Nutrition in Children with Chronic Kidney Disease

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Levitt R, Zaritsky JJ, Mak RH
Pediatric Kidney Disease Textbook 2016

Aims of Nutrition Management in children with CKD

- Enable normal growth and development
- Minimize mortality and co-morbidities
- Maintain normal body habitus and electrolytes
- Delay CKD progression

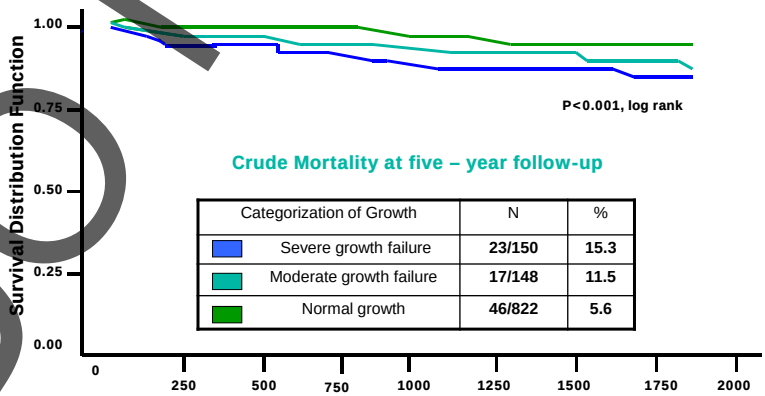
Height Status of children with CKD

Age range (years)	Height SDS after 1 month on dialysis	Height SDS at transplantation
0–1	–2.45	–1.98
2–5	–1.98	–2.34
6–12	–1.69	–2.07
>12	–1.30	–1.49

Abbreviation: SDS, standard deviation score. Permission obtained from the North American Pediatric Renal Trials and Collaborative Studies Online.[9]

Rees L, Mak RH. Nature Reviews Nephrology 7:615-623, 2011

Impact of growth failure on mortality in children with ESRD



Crude Mortality at five – year follow-up

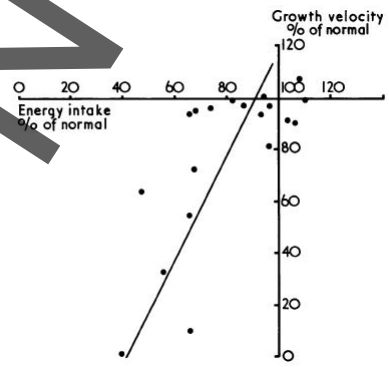
Categorization of Growth	N	%
Severe growth failure	23/150	15.3
Moderate growth failure	17/148	11.5
Normal growth	46/822	5.6

Furth S et al Ped Nephol 2002

Nutrition & Growth in CKD

- **Energy**

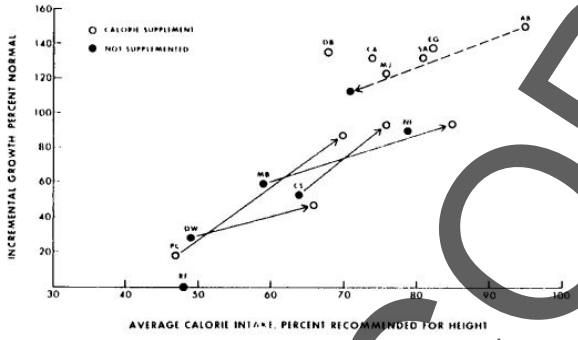
Growth correlates with energy intake in children with CKD



Relation between growth velocity, expressed as percentage of expected 50th centile velocity, and energy intake, expressed as percentage of that recommended for same age (r=0.72; P<0.001)

Betts PR, Magrath G. British Med J 2:189-193, 1974

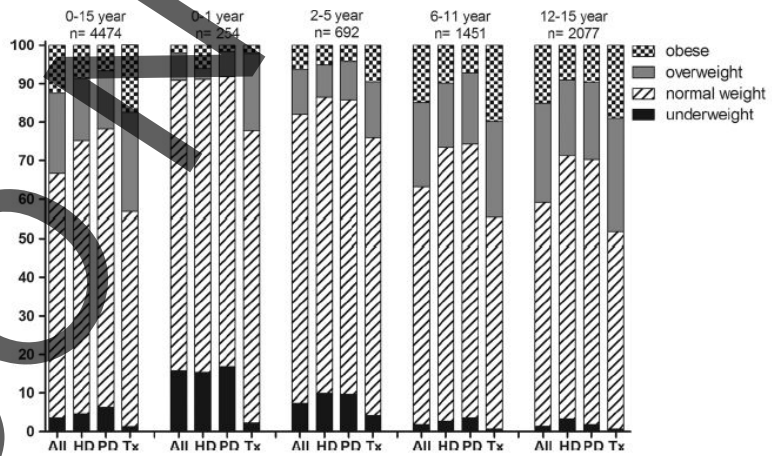
Calorie supplements improve growth in children with CKD



Calorie intake and incremental growth of children on hemodialysis

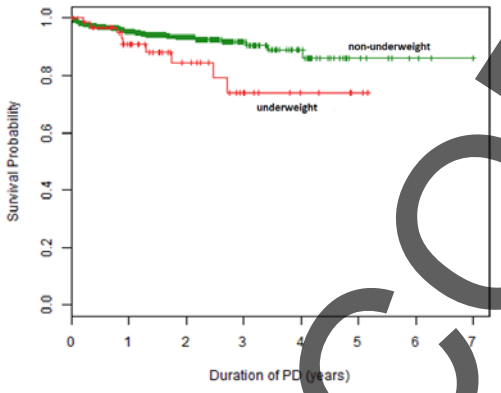
Simmons JM et al. N Engl J Med 285:653-656, 1971

Prevalence estimates for body habitus status stratified by treatment modality and age



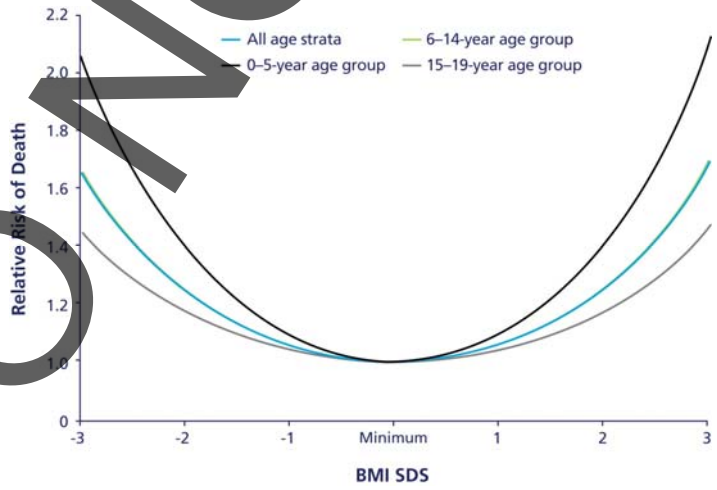
Bonthuis M et al. Nephrol Dial Transplant 2013.

Impact of weight status on survival



Schaefer F et al Sci Rep 2019

BMI and mortality in children with ESRD



Wong et al AJKD 2002

Energy intake recommendations in children with CKD

1. Initial recommendation in CKD 2-5 – same SDI as children of same chronological age
2. In children with suboptimal weight and growth, intake should be towards the high end of SDI or slightly above
3. In overweight children, adjust intake to achieve appropriate weight gain without compromising nutrition

Shaw V & Pediatric Renal Nutrition Task Force Ped Neph 2019

Nutrition in children with CKD

- Energy
- **Protein**

Protein intake recommendations in children with CKD

1. Target protein intake in CKD 2-5 at upper end of SDI for optimal growth
2. Lowest end of SDI range is minimal safe amount
3. Protein intake should be higher in children on dialysis to account for dialysis losses
4. In children with high BUN, protein intake should be at lower end of SDI after excluding offer causes of high BUN

Shaw V & Pediatric Renal Nutrition Task Force Ped Neph 2019

Nutrition prescription in children with CKD

1. Breast feeding preferred in infants
2. Whey dominant infant formulas if 1) not possible
3. Breast milk or formula fortified for fluid restriction
4. Dietary supplements introduced gradually to maximize acceptance and tolerance
5. Solid food, progression to texture and content.
6. Balanced diet and food choices

Shaw V & Pediatric Renal Nutrition Task Force Ped Neph 2019

Nutrition prescription in children with CKD

7. Oral feeding is preferred.
8. Oral stimulation if 7) not possible, to avoid food aversion
9. Prompt intervention once weight percentile deteriorates
10. Nutrition supplements for inadequate diet intake after medical intervention for e.g. GI reflux
11. Supplemental or exclusive enteral tube feeding to improve nutritional status for inadequate oral intake.

Shaw V & Pediatric Renal Nutrition Task Force Ped Neph 2019

Nutritional Assessment

- **Dietary Assessment**
- Every 2 weeks to once a year
- Depending on age and CKD stage
- Prospective or retrospective

Nutritional Assessment

- **Dietary Assessment**
- Maconutrients:
- Vitamins
- Minerals

Nutritional Assessment

Anthropometric Assessment

- Height, weight, head circumference
- Percentile charts
- Growth WHO charts < 2 yr
- CDC charts > 2 yr
- BMI should be relative to height age (because of growth failure & delayed bone age)

Nutrition in children with CKD

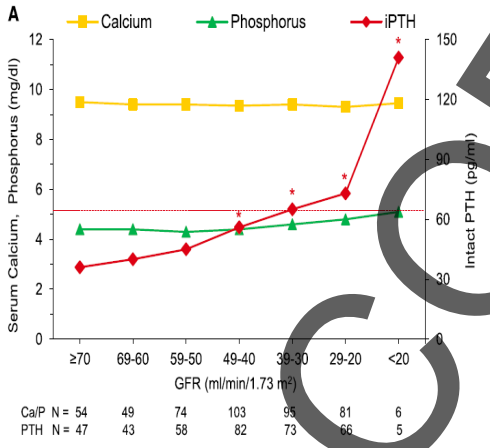
- Energy
- Protein
- Mineral Bone Disorder

Growth failure and bone disease in children with CKD

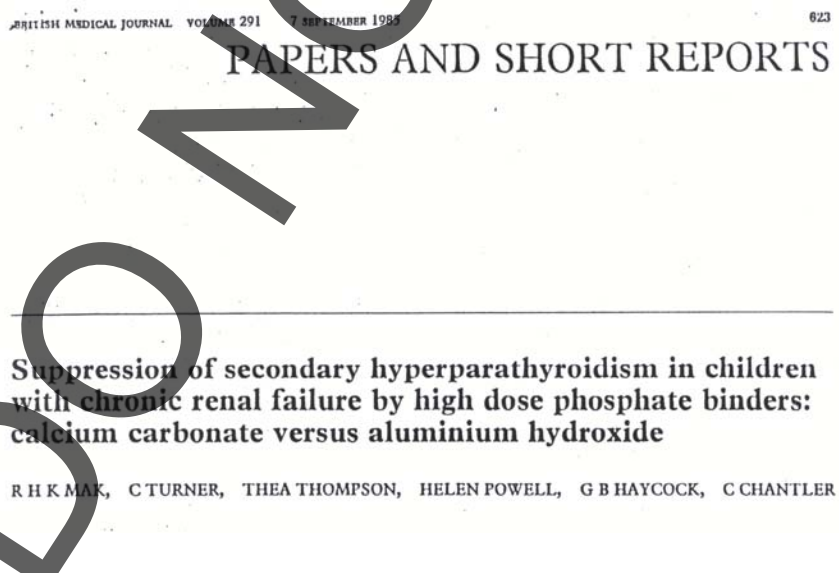
	Total cohort[a]
Height <−2 SD	153 (61.9%)
Clinical manifestations of bone disease	91 (36.8%)
Deformities	63 (25.5%)
Pathological fractures	33 (13.4%)
Aseptic bone necrosis	32 (13.0%)
Mild disabling bone disease	26 (10.5%)
Severe disabling bone disease	18 (7.3%)
Invalidating bone disease (all)	44 (17.8%)

Groothoff J et al. Kidney Intl 63:266-275, 2003

Mineral and hormone values according to estimated GFR in children with CKD



Portale A et al. CJASN 9:344-353, 2014

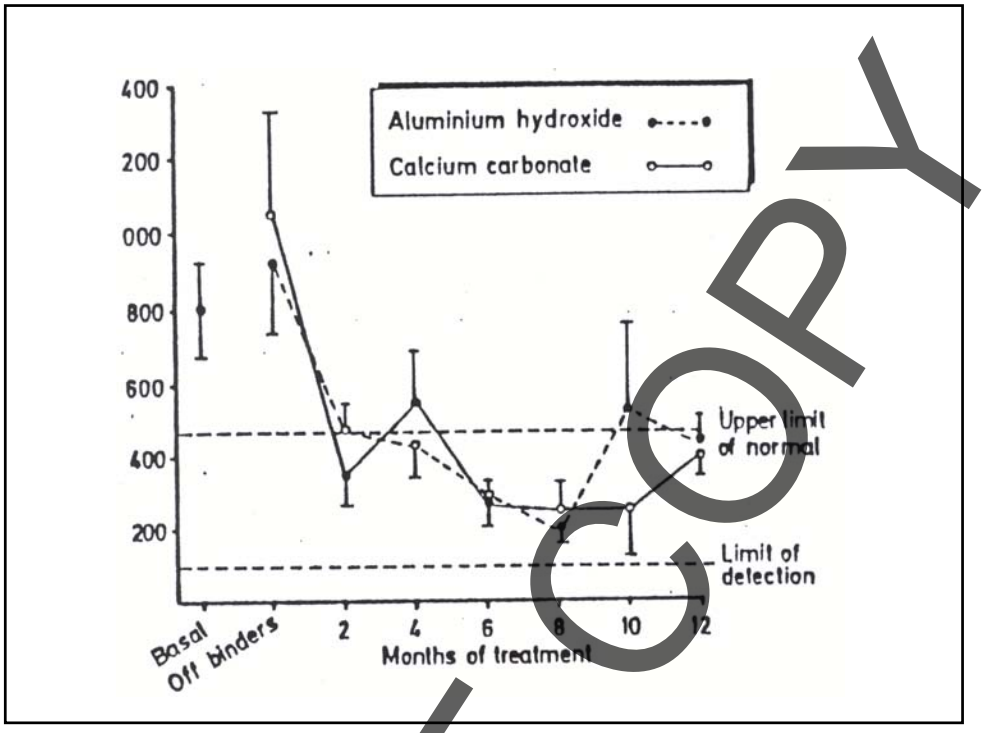


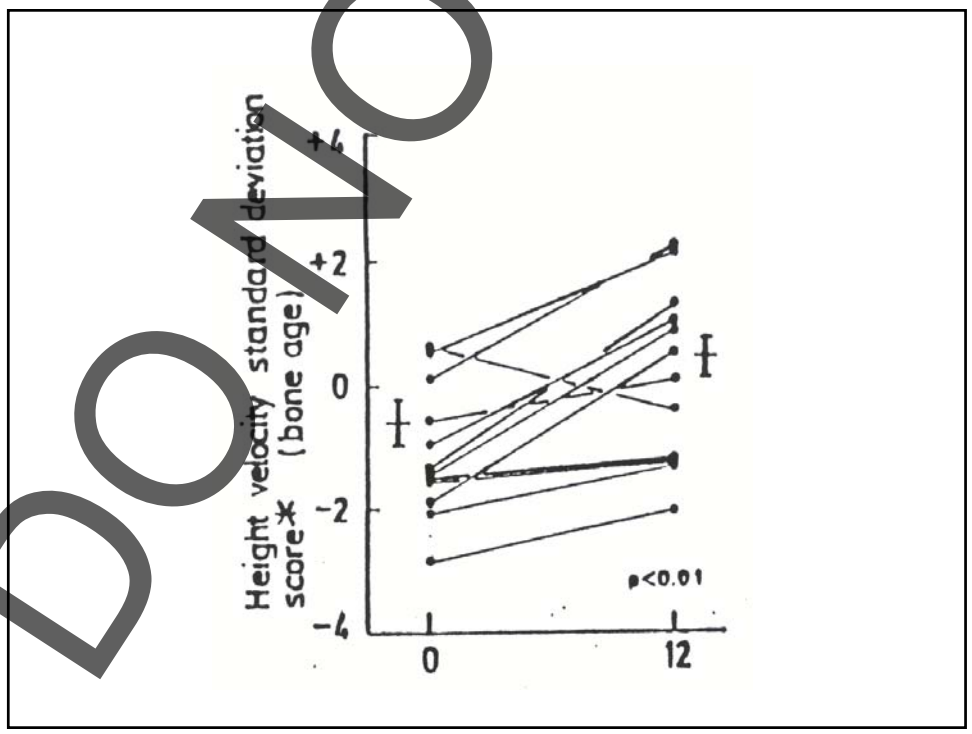
BRITISH MEDICAL JOURNAL VOLUME 291 7 SEPTEMBER 1985 623

PAPERS AND SHORT REPORTS

Suppression of secondary hyperparathyroidism in children with chronic renal failure by high dose phosphate binders: calcium carbonate versus aluminium hydroxide

R H K MAK, C TURNER, THEA THOMPSON, HELEN POWELL, G B HAYCOCK, C CHANTLER


Aluminium hydroxide
Calcium carbonate
400
200
000
800
600
400
200
Upper limit of normal
Limit of detection
Basal Off binders
2
4
6
8
10
12
Months of treatment


Height velocity standard deviation score* (bone age)
+4
+2
0
-2
-4
p<0.01
0
12

Long term outcome of PTH suppression

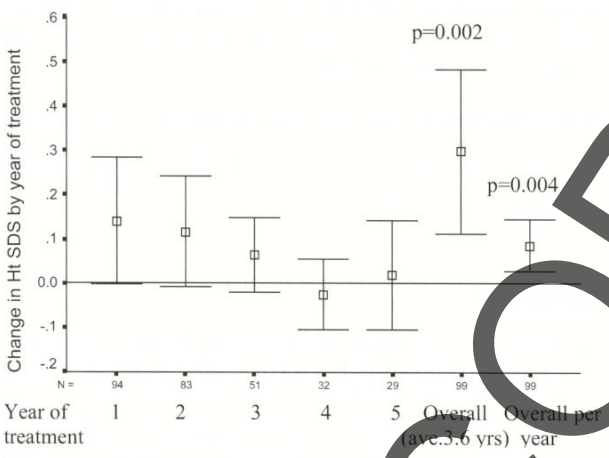
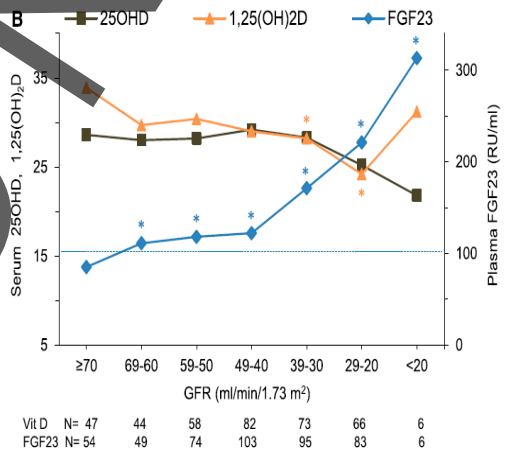


Fig. 1 Change in height standard deviation score (SDS) per year by year of treatment (*error bars* represent 95% confidence intervals), with overall data also shown in last two data points

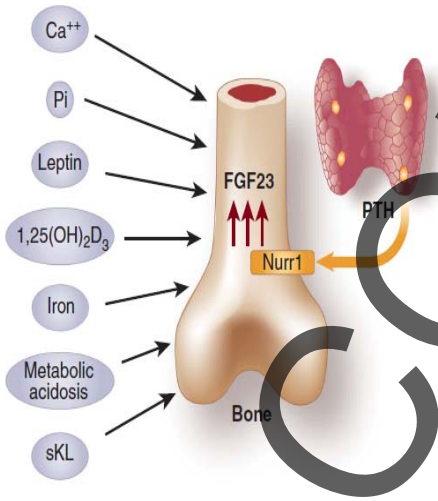
Tamanaha K, Mak RH et al Ped Neph 1987

Mineral and hormone values according to estimated GFR in children with CKD



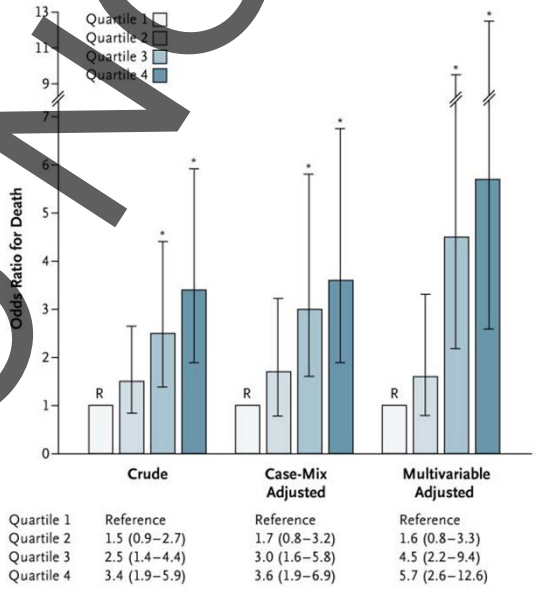
Portale A et al. CJASN 9:344-353, 2014

Schematic representation of currently known inducers of FGF23 production



Lanske B et al. Kidney Intl 86:1072-1074, 2014

Serum FGF-23 & Morality in CKD



	Crude	Case-Mix Adjusted	Multivariable Adjusted
Quartile 1	Reference	Reference	Reference
Quartile 2	1.5 (0.9–2.7)	1.7 (0.8–3.2)	1.6 (0.8–3.3)
Quartile 3	2.5 (1.4–4.4)	3.0 (1.6–5.8)	4.5 (2.2–9.4)
Quartile 4	3.4 (1.9–5.9)	3.6 (1.9–6.9)	5.7 (2.6–12.6)

Gutierrez OM et al NEJM 2008

CKD-MBD Management 2017 LEVEL 1 (We recommend)

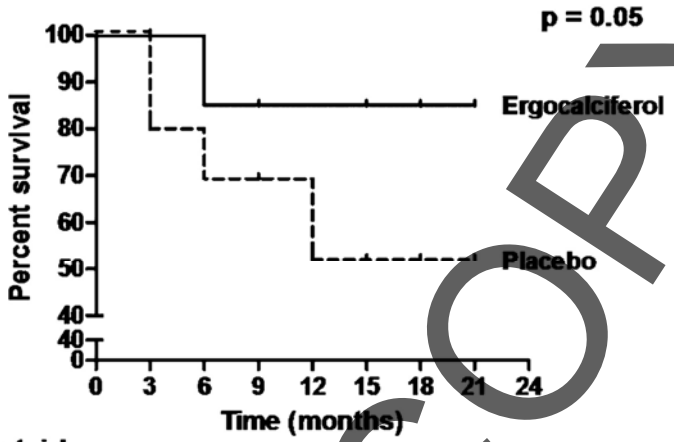
- In patients with CKD stages 3-5, therapeutic decisions should be made on laboratory trends rather than single values. (1C)
- For CKD stage 3-5, oral aluminum-containing PO4 binders should be avoided. For CKD stage 5, aluminum contamination of dialysate should be avoided. (1B)
- For CKD stage 2-5, infants should be measured quarterly and children should be measured annually. (1C)
- For CKD stage 2-5, growth retarded children should be treated with growth hormone after first addressing malnutrition and biochemical abnormalities related to CKD-MBD (1A)

KIDGO. Kidney Intl Suppl 7:1-59, 2017

CKD-MBD Management 2017 LEVEL 2 (We suggest)

- In patients with CKD 3-5, we suggest lowering elevated phosphate levels toward the normal range (2C)
- In adult patients with CKD 3-5, we suggest avoiding hypercalcemia (2C).
- In children with CKD 3-5, we suggest maintaining serum calcium levels in the age-appropriate normal range (2C)
- In patients with CKD 5, we suggest using dialysate calcium concentration between (2.5 and 3.0 mEq/L) (2C)

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



Number at risk

Ergocalciferol	20	20	19	17	16	12	9	5
Placebo	20	20	15	13	12	8	5	4

Rukshana Shroff et al. CJASN 2012;7:216-223

CJASN

Vitamin D therapy

- In patients with CKD 3-5 not on dialysis, we suggest that calcitriol and vitamin D analogs not be routinely used (2C).
- It is reasonable to reserve the use of calcitriol and vitamin D analogs for patients with CKD 4-5 with severe and progressive hyperthyroidism (not graded).
- In children, calcitriol and vitamin D analogs may be considered to maintain serum creatinine levels in the age appropriate normal range (not graded)
- In patients with CKD 5 requiring PTH-lowering therapy, we suggest calcimimetics, calcitriol or vitamin D analogs, or a combination of calcinmimetics

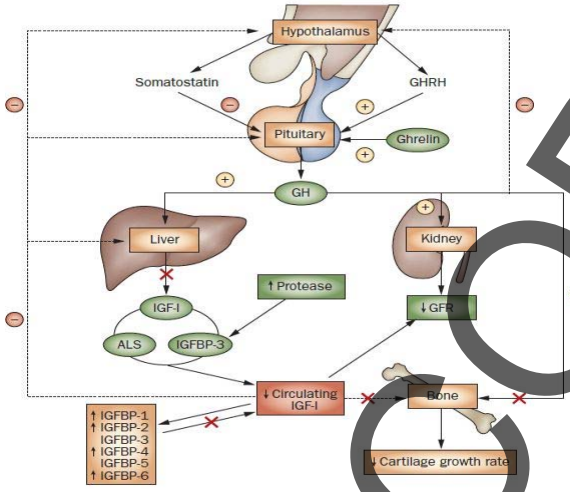
Phosphate-lowering therapies

- Dietary phosphate restriction - quality of phosphate sources (animal vs vegetarian)
- Dialysis frequency
- Phosphate binders
  - Aluminum based
  - Calcium-containing binders
  - Sevelamer
  - Lanthanum
  - Magnesium
  - Novel iron based binders: sucroferric oxyhydroxide and ferric citrate
- Phosphate transport inhibitors: Tenapanor and nicotinamide

Nutrition in children with CKD

- Energy
- Protein
- Mineral Bone Disorder
- **Growth hormone axis**

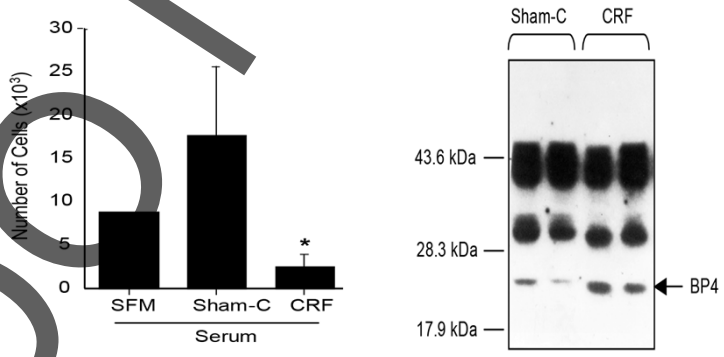
The deranged GH and IGF-I axis in CKiD



Rees L, Mak RH. Nature Reviews Nephrology 7:615-623, 2011

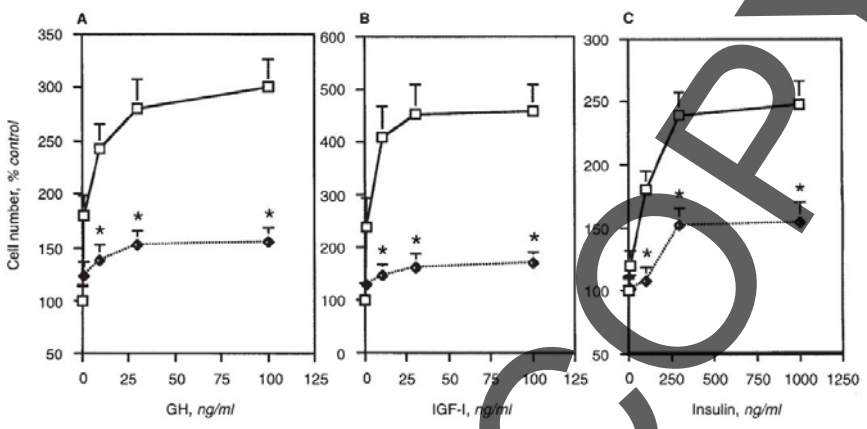
Impact of IGFBP in CKD growth

Growth of growth-plate chondrocytes in uremic sera



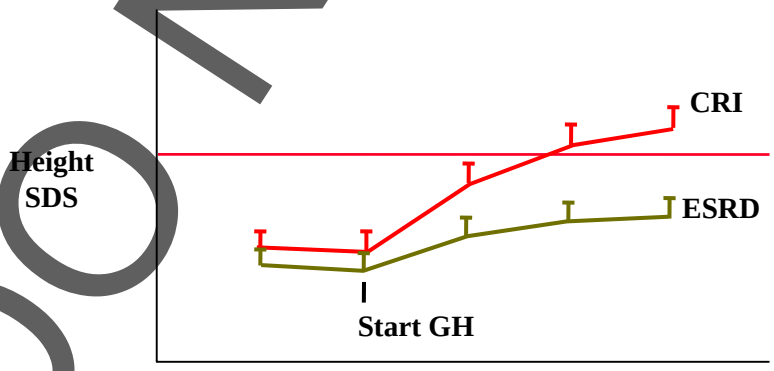
Mak RH, Chang SL, Pak YK.
Experimental & Molecular Medicine 36:243-250, 2004

Ex-vivo Growth-Plate Chondrocytes from CRF rats Are Resistant to GH, IGF-I and Insulin

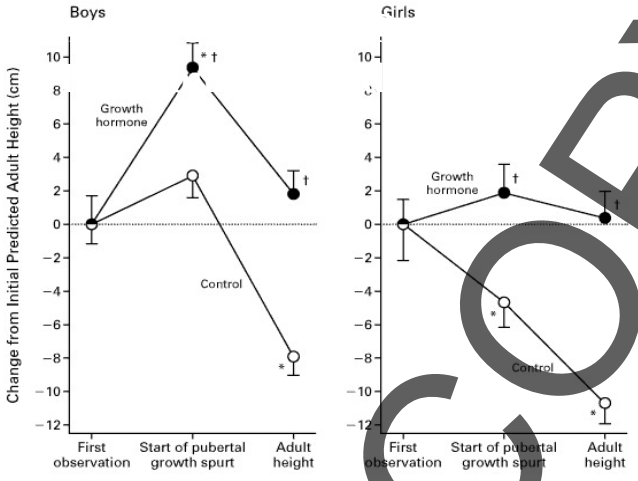


Mak RH, Pak YK. Kidney International 50:400-406, 1996

Efficacy of GH Therapy in Children with CKD



Tönshoff B, et al. J Nephrol 1995



Haffner D et al. N Engl J Med 2000;343:923-930.

Safety of GH Therapy: Issues Specific to CKD

- No acceleration in bone age
- No acceleration in progression to ESRD
- Transient elevation in insulin levels
- No change in glucose levels or Hb A1C
- Infrequent anti-GH antibody does not affect growth outcomes

Fine RN, et al. J Pediatr 1994
Hokken-Koelega AC, et al. Lancet 1991
Hokken-Koelega AC, et al. J Clin Endocrinol Metab 1994
Saenger P, et al. Pediatr Nephrol 1996
Haffner D, et al. Pediatr Res 1998
Hertel NT, et al. J Pediatr Endocrinol Metab 2002

NKF K/DOQI Recommends Correction of GH-Independent Variables Prior to GH

GUIDELINE	
	Prior to considering the use of GH therapy, correct: • Insufficient intake of energy, protein, and other nutrients • Acidosis: HCO_3 <22 mmol/L may require oral alkali therapy or increased HCO_3 content in dialysate • Hyperphosphatemia (serum phosphorus should be less than 1.5 x the upper limit for age) • Secondary hyperparathyroidism: Maintain intact PTH at level appropriate to CKD stage

NKF K/DOQI Pediatric Guidelines for Nutrition in Chronic Renal Failure, 2000

Aims of Nutrition Management in children with CKD

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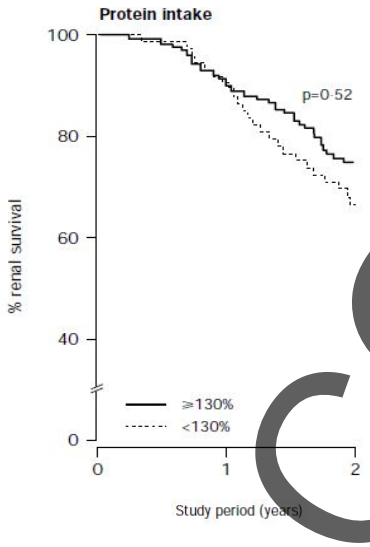
- Maintain normal body habitus and electrolytes
- Delay CKD progression

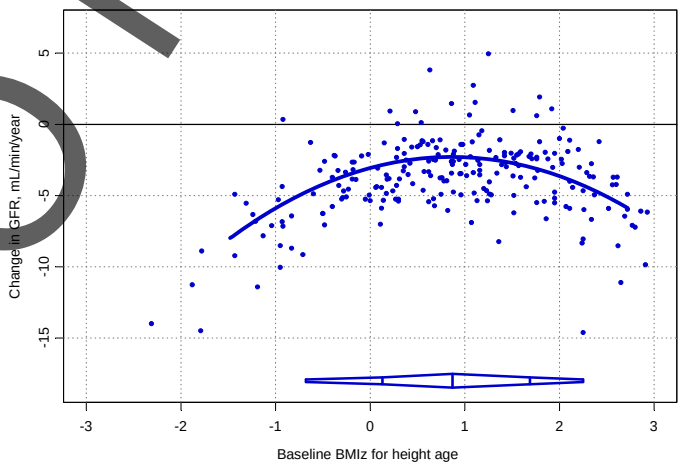
Impact on low protein diet in children with CKD



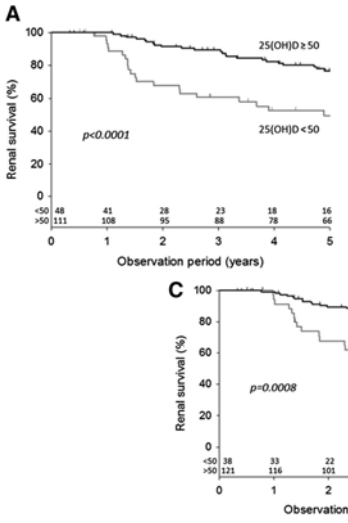
Wingen A-M et al. Lancet 349:1117-1123, 1997

Chronic Kidney Disease in Children

BMI & CKD Progression



25(OH)D levels predict 5-year renal survival.

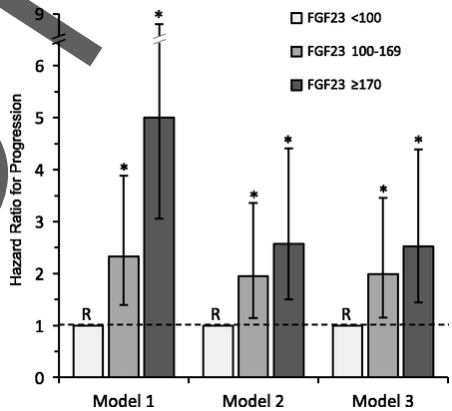


Rukshana Shroff et al. JASN 2016;27:314-322

JASN

Chronic Kidney Disease in Children

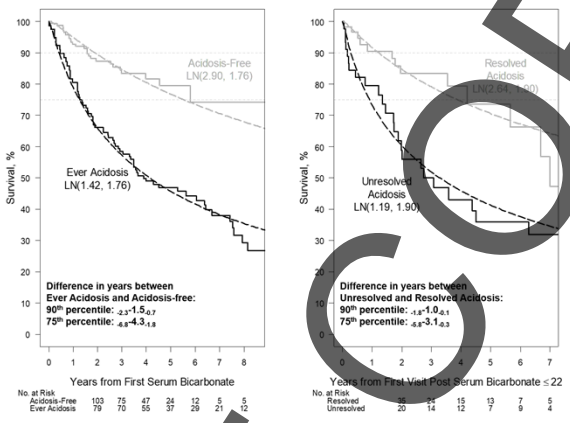
Impact of FGF-23 on CKD progression



Portale AA et al CJASN 2016

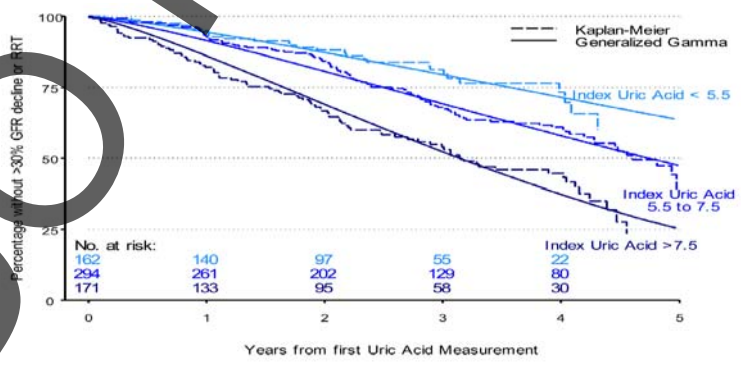
Chronic Kidney Disease in Children

Acidosis and CKD progression



Chronic Kidney Disease in Children

Hyperuricemia and CKD Progression



Rodenbach KE et al. Am J Kidney Dis 66:984-992, 2015

Aims of Nutrition Management in children with CKD

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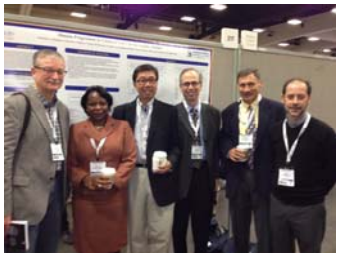
- Minimize mortality and co-morbidities
- Maintain normal body habitus and electrolytes
- Delay CKD progression

Acknowledgements



Funding:

- ***NIH R24HD050837, U01 DK-03-12***
- ***US-Israel Science Foundation, Cystinosis Research Foundation***

1. The following statements are correct about energy homeostasis & growth in children with CKD
   a. Total calorie intake is most important in promoting growth
   b. Increasing energy intake will improve both height and weight equally
   c. Children with CKD have higher caloric needs
   d. Undernutrition or low BMI is a growing problem currently
   e. Linear growth correlates best with mortality & mobidity

Levitt R, Zaritsky JJ, Mak RH
Pediatric Kidney Disease Textbook 2016

2. Bone Mineral Disorder in children with CKD
    a. Dietary phosphorus restriction should start with CKD stage 4-5
    b. PTH should be maintained below 2X normal range for all stages of CKD
    c. Phosphorus binders : total dosage is the most important, not administration times
    d. 1,25 vitamin D level is the most important vitamin D level to monitor
    e. Bone mineral disorder should be optimized before growth hormone consideration

Oliveira E et al. Pediatr Nephrol 33:789-798. 2018

3. BMI in children must be expressed as a percentile or Z-score adjusted by:
    a. Age
    b. Ethnicity
    c. Height age
    d. CKD staging
    e. Parental BMI

Levitt R, Zaritsky JJ, Mak RH
Pediatric Kidney Disease Textbook 2016

4. Considerations before starting growth hormone in children with CKD involves:

a. Insufficient intake of energy, protein, and other nutrients
b. Acidosis: HCO_3 <22 mmol/L may require oral alkali therapy or increased HCO_3 content in dialysate
c. Hyperphosphatemia (serum phosphorus should be less than 1.5 x the upper limit for age)
d. Secondary hyperparathyroidism: Maintain intact PTH at level appropriate to CKD stage
e. All of the above

Levitt R, Zaritsky JJ, Mak RH
Pediatric Kidney Disease Textbook 2016

5. Nutritional assessment in CKD

a. Frequency should be yearly for all ages
b. Frequency should be the same for all CKD stages
c. A 3-day dietary assessment can be done any time of the week to provide convenience
d. Energy requirment may be more than 100% RDA to allow for catch up growth
e. Energy requirement should be 100% RDA for all children

Levitt R, Zaritsky JJ, Mak RH
Pediatric Kidney Disease Textbook 2016

Answers

1. e
2. e
3. c
4. e
5. d