Chylothorax: recent advances

Arunabh Talwar, M.D.

Division of Pulmonary & Critical care medicine
North-Shore University Hospital, Manhasset, NY
Chylothorax

Effusion of lymph in the pleural cavity due to disruption of thoracic duct
Development of Thoracic duct
Chyle: normal physiology

- Thoracic duct transports intestinal and skeletal lymph
- 2.5 L/day chyle emptied into venous system
- Flow varies from 14 ml/hr to 100 ml/hr postprandial
- Chyle flow increases with serotonin, nor-epinephrine, dopamine; decreases with starvation, intestinal rest, opiates

Paes ML. BJ Hosp Med 1994; 51:482
Normal characteristics of chyle

**Characteristics:**
- Milky appearance
- pH: 7.4-7.8
- Specific gravity 1.012-1.025
- Sterile
- Fat globules staining with sudan III
- Lymphocytes 400-6800/mm³
- Erythrocytes 50-600/mm³
Normal Composition of Chyle

Total protein 21-59 g/l
  Albumin 12-41.6 g/l
  Globulin 11-30.8 g/l
  Fibrinogen 160-240 mg/l
Total fat 4-60 g/l
  Triglycerides- above plasma value
  Cholesterol- plasma value or lower
Sugar 2.7-11.1 mMol/l
Urea 1.4-3.0 mMol/l
Electrolytes- similar to plasma value
Pancreatic exocrine enzymes present
Lipoprotein electrophoresis- present
chylomicron band
Cholesterol/triglyceride ratio < 1
Cholesterol crystals: rectangular, notched plates. Wet preparation, Brightfield light

Cholesterol crystals: In Polarized Light
Clinical manifestations

- Infants:
  - respiratory distress

- Adults:
  - dyspnea,
  - Chest discomfort,
  - Pleuritic chest pain is rare (chyle is non-irritant to the pleura)
Diagnostic work-up

- X-ray Chest: AP and lateral
- Lymphangiogram
- Lymphangioscintography
- CT chest
Biochemical diagnosis

- Presence of chylomicrons
- Pleural fluid Triglyceride levels >110 mg/dl
- Pleural TG / serum TG >1; Pleural chol / serum chol <1
- Pleural TG / pleural chol > 1
- Pitfalls:
  - I) Pts with hypertriglyceridemia may have elevated TG levels in pleural fluid as well
  - incidental leakage of TPN fluid in pleural cavity
- If pleural fluid TG 50-100 mg/dl, consider lipoprotein analysis
- Chylothorax: fluid always transudative except in nephrotic synd and cirrhosis

Lipoprotein profile of chyrous and non-chyrous pleural effusion
Causes of Chylothorax

I. TRAUMA

Surgical Trauma
- Coronary artery bypass
- Congenital heart disease repair
- Bochdalek herniorraphy
- Esophageal resection
- Esophagoscopy
- Celiac plexus block
- Radical neck dissection
- High translumbar aortography
- Superior venacava or subclavian vein catheterization
- Amputation of upper arm
- Gastric resection

Non-Surgical Trauma
- Penetrating gunshot or stab wound
- Blast or crush injuries
- Weight lifting or straining
- Severe bout of coughing or vomiting
- Vigorous stretching while yawning
Causes of Chylothorax

II. INFECTIONS
• Filariasis
• Bilharziasis
• Tuberculosis
• Syphilis

III. IDIOPATHIC
• Neonatal spontaneous
• Down’s syndrome
• Noonan’s syndrome
• Turner syndrome
• Maternal polyhydramnios
• Diaphragmatic defects
• Pulmonary hypertension

IV. NEOPLASMS
• Lymphomas
• Chronic lymphatic leukemia
• Bronchogenic Carcinoma
• Gallbladder Carcinoma
• Multiple Myeloma
• Wilms tumor
• Prostate carcinoma
• Uterine cancer
• Stomach cancer
• Pulmonary Kaposis
• Lymphosarcoma
• Mediastinal lymphangioma
• Metastatic carcinoid tumor
Causes of Chylothorax

MISCELLANEOUS

- Behcet’s syndrome
- Amyloidosis
- Sarcoidosis
- Cirrhosis
- Heart failure
- Tuberous sclerosis
- Nephrotic syndrome
- Gorham’s syndrome
- Post irradiation
- Pregnancy
- Retrosternal goiter
- Hypothyroidism

- Yellow nail syndrome
- Lymphangiomatomyomatosis
- Congenital lymphangiectasia
- Thoracic duct atresia
- Jaffe Campanacci syndrome
Complications of chylothorax

- Malnutrition
- Lymphopenia with T-cell deficiency (Breaux JR. J Trauma 1988; 28; 705)
- Hypoalbuminemia
- Water and electrolyte loss
- Increase risk of infections
- Watch for?? Lipophilic drugs like Amiodarone, Digoxin: subtherapeutic serum levels with normal to high levels in the chylous drainage (Taylor MD. Chest 1998; 114: 1482)
Spontaneous chylothorax

- Presents with supraclavicular swelling and left or bilateral chylothorax in women after mild effort
- No underlying cause established
- ?Fixation of the thoracic duct to by previous trauma, infection,
- ?Anomaly of the underlying vertebrae and sudden overstretching of the fixed duct by strenuous activity
- Sudden increase in duct pressure from coughing, especially after a heavy meal

Pantin et al. Resp Med 1989; 83:445
# Incidence of chylothorax in esophageal resections

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>No. of resections</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skinner et.al.</td>
<td>1983</td>
<td>80</td>
<td>2</td>
</tr>
<tr>
<td>Hankins et.al.</td>
<td>1987</td>
<td>26</td>
<td>4</td>
</tr>
<tr>
<td>King et.al.</td>
<td>1987</td>
<td>100</td>
<td>1.0</td>
</tr>
<tr>
<td>Orringer et.al.</td>
<td>1988</td>
<td>320</td>
<td>3.4</td>
</tr>
<tr>
<td>Woods et.al.</td>
<td>1989</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>Tam et.al.</td>
<td>1989</td>
<td>316</td>
<td>0.6</td>
</tr>
<tr>
<td>Bolger et.al.</td>
<td>1991</td>
<td>537</td>
<td>2.0</td>
</tr>
<tr>
<td>Dougenis et.al.</td>
<td>1992</td>
<td>255</td>
<td>3.9</td>
</tr>
</tbody>
</table>
Indications for surgery

• Chyle leak greater than 1 L per day for more than 5 days (or > 10 ml / Kg)
• Persistent leak for more than 2 weeks despite conservative management
• Nutritional or metabolic complications
• Loculated chylothorax, fibrin clots or incarcerated lung

Merrigan et. al. BJS 1997; 84: 15-20
Causes of chylothorax along with chyloperitoneum

- Nephrotic syndrome
- Malignancy: Wilm’s tumor, Gall bladder Ca, Uterine Ca, Stomach Ca, Lymphoma
- Retroperitoneal surgery
- Hypothyroidism
- Sarcoidosis
- Yellow Nail Syndrome
- Idiopathic
- Alcoholic pancreatitis
- Primary Lymphatic Disorders:
  - Primary Lymphatic dysplasia
  - Lymphangioleiomyomatosis (LAM)
Pseudochylothorax

• Pleural fluid that is milky but not associated with disruption of Thoracic duct
• More likely to result from long standing pleural effusions >5 yrs duration
• Cholesterol levels >200 mg/dl
• Presence of cholesterol crystals
• Thickened pleura
• Commonest reported cause is TB
• Acute pleurisy- LDL fraction
• Chronic pleurisy- marked shift to HDL fraction
• Pseudochylothorax- peak in HDL

Halm et.al. Respiration 1998; 58-94
<table>
<thead>
<tr>
<th></th>
<th><strong>Chylothorax</strong></th>
<th><strong>Pseudochylothorax</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presentation</strong></td>
<td>Usually acute</td>
<td>Always chronic</td>
</tr>
<tr>
<td><strong>Pleural surface</strong></td>
<td>Smooth</td>
<td>Thickened/calcified</td>
</tr>
<tr>
<td><strong>Mechanism</strong></td>
<td>Chyle leakage</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Cause of opalescence</strong></td>
<td>Chylomicrons</td>
<td>Cholestrol crystals or lecithin-globulin complexes</td>
</tr>
<tr>
<td><strong>Addition of ethyl ether</strong></td>
<td>Clearing of opalescence</td>
<td>Opalescence persists</td>
</tr>
<tr>
<td><strong>Creamy layer on standing</strong></td>
<td>yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Triglyceride levels</strong></td>
<td>high</td>
<td>Usually low</td>
</tr>
<tr>
<td><strong>Cholesterol</strong></td>
<td>low</td>
<td>Usually high</td>
</tr>
<tr>
<td><strong>Chylomicrons</strong></td>
<td>yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Neoplasm, trauma, congenital</td>
<td>T.B, RA, CHF</td>
</tr>
</tbody>
</table>
Complications of pseudochoxylothorax

- Respiratory insufficiency
- Infections
  - Reactivation of TB
  - Secondary Empyema
  - Fungal infection, esp Aspergillus
- Fistula: Bronchopleural/Pleurocutaneous

Hillerdal G. Eur Resp J 1997; 10: 1157
Management of pseudochoyloothorax

Review of 174 cases, majority males

- Repeated thoracentesis if pt. has dyspnea
- Surgical decortication if recurrent symptomatic case
- Serum ADA levels not helpful

Zamalloa AG et.al. Medicine 1999; 78: 200-7
Pediatric Chylothorax

• Group 1: Chylothorax occurs after direct trauma (post-surgical)
  – Incidence after cardiothoracic surgery 2.5%
• Group 2: secondary to obstruction/ high pressure in SVC. e.g.Fontan and Senning procedure
  – Duration is longer and higher volume drainage as compared to group 1
• Group 3: congenital chylothorax
• Group 2 & 3: higher risk of failure to conservative management (p= <.005)

Beghetti M. J Ped 2000; 136: 653-8
Congenital Chylothorax

- 50% present in first 24 hr of life, 70% within first week
- Acute respiratory distress
- Initially serous, turns chylous after milk feeding
- Increased venous pressure during delivery leads to thoracic duct rupture
- Commonest cause of pleural effusion in neonatal period
- Assc with Turner, Noonan, Down syndrome

AlTawil K. AMJ Perinatology 2000; 17: 121-6
Yellow Nail Syndrome

- Triad: Dystrophic yellow nail (89%), lymphedema (80%), pleuro-pulmonary symptoms (63%)
  - Chylothorax, Bronchiectasis, Rhino-sinusitis
- Hypoplasia of lymphatic vessels
- Twice as common in females
- Associated with RA, AIDS, TB, Breast and Gall bladder Ca., certain immunological disorders, mycosis fungoides

Gorham’s syndrome

- Hemangiomatosis or Disappearing Bone Disease
- Massive osteolysis due to intraosseous proliferation of lymphatic vessels
- Chylothorax in 17% cases due to direct extension of lymphatic dysplasia or by damage to thoracic duct by bone involvement

Willkinson IB. Thorax 1996; 51(12):1275
Pulmonary Lymphangiomatomyomatosis (LAM)

- Proliferation of immature smooth muscle throughout the peribronchial, perivascular, perilymphatic space
- Exclusively in women of reproductive age
- Chylothorax in 50%, pneumothorax 5%
- May be part of Tuberous sclerosis (seizures, adenoma sebaceum, mental retardation)

Izumi T. Int Med 2000, 39: 738
LAM

- Diagnosed on Lung Biopsy
- Anti HMB45 antibody positive
- Frequently associated with renal angiomyolipoma and uterine leiomyoma
- Treatment: Hormonal RX
  Lung Transplant
Goals of conservative Rx

- Obliterate the pleural space
- Improve dyspnea
- Prevent dehydration
- Maintain nutritional balance
- Minimize chyle production
- At least 50% traumatic chylothorax resolve on conservative management (Robinson CLN. Ann Thorac Surg 1985; 39: 90-5)
- Non-traumatic chylothorax: success of conservative Rx depends upon the underlying cause
Conservative Management: Nutrition

• **Medium chain triglyceride (MCTs):**
  – Directly absorbed into portal system bypassing the intestinal lymphatics and decreasing thoracic duct flow; decrease quantity and total duration of chyle loss
  – Trioctanoin (C8:O) may be preferred MCT
  – Success is variable: a) oral feeding increases lymph flow; b) not all MCTs absorbed via portal system
  – Deficiency of Linoleic acid, present in long chain triglycerides

• **TPN**
  – Not only minimizes chyle flow but provides complete adequate nutrition
  – Fistula closure rate is higher with TPN as compared to MCT (Ramos et.al. J Paren Ent Nutr 1986; 10:519)
  – Risk of infection
Conservative Management

- Intravenous Immunoglobulins as an adjunct (Mohan et al. Ped Anesth 1999; 9, 89)
- Radiation therapy in malignancies involving mediastinum
- Steroids for Sarcoidosis, lymphangiectasia
- Somatostatin analogs
Conservative management

• Treatment of underlying disorder
• Chest tube drainage
  – Relieves the dyspnea
  – Re-expands the collapsed lung
  – Obliterates the pleural space
  – Measurement of chyle production
  – Pleurodesis can be performed
  – Complications: Blockage and sepsis
• Repeated thoracentesis
  – Usually done in neonates for congenital chylothorax
Post-surgical chylothorax

- 850 esophagectomies
- Chylothorax 2.7% (23 pts)
- 14 successfully managed with medical Rx
- 9 pts (>10 ml/Kg drainage at day 5) required surgical management: 2 died from sepsis
- Daily chylous output of <10 ml/Kg at day 5 was a predictor of success of medical Rx

Dugue L. BJS 1998; 85: 1147
Lymphangiography

• May help identify the site of leakage
• Identify lymphangiectasia and enlarged lymph nodes
• Delineates the anatomy of thoracic duct, its variations particularly for videoscopic thoracic surgery
• Absence of demonstrable leak associated with opacification of lymphatic system all the way to jugulosubclavian junction suggests increase likelihood of response to conservative Rx (Vallieres E. Ann Thorac Surg 1993; 55: 1006)
CT scan post lymphangiography: visualization of leak
Lymphoscintigraphy

$I^{123}$ labelled fatty acid derivative idophenylpentadecanoic acid (IPPA) : oral administration
Octreotide (somatostatin analog)

- Acetate salt of a cyclic octapeptide
- Synthetic analog of somatostatin
- Inhibitory Neuropeptide
- Inhibits Growth hormone, glucagon and insulin
- Suppresses LH response to GnRH
- Suppresses TSH
Octreotide (somatostatin analog)

• Decreases splanchnic blood flow
• Inhibits gallbladder contractility and decrease bile secretion
• Inhibits the release of several GI hormones (gastrin, secretin, serotonin, VIP, motilin, pancreatic polypeptide)
• Blocks the exocrine function of the stomach and pancreas and therefore inhibits absorption of TG
• Decreases motility of the stomach and gut
Octreotide

- 5 subtypes of human somatostatin receptors (Type 1 and 5 found in GI tract)
- Octreotide has affinity for receptor type 2 and 5
- Given subcutaneous or intravenous
- S/E: hyperglycemia, nausea, abdominal cramps, diarrhea, malabsorption of fat, and flatulence, cholesterol gall stones
Surgical options

• Ligation of the thoracic duct (95% success rate)
  – Thoracoscopy
  – Thoracotomy
• Thoracic duct embolization
• Thoracosopic pleurodesis
• Pleuro-peritoneal shunt
• Thoracic duct to Azygous vein anastomosis
• Pleurectomy
Post-surgical chylothorax Rx

- 1787 esophagectomies, 1980-1998
- Chylothorax 1.1% (19 pts)
- Group A: 11 managed conservatively, 4 (36%) had resolution, 7 needed surgical Rx, 1 mortality, median length of stay 36 days
- Group B: 8 patients managed with early surgery (thoracic duct ligation), no complications/mortality, median length of stay 22 days
- Early surgery avoids nutritional, immunological depletion and decreases length of stay

Merigliano et.al. JTCVS 2000; 119:453
Identification of site of leakage

• Damage to thoracic duct rarely recognized during initial surgery
• Lymphangiography
• Intra-op identification of leak:
  – Oral or nasogastric cream administration
  – Evans blue dye subcutaneously
Normal Pleural surface appearance and in chylothorax on Thoracoscopy
Other surgical options

• Lung transplant for lymphangiomatomyomatosis (LAM)

• In pts with chylothorax and chyloperitoneum:
  – Peritoneo-venous shunting
  – Fibrin glue to close the leak in diaphragm

• In fetus: intrauterine thoracocentesis and/or pleuro-amniotic shunt
Pleurodesis for chylothorax

• 19 patients
• Lymphoma related chylothorax
• Talc pleurodesis (4-8 g), 24 hemithoraces treated
• Mean duration of chest tube: 4 days (range 3-10 days)
• No recurrence of pleural effusion at 90 days
• ARDS in 1 pt (4.1%), 8 pts died from malignancy related causes
• Others used Tetracycline, fibrin glue, OK-432 and bleomycin

*Mares DC, Mathur PN. Chest 1998; 114: 731-5*
Pleuro-peritoneal Shunt

- Useful when surgery contraindicated (e.g. premature infants, medically unstable pts)
- Shunt occlusion in 10%
- Contraindications
  - IVC thrombosis
  - High right atrial pressure > 25 mm Hg (seen in children with congenital heart disease)
  - Presence of chylosus ascites
• Provide prompt lasting palliation
• Relieve dyspnea
• Retain nutrients
• Avoid repeated thoracentesis
• Decrease time of hospitalization and cost
Pleuroperitoneal shunt
Suspect chylothorax

Confirm Diagnosis

Chest tube drainage
TPN
Somatostatin

If Improve
Continue conservative Rx

If No improvement
Pleurodesis
Surgery (Thoracic duct ligation)
Pleuro-peritoneal shunt
Ventilator strategy

- Increasing mean airway pressure (MAP) by pressure control ventilation and adding PEEP may be helpful in pts with persistent chylous leak and poor surgical candidates (Ragosta KG, Crit Care Med 2000; 28: 1208).
- Adding PEEP allows approximation of visceral to parietal pleura thereby sealing the injured lymph duct.
- Relationship between MAP and intrathoracic pressure is not always predictable, nor are changes uniform throughout thoracic cavity.
Embolization of Thoracic Duct

Hoffer EK. AJR 2001; 176: 1040
Hoffer EK. AJR 2001; 176: 1040
Nitric Oxide in post-op Chylothorax

Thank You