CASES IN PEDIATRIC CLINICAL NUTRITION

INSTRUCTOR:

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OUTLINE:

- *I. Iron deficiency anemia (IDA)*
  - *a. Mechanisms IDA*
  - *b. Iron requirements*
  - *c. Health effects ID*
  - *d. Treatment ID*
- *II. Severe malnutrition/kwashiorkor*
  - *a. Protein requirements in children*
  - *b. Kwashiorkor vs Marasmus*
  - *c. Pathophysiology of severe malnutrition*
  - *d. Refeeding Syndrome*
    - *i. Pathophysiology*
    - *ii. Manifestations*
    - *iii. Treatment*
- *III. Parenteral and enteral nutrition*
  - *a. Parenteral Nutrition*
    - *i. Components*
    - *ii. Indications*
    - *iii. Method of delivery*
  - *b. Enteral nutrition*
    - *i. Feeding tubes*
    - *ii. Indications*
    - *iii. Benefits*
- *IV. Cystic Fibrosis (CF)*
  - *a. Background*
  - *b. Nutrition in CF*
  - *c. Exocrine pancreatic insufficiency*
    - *i. Pathophysiology*
    - *ii. Symptoms of fat malabsorption*
  - *d. CF nutrition supplementation*

OBJECTIVES: After studying this unit you should be able to:

1. Explain why infants and toddlers are at high risk for iron deficiency anemia.
2. Understand the physiology of starvation and the pathophysiology of refeeding syndrome and identify patient signs and symptoms associated with refeeding syndrome.
3. Recognize the most common indications for use of parenteral nutrition and enteral nutrition and the risk/benefit associated with each method of feeding.
4. Appreciate the role of nutrition in long term health for patients with Cystic fibrosis and describe the most common nutrition interventions for pancreatic insufficient patients.

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Cases in Pediatric Clinical Nutrition

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Clinical Case

An 26 month old infant presents to your office for her annual well child check. Her growth is tracking along the 60th% for weight and 50th% for length. She is a 'picky eater' who eats mostly fruit and vegetables in addition to cow's milk, about 50 ounces per day. Mom states that she has seemed a little pale in the last few weeks or so, but she is also getting over a cold.

ROS: negative for fatigue, sleepiness, blood in stool

Meds: No medication

FamHx: negative for anemia or other blood disorders

Physical Examination:

Vital Signs: Temperature 37.5 degrees C, Blood Pressure 90/52 mmHg, Pulse 145 beats/minute, Respiration 16 breaths/minute

General appearance: She is a pale appearing, active toddler

Eyes: No scleral icterus. Pale conjunctiva.

Mouth: Dental caries.

Chest: Clear.

Heart: Mild tachycardia, grade II/VI systolic ejection murmur heard best over the upper left sternal border.

Abdomen: No hepatosplenomegaly.

Rectal: Dark brown, soft stool, negative for occult blood.

Laboratory: CBC: White blood count (WBC) 6,100, Hemoglobin (Hgb) 6.2 g/dL, Hematocrit (Hct) 19.8%, Platelet count 589K, MCV 54 fL, RDW 21%. Reticulocyte count is 1.8%. The lab reports microcytosis, hypochromia, mild anisocytosis, and polychromasia. There is no basophilic stippling.

Iron Deficiency Anemia (IDA)

- ID is the most common micronutrient deficiency in the world
- Children at high risk because of their rapid growth/development leading to high iron requirements
- Globally 25% of preschool children have IDA
- IDA Develops in 3 Stages
  - Iron Depletion
  - Iron-deficient erythropoiesis
  - Iron Deficiency Anemia
- Mechanisms of iron deficiency in young children on cow's milk (CM)
  - Low iron content of CMA
  - Occult intestinal blood loss associated with CM consumption during infancy
  - Inhibition of non-heme iron absorption by calcium and casein

Development of IDA in Infants and Toddlers

- Iron Depletion
  - 80% of iron is accreted during 3rd trimester of pregnancy
- Iron Absorption
- Iron Requirements
  - Preterm infants: 2-4 mg/kg/day
  - Term infants
    - 0-6 months: 0.27 mg/day
      - BM: 0.35mg/L (how much BM does a baby drink in a day? 0.78L/day)
    - 6-12 months: 11mg/day
  - Toddlers (1-3 yrs): 7 mg/day

Health Effects of ID

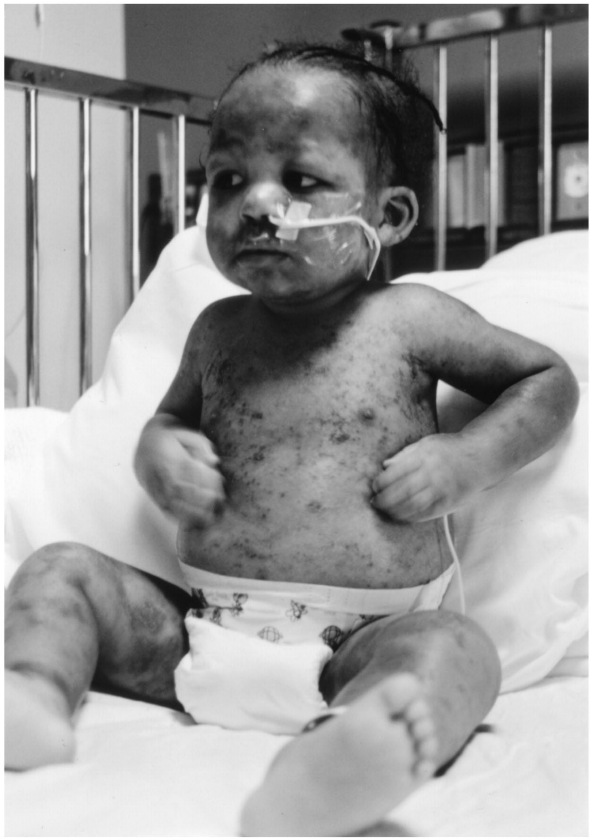
- The main public health problem associated with ID in childhood is the risk of poor neurodevelopment; however, some other physiological manifestations have been attributed to ID in young children, including growth retardation and impaired immune response.
- Cognitive deficits 1-2 decades after iron-deficient insult
- Prevention of ID
  - Umbilical cord clamping
  - Dietary Intervention
  - Role in prevention of lead poisoning

Treatment

- Preterm infants being fed breast milk should be supplemented with iron through 12 months of age
- Term infants usually have enough iron stores until 4-6 months of age
  - Exclusively breastfed term infants receive an iron supplementation of 1 mg/kg per day starting at 4 months of age
- Iron sources in diet
  - Heme sources: red meat
  - Non-heme sources: legumes, iron-fortified cereals
- Universal screening with Hg and risk factors at 12 months old

Clinical Case

You are the resident admitting an 18 month old male for edema. 1 month ago he developed intermittent periorbital swelling which has progressively gotten worse where is now swollen in abdomen, face, extremities. Two weeks before admission, he became increasingly irritable, less active, and started drinking poorly. The mother denied any history of diarrhea or bulky, greasy stools. Several episodes of vomiting occurred during the 3 days before admission. There was no fever.



Diet: He was exclusively breast fed until 13 months of age at which time he weaned to cow's milk and mother felt this worsened his eczema so the family put him on 'rice milk'. On average he consumed 25 ounces of the rice drink daily and 2 teaspoonfuls of solid foods per day.

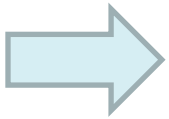
Physical Exam and Laboratory Work Up

- VS: afebrile, RR 20, HR 95, BP 70/40
- Growth: weight 8.8kg (<3rd%), height 78cm (3rd%)
- PE: generalized edema, hyperpigmented and hypopigmented skin lesions, irritability, and thin, sparse hair, Bilateral otitis media with effusion

- Labs: Albumin 1.0 g/dL (nml 3-5), Potassium 3.4 mmol/L, BUN <0.5 mg/dL, Phosphorus, 2.2 mg/dL, alkaline phosphatase, 104 U/L; Hemoglobin, 8.0 g/dL (80 g/L); MCV 78.4 fL, normal liver function, UA negative for protein

Etiology of Hypoalbuminemia

1. Excessive losses (urine, stool)
2. Decreased protein synthesis (liver disease)
3. Deficient Protein Intake



Consequences

- Low oncotic pressure leading to 3rd spacing (edema, pleural, pericardial effusions
- Hypogammaglobulinemia

Protein Requirements

Category	Protein (g/kg/day)
Very Low Birth Weight (<1500g)	3-4
Preterm	2.5-3
Infant/Neonate	2-2.5
Infant	1.5-2
Preschool/ school age	1-1.5
Adolescent	0.8-1.5

Protein is essential for growth; structure, enzymes, substrates, neutrotransmitters, transporters, etc.

Nutritional Comparison of Cow's Milk and Plant-Based "Milks"

Per 1 cup (240mls)	Cow's Milk	Vegetable Milks*								
		Almond	Cashew	Coconut	Flax-Seed	Hemp	Oat	Pea	Rice	Soy
Calories	150	30-100	25-80	45-90	55	70-170	130	115	110	90
Protein (g)	8	1-5	0-1	0-1	0	2-4	4	8	1	6
Fat (g)	8	3	2-3.5	5	2.5	5-6	2.5	5	2.5	3.5
Carbohydrates (g)	13	9-22	1-20	8-13	9	1-35	24	11	20	15
Sugars (g)	12	7-20	0-18	0-9	9	0-23	19	10	13	9
Calcium (mg)	300	300	100-450	100-450	300	400	350	450	300	400
Vitamin D (IU)	120	110	125	125	100	150	120	150	120	120

Our patient:
Daily protein intake ~1.7 g
1.3 g of protein from the rice drink and 0.4 g of protein from other sources
Average daily caloric intake was 405 calories per day
395 calories from the rice drink and 10 calories from other sources
Minimum protein requirement: 10g/day (~1g/kg/day)
Minimum calorie requirement: 800 kcals (80kcal/kg/day)

Kwashiorkor vs. Marasmus

Clinical Diagnosis of Severe Acute Malnutrition		
Result (Indicator)	**Measure**	**Cut-off for diagnosis**
Severe wasting (marasmus)	Weight-for-height or BMI	Z-score <-3
Bilateral Edema (kwashiorkor)	Clinical exam	Edema

Kwashiorkor
- Severe protein malnutrition
- Marked muscle atrophy
- Abdominal distention (+/- hepatomegaly)
- Think, dry, peeling skin
- Dry, hypopigmented hair
- Skin lesions/dermatitis
- Growth retardation
- Bilateral extremity swelling
- More than just dietary protein deficiency

Marasmus
- Wasting syndrome
- Energy deficiency
- No edema
- Marasmus and kwashiorkor often coexist

Pathophysiology of Severe Malnutrition

- Cardiovascular:
  - Output and SV reduced when lean body mass loss
- Liver:
  - Hepatic gluconeogenesis is reduced (hypoglycemia) and decreased metabolism of toxins, reduced synthesis of protein
- GI:
  - Mucosal atrophy in small bowel impairs digestions, electrolyte abnormalities (Mg, K) slow motility, diminished gut barrier can lead to bacterial translocation
- Immune:
  - T cell immunity, IgA levels, complement levels, and phagocytosis are diminished
- Endocrine:
  - Low insulin levels, cortisol level increased
- Metabolism/circulation:
  - basal metabolic rate reduced
- Skin and glands:
  - Atrophied fat, loose skin folds, may be hard to judge hydration status

Starvation Pathophysiology

Day 1 – Day 3: liver glycogen depleted, decreased insulin (small increase in glucagon and growth hormone)

Day 7: catabolism of fat (lipolysis) and protein for hepatic gluconeogenesis → (anaerobic conversion of glucose to ATP can occur throughout this time period)

Day 8-10: source of energy shifts from fat to ketone bodies

Day 30 and beyond: muscle catabolism of lean muscle, leading to death

- In small children, less liver glycogen, fat, and protein stores can hasten starvation process.
- The arrows represent continuation of the previous day(s) aforementioned processes until the next annotated day is highlighted.

Refeeding Syndrome Pathophysiology

- Refeeding potentiates intracellular electrolyte shift to accommodate cellular processes

Malnutrition/Starvation

Gluconeogenesis, protein and glycogen catabolism	Protein, fat, vitamin, and mineral depletion; Salt, fluid, and electrolyte (notably phosphate, potassium, and magnesium) balance shifts

Nutritional Replacement

Reestablishment of vital nutrients	Hyperglycemia; Insulin secretion - glucose uptake; Synthesis of protein & glycogen; Intracellular shift of phosphate, potassium, magnesium; Thiamine depletion

Refeeding Syndrome

Hypophosphatemia, hypokalemia, salt and fluid retention; thiamine deficiency

Refeeding Syndrome Manifestations

	Hypophosphatemia	Hypokalemia	Hypomagnesemia	Vitamin/thiamine deficiency	Hyperglycemia	Fluid overload	Trace element deficiency
Cardiac	• Sudden death • Arrhythmia • Heart failure • Hypotension • Shock	• Arrhythmia	• Arrhythmia		• Hypotension	• Heart failure	• Arrhythmia • Heart failure
Pulmonary	• Dyspnea • Respiratory failure • Impaired diaphragm function	• Respiratory failure			• Respiratory failure		
Musculoskeletal	• Weakness • Myalgia • Rhabdomyolysis	• Weakness • Rhabdomyolysis • Muscle necrosis	• Weakness		• Weakness • Rhabdomyolysis • Muscle necrosis	• Edema	
Hematologic	• Hemolysis, • Thrombocytopenia • Leukocyte dysfunction						
Gastrointestinal		• Nausea • Vomiting • Constipation	• Nausea • Vomiting • Diarrhea		• Nausea • Vomiting • Constipation		
Neurologic	• Confusion • Delirium • Paresthesia • Paralysis • Seizures • Hallucinations	• Paralysis	• Tremor • Tetany • Seizures • Altered mental status • Coma	• Encephalopathy	• Paralysis		• Encephalopathy
Other	• Metabolic acidosis • Insulin resistance • Acute tubular necrosis	• Death	• Refractory hypokalemia & hypocalcemia • Death	• Lactic acidosis • Death	• Infection • Death	• Death	• Metabolic acidosis

Refeeding Syndrome : Identification and Prevention

- The general principles of reduced energy intake, poor absorption, and/or increased metabolic demands give rise to a variety of presentations and illnesses.
- Risk factors: anorexia, prolonged fasting (>5 days), loss of 10% of body weight in 1-2 mos, complex health care needs
- Dietary Start/Advancement
  - Start at 25-50% of caloric requirements
  - Advance over 3-7 days
  - Frequent electrolyte monitoring and replacement

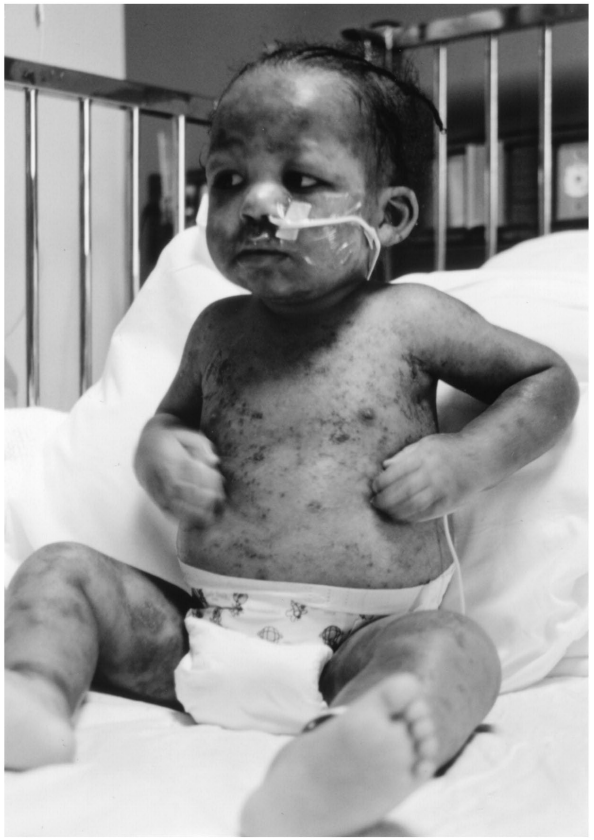
Pulcini, Zettle, Srinath, Peds In Review, 2016;37:12.

Nutrition Focused Physical Exam

Area	Normal Findings	Abnormal Findings	Related Nutrition Deficiencies
Hair	Smooth and symmetrically distributed	Poor quality	Zinc, essential fatty acid, biotin, protein-calorie
		Alopecia	Protein, zinc, biotin, essential fatty acid, selenium
Eyes	Bright, shiny, clear, pink moist membranes	Dull, dry membranes with Bitot spots	Vitamin A
		Burning itching with photophobia	Riboflavin
Lips/mouth	Pink, free of lesions	Dry, swollen	B6, folate, riboflavin, niacin, B_{12}, Fe
		Dry mucous membranes	Dehydration
		Dry mouth	Zinc
Tongue	Moist pink with slightly rough texture	Magenta and edematous	Riboflavin, niacin, folate, B_6, B_{12}, Fe
		Enlarged in congenital anomalies	May lead to feeding issues
		Candidiasis lesions or thrush	Vitamin C, Fe
Gums	Pink without lesions	Bleeding and inflamed	Vitamin C
Teeth	Normal eruption begins at 4–12 mo	Delayed eruption	Severe malnutrition
		Dental caries	Vitamin D
Skin	Uniform color without rashes, tears, or flaking	Pallor	Fe, folate, B_{12}
	Cool to touch	Dry, scaly	Vitamin A, essential fatty acid
		Dermatitis	Essential fatty acid, zinc, niacin, riboflavin, tryptophan
Nails	Symmetrical and smooth	Transverse lines	Protein
		Flaky	Magnesium
		Poorly blanched	Vitamin A, vitamin C

Back to our case:

- Gradual refeeding, initially via a nasogastric tube because of severe anorexia
- Supplements of potassium, phosphorus, multivitamins, zinc, and folic acid were provided.
- Rising serum albumin and total resolution of the edema within 3 weeks.
- At follow-up 1 year later he continued to do well on a regular diet supplemented with a milk-based pediatric nutritional supplement.



Carvalho, Kenney, Et al. Ped, 2001;107:4.

Clinical Case

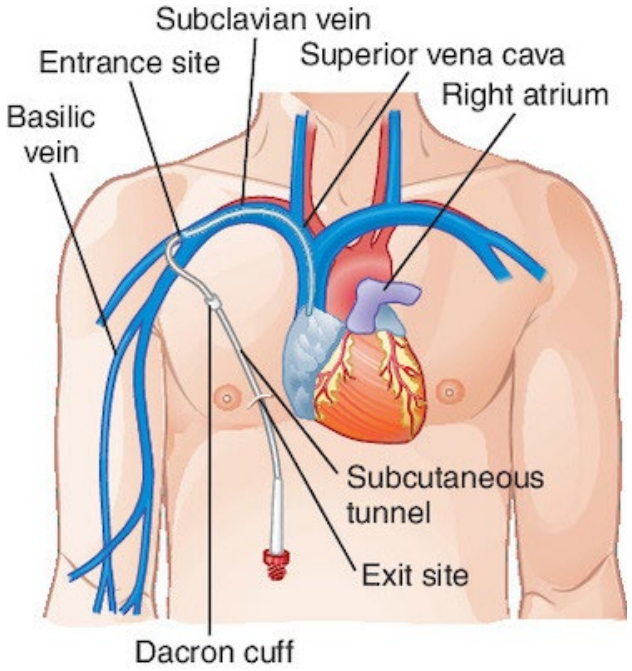
- You are the pediatric resident on the NICU rotation when you are called to the delivery of a preterm infant. The infant is born via C-section for non-reassuring fetal tracing in the setting of severe maternal pre-eclampsia. After initial resuscitation the baby is transported to the NICU in stable but critical condition. The next day on rounds the team is discussing the plan to provide nutrition to the infant. The team agrees on initiation of parenteral nutrition.

What is Parenteral Nutrition (PN)?

- Complex solution of macronutrients, micronutrients, fluid, electrolytes, and additives
- Indicated in patients when GI tract is not functional or cannot be accessed or when nutrient needs exceed that what can be provided through enteral nutrition (EN)
- ONLY use when there is no reason to use EN

How is Parenteral nutrition given?

- Ideally via central venous access via a central line
  - Tip of a central catheter is at the junction of the SVC and IVC with the right atrium
- Risk of central lines
  - Procedure for placement
  - Risk of infection
  - Risk for clots
- PN is ordered daily based upon calories, electrolytes, growth of patient
- Compounded by pharmacy

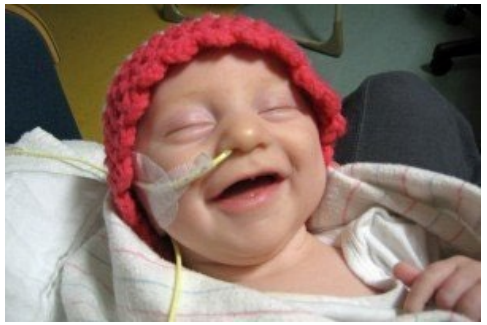


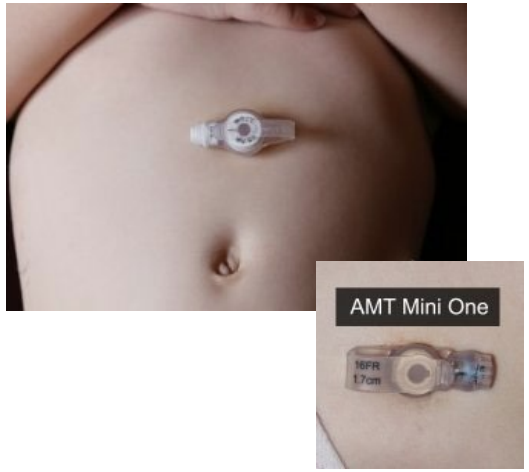
Back to the case

- The following day on rounds (DOL 2) the team states they want to start enteral nutrition in the form of ‘trophic feeds’ in this infant. They will be giving maternal breast milk. Via what route should this infant receive breast milk?

Enteral Nutrition

- Involving or passing through the intestine, either naturally via the mouth and esophagus, or through an artificial opening
- Feeding tubes
  - Orogastric
  - Nasogastric, nasoduodenal, nasojejunal
  - Gastric, Gastrojejunal
  - Jejunal





Indications
- Inadequate oral intake
- Airway protection
- Inadequate intestinal function
- Therapeutic
  - Crohn's disease, IEM, eosinophilic esophagitis

Contraindications
- GI bleeding
- Ileus
- Free air
- Pneumatosis
- Hemodynamic instability

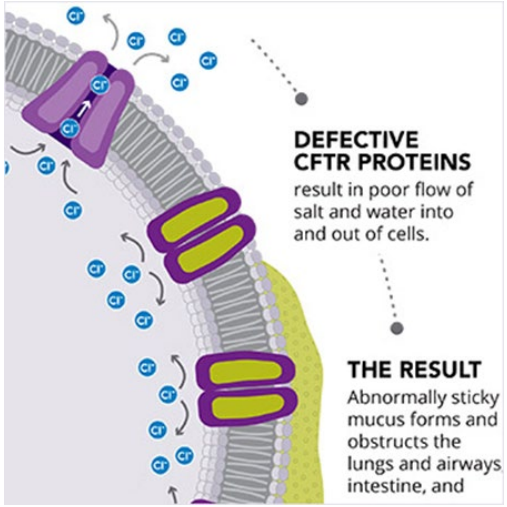
Clinical Case

- You are seeing a 2 week old infant whom was referred to the Cystic Fibrosis Clinic after screening positive on the newborn screen. Her mother reports that she has had approximately 8-9 stools per day which are described as shiny. She has 2-3 episodes of vomiting per day. Her birth weight was 7lbs 5 oz and at 2 weeks old she is 6lbs 10 ounces. She breast feeds every 1-2 hours for ~20 minutes. Mom has started to offer formula after each feed because she seems 'ravenous'.

- While we await confirmation of a diagnosis of CF what can we do to improve her nutrition?

Cystic Fibrosis Basics

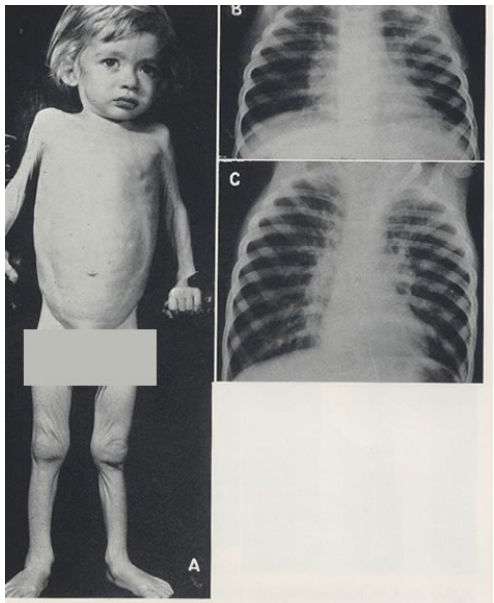
- Cystic fibrosis is the MC inherited disease in white populations, with an incidence of 1 in 2500 newborns
- Autosomal recessive inheritance, mutation in CFTR gene
- Poorly/ Non-functioning CFTR is unable to move chloride out of the cell, causing mucous to build up in airway lining
- Same process occurs in the pancreas leading 'Exocrine Pancreatic Insufficiency'
  - Inability to secrete enzymes (lipase and protease) required for digestion of fat and protein



https://www.vrtx.com/all-cf/understanding-cf

Nutrition in CF

- Increased energy needs and increased energy losses
  - 110-120% of energy needs of the healthy population
- Adequate nutrition and anthropometric markers have been associated with improved survival, decrease in pulmonary exacerbations

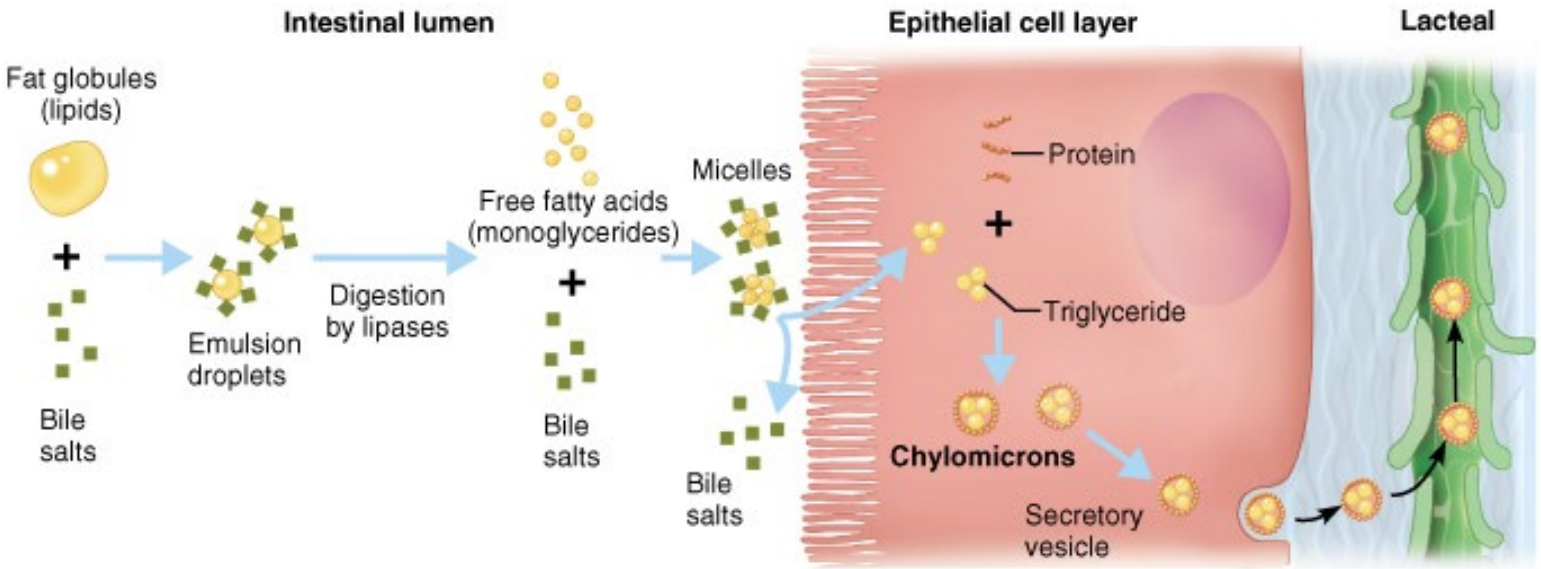


igure 7. A. Patient with Cystic Fibrosis of the Pancreas at two years, ve months. B. Lungs at one year, two months. C. Lungs at two years, ve months. When infection becomes established in the viscid secretion the bronchioles at an early age, and persists, the lungs show progres- ve development of peribronchial infiltration and emphysema. The utritional state deteriorates with advance of the infection. (Repro- uced from Plate V, May, C. D. and Lowe, C. U., Fibrosis of the ancreas in Infants and Children, *J. Pediat., 34*:663 (1949) with per- mission of C. V. Mosby, St. Louis.)

GOALS

- Infants and children <2 yo weight for length >50th% (CDC 2000)
- Children >2, BMI >50th% (CDC)
- Adults: BMI >22 in women, >23 in men

Exocrine Pancreatic Insufficiency (EPI)

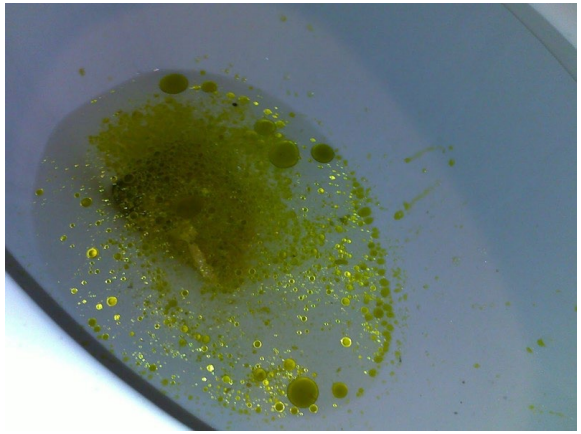


CF patients require 50% of calories from fat.

Symptoms of Fat Malabsorption

- Steatorrhea
- Excessive gas, bloating
- Poor weight gain, weight loss
- Short stature
- Hypoproteinemia; edema
- Meconium ileus
- Rectal prolapse
- Deficiencies in vitamins A, D, E, K (fat soluble vitamins)

The clinical manifestations of fat malabsorption include bulky, loose, greasy, foul smelling stools that are difficult to flush.



Current standard for diagnosis in pediatric patients is a fecal elastase.

CF Nutrition Supplementation

- EPI patients will take pancreatic enzyme replacement therapy (PERT)
  - Capsule that contains porcine lipase and amylase and aid in breakdown of fats within the intestinal lumen
  - Given starting in early infancy with each meal
- Fat soluble vitamin supplementation
- Supplemental calories
  - Oral formulas
  - Gastrostomy or other tube feeds

- Start PERT
- Reinforce formula supplementation for time being
- Confirm that infant is taking prescribed vitamin D

FAT SOLUBLE VITAMINS

Fat Soluble Vitamins	Deficiency	Toxicity	Assessment
Vitamin A	Night blindness, Bitot's spots, xerophthalmia, poor bone growth, impaired resistance to infection (measles), follicular hyperkeratosis	Alopecia, ataxia, muscle and bone pain, cheilitis, conjunctivitis, headache, hepatotoxicity/cirrhosis, hyperlipidemia	Serum retinol, Serum retinol binding protein Serum esters for toxicity
Vitamin D	Rickets/osteomalacia, dental caries, hypocalcemia/ hypophosphatemia	Hypercalcemia (nausea/vomiting, weakness, fatigue, diarrhea, anorexia, headache, confusion, psychosis, and/or tremor); hypercalcuria	Serum vitamin D 25-OH, Serum parathyroid hormone (PTH)
Vitamin E	Hyporeflexia spinocerebellar & retinal degeneration; peripheral neuropathy, proximal muscle weakness, cognitive & behavioral abnormalities	Impaired neutrophil function, coagulopathy, thrombocytopenia, cerebral hemorrhages	Serum alpha-tocopherol, ratio of serum alpha tocopherol to total lipids is more accurate reflection of vitamin E stores Ideally when fasting
Vitamin K	Bleeding, bruising, abnormal bone matrix synthesis	High doses of K3 have been associated with red blood cell (RBC) instability and hemolysis	INR ≥ 1.2, PIVKA > 4 ng/mL; indirectly ↓ levels of vitamin-K- dependent clotting factors (II, VII, IX, and X)

Questions?