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Chylothorax and other Lymphatic Flow Disorders: Etiology and Management

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Objectives

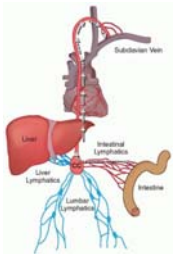
1. Understand the anatomy, function and disorders of the lymphatic system
2. Describe the adverse consequences of lymphatic flow disorders
3. Define the medical nutrition management of lymphatic flow disorders
4. Discuss a case report and relate learning to one's own practice


Anatomy of the Lymphatic System

- Complex network of lymphatic vessels throughout the body
- Lymphatic fluid is produced in:
 - Soft tissues
 - Organs
- Intestines and liver produce the majority (80%) of lymphatic fluid
 - Liver is largest producer of lymph and delivers hepatic proteins, particularly albumin, into bloodstream


Anatomy of the Lymphatic System 

- Lymphatic fluid flows from the organs (liver, intestines, tissues, lungs) **peripherally to centrally**
- Cisterna chyli collect the streams of fluid into one main channel called the thoracic duct
- The thoracic duct drains into the venous system through lympho-venous connections at the junction of the left subclavian and jugular veins

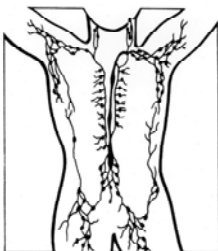



Lymphatic System Function 

- **Defense**
 - key role in immune system
- **Transport**
 - cells, fatty acids, proteins, macromolecules
- **Circulation**
 - returns excess interstitial fluid from tissues to venous system



Lymph Fluid 


- Chyle
- T cells
- Antithrombin 3 (AT3)
- Proteins
 - albumin, fibrinogen, immunoglobulins
- Electrolytes
- Trace elements




Diagnosis of Chylothorax 

- **Signs and Symptoms**
 - ▣ Cough, dyspnea
 - ▣ Nausea and vomiting
 - ▣ Pleural effusion on chest radiograph
- **Thoracentesis**
 - ▣ White, milky or yellow serous fluid
 - ▣ Biochemical analysis confirmed chylous





What is Chyle? 


- Chyle is composed of lymph and emulsified fatty acids as chylomicrons
- Chyle is formed in the intestinal lacteals during digestion of fat
- Role in absorption of fat soluble vitamins
- Role in reabsorption of proteins lost through capillary leakage

Biochemical Analysis of Chyle 


Body Fluid Biochemical Analysis	
Triglycerides	>110 mg/dL
Total lipid content	0.4-4.0 g/dL
Cholesterol	<220 mg/dL
Lymphocytes	>70%
White blood cell	>1000 per μ L
Total protein	>3 g/dL
pH	Alkaline (7.4-7.8)

Lymphatic Disorders 


- **Traumatic Leaks**
 - Chylothorax
 - Chylous ascites
 - Chylous pericardium
- **Lymphatic Malformations**
 - Lymphoma
 - Lymphangiomatosis
 - Gorham's disease
- **Idiopathic Leaks**
 - Congenital chylothorax
 - Increased incidence with Noonan, Turner, and Trisomy 21
 - Trauma, infection, malignancy
- **Pulmonary Lymphatic Perfusion Syndrome (PLPS)**
 - Plastic Bronchitis
- **Protein Losing Enteropathy**

Etiology of Chylothorax 

- **Trauma**
 - Iatrogenic injury during surgery in the posterior mediastinum
 - **High risk surgeries:** Systemic-to-pulmonary shunts, aortic arch augmentation, vascular ring repair, delayed chest closure
- **Elevated CVP**
 - Increased pressures cause significant burden on lymphatic circulation and decreased ability of lymph to drain into the vascular system
 - Single ventricle palliation surgeries at increased risk
- **Central venous thrombosis**
 - Presumed mechanism is occlusion of the thoracic duct drainage and subsequent obstruction of the flow of chyle into venous system


Protein Losing Enteropathy (PLE) 

- Condition of the GI tract that results in **net loss of proteins**
- PLE is characterized by:
 - Abnormal enterocyte membrane structure resulting in severe protein loss into the intestinal tract
 - As the protein loss exceeds the patient's ability to resynthesize the lost proteins, serum albumin will dramatically decrease
 - Decreased absorption of nutrients from the small intestine

Protein Losing Enteropathy (PLE) 

- Elevated CVP → overproduction of liver lymph
- Results in dilation of hepatoduodenal lymphatic ducts and duodenal lacteals
- Liver Lymphangiography
 - Documents lymphatic leakage by injecting isosulfan blue dye into liver lymphatic ducts
 - Endoscopy imaging shows subsequent visualization of blue dye leaking into the duodenal lumen


Dori 2016; Itkin 2017

Protein Losing Enteropathy (PLE) 


- **Signs and Symptoms**
 - Abdominal bloating, diarrhea, bowel inflammation, malabsorption
 - Hypoalbuminemia, hypoproteinemia
 - Ascites, soft tissue swelling, pleural effusions
 - Electrolyte disturbances
 - Malnutrition secondary to malabsorption
- **Diagnosis**
 - Suspected by history, physical exam, s/s
 - Gold Standard: elevated 24 hr **stool α -1-antitrypsin** clearance study

Adverse Effects of Chylothorax and Chylous Loss 




Immunological and Hematologic Effects 


- Impaired cell-mediated immunity from lymphocyte depletion
 - 70-90% T cells
 - Lymphocytopenia
 - Decreased serum levels of antibodies and gamma-globulins
- Increased risk of infection and sepsis
- Increased risk of coagulopathy and thromboembolic events

Electrolyte and Fluid Disturbances 


- 2 – 4 L/day of chyle are transported through lymphatic system
- Profound losses may cause:
 - Electrolyte imbalances (hyponatremia, hypocalcemia, hypokalemia)
 - Metabolic acidosis (alkaline pH of chyle)
 - Hypovolemia
 - Hemodynamic instability
- Hypervolemia
 - Inadequate lymphatic drainage or overproduction of lymph leading to respiratory failure and anasarca
 - Secondary to replacement of fluids (FFP, PRBCs, albumin, etc.)

Protein Loss 

- Lymph is the only means for protein that has left the vasculature to be returned to the blood
 - Returns ¼ to ½ of circulating plasma proteins
- Hypoproteinemia
 - Albumin, fibrinogen, immunoglobulins, enzymes (amylase, lipase, alanine aminotransferase)
- May have problems maintaining intravascular volume due to transcapillary fluid shifts

Fat Soluble Vitamins 


- Fat soluble vitamins are transported in chyle
- Additional supplementation may be recommended for patients on a restricted oral/enteral regimen
- Water soluble forms of vitamins A, D, E and K may be better utilized with high-output losses or malabsorption
- Laboratory monitoring should be part of a routine nutrition assessment

Other Adverse Effects 


- Respiratory Failure:
 - ▣ Chylous fluid accumulation in the pleural space can create restrictive lung disease and contribute to respiratory insufficiency and need for ventilator support
- Prolonged ICU and hospital admissions

Clinical Nutrition Management 




Management of Chylothorax 

- Management is multifactorial
- Conservative therapies are directed to reduce intestinal lymphatic flow and decrease chyle production through **diet modifications** and/or medications
- Registered Dietitians play an integral role in:
 - ▣ Delivering adequate nutrition for growth and development
 - ▣ Recommending nutrient supplementation
 - ▣ Providing nutrition education and counseling


Dietary Management for Chylothorax 

- Minimize intake of **long-chain triglycerides (LCT)**
 - ▣ Absorbed and transported to the bloodstream by the intestinal lymphatics as chylomicrons
- Enrich diet with **medium-chain triglycerides (MCT)**
 - ▣ Absorbed directly into the portal circulation and do not stimulate an increase in lymphatic flow
- Oral diet modifications or specialized enteral formula regimens

Postoperative Chylothorax 


- Upon diagnosis, a very low fat regimen should be ordered
- Literature recommends a low fat regimen for **4 – 6 weeks** after resolution of chylous drainage
- Once chylothorax has resolved, there is no further preventative effect of using a restricted diet
- Remaining on a low fat diet longer than necessary is not nutritionally appropriate and may be harmful in the long-term

Wu 2006, Densupsoontorn 2014, Panthongviriyakul 2008, Cormack 2004, Cabrera 2010, Beghetti 2000


Postoperative Chylothorax 


- One study measured fat soluble vitamins and fatty acid levels in patients with CHD who developed chylothorax after cardiac surgery
- Levels taken at baseline and after 28 days on MCT-rich diet
- Administration of MCT-rich diet for 28 days (range 27-31 days) was an effective treatment
- Results showed a reduction in vitamin E status and linoleic acid levels from baseline, but without any symptoms of deficiency

Densupsontorn 2014

Low Fat Diet 

- Estimate ≤10% of EER from fat
 - 1-10 years of age: ~10-20 grams/day
 - >10 years of age: ~15-25 grams/day
- Considerations
 - Divide between meals & snacks
 - Tolerance to LCT intake is patient specific
- MCT supplementation may enhance energy intake
 - MCT oil or MCT modular



Skimmed Breastmilk 


- Literature demonstrates safety and efficacy of skimmed breast milk with the fat removed via centrifugation for the medical nutrition management of chylothorax in infants
- **Content**
 - Caloric Density: 10–14 cal/oz*
 - Fat Content: 0.5%–1.5%*
 - Requires addition of calories, protein, MCT and essential fatty acids
- **Benefits**
 - Immunological properties and improved gastrointestinal tolerance

*Fogg 2016, *Kocel 2016*

Comparison of Specialized Formulas				
High MCT and/or Low LCT Formulas for use of Chyllothorax				
Formula	MCT:LCT Ratio	Percent calories from LCT Fat	LCT Fat grams per 100 calories	
Enfaport™ (Mead Johnson)	83:17	7.8	0.9	Contains milk-proteins
Lipistart® (Nestlé)	80:20	7.6	0.82	
Monogen® (Nutricia)	83:17	4.5	0.5	
Portagen® (Mead Johnson)	87:13	5.5	0.6	
Tolerex® (Nestlé)	0:100	2	0.2	Elemental, 100% free amino acids
Vivonex® Pediatric (Nestlé)	70:30	7.5	0.87	
Vivonex® T.E.N. (Nestlé)	0:100	3	0.3	


Nutrition Management

- ❑ Parenteral Nutrition
 - ❑ Fasting decreases intestinal blood flow, which may result in a secondary reduction in lymph flow
 - ❑ Aggressive nutrition intervention for malnutrition
 - ❑ Cannot tolerate restricted enteral fat regimen
- ❑ Intralipids are safe
 - ❑ Delivered directly into the bloodstream
 - ❑ Do not stimulate lymph production
 - ❑ Do not pass through the lymphatic system via chyle




Considerations of Restricted Fat Diets

- ❑ But...Children need fat/kg/body weight
 - ❑ Energy requirements
 - ❑ Growth
 - ❑ Neurological development
 - ❑ Long term health
 - ❑ Prevent essential fatty acid deficiency



Essential Fatty Acids

- EFAs
 - Omega-3: α-Linolenic Acid
 - Omega-6: Linoleic Acid
- Function
 - Formation of phospholipid cellular membranes
 - Integrity of epidermal water barrier in the skin
 - Development and function of the brain, retina and nervous systems
 - Regulate BP, blood viscosity, vasoconstriction
 - Role in immune and inflammatory response




Essential Fatty Acid Requirements

- Linoleic acid
 - 1-4% of calories
- α-linolenic acid
 - 0.2-1% of calories
- Supplementation
 - Fish, leafy vegetables, seeds, nuts, flax, eggs, wheat germ
 - Walnut, flax seed, canola, chia seed oils
 - Anecdotally, flaxseed oil can increase mucus production and cause GI side effects

Dietary Reference Intakes Adequate Intakes (AI) for EFA		
Life Stage Group	α-Linolenic Acid AI (g/d)	Linoleic Acid AI (g/d)
Infants		
0-6 months	0.5	4.4
7-12 months	0.5	4.6
Children		
1-3 years	0.7	7
4-8 years	0.9	10
Males		
9-13 years	1.2	12
14-18 years	1.6	16
Females		
9-13 years	1.0	10
14-18 years	1.1	11


Essential Fatty Acid Deficiency

- Hair loss
- Eczema, dermatitis, folliculitis
- Growth retardation
- Developmental delay
- Xerosis
- Poor wound healing
- Increased susceptibility to infection
- Hypertension
- Hematologic disturbances
 - hemolytic anemia
- Fatty infiltrations of the liver
- Hypertriglyceridemia


How do we define EFA deficiency? 

- Measure absolute serum levels
 - Low Linoleic Acid (LA)
 - Low α -Linolenic Acid (ALA)
 - Elevated Mead Acid
 - Elevated Triene:Tetraene (T:T) ratio
 - Mild deficiency ≥ 0.05
 - Moderate deficiency ≥ 0.2
 - Severe deficiency ≥ 0.4


Holman 1960

Vitamin/Mineral Lab Monitoring 


- Vitamin 25(OH)D
- Vitamin A, E
- Prothrombin times (PTT)
- Zinc
- Copper
- Ceruloplasmin
- Selenium
- Check if concern for:
 - Suboptimal intake
 - Chronic drainage/losses
- Monitor monthly if abnormal
- Monitor EFA profile Q 2-4 months if normal but remains on a long-term restricted diet

Nutrition Management of PLE 


- No gold standard nutrition recommendations exist
- High-protein (≥ 2 g/kg/day)
- Reduced LCT, MCT-enriched diet
- Diet modifications may augment a patient's nutritional intake and absorption, which may improve morbidity and success of other medical therapies
- High risk for malnutrition

Neonatal Congenital Chylothorax 

- Idiopathic condition that presents as a pleural effusion in utero or in the early days of life due to the development of abnormal pulmonary lymphatic flow
- May require prolonged diet modifications with slow reintroduction of fat as the lymphatic system is immature, and they have an inability to collateralize until around 8-10 months of age

MR Lymphangiography and Embolization 

- Dynamic Contrast Magnetic Resonance Lymphangiography
 - Lymphatic system is accessed through lymph nodes and contrast is injected to determine the anatomy and flow pattern of lymph in the central lymphatic system
- Lymphatic Embolization
 - Under fluoroscopic guidance, a needle is inserted percutaneously through the abdomen into the cisterna chyli
 - Guidewire and microcatheter are advanced into the thoracic duct
 - Injection of lipiodol occludes the pathologic lymphatic network and supplying vessels


Other Considerations and Challenges 

- Coagulation
- Pain
- Illness-associated anorexia
- Malnutrition
- Fluid management
- Wound care
- Child life/psych




Case Study





Case Study


- DW is a female with a PMH of hypoplastic left heart syndrome, interrupted IVC and azygous continuation to the left SVC, and heterotaxy syndrome. She initially had a Stage 1 palliation with BT shunt after birth, followed by a Kawashima operation. She subsequently developed pulmonary arteriovenous malformations, and underwent a Fontan with hepatic inclusion at 17 months old and was discharged home.
- At 18 months of age, she presented with left chylous pleural effusion. She underwent cardiac cath, thoracentesis, and left pleural pigtail catheter.
- Diet History: Regular diet and breast milk, although weaning




Case Study

Body Fluid Composition	
Type of Body Fluid	Pleural
Appearance	Cloudy
Fluid Color	Yellow
Lymphocytes	91 %
Total Protein	3.5 g/dL
Triglyceride	225 mg/dL
White blood cells	2128 / μ L


- **Drainage day 1-10:**
 - Avg 341 mL/day (32 mL/kg/day)
 - Range 220-700 mL/day
- **Lab Abnormalities:**
 - Na 139 → 133 (L)
 - Albumin 3.9 → 2.9 (L)

Case Study 


- **Nutrition Assessment**
 - EER: 100-110 kcal/kg @ 10.5 kg = 1050-1150 kcal/day
 - Anthropometrics: well nourished on admission
 - Nutrition concerns: intermittent nausea, poor appetite

Case Study 

- **Nutrition Intervention**
 - Ordered for a low fat diet
 - 10% EER from fat = 11-13 grams fat/day
 - She was eating fruits, starches, fat free dairy products, small amount of lean meats
 - Ordered for Monogen® with DHA & ARA 30 cal/oz
 - Drinking ~16 ounces per day (~2.2 g LCT)
- Drainage gradually slowed and CT removed after 20 days

Case Study 


- Discharged home after 3 week admission with plan to continue the low fat regimen given concern for underlying lymphatic abnormality
- Mom continued to express fear of giving oral fat; may likely be receiving <10 g/day by mouth
- After 8 weeks of remaining on a low fat regimen, EFA profile and zinc levels were checked

Case Study 


- Essential Fatty Acid Profile after 8 weeks on low-fat diet

	Result	Reference Range
α-Linolenic acid	35	20–200 nmol/mL
Linoleic acid	1211	1210–4300 nmol/mL
Mead Acid	164 (H)	1–35 nmol/mL
Triene:Tetraene ratio	0.427 (H)	0.004–0.05
Zinc	74	60–120 mcg/dL


- Labs notable for severe EFA deficiency for which EFA supplementation with walnut and flaxseed oil was started
- Educated parents on optimizing EFA intake in the diet

Case Study 


- Learning points:
 - Increased deficiency risk after 4 weeks on a restricted diet
 - Close nutrition laboratory monitoring is imperative
 - Preventative supplementation may be beneficial when EFA and micronutrient intake is suboptimal
 - Parental education is vital to help understand diet modifications, risks, and importance of supplementation


Summary 

- Lymphatic system is vital for immunity and transport of protein, fat, and fluid
- Conservative management of chylothorax is with diet modifications
- Children are at high risk for protein-calorie malnutrition, essential fatty acid and other micronutrient deficiencies
- Further research is needed to better define nutrition recommendations for other lymphatic disorders


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Questions? 




"Looks aren't everything. It's what's inside you that really matters. A biology teacher told me that."

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