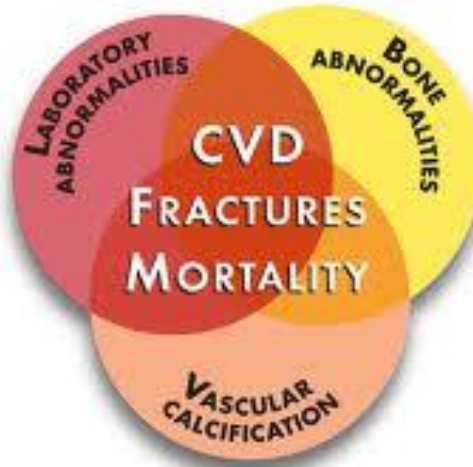
Hypocalcemia  
Hyperphosphatemia

HyperPTH  
Decreased 1-25 D

Prurit  
Skin necrosis

Keratitis  
Corneal calcifications

CHRONIC KIDNEY DISEASE—  
MINERAL AND BONE DISORDER



CKD-MBD

Renal osteodystrophy

Growth retardation  
GH resistance

Proximal myopathy

Vascular calcifications

$\text{GFR} < 60 \text{ mL/min per } 1.73 \text{ m}^2$



# First challenge: bone and growth

N=249 young adults with ESRD  
between 0 and 14 years, born before 1979



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## Total cohort<sup>a</sup>

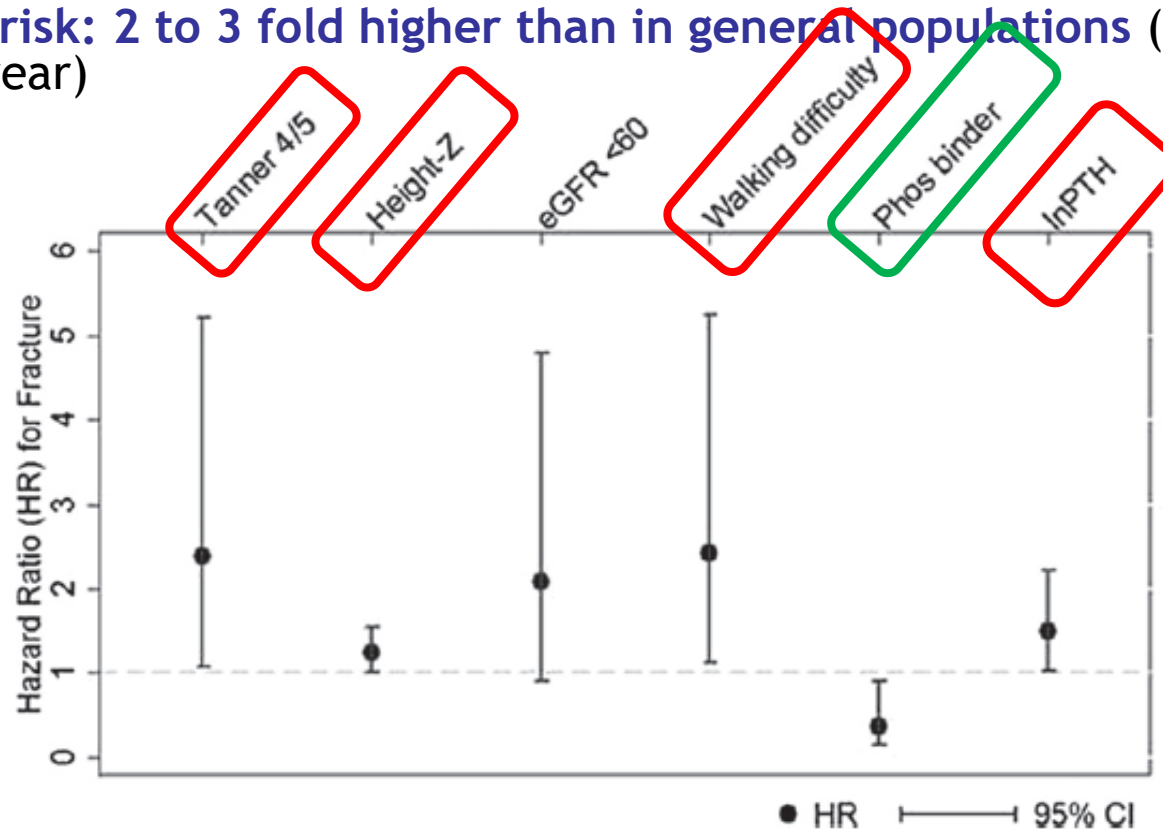
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|   |             |
|---|-------------|
| Height < -2 SD                          | 153 (61.9%) |
| Clinical manifestations of bone disease | 91 (36.8%)  |
| Deformities                             | 63 (25.5%)  |
| Pathological fractures                  | 33 (13.4%)  |
| Aseptic bone necrosis                   | 32 (13.0%)  |
| Mild disabling bone disease             | 26 (10.5%)  |
| Severe disabling bone disease           | 18 (7.3%)   |
| Invalidating bone disease (all)         | 44 (17.8%)  |

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# Fracture risk in CKD children

- CKiD cohort, 537 CKD children
- Median age at baseline 11 years, 16% past of fracture
- Median follow-up 3.9 years, 43 boys and 24 girls with fracture
- **Fracture risk: 2 to 3 fold higher than in general populations** (113/10000 persons/year)



**Figure 1.** Final multivariable Cox regression model: correlates of incident fracture.

<sup>a</sup>HR for males  $\geq 15$  years versus females  $\geq 15$  years =  $(3.94 \times 0.67) = 2.6$ . <sup>b</sup>PTH natural log transformed.

# Causes of bone impairment in pediatric CKD

- Growth failure, impaired GH-IGF1 axis
- Inadequate intake of calories and proteins / nutrition
- Muscle deficits
- Hypogonadism / delayed puberty
- Acidosis
- Inflammation
- Vitamin D deficiency
- Hyperparathyroidism
- Long-term use of corticosteroids and other drugs



# Drugs inducing bone toxicity

- **Calcineurin inhibitors**

- Increased RANKL expression
- Activation of osteoclastic activity
- VDR inhibition

- **mTor inhibitors**

- Animal models +++, clinical data
- Impaired growth
- Direct toxicity on growth plate

- **Anti-epileptic drugs**

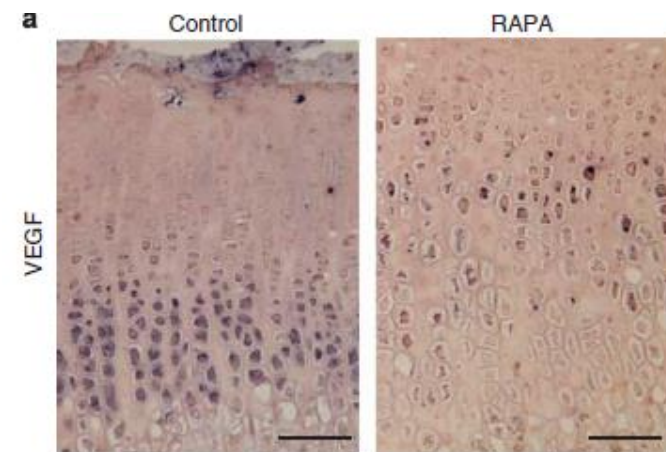
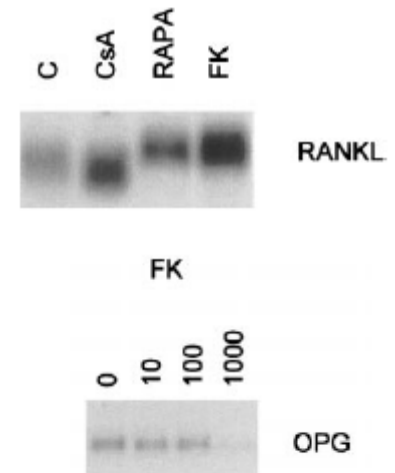
- Secondary rickets

- **Anti-acid drugs**

- Hypophosphatemia
- Impaired mineralization

- **Long-term use of heparin**

- **This list is not exhaustive!**



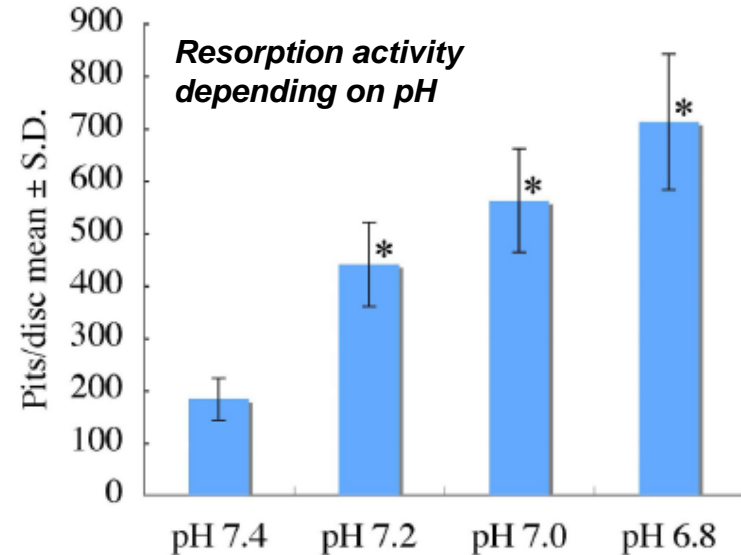
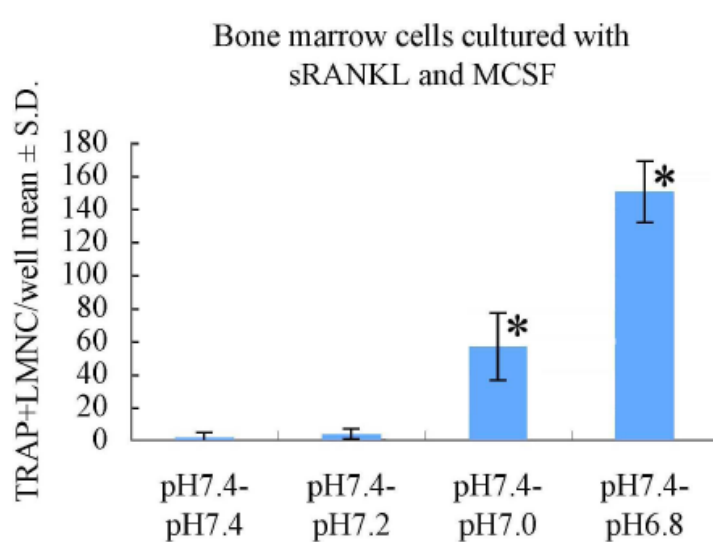
Hofbauer, 2001

Fukunaga 2004

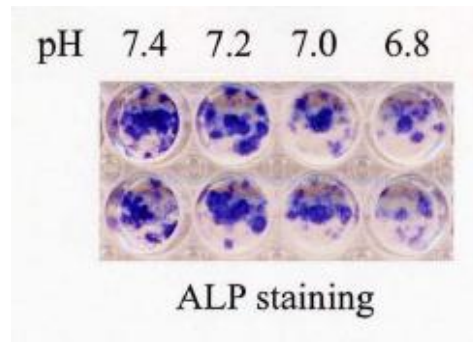
Lee, Am J Nephrol 2011

# Acidosis and bone metabolism

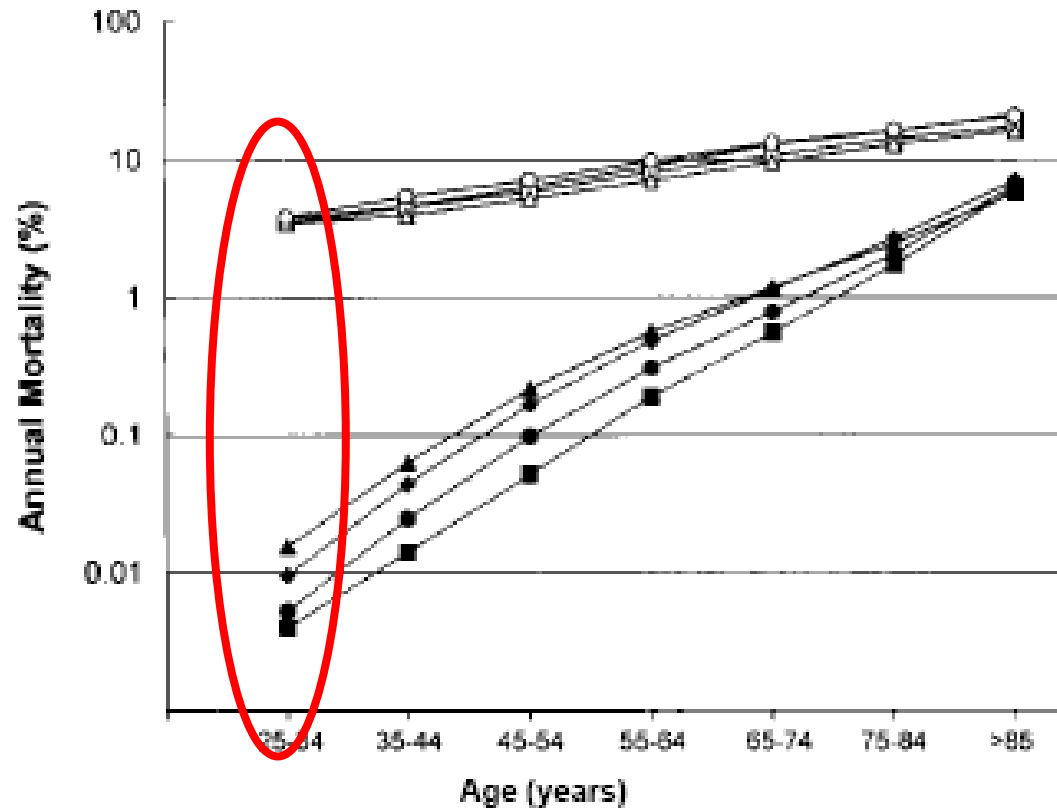
- Stimulation of osteoclastic differentiation
- Stimulation of osteoclastic resorption



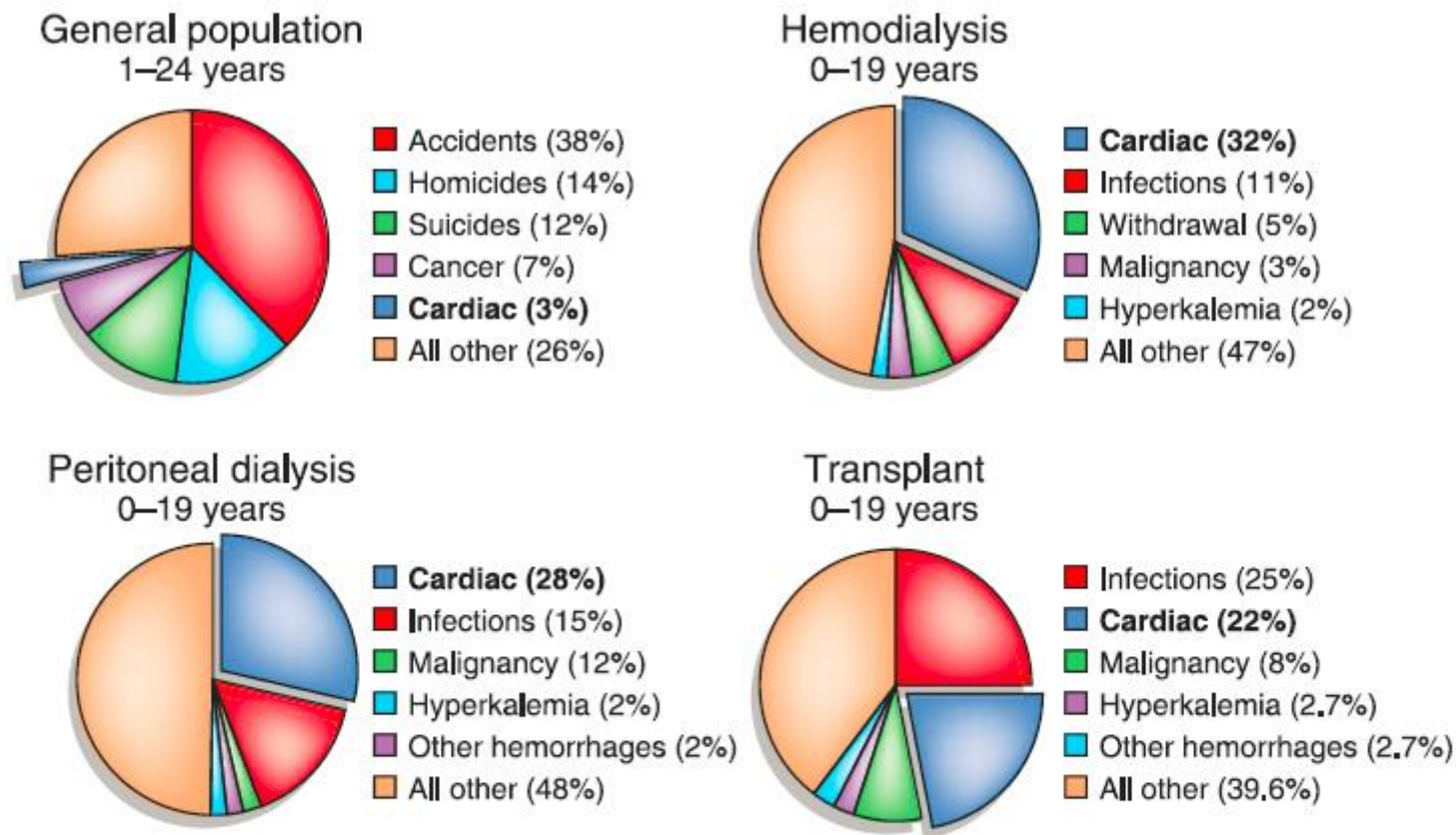
- Inhibition of osteoblastic differentiation



## Second challenge: cardiovascular disease

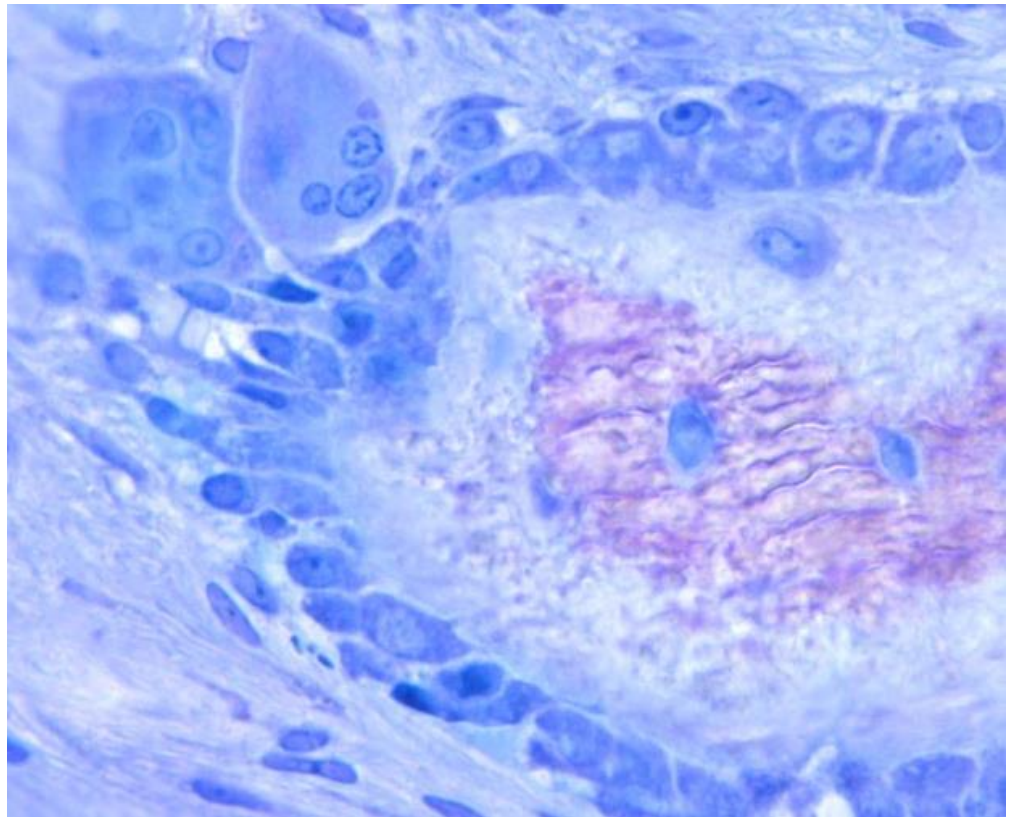
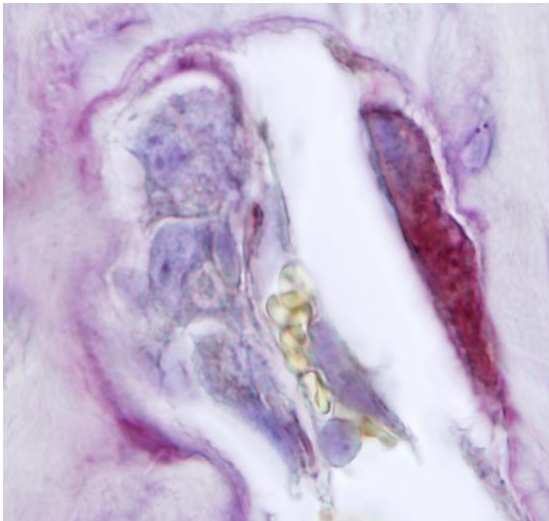


# Cardiovascular disease as the leading cause of mortality in CKD children



**Figure 1.** Leading causes of death in general pediatric population and in children on renal replacement therapy. Data are presented as percentages. Data for dialysis and transplant patients are from the USRDS (2011).<sup>2</sup> Data for general pediatric population are from Mathews et al. (2011).<sup>1</sup>

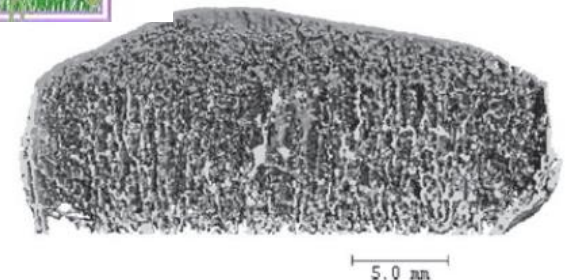
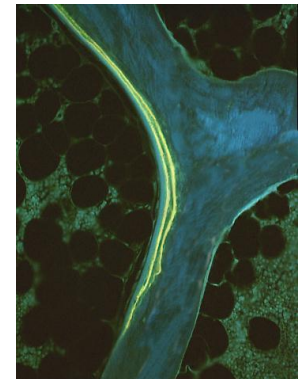
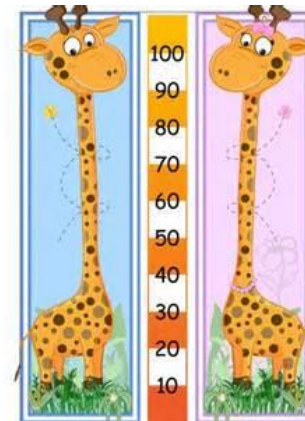
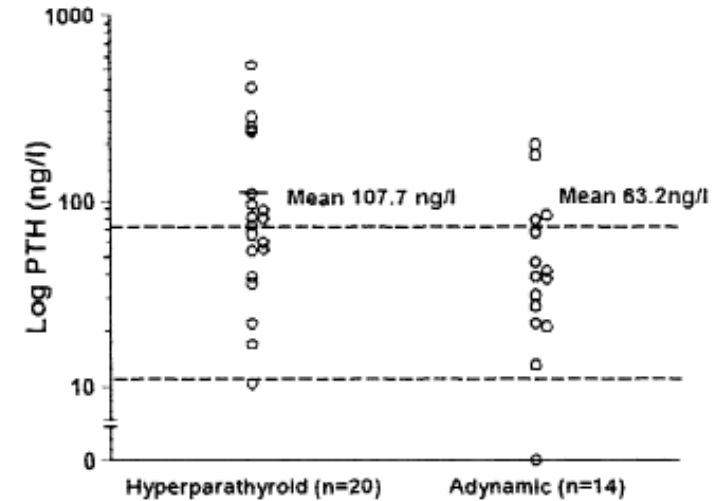
# Evaluating CKD-MBD in pediatrics





# How to evaluate CKD-MBD in pediatric CKD in daily practice?

- Growth
- Biomarkers
  - Calcium, phosphate
  - PTH, 25OH-D
  - ALP
  - **ESPN next week**
- Dual X-ray absorptiometry: DXA
  - **ESPN next week**
- Cardio-vascular evaluation
  - Ambulatory BP monitoring
  - Cardiac US
- Research tools
  - FGF23, sclerostin, bone biomarkers
  - Bone MRI, pQCT, HR-pQCT, US...
  - Bone biopsy: **ESPN next week** !
  - Carotid IMT, PWV





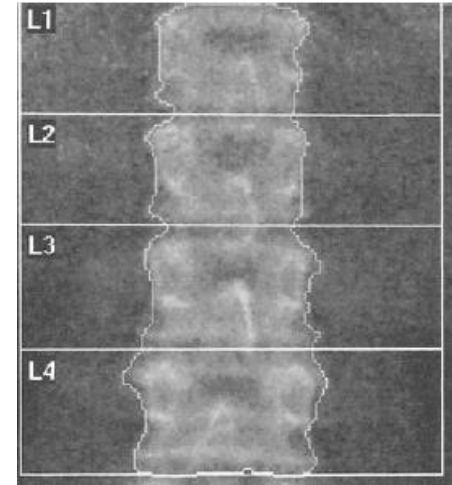
**Do you perform DXA scans in the CKD children followed in your centre?**

- **Yes**
- **No=> 73%**

# In daily practice: dual X-ray absorptiometry?

- **Advantages**

- “Gold standard” for assessing bone mineral density
- Minor irradiation: 2.7 to 3.6  $\mu\text{Sv}$
- Not expensive and easily available
- Evaluation of body composition



- **Limitations**

- **Bidimensional technique:** major technical concern in pediatrics
- Systematic underestimation of BMD in children with poor growth
- **No distinction between cortical and trabecular bone**
- **No evaluation of geometry and microarchitecture**
- BUT **prediction of fracture risk in CKD adults**

# In daily practice: dual X-ray absorptiometry?

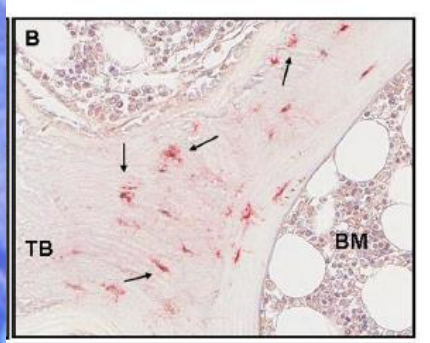
- **Daily practice**

- **Adults**, KDIGO 2009: DXA no longer recommended
- **Adults**, new KDIGO 2017 : it is suggested to test BMD to assess fracture risk if results will impact treatment decisions
- **In CKD children: DXA no longer recommended in 2011**
- **But... 2013 ISCD position in pediatrics**
  - Height-adjusted Z-scores
  - Total body less head and posterior-anterior spine
  - **DXA when the patient may benefit from interventions** to decrease their elevated risk of a clinically significant fracture and when the DXA results will influence that management

**Have you already performed at least one bone biopsy in the CKD children followed in your centre?**

- **Yes**
- **No=> 100%**

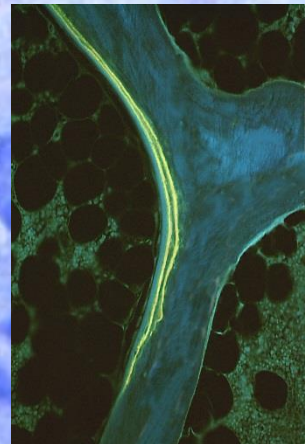
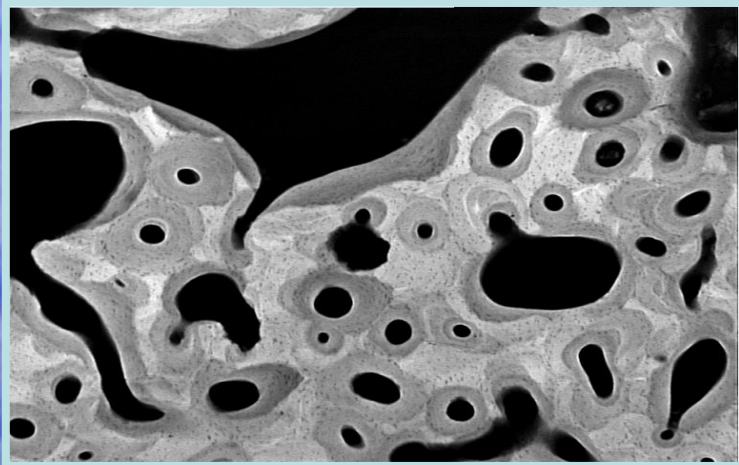
# The gold standard: bone biopsy at the iliac crest



**‘Standard’ histomorphometry**  
**Immuno-chemistry**  
**Micro-radiography**

**FTIRM** *Fourier Transform InfraRed Microspectroscopy*

...



# The gold standard: bone biopsy at the iliac crest

- Limitations

- Procedure
- Needle: Bordier *versus* Jamshidi
- Interpretation

- Indications

- K-DIGO 2009: detailed list of indications
- K-DIGO 2017: **in patients with CKD 3a-5 it is reasonable to perform a BB if knowledge of the type of renal osteodystrophy will impact treatment decisions**

- Perspectives

- **EUROD initiative**
- CKD-MBD working group of the ERA-EDTA
- Chair: P Evenepoel
- Mainly for adult patients
- An opportunity for European children???



Trocart de Meunier (8mm Ø)



Trocart de Jamshidi ou Bell, (4 mm Ø, 8G)





# Clinical consequences of pediatric renal osteodystrophy

Adynamic bone  
« *Low PTH* »

Osteitis fibrosa  
« *High PTH* »

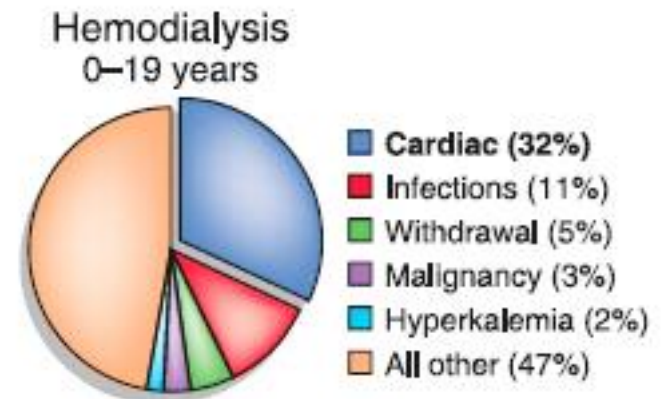
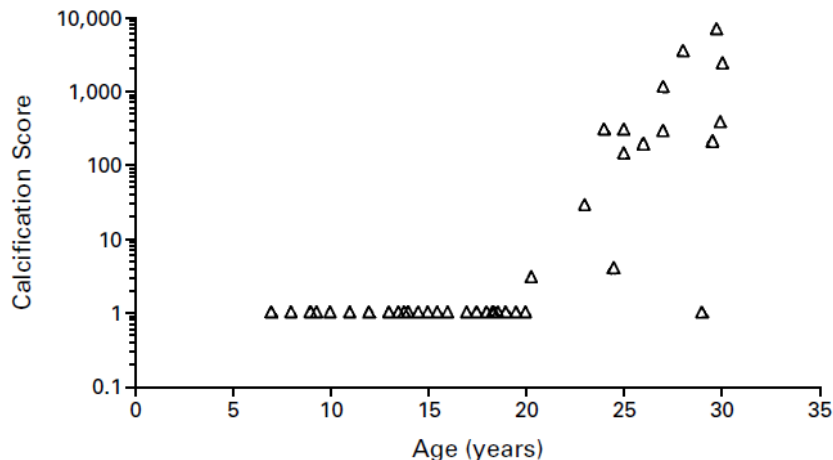
Mainly due to vitamin D analogs and calcium salts

**Growth retardation +++**

Calcifications +++

Fractures +++

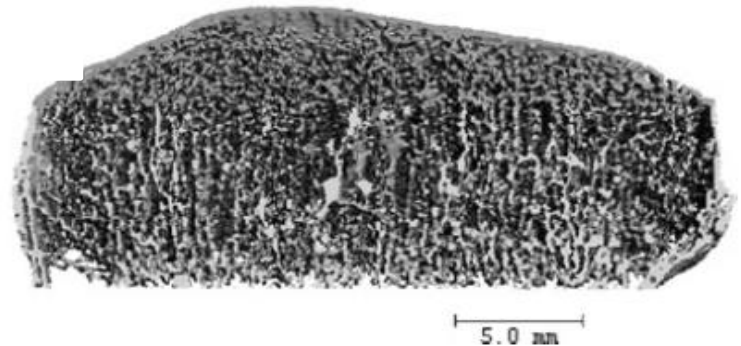
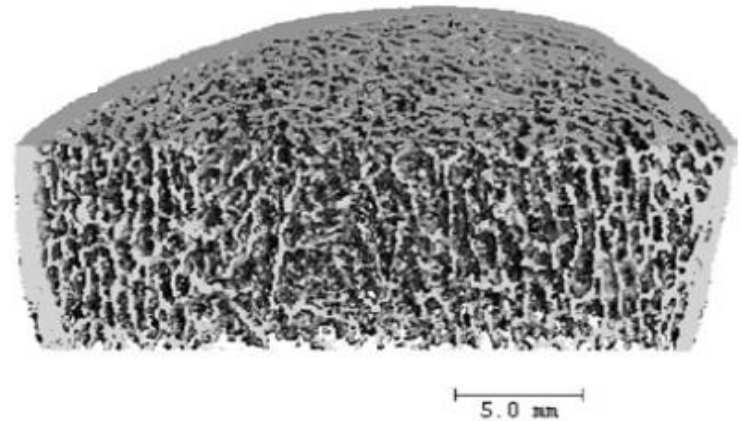
**Growth retardation +**  
Calcifications +++



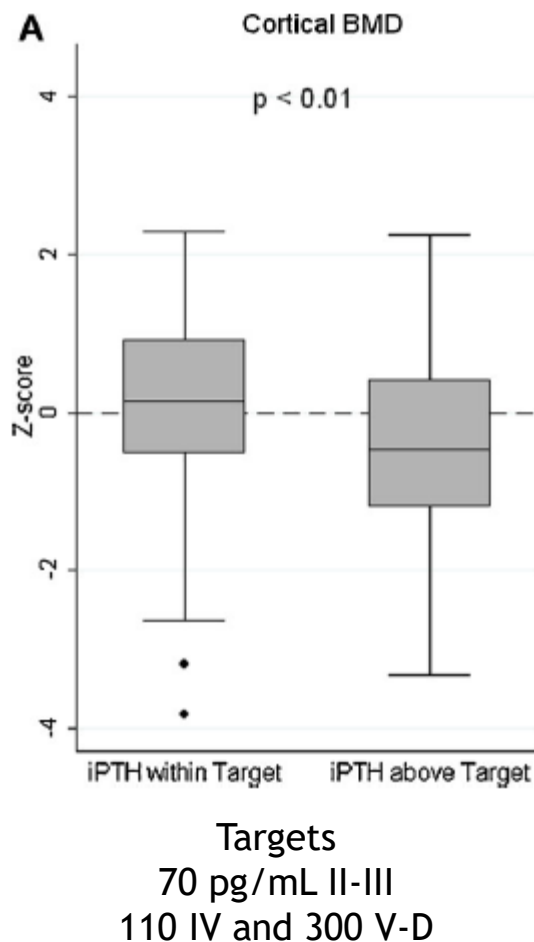
Salusky and Kuizon, 2004  
Goodman NEJM 2000  
Mistnefes 2012

# 3D bone imaging techniques: pQCT, HR-pQCT, etc

- **High Resolution Peripheral Quantitative Computed Tomography**
  - Resolution 82  $\mu\text{m}^3$
  - Irradiation  $\approx$  DXA (5  $\mu\text{Sv}$ )
  - Acquisition time: 3 minutes
  - Radius and tibia
- **Bone mineral density**
  - Total, cortical, trabecular
- **Bone microarchitecture**
  - Trabecular parameters
  - Cortical thickness / porosity
- **Biomechanical evaluation**
  - FEA: finite element analysis
  - Stiffness and failure load



# Cortical impairment and hyperparathyroidism



- **156 CKD II-III children**
  - 69 II-III: 42 (**2-521**) pg/mL for PTH
  - 51 IV-V: 140 (**8 to 770**) pg/mL
  - 36 dialysis: 267 (**10 to 1139**) pg/mL
  - Aged 5-21 years
- **831 healthy controls**
- **Tibia pQCT**
- **Secondary hyperparathyroidism associated with**
  - **Significant reduction in cortical vBMD and area**
  - **Increased cortical porosity**
  - **Greater trabecular vBMD in younger participants: anabolic effect of PTH?**

# Cortical impairment and hyperparathyroidism

- 171 patients aged 5-21 years with CKD stage 2-5D at enrollment
- 89 patients one year later
- Tibia pQCT
- **Predictors of Cortical vBMD Z-scores at baseline**
  - Lower calcium
  - Lower 25-D
  - Higher PTH
  - Higher 1-25 D
  - Independently associated with **lower cortical vBMD** at baseline
- **Cortical vBMD Z-score at baseline: associated with increased fracture risk during follow-up**
  - Hazard ratio for fracture 1.75 (95%CI: 1.15-2.67, p=0.009) per SD lower baseline cortical vBMD

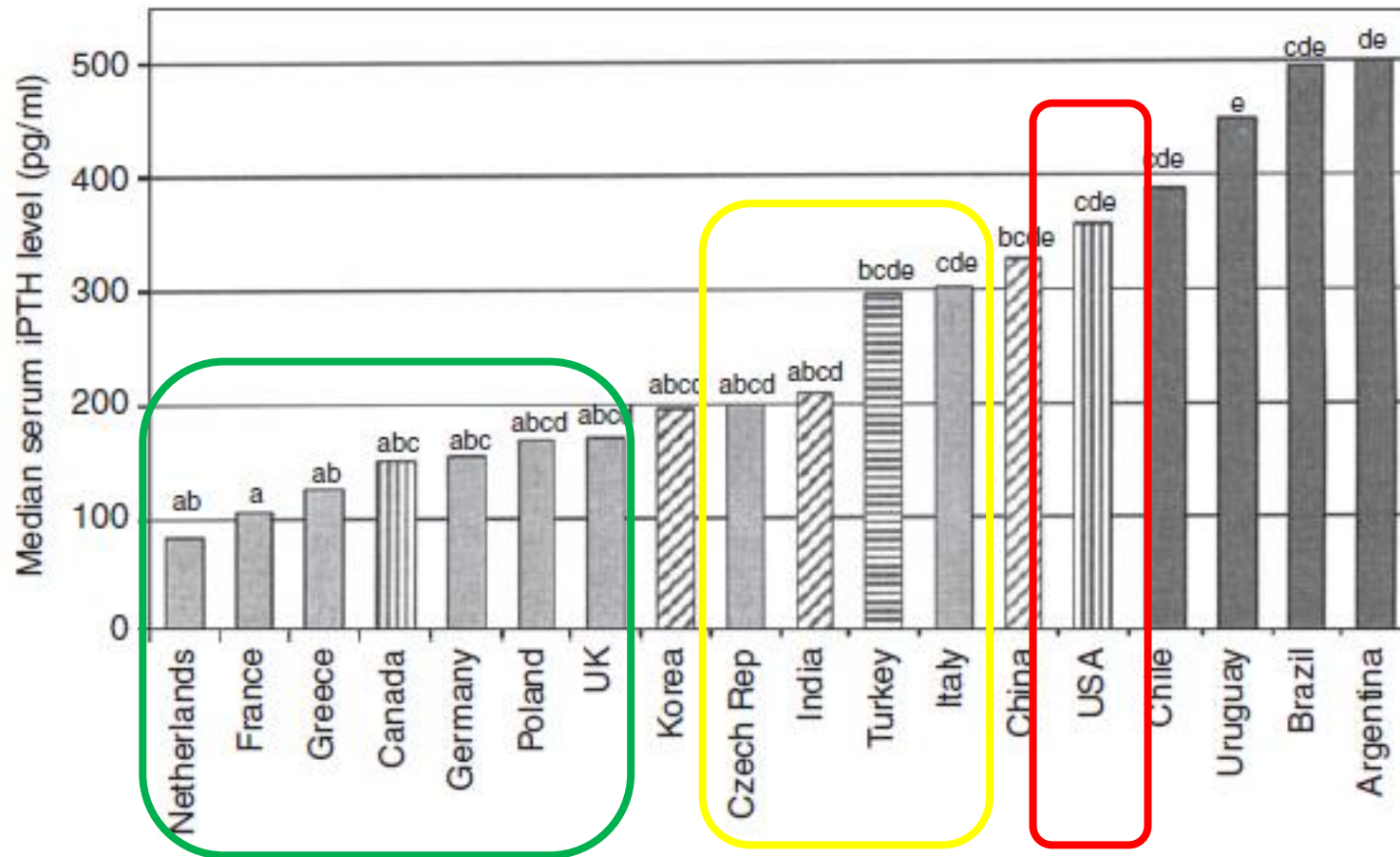
# Lower PTH levels in pre-dialysis and bone quality

|                                      | CKD patients     | Healthy peers                           |
|--------------------------------------|------------------|---|
|                                      |                  | Matched on age, gender and Tanner stage |
| N                                    | 32               |   |
| Age (years)                          | 12.9 [10.2-17.9] | 12.6 [10.0-17.8]                        |
| eGFR (ml/min/1.73 m <sup>2</sup> ) * | 33 [11-72]       | 102 [73-135]                            |
| PTH (pg/mL) *                        | 81 [9-359]       | 18 [9-34]                               |
| 25-OH D (nmol/L)                     | 70 [32-116]      | 60 [31-123]                             |
| <b>Geometry</b>                      |                  |   |
| - Tt.Ar [mm <sup>2</sup> ] *         | 588 [337-968]    | 626 [442-956]                           |
| - Ct.Ar [mm <sup>2</sup> ] *         | 66 [35-121]      | 82 [26-170]                             |
| - Ct.Th [mm <sup>2</sup> ]           | 0.69 [0.33-1.32] | 0.80 [0.28-1.48]                        |
| - Tb.Ar [mm <sup>2</sup> ]           | 506 [265-886]    | 543 [360-804]                           |
| <b>Density</b>                       |                  |   |
| - Tt.vBMD [mg/cm <sup>3</sup> ]      | 265 [186-365]    | 259 [217-369]                           |
| - Tb.vBMD [mg/cm <sup>3</sup> ]      | 201 [126-268]    | 187 [151-250]                           |
| - Ct.vBMD [mg/cm <sup>3</sup> ]      | 740 [621-898]    | 733 [607-913]                           |
| <b>Trabecular structure</b>          |                  |   |
| - BV.TV                              | 0.17 [0.11-0.22] | 0.16 [0.13-0.21]                        |
| - Tb.N [mm <sup>-1</sup> ]           | 1.72 [1.38-2.62] | 1.79 [1.58-2.43]                        |
| - Tb.Th [μm]                         | 0.09 [0.06-0.12] | 0.09 [0.07-0.12]                        |
| - Tb.Sp [μm]                         | 0.49 [0.30-0.65] | 0.47 [0.33-0.54]                        |
| - Tb.Sp.SD [μm]                      | 0.20 [0.12-0.35] | 0.20 [0.13-0.23]                        |

No differences for cortical porosity and biomechanical properties (FEA)

# When interpreting results of clinical studies on pediatric renal osteodystrophy...

## Remember that PTH levels depend on geography!





# PTH levels are associated with...

- Longitudinal growth (>500 pg/mL)
  - Vascular calcifications
  - Anemia
  - Left ventricular hypertrophy
  - Cardiovascular disease
- 
- Data from the IPPN registry
    - More than 1800 children
    - 87 centers
    - 31 countries

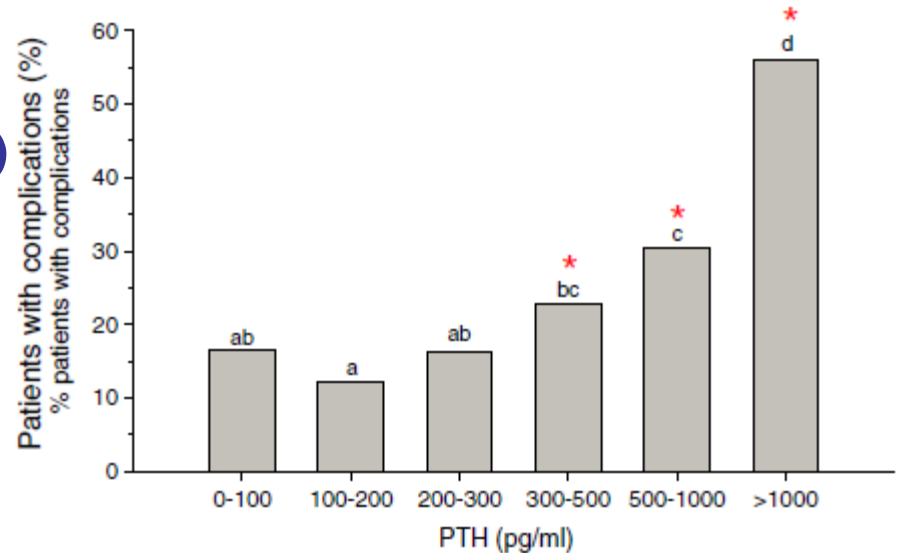


Fig. 3 Percentage of patients with alterations of bone and mineral metabolism (bone pain, limb deformities, extraosseous calcifications, radiological osteomalacia and/or osteopenia) stratified by time-averaged mean parathyroid hormone (PTH) levels. Groups sharing same letters do not differ significantly; (Fig. adapted from 39; used with permission)



## Searching the optimal PTH target in dialysis...



- **K-DOQI 2005**
  - PTH 3-5 times above the upper normal limit : **200-300** pg/mL
- **European guidelines 2006**
  - European Pediatric Dialysis Working Group
  - Keep PTH levels within 2-3 times the upper normal limit: **120-180** pg/mL
- **K-DIGO 2017**
  - PTH 2-9 times above the upper normal limit : **120-540** pg/mL
- **Limited clinical evidence**
- Data from IPNN in PD: optimal range 1.7-3 times above the upper normal limit: **100-200** pg/mL

# KDIGO 2009: one main point to keep in mind!

- It is recommended that therapeutic decisions are based on trends rather than on a single laboratory value, taking into account all available CKD-MBD measurements

| 14-year old boy<br>HD<br>CAKUT | M1                  | M2                  | M3                  |
|--------------------------------|---------------------|---------------------|---------------------|
| Calcium (mmol/L)               | 2.29                | 2.26                | 2.29                |
| Phosphorus<br>(mmol/L)         | 1.56<br><i>2.15</i> | 1.67<br><i>2.03</i> | 1.96<br><i>1.96</i> |
| 25 OH (nmol/L)                 |                     |                     | 43                  |
| PTH (15-65 pg/mL)              | 500                 | 688                 | 830                 |
| <i>PTH (pg/mL)</i>             | <i>1200</i>         | <i>920</i>          | <i>830</i>          |

# KDIGO2017: what's new (1)?

- **Evaluation of fracture risk / osteoporosis**
  - BMD assesement and bone biopsy to be considered if clinical management can be modified by the results
- **Treatment of CKD-MBD targeted at lowering high serum phosphate and maintaining serum calcium**
  - Suggested to lower elevated phosphate levels toward the normal range
  - Suggested to maintain serum calcium in the age-appropriated normal range
  - In adults suggested to restrict the dose of Ca-based binders
  - In children reasonable to base the choice of phosphate-lowering treatments on serum calcium levels
  - Suggested to limit dietary phosphate intake and to consider phosphate source (e.g., animal, vegetal and additives) to make dietary recommendations

# KDIGO2017: what's new (2)?

- **Treatment of abnormal PTH levels in CKD-MBD**
  - Optimal levels in pre-dialysis non known => evaluate for modifiable factors: hyperphosphatemia, hypocalcemia, high phosphate intake and vitamin D deficiency
  - Pre-dialysis in children: calcitriol and vitamin D analogs may be considered to maintain serum calcium levels in the age-appropriate normal range
  - Dialysis: suggested to use calcimimetics, vitamin D analogs or a combination to decrease PTH levels
- **Treatment of bone with bisphosphonates, other osteoporosis medications and rhGH**
  - In patients with biochemical CKD-MBD abnormalities and low BMD and/or fragility fractures, suggested that treatment choices take into account the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy

# For clinical practice in children : the 2006 European guidelines are still of interest

- R1: clinical, biological and radiological follow-up

**Table 1** Frequency of measurements for biochemical and radiological markers of renal osteodystrophy

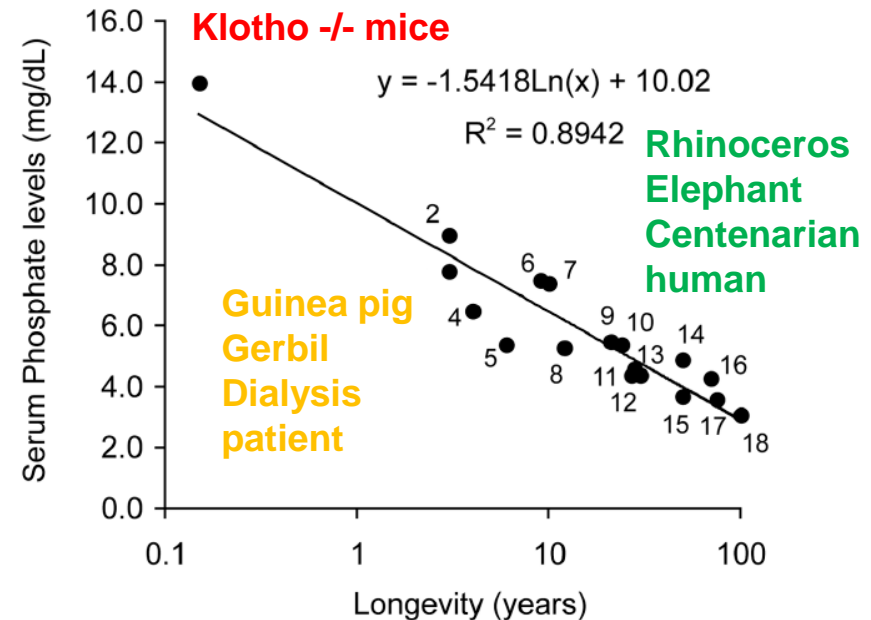
| Marker <sup>1</sup>               | Frequency of measurement (every x month) |                           |                                 | Target   |
|-----------------------------------|--|---------------------------|---------------------------------|--|
|                                   | GFR<br>59–30                             | GFR<br>29–15              | GFR <15, dialysis<br>(Evidence) |  |
| Calcium or<br>Ionized calcium     | 6  | 3                         | 1                               | Normal range (corrected calcium) <sup>2</sup><br>Normal range <sup>2</sup>   |
| Phosphate                         | 6  | 3                         | 1                               | Normal range for age band  |
| Calcium phosphorus<br>product     | 6  | 3                         | 1                               | $\leq 5.0 \text{ mmol}^2/\text{l}^2$<br>Target range $3.3\text{--}4.4 \text{ mmol}^2/\text{l}^2$ <sup>3</sup>                                  |
| Alkaline phosphatase              | 6  | 3                         | 1                               | Normal range for age band  |
| Serum bicarbonate/<br>base excess | 6  | 3                         | 1                               | Normal range, at least: bicarbonate $>22 \text{ mmol/l}$<br>Base excess $>-5 \text{ mmol/l}$   |
| Intact PTH/whole PTH              | 6  | 3                         | 1                               | Normal range in moderate CRF<br>(GFR $>29 \text{ ml/min/1.73m}^2$ )<br>Up to 2–3 times upper limit of normal<br>in advanced CRF or on dialysis |
| 25-(OH) vitamin D <sub>3</sub>    | As indicated <sup>4</sup>                | As indicated <sup>4</sup> | As indicated <sup>4</sup>       | $>20 \text{ ng/l}$   |
| Left hand and wrist X-ray         |  |                           | 6–12                            | No radiological signs of hyperparathyroidism<br>No Looser zones or osteopenia  |

Calcium: mmol/l in mg/dl:  $\times 4$ , phosphate mmol/l in mg/dl:  $\times 3.0969$ ; calcium phosphorus product:  $\text{mmol}^2/\text{l}^2$  in  $\text{mg}^2/\text{l}^2$ :  $\times 12.387$ . <sup>2</sup> Corrected calcium (mg/dl) = measured calcium concentration (mg/dl) +  $0.8 \times [4\text{-measured albumin concentration (g/dl)}]$ ; corrected calcium (mmol/l) = measured calcium concentration (mmol/l) +  $0.2 \times [4\text{-measured albumin concentration (g/dl)}]$ . <sup>3</sup> Depending on age. <sup>4</sup> Only in patients with suspected vitamin D deficiency



# For clinical practice in children : the 2006 European guidelines are still of interest

- **R2: acidosis correction**
  - Nutrition
  - Dialysis intensification
  - Sodium bicarbonate / citrate
- **R3: phosphate control**
  - Target depending on age +++
  - As soon as  $GFR < 40 \text{ mL/min/1.73 m}^2$
  - Cardiovascular risk factor
- **R4: first nutrition for phosphate control**
- **R5: then dialysis intensification**
- **R6: and last aluminum-free binders**
  - Calcium-based first
  - If hyperCa: non Ca non Al binders



# For clinical practice in children : the 2006 European guidelines are still of interest

- **R7: avoid 25-D deficiency** (but **outdated by the 2017 ESPN guidelines**)
- **R8: avoid hyperPTH**
  - Active vit D analogs (but **outdated by the 2017 ESPN guidelines**)
- **R9: PTH target: 2-3 upper normal limit in ESRD**
- **R10: if increased PTH levels and phosphate < 2 mmol/L**
  - Active vit D analogs
  - Very few data for calcimimetics (in the mean time 2017 European approval by EMA for cinacalcet in pediatric dialysis)

# For clinical practice in children : the 2006 European guidelines are still of interest

- **R11: no rhGH in case of severe hyperparathyroidism**
  - Before rhGH: nutrition and acidosis correction => *EPSN guidelines coming soon (D Haffner)*
- **R12: in case of hyperCa**
  - Stop vit D analogs
  - Stop Ca-based binders
  - Decrease the calcium concentration in the dialysate
- **R13: PxCa product**
  - To keep it below 5 mmol<sup>2</sup>/L<sup>2</sup>
- **R14: parathyroidectomy**
  - Rarely performed

# CKD-MBD

## *A balance between bone and vessels*

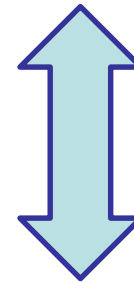


Renal osteodystrophy

Fracture risk

Growth retardation

Bone pains and deformations



**Adults**

The better the bone  
The better the vessels

Vascular calcifications

Pathophysiology

Same biomarkers than bone

Vitamin D, PTH, FGF23...

# Bone and vessels in children with CKD

## Is there a relationship?

- Cross-sectional study (local ancillary from the 4C cohort)
  - 32 teenagers pre-dialysis CKD
    - **Bone** assessment HR-pQCT
    - **Vascular** evaluation, ABPM



- **The greater the trabecular thickness and density**
- The greater the ABPM, and notably the diastolic and the mean BP
- Two major determinants for blood pressure (mean and diastolic, night, day, and 24-hour) by multivariable analyses: serum calcium and trabecular thickness

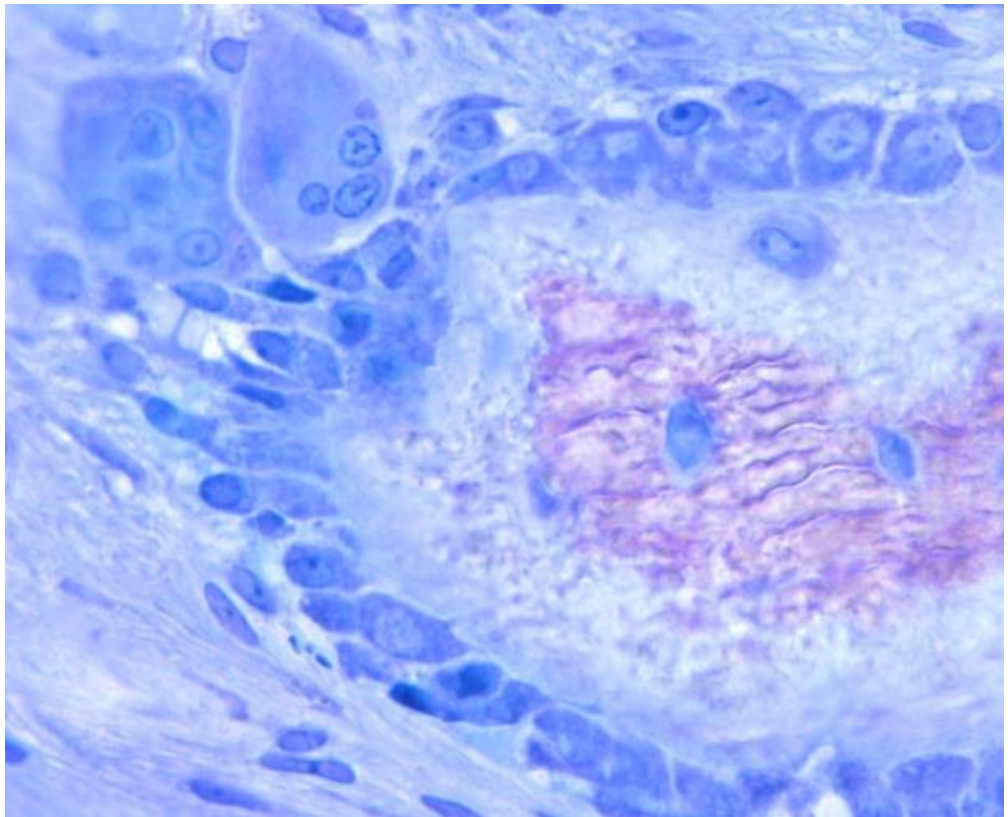
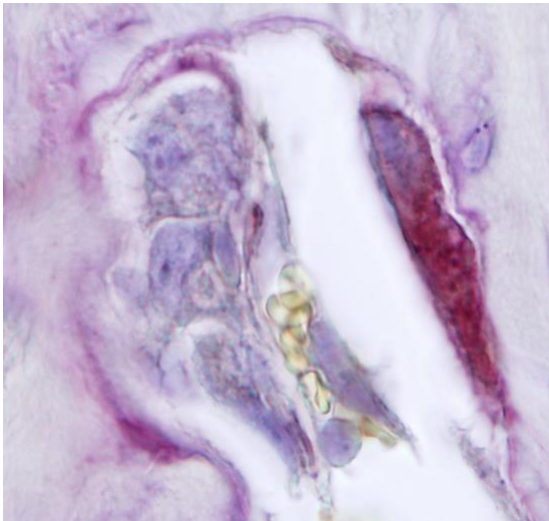
=> In a growing skeleton: 'the better the bone, the worse the vessel'

# So... do we give too much calcium to CKD children (at least in Lyon)?

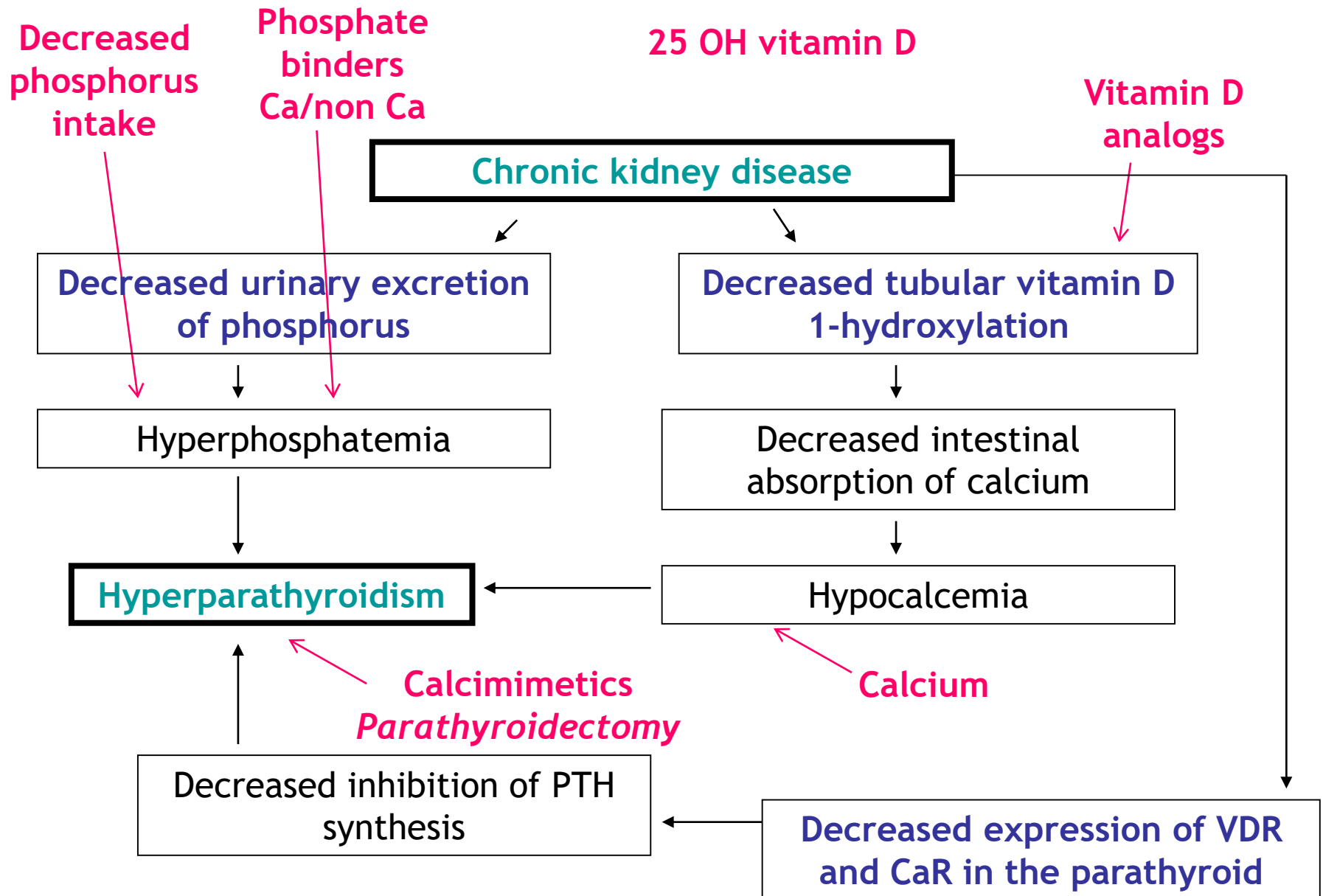
- **Not giving enough calcium supplements may be deleterious for bone in pediatric CKD**
- **Histomorphometry:** defective skeletal mineralization associated with lower calcium levels.
- **Histomorphometry:** 160 children on PD; serum calcium concentrations inversely related to mineralization (but not turnover)
- **Tibial pQCT:** lower calcium levels independently associated with baseline and progressive cortical deficits
- **Recent data from CKiD:** phosphate binder treatment (predominantly calcium-based) associated with a significant lower fracture risk
- All these data thus provide **a strong rationale for giving calcium supplementation in pediatric CKD**, at least for bone quality and quantity.
- **Giving too much calcium supplements may also be deleterious for vessels**
- Meta-analysis in adults: increased mortality risk with calcium-based phosphate binders
- No specific pediatric data



# Management of CKD-MBD in children



## The cornerstones of CKD-MBD management



# Native vitamin D therapy and prevention of secondary hyperparathyroidism in pediatric CKD

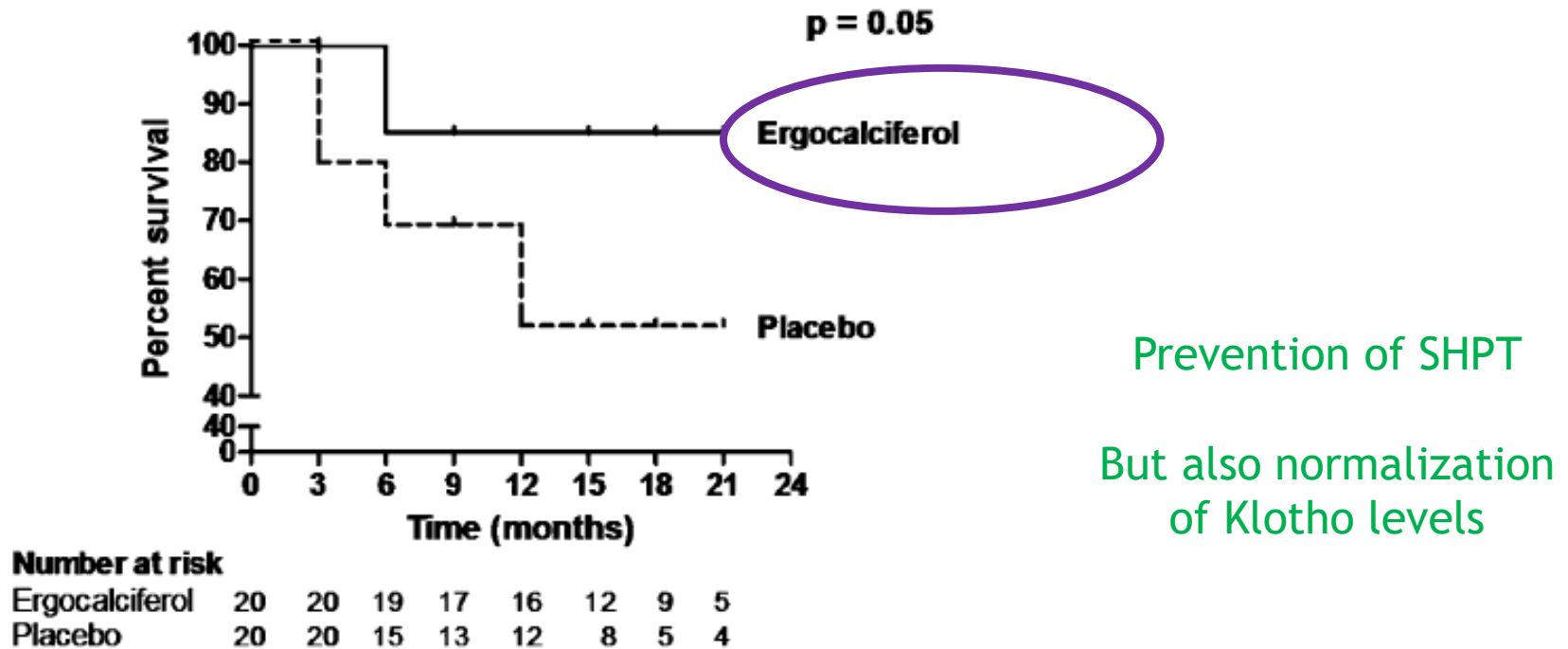


Figure 3. | Time to development of secondary hyperparathyroidism in ergocalciferol and placebo-treated patients.

Randomized controlled trial  
Ergocalciferol *versus* placebo, 20 CKD 2-4 per group

# Practical summary of the native vit D European guidelines

- Target 75-120 nmol/L
- Daily supplementation, D2 or D3; if sequential D3

| Intensive replacement phase |                          |  |  |
|-----------------------------|--------------------------|--|--|
| Age                         | 25(OH)D serum (nmol/L)** | Vitamin D supplementation dose (daily) | Monitoring   |
| < 1 year                    |                          | 600 IU / day                           | - Serum calcium and urinary calcium levels – 1-3 monthly based on CKD stage<br>- 25(OH)D level: after 3 months |
| >1 year*                    | < 12                     | 8000 IU / day                          |  |
|                             | 12 - 50                  | 4000 IU / day                          |  |
|                             | 50 – 75                  | 2000 IU / day                          |  |
| Maintenance phase           |                          |  |  |
| < 1 year                    | >75***                   | 400 IU / day                           | - 25(OH)D level: 6-12 monthly  |
| >1 year*                    |                          | 1000 - 2000 IU /day based on CKD stage |  |

\* Consider adjusting dose by body size (weight or body surface area)

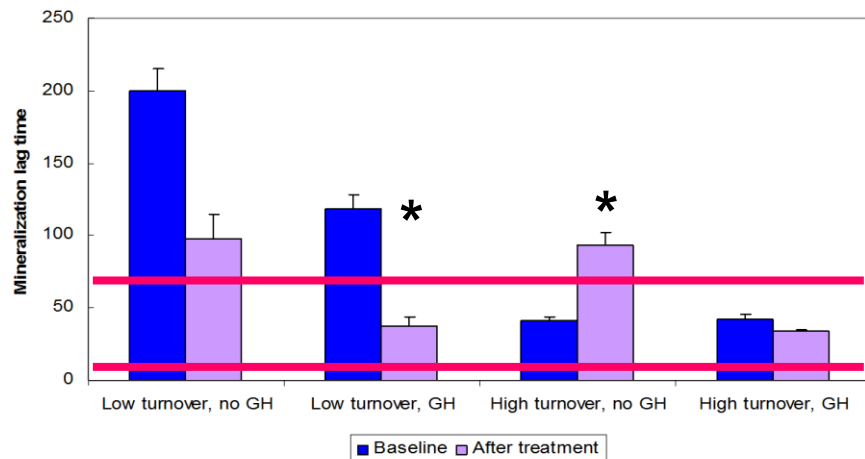
\*\* To convert nmol/L to ng/ml divide by 2.5

\*\*\* If levels remain <75nmol/L, then give doses as per the 'Intensive replacement' schedule for a further course of intensive replacement and recheck levels

# rhGH therapy improves mineralization, whatever the type of the underlying osteodystrophy

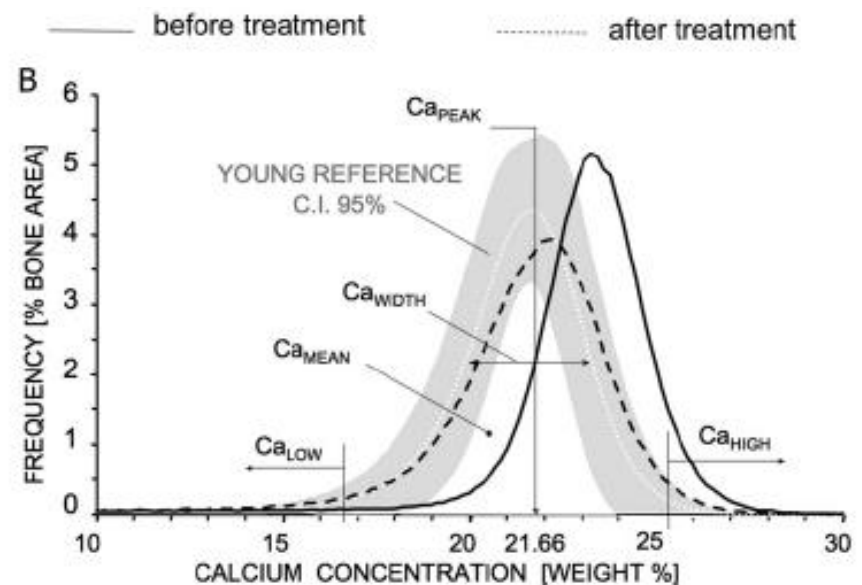
## • Study from USA

- Randomized trial: 33 children, PD
- **Low Turnover LTO**, n= 14, rhGH or nothing
- **High Turnover HTO**, n= 19, GH + calcitriol IP or calcitriol IP
- rhGH for 8 months



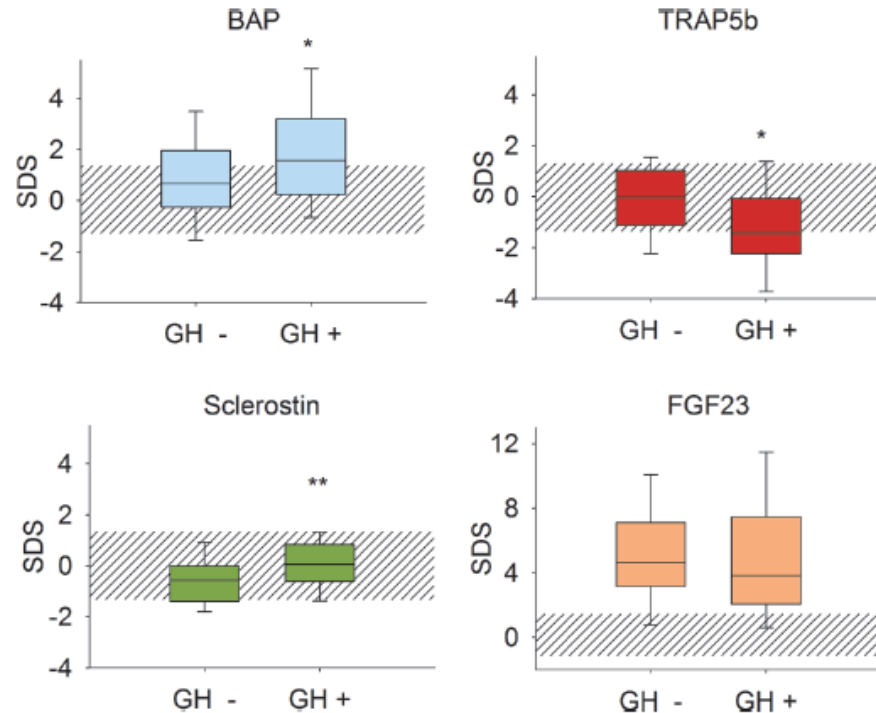
## • Study from Austria and Poland

- 18 children, hemodialysis
- rhGH for one-year
- Paired analysis before/after
- **Baseline: high prevalence of low bone turnover**



# Markers of bone metabolism are influenced by GH therapy in pediatric CKD

- **European study 4C**
  - 556 children
  - CKD
  - eGFR 10-60
  - Age 6-18 years
  - 41 rhGH
  - 41 matched controls

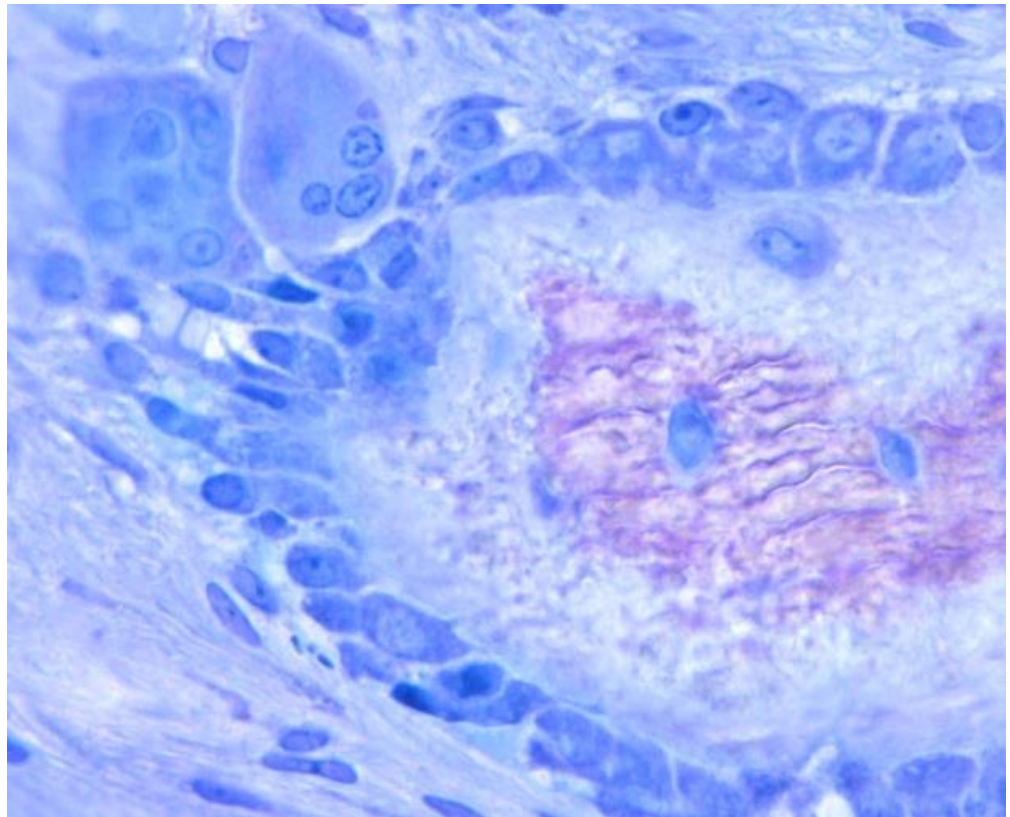
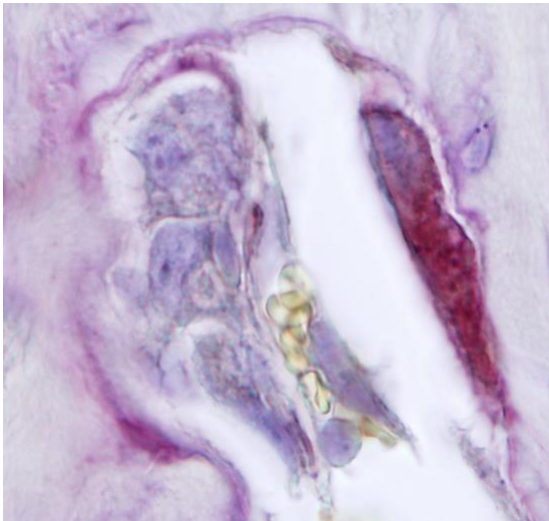


**Fig 3. Distribution of serum bone marker concentrations in children with and without rhGH treatment (n = 41 per group).** Data are expressed as standard deviation scores (SDS). The shaded area depicts the normal range (5<sup>th</sup> to 95<sup>th</sup> percentile of biomarker concentrations in healthy children)<sup>8</sup>. Asterisks indicate significant deviation from distribution in the reference population (\*: p < 0.05, \*\*: p < 0.01).

doi:10.1371/journal.pone.0113482.g003



# Conclusion and perspectives



# CKD-MBD in pediatric CKD...

## Which management in 2018?

- **A global management**
  - Denutrition
  - Anemia
  - **Acidosis**
- **A management focused on mineral metabolism**
  - **Nutritional intake: phosphate**
  - **Native vitamin D deficiency: target 75-120 nmol/L**
  - **Phosphate binders**
    - Calcium carbonate
    - Sevelamer
    - Lanthanum
    - New binders currently evaluated => sucroferric oxyhydroxide
  - **Vitamin D analogs**
  - **Calcimimetics**
    - Cinacalcet
  - **Dialysis intensification**
  - *Parathyroidectomy*
- **And a management targeting not only growth but also bone**
  - Recombinant growth hormone therapy

# Take-home messages

- **CKD-MBD: Bone and vessels**
- **A close interaction between these two compartments**
- **A growing skeleton**
- The question of calcium supplementation in pediatric CKD remains open
- Exact threshold that would become too much?
- International trials required...
- **On the long-term**
- Bone pain, fracture, deformations
- Vascular calcifications, but also...
- Quality of life
- Social and professional reintegration
- Improved self-esteem

