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NUTRITION MANAGEMENT OF INFANT WITH RENAL DISASES

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OBJECTIVES

* To understand why premature infants are at higher risk for renal failure
* To learn unique nutrition requirements of premature infants
* To review causes of CKD (Chronic Kidney Disease) in newborns
* To apply pediatric renal nutrition goals in the setting of premature/term infants with CKD

OUTLINE

1. NICU basics
2. Nephrogenesis and prematurity
3. Premature nutrient requirements
4. Renal Disease in Neonates
5. Intervention – Medical and Nutrition

1. NICU BASICS

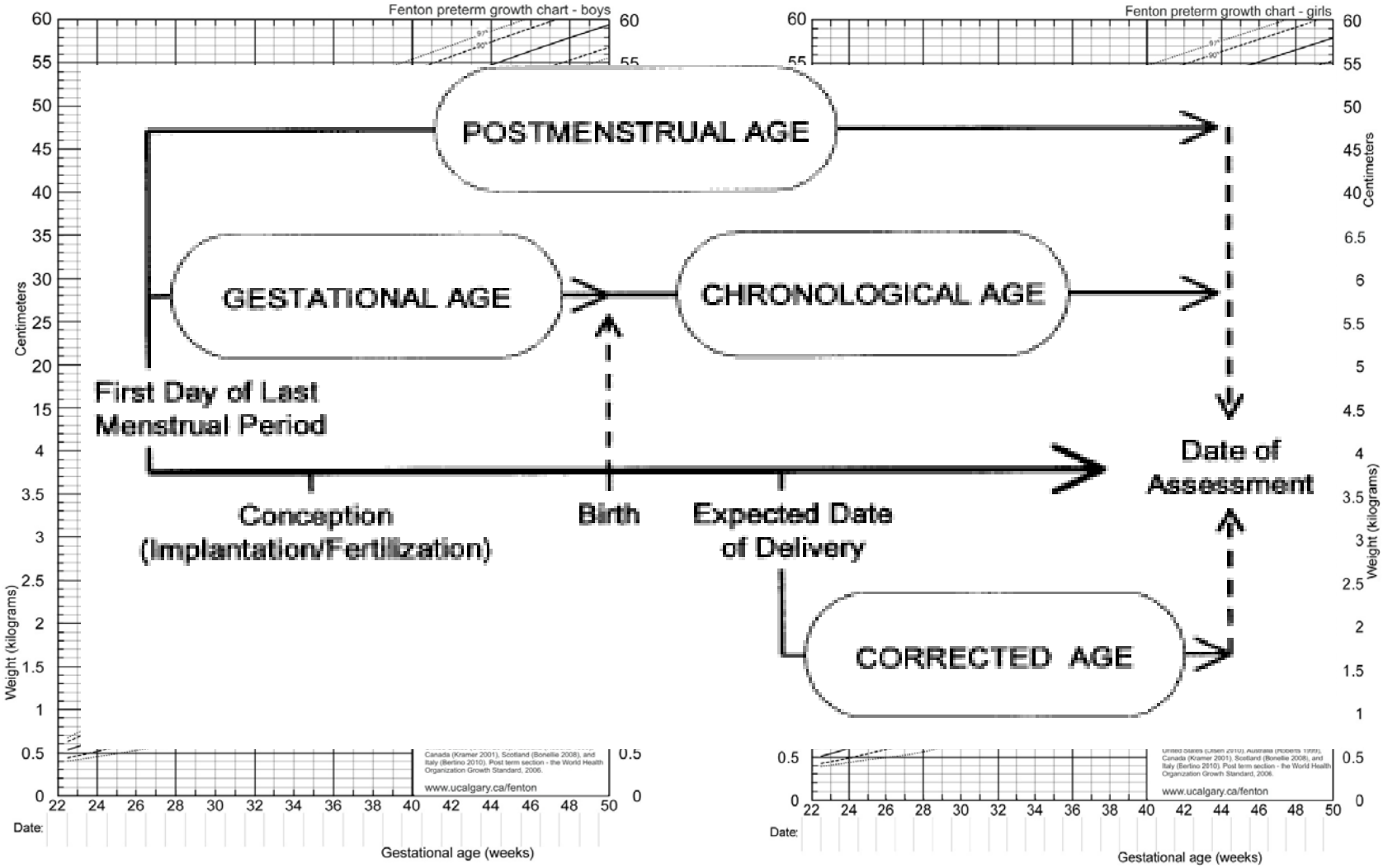
Newborn classifications
Anthropometric goals
Growth charts

Classifications

Gestational Age	Premature: <37 wks Term: 37 – 42 wks Post-term: >42 wks
Birth Weight	LBW: <2500 g VLBW: <1500 g ELBW: <1000 g
Weight for Age	SGA: <10th percentile AGA: 10th to 90th percentile LGA: >90th percentile

Anthropometric Goals

Premature	15-20 g/day .8-1.1 cm/week (length) .5-.6 cm/week (HC)
Term	20 – 30 g/day .69-.75 cm/week (length) .5 cm/week (HC)



Fenton Growth Chart (Boys)

Fenton Growth Chart (Girls)

2. NEPHROGENESIS AND PREMATURITY

Nephrogenesis and Prematurity

* Nephrogenesis starts 22 days after conception and start function at 37 days.
* Continues until **36 wks gestation** - then it's over!
* **60% of nephrons** are formed during the 3rd trimester
* **Autopsy studies have shown a very strong correlation between BW, GA, and glomerular number and size**

Consequences

Franke D. et al, 2010

* 435 children with CKD
* Prevalence of SGA was 3 X higher in children with CKD compared to normal controls
* 1/3 of children with CKD born premature

Greenbaum et al, 2011

* Analysis of CkiD study
* 400 children with CKD
* 17% were LBW
* 14% were SGA
* 40% were in a NICU
* LBW and SGA higher incidence of short stature

TAKE HOME MESSAGE

* Assume some degree of renal insufficiency when assessing premature infants in the NICU
* Remember the higher risk these children will have for CKD as they get older

3. PREMATURE NUTRIENT REQUIREMENTS

NORMAL NUTRIENT NEEDS FOR PREMATURE INFANTS

	PARENTERAL	ENTERAL
Calories *120 kcals/kg is typical initial goal	90-100 kcals/kg	110-150 kcals/kg*
Protein	3.2-4.0 g/kg	3.4 – 4.4 g/kg
Sodium	3-5 meq/kg/d	3-5 meq/kg/d
Potassium	2-3 meq/kg/d	2-3 meq/kg/d
Calcium Term: 210 mg/day	60-80 mg/kg/d	100 – 220 mg/kg/d
Phosphorous Term: 100 mg/day	45-60 mg/kg/d	60 – 140 mg/kg/d
Fluid *150 mls/kg is typical goal	90-180 mls/kg/d	90-220 mls/kg/d*

Tsang 2005

Protein Needs by Gestational Age

Adapted from Tsang, et al 2005

For a complete listing of all nutrient requirements recommended see Tsang, et al 2005

Gestational Age	Protein (g/kg)
26 - 30 weeks	3.8 – 4.4
30 - 36 weeks	3.4 – 4.2
36 – 40 weeks	2.8 – 3.4

In General, Nutrient Needs are Higher for Premature Infants.

Goal is to Provide Nutrient Concentrations that will match Fetal Accretion Rates.

4. RENAL DISEASE IN NEONATES

A. Acute Kidney Injury (AKI)

Incidence of AKI

TABLE 1

Recent Estimates of AKI Incidence in Various Neonatal Populations

Study	Study Population	AKI Definition	Number of Infants	AKI Incidence
Viswanathan et al[141]	Extremely LBW (<1000 g)	Serum creatinine ≥1.5 mg/dL or urine output <1 mL/kg/h	472	12.5%
Koralkar et al[142]	Very LBW (<1500 g)	AKIN[55]	229	18%
Selewski et al[143]	Asphyxiated newborns undergoing therapeutic hypothermia	AKIN	96	38%
Kaur et al[144]	Infants ≥34 wk gestation with asphyxia (Apgar <7 at 1 min after birth)	AKIN	36	41.7%
Blinder et al[145]	Infants <90 d old with congenital heart disease undergoing surgery	AKIN	430	52%
Gadepalli et al[146]	Infants with congenital diaphragmatic hernia requiring extracorporeal membrane oxygenation	RIFLE[147]	68	71%

Box 1.

Proposed neonatal AKI classification

Modified from Jetton JG, Askenazi DJ. Update on acute kidney injury in the neonate. Curr Opin Pediatr 2012;24(2):191–6.

Stage	SCr	Urine Output
0	No change in SCr or increase <0.3 mg/dL	≥0.5 mL/kg/h
1	SCr increase ≥0.3 mg/dL within 48 h or SCr increase ≥1.5–1.9 × reference SCr[a] within 7 d	<0.5 mL/kg/h for 6–12 h
2	SCr increase ≥2 to 2.9 × reference SCr[a]	<0.5 mL/kg/h for ≥12 h
3	SCr increase ≥3 × reference SCr[a] or SCr ≥2.5 mg/dL or Receipt of dialysis	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

[a] Baseline SCr is defined as the lowest previous SCr value.

Jetton JG, Askenazi DJ. Acute kidney injury in the neonate. Clin Perinatol. 2014; 41:487-502.

AKI
Causes

* Prerenal
* Renal (Intrinsic)
* Postrenal

Remember that AKI can occur in both non-CKD babies as well as CKD babies

AKI
PRERENAL

* Usually due to **inadequate renal perfusion**
  * Dehydration
* Kidney is intrinsically normal
  * But remember nephrogenesis not complete if premature
* **Most common reason for AKI in NICU**
* Can lead to CKD if not corrected: ATN and/or acute cortical necrosis with scarring

AKI
INTRINSIC

* **ATN** - from ischemic/hypoxic events
* **Drug Induced** - Gentamicin, Tobramycin, Ibuprofen, Indomethacin
* **Vascular Insults** – Renal (artery or vein) Thrombosis
* **Infectious** – Sepsis, Pyelonephritis

AKI
POSTRENAL

* Obstructive Uropathy
* Post Urethral Valves
* Neurogenic Bladder

4. RENAL DISEASE IN NEONATES

B. CHRONIC KIDNEY DISEASE (CKD)

Disorders resulting in neonatal CKD

Adapted from Flynn JT, Mitsnefes M, Pierce C, et al. Blood pressure in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children study. Hypertension 2008;52(4):631–7.

- Aplastic/hypoplastic/dysplastic kidneys[a]
- Autosomal dominant polycystic kidney disease
- Autosomal recessive polycystic kidney disease[a]
- Obstructive uropathy (posterior urethral valves)[a]
- Pyelonephritis
- Reflux nephropathy
- Renal infarct[a]
- Syndrome of agenesis of abdominal musculature[a]

[a] May result in need for dialysis in neonatal period.

Classification of CKD in Neonates

* The typical diagnostic criteria of GFR < 60 (KDOQI) does not apply until > 2 years old.

* The updated Schwartz formula: *eGFR= 0.413xheight/Scr does not apply in children 0 – 2 yrs old*

* *Normal GFR in newborn period is significantly < 60*

Glomerular filtration rate (GFR) in healthy infants as assessed by inulin clearance

Age	Mean GFR ± SD (mL/min/1.73 m^2)
Preterm babies	
1–3 d	14.0 ± 5
1–7 d	18.7 ± 5.5
4–8 d	44.3 ± 9.3
3–13 d	47.8 ± 10.7
8–14 d	35.4 ± 13.4
1.5–4 mo	67.4 ± 16.6
Term babies	
1–3 d	20.8 ± 5.0
3–4 d	39.0 ± 15.1
4–14 d	36.8 ± 7.2
6–14 d	54.6 ± 7.6
15–19 d	46.9 ± 12.5
1–3 mo	85.3 ± 35.1

Abbreviation: SD, standard deviation.

Adapted from Schwartz GJ, Furth SL. Glomerular filtration rate measurement and estimation in chronic kidney disease. Pediatr Nephrol 2007;22(11):1840.

KDIGO classification schemata for CKD for ages less than 2 years

Neonatal CKD Classification	GFR
Normal GFR	GFR ≤1 SD below the mean
Moderately reduced GFR	GFR >1 SD to ≤2 SD below the mean
Severely reduced GFR	GFR >2 SD below the mean

Abbreviations: KDIGO, Kidney Disease: Improving Global Outcomes; SD, standard deviation.

Adapted from Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International Supplements 2013;3(1). Jan 1; with permission.

Factors Influencing Lab Assessment

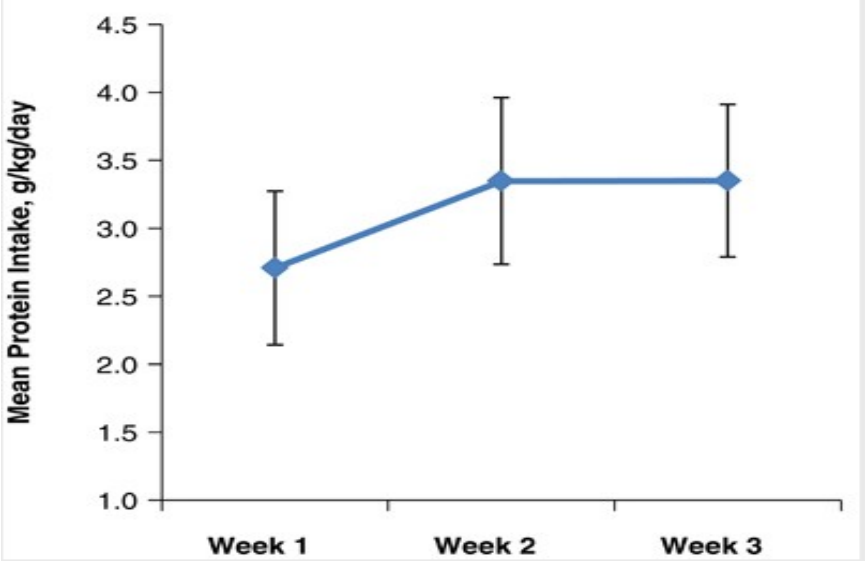
BUN

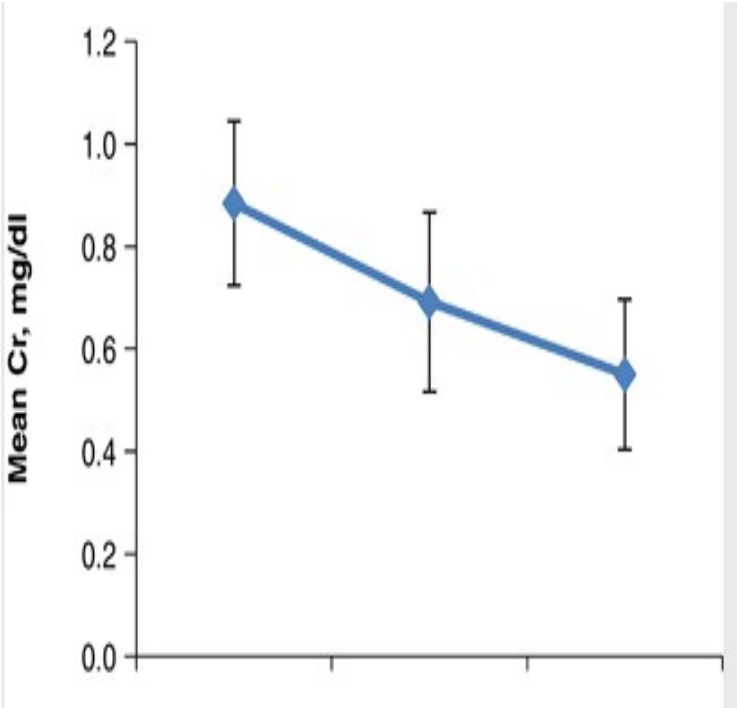
* Normal BUN levels are higher with lower GA and BW
* Elevated BUN levels are often cited as reason for limiting AA or protein intake

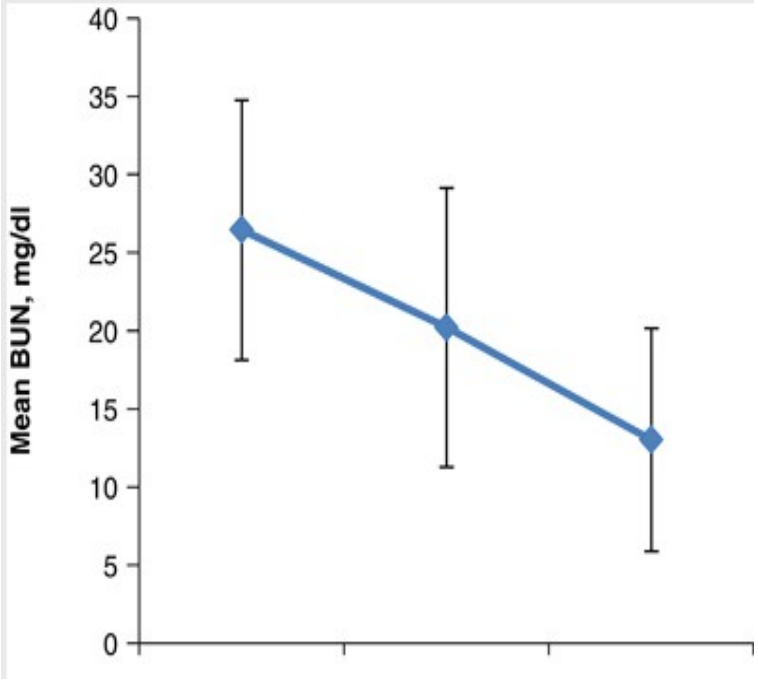
BUN

* **Weintraub AS et al. Impact of renal function and protein intake on blood urea nitrogen in preterm infants in the first 3 weeks of life. J of Perinatol. 2015; 35: 52-56.**

* 249 infants, all <30 wks gestation at birth
* Provided recommended protein/AA intakes over the 1st 3 weeks of life (range: 2.1 – 3.9 g/kg)
* Measured BUN, Cr and protein/AA intake for each week







Weintraub AS et al 2015

Creatinine

* High at birth; reflects mother's level.
* Transient increase (2 -5 days) initially reflecting diuresis. Can take up to 3-4 wks to normalize in a premature infant.
* These higher levels the 1st month also reflect incomplete nephrogenesis.
* Normal range:
  * Newborn: .3-1.0 mg/dl
  * Infant: .2-.4 mg/dl

Factors Influencing Lab Assessment

Phosphorus

* Normal reference range 4.2 – 8.5mg/dl
* Premies have very high phosphorous requirements.

Potassium

* Hyperkalemia is common but may not be real.
* Beware of false elevation due to frequent heel sticks and hemolysis.
* Potassium will be elevated if baby is acidotic.

Sodium and Water

* Term and preemies undergo 10 – 20% loss of ECF immediately after birth.

* Term: regains BW in 7-10 days
  Preterm: regains BW in 14-21 days

* Fluid loss accompanied by Sodium loss.

* In Preemies: Renal Na losing state is greater and more prolonged. Most normal premies may temporarily require Na suppl. (even without dx of CKD)

Sodium and Water

* Fractional Excretion of Sodium (FENa) is inversely related to GA. The lower the GA, the higher the loss of Na.

* FENa: [(UNa/PNa)/(UCr/PCr] X 100%

  - **Normal FENa is <1%.**

* If there is AKI/CKD, with normal or high urine output, the Na supplementation needed may be higher.

- Examples are recovering ATN in AKI and obstructive uropathy with tubular damage in CKD. (Exception: anuric/oliguric and not on dialysis)

5. INTERVENTION

Medical and Nutrition

INTERVENTION:
A. Medical

* Management of fluid balance
* Management of electrolytes
* Acid/Base Balance
* Renal Replacement Therapy (RRT)

MANAGEMENT OF
FLUID BALANCE

* **Maintenance fluid = 100 ml/kg/d**
* Typical fluids to meet kcal needs with 24 Kcals/oz feedings = 150mls/kg
* If **Anuric/Oliguric** may need severe fluid restrictions (i.e. **60 – 80 ml/kg/d**)
* Requires concentration of formulas (up to 60 kcals/oz) and/or concentration of TPN
* **If Polyuric,** fluid needs may increase up to **200-250mls/kg/d** (examples would be in babies with concentrating defects)

MANAGEMENT of ELECTROLYTES
HYPONATREMIA

* May require fluid restriction
* May require Sodium supplementation
  * If very premature
  * If there is a sodium losing component with renal failure
    * Calculate FENa
  * If baby is on peritoneal dialysis
* Sodium can be increased in TPN or NaCL added to formula
* Phos and bicarb supplementation will also increase the Na supplementation

MANAGEMENT of ELECTROLYTES
HYPERKALEMIA

* Hyperkalemia is common
* Beware of false elevations (i.e. heel sticks)
* Change feedings to lower K content
* Remove K from TPN or titrate down
* Kayexalate can be added to formula followed by decanting
  * 1 g kayexalate for each meq of K removed
  * Range of 0.5-1.5g Kayexalate per 100 mls EBM or formula
* Dialysis may be necessary

MANAGEMENT of ELECTROLYTES
HYPERPHOSPHATEMIA

* Remember… the normal reference range for phosphorous
  * For premies: 4.2 – 8.5mg/dl
  * For term: 4.2 – 7.0mg/dl

* If phosphorous is above those ranges
  * Use Low Phos formula (Kindergen) and/or Breast Milk
  * Add liquid Calcium Carbonate to formula to bind

* Phos is likely to go too low once dialysis started
  * Titrate down or stop dose of calcium carbonate
  * May need phos supplementation (sodium phosphate: 93 mg/ml)

MANAGEMENT of ELECTROLYTES
ACID/BASE BALANCE

* Metabolic Acidosis
  * Very common in AKI
  * Ongoing issue in CKD
* Treated with Sodium Bicarbonate, Sodium Citrate or Dialysis
* Remember…
  * **Acidotic babies will not gain weight or grow**
  * Treatment will add to sodium intake so it needs to be accounted for if you are also using NaCl
  * Acidosis can cause the hyperkalemia!

INTERVENTION
RRT

* **Peritoneal Dialysis** is predominant choice
* Literature cites premies as low as 930 g getting long term PD and smaller for short term PD

* **Hemodialysis:** depends on expertise available

* **CRRT:** depends on expertise
  * As low as 1500 g
  * HD and CRRT not good long term options due to frequent clotting and infection.

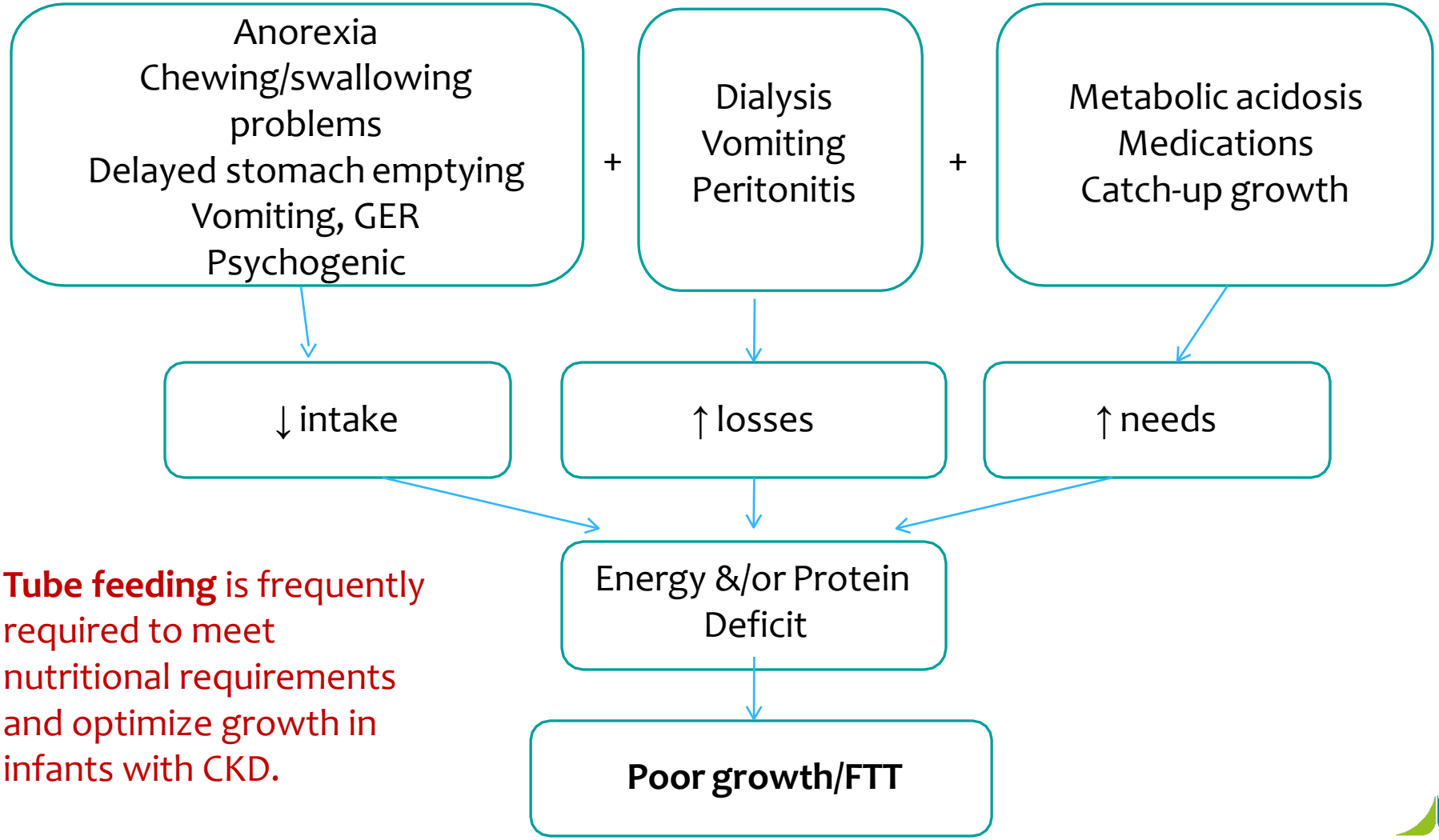
INTERVENTION

B. NUTRITION

Phases of Growth

	Fetal	Infant	Childhood	Pubertal
From:	Conception to birth	Birth -18 mos	18 mos -12 yrs	Onset of puberty
% of total growth	30%	15%	40%	15%
Dependent on:	Nutrition Placenta	Nutrition Good Health	Growth H Thyroid H. Good Health	Testosterone Estrogen Growth hormone Good Health

Nutritional Challenges In Infants with CKD



Tube feeding is frequently required to meet nutritional requirements and optimize growth in infants with CKD.

NUTRITION
Calories

Term Infants

Table 2. Equations to Estimate Energy Requirements for Children at Healthy Weights

Age	Estimated Energy Requirement (EER) (kcal/d) = Total Energy Expenditure + Energy Deposition
0-3 mo	EER = [89 × weight (kg) − 100] + 175
4-6 mo	EER = [89 × weight (kg) − 100] + 56
7-12 mo	EER = [89 × weight (kg) − 100] + 22

NFK KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update

NUTRITION
Protein

* Term Infants

Table 12. Recommended Dietary Protein Intake in Children with CKD Stages 3 to 5 and 5D

	DRI				
Age	DRI (g/kg/d)	Recommended for CKD Stage 3 (g/kg/d) (100%-140% DRI)	Recommended for CKD Stages 4-5 (g/kg/d) (100%-120% DRI)	Recommended for HD (g/kg/d)*	Recommended for PD (g/kg/d)†
0-6 mo	1.5	1.5-2.1	1.5-1.8	1.6	1.8
7-12 mo	1.2	1.2-1.7	1.2-1.5	1.3	1.5

NFK KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update

CALORIE AND PROTEIN RECOMMENDATIONS

Premature

	KCALS	PROTEIN
CONSERVATIVE	110 – 150 kcals/kg	3.4 – 4.4 g/kg
PERITONEAL DIALYSIS	110 – 150 kcals/kg	?
HEMODIALYSIS	110 – 150 kcals/kg	?

- No published references on Protein needs for Premies on dialysis
- If term baby recs. are to increase Protein intake by .1-.35 g/kg/day (K/DOQI 2008) then a conservative approach would be to increase preemies protein intake above normal needs by .1g/kg (for HD) and .35 g/kg (for PD)
- **With HD protein needs increase: 3.5-4.5 g/kg/day**
- **With PD protein needs increase: 3.75-4.75g/kg/day**

Protein Recommendations by Gestational Age

Gestational Age	Conservative* g/kg	PD g/kg	HD g/kg
26 – 30 wks	3.8 – 4.4	4.15 – 4.75	3.9 – 4.5
30 – 36 wks	3.4 – 4.2	3.75 – 4.55	3.5 – 4.3
36 – 40 wks	2.8 – 3.4	3.15 – 3.75	2.9 – 3.5

*Adapted from Tsang, 2005

INTERVENTION
Nutrition

* Monitor growth parameters closely
* **Start by determining fluid needs**- anuric, oliguric, normal, polyuric? - with or without dialysis?
* Make modifications to calorie or protein intake based on your assessment of current calorie intake, protein intake, growth.
* **Monitor BUN:Cr Ratio**
  * Normal ratio is 10-20: 1
  * If ratio is high: perhaps not enough calories, too much protein or breakdown of lean body mass, dehydration, needs more dialysis?
  * If ratio is low: not enough protein, fluid overload

INTERVENTION NUTRITION

Vitamins and Minerals

* Need to meet the requirements of the Term or Premature Infant
* If K or Phos restriction warrants a change from normal premature feedings, then **MVI** supplements will be needed
* Use **single Mineral supplements** to provide mineral requirements (i.e. $CaCO_3$, Ferinsol, NaPhosphate, KCl)
* Watch **Calcium and Phosphorous** levels closely
  * Remember the increased needs of premies
  * May need both Calcium and Phos. supplementation
* Watch **Sodium** levels closely.
  * Premies, Polyuric, and PD babies tend to be salt wasters.
* May need additional **B vitamins** and **Vit C** if on dialysis.

First Nutrition

- Breast feeding
- Expressed breast milk
- Formula
- Concentrate EBM or formula with modular products to achieve goal intake

- Delay transition to Cow's milk due to nutrient profile

FORMULA DECISIONS
GENERAL CONSIDERATIONS

* **Nutrient needs are high for premies.** But because of high serum K and Phos with renal failure…. Premature formulas are discontinued and Fortified Breast Milk is stopped.
* Usual practice is to start kindergen or unfortified Breast Milk: then concentrate as needed
* Supplementation of individual nutrients may be necessary: MVI, iron , Na, Ca and Phos
* Individual nutrient supplementation will likely increase once dialysis is started

Nutrient Content Comparison per 100 kcal

Source (kcal/oz)	mL	Pro(g)	Na(mg)	K(mg)	Ca (mg)	P(mg)
Human Milk (20)	142	1.5	25	75	46	20
Similac PM 60/40 (20)	**147**	**2.2**	**23**	**80**	**56**	**28**
Kindergen (30)	**100**	**1.5**	**46.4**	**24**	**22.4**	**18.6**
Cow's Milk	**159**	**5.1**	**79**	**248**	**200**	**148**

IDEAL FORMULA: LOW RENAL SOLUTE, LOW P, K, and HIGH Calories

FORMULA DECISIONS

CONCENTRATING

* **Determine urine output status of infant:** anuric, oliguric, normal, polyuric
* **Determine fluid status of infant:**

  dehydrated, normal hydration, edemetous
* If fluids restricted to maintenance fluid (100 ml/kg) Requires **36 kcals/oz** to meet basic **premie needs** and **32 kcals/oz** to meet **term needs**.
* If more fluid restricted (ie 60-80 ml/kg) then greater concentration required.

FORMULA DECISIONS

CONCENTRATING

- Increase formula powder to fluid (water or breast milk) ratio until protein needs are met
- Use carbohydrate/fat modulars for additional concentration if necessary to meet calorie goals

Modular Products

FORMULA DECISIONS

DILUTION

* If highly polyuric, formula may need to be prepared to less than 20 kcals/oz
* There are 2 ways to do this:
  * Prepare recipes for less than 20 kcals/oz –(i.e. 14, 16, 18 etc)
  * Prepare 20 kcals/oz feedings but instruct on giving additional water

Thank You !