

Octreotide use for chylothorax – a review

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Conflict of interest

I was on the speaker's bureau for Ovation
Pharmaceuticals in 2007.

Objectives

- ◆ **Discuss pathophysiology of Chylothorax**
- ◆ **Describe the management of Chylothorax and experience with Octreotide**

What is Chyle?

- ◆ **Lymphatic fluid that contains fat (chylomicrons), protein (albumin, globulin), lymphocytes (70-90%) and enzymes (lipase and amylase). Specific gravity 1012-1025.**
- ◆ **Milky appearance is from chylomicrons**
- ◆ **In adults up to 2 - 4 L of chyle is transported per day (1.38 ml/kg/h)**
- ◆ **Flow depends on oral intake – fat.**
- ◆ **Sterile**

Anatomy of Thoracic Duct

- ◆ Thoracic duct begins at cisterna chyli at the level of second lumbar vertebra.
- ◆ Duct ascends into thorax via aortic hiatus and travels in the posterior mediastinum to the right aorta and posterior to esophagus. The duct terminates at the junction of the left subclavian and internal jugular veins.
- ◆ Considerable variations can occur during development.
- ◆ Numerous valves are present along the lumen and a large bicusped valve at the duct-vein junction.

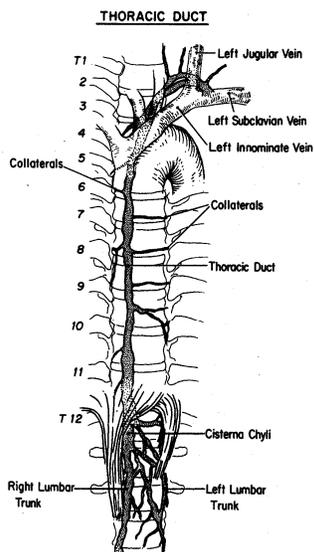
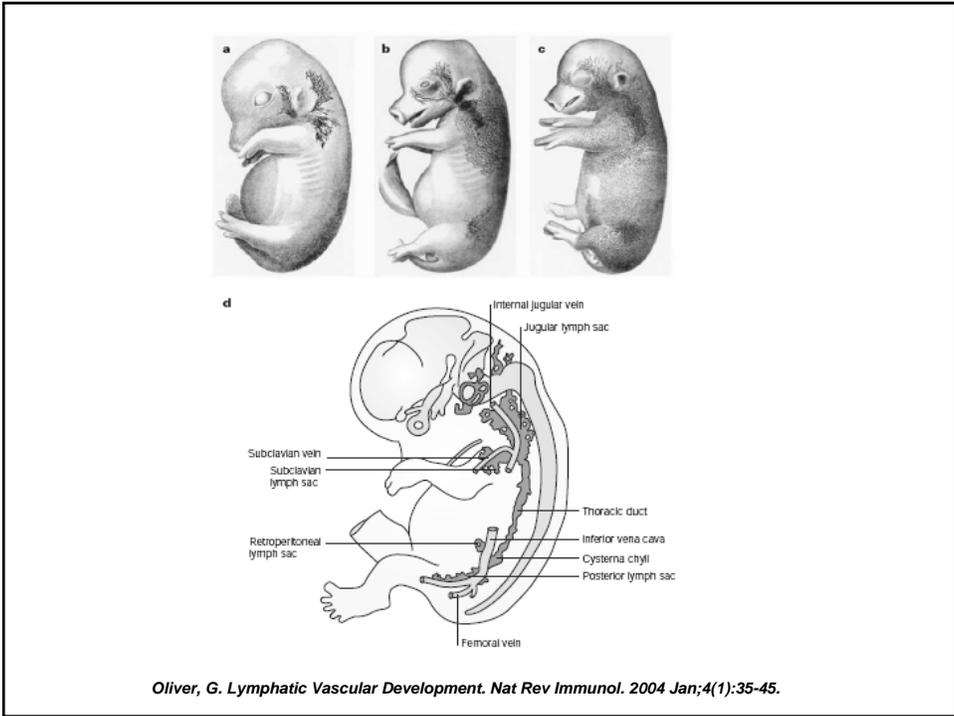


Figure 58-12 Schematic representation of most common anatomical arrangement of the thoracic duct. (From DeMeester TR, Lafontaine E: *The pleura*. In Sabiston DC, Spencer FC, editors: *Gibbon's surgery of the chest*, ed 4, Philadelphia, 1983, WB Saunders. Reprinted with permission.)



Incidence

- Congenital chylothorax occurs in 1:1,000 births
- Steady increase in the number of cases diagnosed prenatally
- Post-operative chylothorax occurs in 2.5 to 4.7% of cases

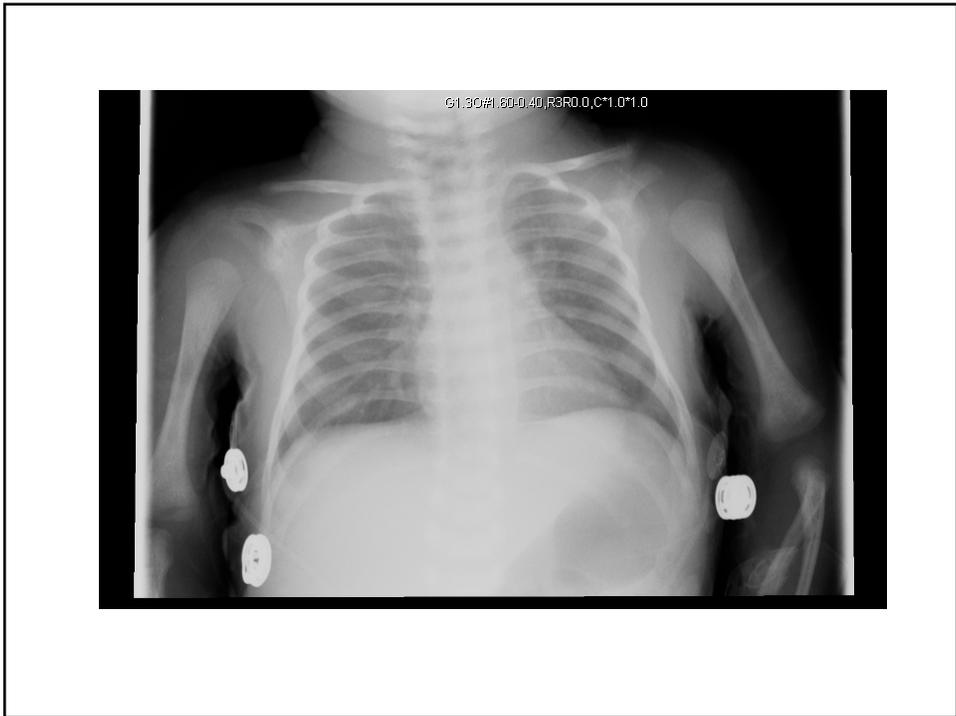
Etiology of Chylothorax

- ◆ **Congenital – Chromosomal, Malformations, Idiopathic**
- ◆ **Postoperative – Cardiac, pulmonary, T-E fistula**
- ◆ **Traumatic – Birth trauma**
- ◆ **Obstructive – Extrinsic or Intrinsic**

Diagnosis

- ◆ Fluid composition
- ◆ Recurring effusion
- ◆ Chest radiography
- ◆ Lymphangiography
- ◆ Follow up blood count (CBC); culture
- ◆ Cardiac Echo
- ◆ Karyotyping





Treatment of Chylothorax

- ◆ **Conservative** - NPO & TPN
- ◆ **(80% success)** - Diet: Rich in MCT
 - Evacuation of effusion
 - Octreotide

Octreotide acetate

- ◆ Sandostatin[®] - a cyclic octapeptide
- ◆ Molecular weight 1019.3
- ◆ Can be given SQ or IV
- ◆ Bioavailability 100%, Vd 21.6±8.5L
- ◆ Elimination half-life 1.7 to 1.9 hours
- ◆ 32% of drug is excreted to urine
- ◆ No pharmacokinetic studies in newborn

Indications for octreotide use in older children and adults

- ◆ **Endocrine disorders**
 - ◆ Acromegaly, Cushing's Syndrome, insulinoma

- ◆ **GI disorders**
 - ◆ Secretory diarrhea
 - ◆ Zollinger Ellison Syndrome
 - ◆ Post gastronomic dumping syndrome
 - ◆ Severe GI bleed

Indications for octreotide use in neonates

- ◆ **Chylothorax not responding to standard medical care**

- ◆ **Severe neonatal hypoglycemia**
- ◆ **Nesidioblastosis**

Octreotide Therapy

Mechanism of Action

◆ Effect on the GI System

- ◆ Decrease in splanchnic blood flow
- ◆ Reduction in the absorption of triglycerides
- ◆ Inhibition of Serotonin, Motilin, VIP, Gastrin
- ◆ Decreased gallbladder contractility and bile flow
- ◆ Reduction in the absorption of triglycerides
- ◆ Reduces gastric and intestinal secretions (antisecretory)

Experience with octreotide

Dose used mcg/kg/day	# of cases	Route of administration	Duration (days)	Diagnosis	Side effects	
1-10	3	IV, IV, SC	3,6,3,6	Neo. Chylothorax Dianphr. Hernia	-	L
11-20	2	IV? IV	3, 4	Hyperinsulinemia chylothorax	NEC	L
21-40	3	IV, IV, SC	10	VSD, IAA Hydrops, TGV	Hypoxia, PPHN	L L
41-80	5	IV q 8h, IV, SC, SC, IV	21,5,7-10, 16	Hypoplastic Lt.H rt Nesideoblastosis Cong. Chylothorax	Hypothyroidism	L L L
81-100	6	All IV	3,8,3,14	Coarctation of aorta, gastroschisis, Cong. Chylothorax	NEC Hyoerglycemia & Hypoglycemia	L L
>100	3	All IV	3,10,10	Pul. Lymphang +TAPVR, ectasia Cong. Chylothorax	-	D L

Review of all papers & infants <3 months of age

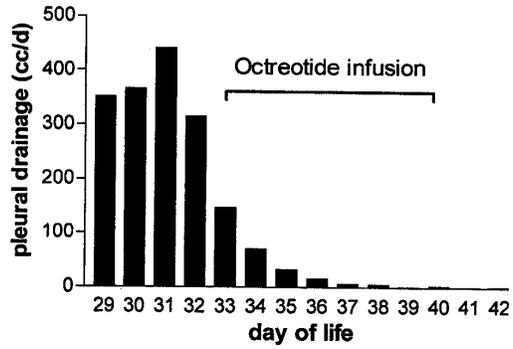
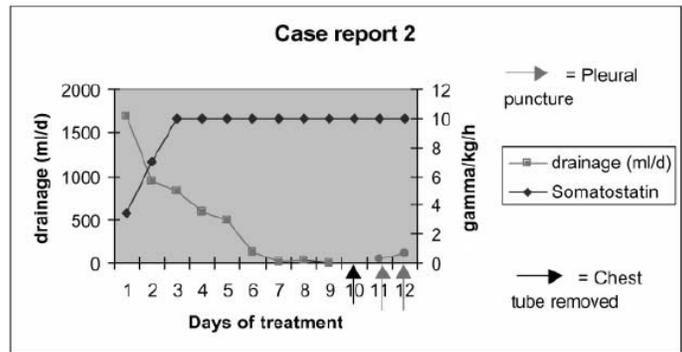


Fig 1. 24-hour pleural drainage on days surrounding octreotide infusion. Pleural effusions were first noted on day 14, and chest tubes were placed on day 24. Drainage averaged 250 to 300 mL/d on days 24 through 28. Octreotide was begun on day 33 and discontinued day 40.

Au M, Weber T, Flemming R, J Ped Surgery. 38:7 2003 p1107



Intensive Care Med (2001) 27: 1084

Side Effects

◆ Transient

- ◆ Loose stools, nausea, flatulence, Hypo or hyperglycemia, liver dysfunction, Distended abdomen, Hypothyroidism
- ◆ Pulmonary Hypertension
- ◆ Hypotension

◆ Serious

- ◆ Necrotizing Enterocolitis
- ◆ Cholelithiasis.

Necrotizing Enterocolitis

Incidence

- 0.3 to 2.4 cases /1000 live births
- >90% cases in infants <2000gms: 4-13%
- Annual number of cases: 2500 cases
- Mortality 10-15%

Pathophysiology of NEC

Multifactorial etiology

Ischemia, immunity and infection

Current concept:

Genetic susceptibility

Enteral feeding: breast versus formula

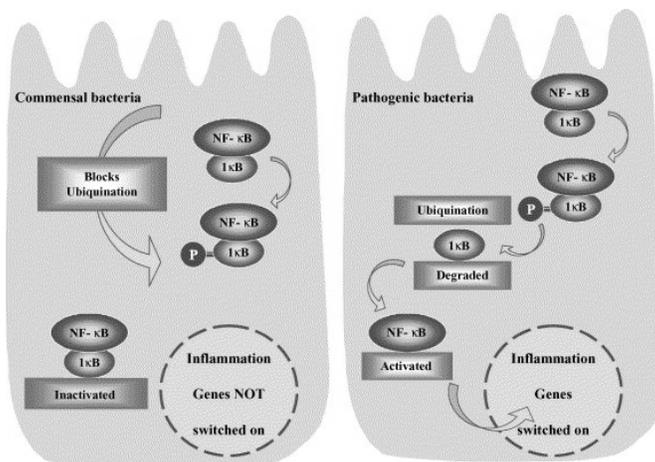
Immature luminal digestion

Bacterial proliferation

Immature barrier function

Inflammatory mediators

Pathophysiology of NEC



Mechanism by which commensal and pathogenic bacteria regulate intestinal inflammation.

Martin , Allan W. Seminars in Fetal and Neonatal Medicine. 11:5 2006 P 372



Treatment of Chylorthorax

- ◆ **Surgical Treatment (for refractory cases)**
 - ◆ Thoracic duct ligation
 - ◆ Pleuroperitoneal shunt
 - ◆ Plurodesis
 - ◆ Pleurectomy

Beghetti M, et al. J Pediatr:2000

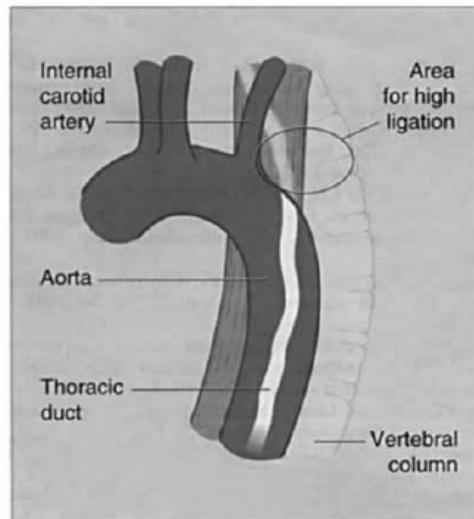


Fig. 2 Area for high ligation: Poirier's triangle between the internal carotid artery, arch of aorta and vertebral column

British Journal of surgery 1997, 84, 19

What we need to know

- **Pharmacokinetics in term and preterm newborns**
- **Dose response relationships**
- **Adverse effects**
- **Multi-center, randomized, controlled studies in post surgical and Congenital chylothorax**