Chapter 12

Miscellaneous Considerations

12.1 Pleural Effusions

Chest tube (CT) drainage that is sanguineous or sero-sanguineous lasts usually for a day or two after an uncomplicated open heart surgical (OHS) procedure. Prolonged (> few days) sanguineous and bloody drainage after OHS may be related to a poor surgical technique or bleeding diathesis.

Meticulous attention to a surgical technique and principles of hemostasis with adequate reversal of anticoagulation prevents the above problem.

Persistent drainage of serous or asanguineous fluid (> few days or a week) is due to collection of fluid in the pleural space (pleural effusion) and should be further evaluated.

12.1.1 Normal Fluid Movement in Pleural Space

Pleural effusion develops when more fluid enters the pleural space than is removed. Normally, 7-15 mL/kg/day (5 to 10 liters/day in an average adult) of protein free fluid flows from parietal pleural surface into pleural space and is absorbed by visceral pleura leaving only < 1-2 mL of fluid in the space with the protein content of < 1.5 gm/100 mL (see Figure 34).

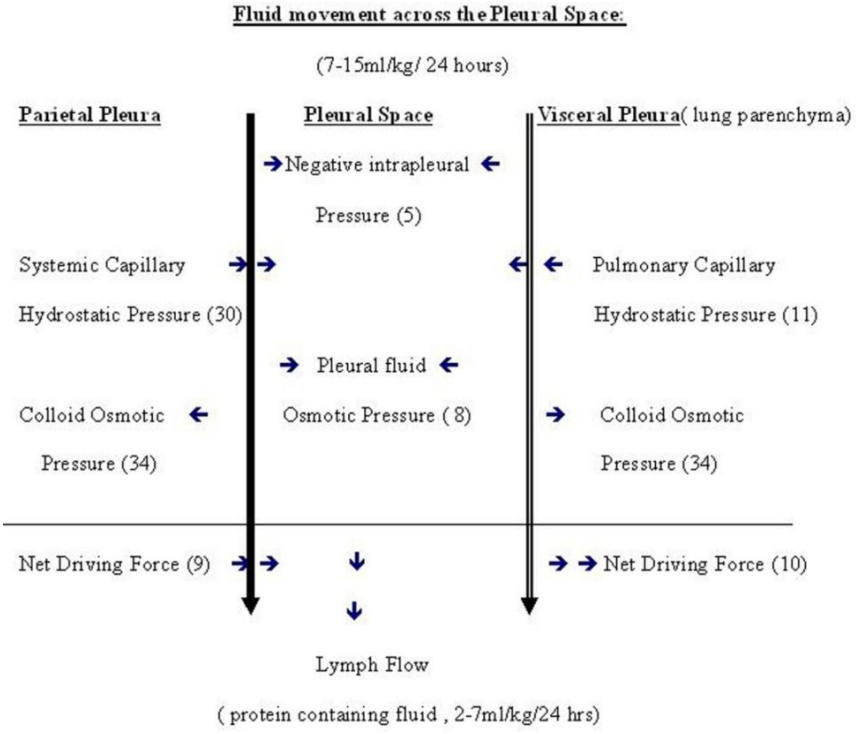

Figure 34 **Diagram depicting pleural and capillary hemodynamics responsible for normal movement of fluid and lymph in the pleural space. The numbers in parenthesis indicate pressures in cm of H_2O. * Adapted and modified from GIBBON'S Surgery of the Chest, ed 4. Philadelphia, WB Saunders CO, 1983.*

The driving forces for the movement of fluid from parietal pleura to pleural space are:

1. Capillary hydrostatic pressure (30 cm H_2O) of parietal vessels (or systemic capillaries).

2. Negative intrapleural pressure (5 cm H_2O).

3. Colloid osmotic pressure (8 cm H_2O) of pleural space fluid.

The opposing force for the above movement of fluid is:

1. Colloid osmotic pressure (34 cm H_2O) of capillary blood.

Fluid moves into the pleural space from parietal capillaries with a net force of (30 cm + 8 cm + 5 cm - 34 cm of H_2O) 9 cm of H_2O.

Fluid from the pleural space is reabsorbed into the viscceral pleural surface capillaries.

Driving pressure for the above fluid movement (pleural space to visceral pleura) is:

Colloid osmotic pressure of visceral (pulmonary) capillaries (34 cm H_2O).

The opposing forces for the above movement of fluid from pleural space to visceral pleura are:

1. Pulmonary capillary hydrostatic pressure (11 cm H_2O).

2. Negative intrapleural pressure (5 cm H_2O).

3. Colloid osmotic pressure (8 cm H_2O) of pleural space fluid.

Fluid moves from pleural space into visceral pleural capillaries with a net force (34 cm - 11 cm + 5 cm + 8 cm H_2O) of 10 cm H_2O.

Protein that is leaked into the pleural space cannot be absorbed by diffusion due to high colloid osmotic gradient in the capillaries, but is removed by lymph.

Normal lymph flow is 2-7 mL/kg/24 hours, leaving only < 1-2 mL of fluid in the pleural space with a protein content of < 1.5 gm/100 mL.

12.1.2 Mechanisms of Formation of Pleural Effusion

↑ Intestitial fluid in the lungs secondary to ↑ pulmonary capillary pressure, ‘e.g., heart failure and Fontan circulation.

↑ Pulmonary capillary permeability (i.e., pneumonias).

↑ Negative intrapleural pressure (i.e., atelectasis).

↑ Pleural membrane permeability and obstructed lymph flow (i.e., pleural malignancy and infection).

↓ Plasma oncotic pressure (e.g., hypoalbuminemia).

12.1.3 Etiology of Pleural Effusions

Infants and children:

The most common cause is nosocomial or community acquired pneumonia.

The postoperative effusions are due to nosocomial pneumonia, heart failure, and Fontan circulation.

Adults:

Most common causes are heart failure, pneumonia, pulmonary embolism, malignancy, and tuberculosis.

Other causes:

Diaphragmatic defects (hepatic hydrothorax).

Thoracic duct rupture (chylothorax).

The pleural effusions are broadly divided into transudative and exudative effusions based on the mechanism of formation.

A. Transudative effusions:

Transudates result from imbalances in hydrostatic and oncotic forces.

Common causes: Fontan circulation, heart failure, and cirrhosis.

Rare causes: Atelectasis, constrictive pericarditis, SVC obstruction, nephrotic syndrome, peritoneal dialysis, and urothorax (uremic effusion).

Transudative effusions usually respond to diuretics.

B. Exudative effusions:

These result from alteration of local factors influencing the accumulation of pleural fluid.

Common causes:

Pneumonia, pulmonary embolism, tuberculosis, and malignancy.

12.1.4 Diagnosis of Prolonged Chest Tube Drainage

Prolonged chest tube drainage during the postoperative period should be thoroughly investigated, and the diagnosis should be ascertained as a cause of the effusion or accumulation of fluid in the pleural space, systematically, as discussed.

(I) Clinical History

1) Perioperative patient with any of the following conditions is prone for pleural effusion.

Congenital heart disease / heart failure with elevated pulmonary capillary pressure, Fontan circulation, trauma to lymphatic / thoracic duct, prolonged postoperative bleeding, bleeding diathesis, perioperative pneumonias, and pulmonary embolism.

The following preexisting conditions in a patient may also influence formation of pleural effusion in the postoperative period.

Auto-immune disease, community acquired pneumonia, pulmonary tuberculosis, and malignancy.

2) Analysis of pleural fluid.

3) Optional and specific diagnostic tests of pleural fluid.

(II) Analysis of Pleural Fluid

A. Gross appearance of pleural fluid:

1) Turbid pleural fluid:

Caused either by cells and debris as in empyema, or by a high lipid levels in chylothorax.

2) Blood-stained fluid (i.e., fluid Hct > 1% of blood Hct):

Post-cardiac surgery (trauma), pulmonary embolism, pneumonia, and malignancy.

3) Pleural fluid Hct > simultaneous blood Hct:

Hemothorax.

B. Biochemical Characteristics:

These differentiates effusions as transudates or exudates.

Light's criteria (100% sensitive) may be used for differentiation of transudates from exudates.

Initially analyze pleural fluid to determine whether the effusion is a transudate or an exudate. Pleural fluid needed for the test is 20 mL for basic and 60 mL if further diagnostic studies are required.

a) Determine concomitant serum and pleural fluid total protein and LDH levels.

b) If the patient was/is on diuretic therapy, determine concomitant serum and pleural fluid albumin also.

Light criteria:

Pleural fluid is transudate if none of the following criteria are met;

Fluid is exudate if one or more criteria are met.

1) Pleural fluid / serum protein levels ratio > 0.5

2) Pleural fluid / serum LDH levels ratio > 0.6

3) Pleural fluid LDH level > 2/3 of the upper normal of serum LDH.

Above criteria are less accurate for transudates due to congestive heart failure and patients on diuretics. Longer is the diuretic therapy, more likely, the fluid will have exudative characteristics.

If there is high suspicion of pleural effusion as a transudate due to congestive heart failure, determine the serum-to-pleural fluid albumin gradient (i.e., serum albumin level – pleural fluid albumin level).

A gradient < 1.2 g/dL is exudative effusion.

A gradient > 1.2 g/dL is transudative effusion.

20% of effusions caused by CHF fulfill criteria for an exudative effusion, post-diuretic use.

In above cases the diagnosis of transudative effusion is most likely if:

1) serum and pleural fluid protein levels difference is > 3.1 gm/dL.

2) Serum and pleural fluid albumin gradient > 1.2 gm/dL.

(III) Optional and Specific Diagnostic Tests of Pleural Fluid

Clinical presentation may determine the need for further biochemical and microbiological studies. Exudative effusions usually require further investigation of pleural fluid as discussed below:

1) WBC count with differential

Pleural fluid is sent in an anti-coagulated tube for total and differential white cell count.

2) pH, glucose, and amylase levels

pH: Fluid is collected anaerobically in a heparinized syringe and analyzed by a blood-gas machine.

pH < 7.20 in parapneumonic effusion indicates the need to drain the fluid.

If a pleural fluid pH value is inconclusive, pleural fluid glucose levels are done.

Glucose:

If pleural fluid glucose level is of < 60 mg/dL, it identifies complicated parapenumonic effusion.

A pH value < 7.30 is associated with poorer response to chemical pleurodesis and ↓ survival in malignant pleural effusions.

Amylase:

If pleural fluid amylase is > upper normal of serum amylase, it suggests esophageal perforation / or a malignancy.

3) Adenosine Deaminase (ADA)

ADA is an enzyme that plays an important role in lymphoid cell differentiation.

ADA level > 40 U/L has 90-100% sensitivity and 85-95% specificity for tuberculous pleurisy.

The specificity for TB is > 95% if exudates are only lymphocytic.

4) Cytological analysis:

10 mL of pleural fluid is adequate for testing.

Cytological analysis is performed in suspected pneumocystis carinii infection, mailgnancy, and in suspected exudative effusions with normal fluid glucose and amylase levels.

Cytology is positive in only 60% of malignant effusions.

Cytology is usually negative with mesothelioma, sarcoma and lymphoma.

5) Staining: Gram stain, acid-fast bacilli (AFB), and fungal (KOH).

AFB staining is positive rarely (in 5%) in tuberculous pleurisy, unless patient has tuberculous empyema.

6) Culture and sensitivity:

It is performed for suspected aerobic and anaerobic bacterial organisms and fungi.

Culture yield is increased if blood culture bottles are inoculated at bedside with a pleural fluid.

Cultures identify microorganisms in 40% of parapneumonic effusions.

If fluid is grossly purulent, culture is positive in 70% of cases.

If tuberculous effusion is suspected, culture of both the pleural fluid and sputum is obtained.

The yield of sputum culture in tuberculous effusion is only 10 to 60%.

Mycobacterium is difficult to be isolated in tuberculous effusion in > 60-70% as tuberculous pleuritis develops due to delayed hypersensitivity. About one third of patients with tuberculous effusion have a negative PPD skin test.

(IV) Further Diagnostic Studies

The following studies are to be done on basis of the gross appearance of the pleural fluid or if a specific condition is suspected.

i) Centrifugation:

It should be performed if the pleural fluid is turbid, milky, bloody, or brown, and if chylothorax is suspected. If supernatant of the pleural fluid remains opaque after centrifugation, study the fluid chemistry for triglyceride, cholesterol and total lipid levels and microscopic examination of the sediment.

Lipoprotein analysis demonstrates chylomicrons in the pleural fluid.

A ratio of pleural fluid to serum creatinine level > 1 confirms urinothorax.

Straw-colored pleural effusion with ammonia (urine) odor suggests urinothorax.

ii) Immunologic studies of the pleural fluid:

Rheumatoid factor titer, antinuclear antibody level, amylase isoenzyme determination, or immunohistochemical studies are performed.

iii) Hematocrit of the pleural fluid:

In hemothorax, the pleural fluid hematocrit is > 50% of the serum hematocrit.

Traumatic thoracentesis:

Traumatic thoracentesis should be differentiated from hemothorax by the following criteria:

a) Non-uniform red discoloration of fluid during aspiration.

b) Clotting of the fluid within minutes (due to presence of platelets).

c) Absence of hemosiderin-laden macrophages.

One may perform 2nd thoracentesis in the following situations:

1. The suspected malignant effusion and initial pleural fluid cytological examination is negative.

2. A parapneumonic effusion with a borderline biochemical indicators for CT tube drainage.

3) Suspected acute tuberculous pleurisy with non-diagnostic pleural adenosine deaminase (ADA) levels.

iv) Blood studies:

Blood cultures (2 tests, preferably from different sites and one-half hour apart) are performed, and ensure determination of serum glucose, amylase, and arterial pH.

Confirmatory diagnosis: After analyzing several tests of the pleural fluid and blood, one can make a confirmatory diagnosis of the etiology of the effusion by ordering more specific tests dictated by clinical suspicion of the disease (see Tables 12.1, 12.2).

Table 12.1 *******Routine Pleural Fluid Tests in Pleural Effusion.*

Test	Test result	Inference and Comments
Glucose	< 60 mg/dL (3.3 mmol/L)	Empyema or complicated parapneumonic effusion, 20% of TB effusions, (< 10%) of malignancy, rheumatoid arthritis. Pleural fluid with low glucose levels also have low pH and high LDH levels
LDH	> 2/3 of normal serum LDH	Any condition causing an exudate. Very high levels of LDH (> 1000 U/L) found in complicated parapneumonic and 40% of tubrculous effusions
LDH fluid/serum ratio	> 0.6	Any condition causing an exudate. If LDH criteria are met, but not protein criteria for exudative effusion, it is parapneumonic or malignancy
Protein fluid/serum ratio	0.5	Any condition causing an exudate. Pleural fluid protein level > 3 gm/dL suggests an exudates. This criteria alone misdiagnoses 10% exudates and 15% transudates
WBC Count and differential	> 10,000/cumm	Empyema, other exudates (not common). WBC count is lower than expected in purulent fluid due to presence of dead WBC cells and debris
Eosinophils	>10%	Diagnosis is non confirmatory in 1/3 of eosinophillic pleural effusions. Presence of air or blood in the pleural space may be the cause
Lymphocytes	>50%	Tuberculosis, pulmonary embolism, post CABG surgery. Pleural lymphocytosis > 90% suggests lymphoma, or tuberculosis
Neutrophils	>50%	pulmonary embolism, parapneumonic effusion. 7% of acute tuberculos pleurisy, and 20% of malignant pleural effusions
Red blood cells	>100,000/cumm	Parapneumonic effusion, pulmonary embolism, trauma, malignancy. Fluid hematocrit of < 1% is insignificant
Adenosine deaminase	>40 units/L	60% empyema, 5% malignancy, rheumatoid arthritis
(ADA)	(667 nkat/L)	30% complicated parapneumonic effusions, >90% of tuberculosis. Due to low prevalence of tuberculous pleurisy, ADA is not routinely done
Cytology	Positive	Malignancy, actively dividing mesothelial cells may mimic adenocarcinoma

Modified from: PORCEL M J, and LIGHT WR, Diagnostic Approach to Pleural Effusion in Adults. Am Fam Physician. 2006.

Table 12.2 **Specific Pleural Fluid Tests in Pleural Effusion.*

Test	Test result	Inference and Comments
pH	< 7.20	Complicated parapneumonic effusion or empyema, < 10% of malignancy, < 10% of tuberculosis, esophageal perforation. Obtain in effusions if infection is suspected. A low pleural fluid pH indicates the need for CT tube drainage in only parapneumonic effusions
Amylase	> Upper normal	Pancreatic disease, malignancy, (< 20% of cases), esophageal rupture. Amylase in esophageal rupture and malignancy is salivary type
Cholesterol	> 45-60 mg/dL	Any condition causing exudate. Obtain in suspected chylothorax and pseudochylothorax. This test alone misdiagnoses 10% exudates, 20% transudates
Triglycerides	>110 mg/per dL	Chylothorax. Obtain if pleural fluid is cloudy or milky. Not all chylous effusions are milky.
HCT fluid / Blood ratio	≥ 0.5	Hemothorax. Obtain if pleural fluid is bloody
NT-pro BNP	> 1500 pg/mL	Heart failure. Do in suspected heart failure, if exudate criteria are met
Polymerase chain reaction (PCR)	Positive	Consider if infection is suspected. Sensitiviy to detect tuberculos pleurisy ranges 40-80%, but much lower if TB cultures are negative.
Interferon	variable points	Consider if ADA is unavailable and tuberculosis is suspected.
Culture	Positive	Confirmation of infection and obtain in all parapneumonic effusions, positive gram stain or culture mandates prompt CT drainage

*Modified from: PORCEL M J, and LIGHT WR, Diagnostic Approach to Pleural Effusion in Adults. Am Fam Physician. 20061220.

12.1.5 Technique for Chest Tube (CT) Drainge

May use conventional CTs (French size) or Blake tubes depending on size of the infant and child. Blake drains (10F, 15F, and 19) are safer and more efficient than conventional CTs.

Advantages of use of Blake tubes:

Blake drains (10F, 15F, and 19F) are safer and more efficient than conventional CTs. Blake drains remove the same amount of fluid drained as with conventional tubes with use of smaller size tubes, and facilitates earlier removal, with fewer occurrences of recurrent effusions.

12.1.6 Pleurodesis

Indications:

Pleural effusion lasting more than a week in postcardiotomy patients.

Methods: Surgical/talc pleurodesis or inntrapleural doxycycline infusion.

Intrapleural doxycycline infusion:

It can be used in neonates, young infants, and children.

Dose: 19.1 mg/kg/dose.

Doxycycline (parenteral form) is diluted in a normal saline to a syringe concentration of 2-8 mg/mL. The total dose is injected through a chest tube, and the patient is rotated according to set protocol. Dose should be remained in the pleural space for at least 6 hours before being drained by CT suction.

Expected results:

Treatment is successful if CT tube output is 0 mL/hr; overall success rate is 90-95%. Treatment success is not related to concentration of doxycycline.

Mean time from dosing to CT tube removal is usually 5 days (range 8 hr-450 hrs). Chest pain is the most common adverse effect.

12.1.7 Post Cardiac Surgery Eosinophilic Pleural Effusions

Increased eosinophil counts are present in blood and pleural fluid.

Allergic response might have caused the persistent effusion.

Pleural effusions are characterized by recurrent and persistent effusions with ↑ eosinophil counts.

Treatment:

Corticosteroid therapy is usually recommended.

Effusions resolve within hours after initiating corticosteroid treatment.

12.1.8 Fontan Circulation and Post-Fontan Pleural Effusion

It is a persistent fluid drainage or pleural effusion lasting > 10 to 14 days after Fontan operation.

1. Incidence:

21% to 45% of post-Fontan patients.

Results in prolonged hospitalization (i.e., > 2 to 3 weeks) in 13% to 45% of patients.

2. Contributing / modifying factors of pleural effusion:

A. Factors associated with decreased incidence of pleural effusions and shorter hospitalizations:

1) Creation of a fenestration.

2) Partial exclusion of the hepatic veins during completion of Fontan.

3) Extracardiac Fontan operation

B. Following factors may not be associated with increased incidence of prolonged effusions:

1) Cardiac function and morphology:

RV or LV morphology, degree of AV valve regurgitation, presence of pulmonary artery stenosis, and diminished ventricular function.

2) Hemodynamic status:

Age, preoperative O_2 saturation, mean pulmonary artery pressure > or < 12 mm Hg, pulmonary vascular resistance (PVR) > or < 2 Wood units, and left ventricular end-diastolic pressure.

3) Surgical procedure:

Type of Fontan; prior bidirectional Glenn procedure.

C. subclinical viral infection:

Upsets the balance required for adequate flow through a Fontan circuit in the early postoperative period.

The viral infection ↑ CVP, ↑ transpulmonary gradient, and results in prolonged pleural effusions. The mean postoperative CVP is statistically related to prolonged pleural effusions.

D. Fontan operation (fenestrated) during the winter respiratory viral season:

If fenestrated Fontan operation is performed during winter months, it may be associated with prolonged pleural effusions.

3. Morbidity of post-Fontan pleural effusion:

Loss of lymphocytes and plasma proteins, as seen in chylothorax.

Reduced cell-mediated and humoral immunity.

Increased risk of postoperative infection.

4. Pleurodesis in post-Fontan pleural effusion:

Indications:

Pleurodesis is usually required in 15 to 17% of effusions.

If CT drainage is prolonged and high-volume, pleurodesis is often indicated..

Initially, the patient should be on a low-fat diet.

If above is not successful, keep the patient NPO and give total parenteral nutrition.

Once the drainage has ceased, the patient is again placed on a low-fat diet.

Pleurodesis is usually done if significant drainage recurs after re-feeding.

12.2 Chylothorax

Chylothorax and chylopericardium are effusions of lymph in the pleural and pericardial cavities, characterized by a milky fluid due to high triglyceride content and presence of chylomicrons.

Chylomicrons are often detected by lipoprotein electrophoresis.

12.2.1 Types of Chylothorax

A). Traumatic chylothorax:

Cardiothoracic operations are principal causes such as:

Congenital heart surgery complicated by elevated venous pressure and / or trauma to the thoracic duct. It may occur in concurrent with chylopericardium.

B). Nontraumatic chylothorax:

Malignant lymphoma is the most common cause.

Other causes: Infection, thrombosis of SVC, lymphangiectasis, metastatic cancers, malformations of lymphatic system, lymphangiectasis, and lymphangioleiomyomatosis.

12.2.2 Postoperative Chylothorax

A. Incidence and Mechanisms of formation of postoperative chylothorax:

Recent ↑ incidence from previously reported 1% or less to 2.5% to 4.7%.

Occurs in children after several cardiothoracic procedures.

Several congenital heart operations are more prone to this complication.

Incidence is attributed to ↑ complexity of the surgery and earlier feeding after surgery. Increased pressure in the systemic vein exceeding that in the thoracic duct, and damage to the duct and / or disruption of accessory lymphatics are possible causes.

B. Cardiac operations associated with chylothorax:

The most frequent cardiac procedures implicated in chylothorax formation are mentioned below.

Repair or reconstruction of the right ventricular outflow tract.

Repair of tetralogy of Fallot.

Repair of pulmonary atresia with or without VSD.

Bidirectional cavopulmonary shunt.

Fontan-type of correction (duration of chylothorax after Fontan is significantly longer).

Right ventricular dysfunction after a cardiac procedure (repair of tetralogy of Fallot) predisposes to ↑ systemic venous pressure and increases the risk of chylothorax formation.

C. Surgical procedures in the vicinity of the thoracic duct:

Systemic-pulmonary arterial shunt, aortic coarctation repair, and ligation of PDA are more prone to this complication.

The location of postoperative chylothorax is left sided 60%, right sided 13%, and bilateral in 27% (in bidirectional Glen and modified Fontan).

12.2.3 Diagnosis of Chylothorax

Milky fluid drains from the chest tube and testing of the fluid depicts:

i) Sudan staining is positive for fat globules.

ii) Triglyceride levels ↑ (> 1.1 mmol/L) or > 110 mg/dL.

Triglyceride < 50 mg/dL usually rules it out, unless the patient has not been on enteral fat intake.

If triglyceride level is indeterminate (i.e., 50 to 110 mg/dL), lipoprotein electrophoresis is required.

iii) WBC count:

Ranges from 90 to 30,500 cells/mm^3 with lymphocyte predominance (> 80%) and sterile culture.

iv) Protein content: The fluid content of protein varies from 2.4 to 77.4 gm/dL.

12.2.4 Conventional Management Strategy of Chylothorax

(I) Conservative Therapy

Chylothorax may resolve in up to 75% to 85% of patients with conservative treatment. The treatment is as follows:

i) Chest tube drainage and pericardiocentesis: In addition to pleural drainage, pericardiocentesis may also be needed to relieve the symptoms of cardiac tamponade. Pericardial catheter may be placed for continuous and complete drainage.

ii) Modified diet:

Non-fat milk or food supplemented with MCT (medium chain triglycerides) oil, vitamins and minerals is recommended.

The above diet may be given for at least 30 days.

iii) TPN with bowel rest:

Patients should be kept on NPO and are given TPN if chyle reaccumulates, or there is no improvement 1 to 2 weeks after MCT-rich diet treatment. The usual trail period for treatment with medium chain triglycerides (MCT) or TPN is up to 30-45 days (average duration 12 days).

Risk factors for failure of conservative management:

1) Persistence of chyle output > 3 weeks duration.

2) Lesions associated with ↑ systemic venous pressure.

(II) Surgical Therapy and Interventions

Indications:

1. The chyle loss of > 100 mL/kg/year of age in children for a 5-day period, i.e., a 11 kg, 2 year old infant with a chyle loss of > 2200 mL/5 days (> 100 ×11 × 2 = > 2200 mL).

2. No decrease of chyle flow after 14 days of conservative treatment (above treatment I) or

3. Onset of evidence of nutritional complications.

4. Surgical intervention is usually indicated for a drainage that lasts > 4 weeks.

Surgical procedures:

Pleurodesis, ligation of the lymphatic ducts, ligation of the thymus gland, and pleuroperitoneal shunting.

12.2.5 Current Management Strategy of Chylothorax

Octreotide therapy (long-acting synthetic analogue of somatostatin):

Octreotide use is suggested prior to surgery in prolonged drainage refractory to conservative management.

i) Mechanism of action of octreotide:

Directly ↓ lymph excretion acting on the vascular somatostatin receptors.

Indirectly ↓ lymph flow, by ↓ splanchnic, hepatic, portal blood flows and inhibiting intestinal motility.

ii) The indications for octreotide therapy:

1) Persistent chyle leak for > 2 weeks of conservative treatment.

2) Significant drainage that exceeds 10 mL/kg/day (octreotide may be started even after 1 week of conservative treatment).

3) Failure of surgical intervention:

Surgical failure due to diffuse chyle leak after extensive surgical dissection or anatomic variations of the thoracic duct, further octreotide therapy may be required.

iii) Administration of octreotide:

Norvatis (subcutaneous octreotide):

Give at a starting dose of 10 ug/kg/day in 3 divided doses.

Increase the dosage by 5 to 10 ug/kg/day every 72 to 96 hours to a maximum of 40 ug/kg/day.

Continuous intravenous infusion:

Dose range: 0.3 to 10 ug/kg/hour (common median dosage is 2.8 ug/kg/hour).

iv) Weaning of octreotide:

Start weaning after 3 days of insignificant chyle output (< 10 mL/day).

Decrease the dose by 10 ug/kg/day daily and the drug is withdrawn rapidly over 3 to 4 days.

v) Complications of octreotide therapy:

A. Established and common:

Hyperglycemia or hypoglycemia, cardiopulmonary side effects, and gastrointestinal disturbance (abdominal distension).

B. Uncertain complications:

Hypoalbuminemia, septicemia, ↓ immune response, and necrotizing enterocolitis.

C. Other complications:

Essential fatty acids deficiency, lymphopenia, pneumonia, bacterial sepsis, and candidiasis.

vi) Expected results and comments on octreotide therapy:

Chylothorax may completely resolve in > 80% of conservative treatment failures about 2 weeks after starting octreotide.

It may reduce total chyle loss and duration of postoperative stay.

Useful adjunctive therapy in the management of postoperative chylothorax.

Octreotide therapy may be started soon the diagnosis of chylothorax is made due to documented clinical benefits and absence of significant complications.

In postoperative chylothorax, though initial conservative management without octreotide use is justified, earlier institution of octreotide in patients at risk of prolonged chyle loss (as those with elevated systemic venous pressure) may be indicated.

12.2.6 Complications of Chylothorax

Essential fatty acids deficiency, lymphopenia, pneumonias, bacterial sepsis, and candidiasis.

12.2.7 Mortality of Chylothorax

Ranges from 7 to 7.8%.

50% of deaths are due to uncontrolled sepsis.

25% of deaths are due to heart failure.

25% of deaths are due to pulmonary hypertensive crisis.

Hospital stay: Duration of stay in survivors ranges from 13 to 135 days (median 32 days).

12.3 Necrotizing Enterocolitis (NEC)

Though the diagnosis and surgical management of NEC in perioperative cardiac patient is beyond the scope of cardiothoracic discipline, its knowledge, early recognition, and management by coordinated efforts of all involved in care of the infant is crucial.

12.3.1 Incidence

Occurs in approximately 25,000 babies per year in a low birth weight infants.

Incidence of NEC increases to approximately 1 in 18 (5.5%) in infants weighing < 1.5 kg.

Premature infants that live longer have a greater chance of developing NEC.

Serious form of NEC in infants has 25% mortality despite current advances in treatment. NEC accounts for 15% of all deaths occurring after 1 week of life in infants of (< 1.5 Kg).

12.3.2 Etiology and Pathogenesis

Definite cause is not known, but more often it is multifactorial.

A. Poor intestinal blood flow and bacterial infection are critical to the development of NEC.

Decreased blood pressure, ↓ blood volume, or ↓ blood oxygen saturation at birth are probable causes. Decreased intestinal blood flow caused by bacteria or other causes and premature infant are two most important factors for developing NEC. Risk factors associated with premature infant for NEC are:

Immature intestinal cells with decreased gastric, pancreatic, and intestinal secretions.

Absence of important breast milk components due to lack of breast - feeding.

B. Poor motility of intestine results in stasis and permits intestinal bacteria to multiply.

C. Administration of antibiotics alters the patient's normal intestinal bacteria.

Infant in ICU with heart / lung failure is exposed to strong "intensive care" bacteria.

D. Feeding formulas provide nutrition for the bacteria in the intestine.

E. Inadequate immune system in premature cannot fight off the infection.

End Result: 1. Necrosis and perforation of the intestine as bacteria enter the intestinal lining in presence of intestinal damage due to ↓ blood supply.

2. Ineffective bacterial killing due to ↓ defense and immune systems.

12.3.3 Pathology of NEC

NEC commonly occurs in the last part of small intestine (ileum) followed by colon. Large and small intestines are involved together in 44% of NEC cases.

NEC involves either a single (in 50%) or multiple portions of the intestine.

In most severe form of NEC, at least 75% of the intestinal necrosis occurs.

Morphology:

Patchy areas of bleeding into the wall of the intestine occurs with gas inside the intestinal wall. Swelling and blood in the intestinal middle layer results in patchy loss of the inner lining. Necrotic bowel segments are interspersed with a normal appearing segments. The intestinal mucosa has multiple ulcers with wide areas of damage. Air in the intestinal wall occurs as a result of gas-forming bacteria

entering the intestinal wall. Tissue reaction to bacteria is only minimal early but is evident later during healing. Stricture formation occurs in 5% to 10% of patients who recover from the initial NEC episode.

12.3.4 Clinical Presentation of NEC

A. Symptoms and Signs:

The typical patient is a premature and in ICU, with medical / surgical problems (disease occurs rarely in the first few days of life).

Patient has recently been fed, and has inability to tolerate feeds.

Vomiting (green/yellow) in 75% and diarrhea in 20% are initial symptoms.

Blood in the stools (massive bleeding is rare) may occur.

Soft distended abdomen is the most common, and it becomes firm and tender with progression of the disease.

Discoloration (red / blue) with swelling of the abdominal wall occurs in 5% of patients.

A mass of intestines occasionally, can be felt on palpation.

Early signs of bacteremia and sepsis are present as mentioned below:

i) Lethargy, low blood pressure, and unstable temperature.

ii) Low heart rate and/or breathing difficulties.

iii) Need for oxygen and mechanical ventilation.

B. Laboratory Findings:

None of the laboratory tests can make absolute diagnosis of NEC.

i) WBC count:

WBC is high or low, a low WBC count suggests severe infection and poorer outcome.

ii) Platelet count:

A low platelet count is frequent, platelets being consumed by bacterial toxins.

Platelet counts < 100,000/$mm^{3'}$ occurs in > 80% of patients.

Decreasing platelet count is probably the most helpful indication of worsening NEC.

iii) Clotting time:

It is prolonged, with increased APTT and PT.

iv) Blood gas analysis:

Metabolic acidosis: Occurs in > 70% to 90% due to ↓ blood flow to the intestine. It also signifies worsening status of NEC patient.

v) Radiological Signs:

♣ NEC may be present even in the absence of all of the following x-ray signs.

i) Pneumatosis intestinalis (air in the wall of the intestine):

It is the hallmark of NEC and occurs in 98% of patients. It is frequently seen in infants who have been fed compared with unfed infants, but eventually is seen in all NEC patients. This sign may come and go and is a common early, rather than a late finding. In severe NEC extensive pneumatosis involves large portions of small and large intestine (see Figure 35).

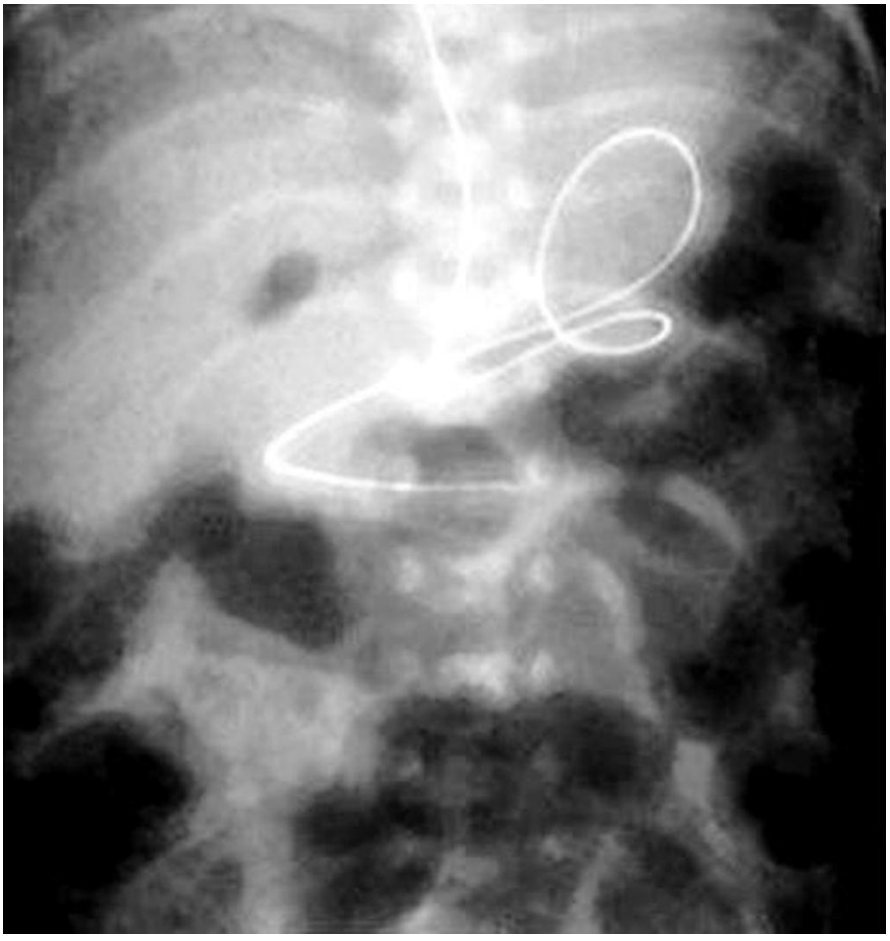

Figure 35 *Antero-posterior roentgenogram of an abdomen of an infant with necrotizing entero-colitis showing dilated large and small intestine with pneumatosis intestinalis. Note small air bubbles and linear gas shadows in the bowel wall.*

ii) Portal vein gas: (Presence of air in the portal vein leading to the liver):

Gas in the intestinal wall is absorbed into the portal venous system.

Portal venous gas comes and goes and accounts for the fact that it is not often seen. Portal vein gas is present in 60% of patients with severe NEC.

iii) Pneumoperitoneum (air outside of the small intestine):

It may be indicative of perforation and is seen in 10% to 20% of patients.

Only 2/3 patients with an intestinal perforation noted at operation, have free air on the x-ray.

iv) Ascites (free fluid in the abdominal cavity):

In 10% of patients, abdominal distension is seen with gas-filled intestinal loops in the center, and is surrounded by a white haziness.

25% patients with surgically proven intestinal perforation have ascites.

15% of proven intestinal perforations have no ascites, no free air on x-rays of the abdomen.

Combination of ascites and portal vein gas has been associated with ↑ mortality rate.

v) Fixed loop sign (non-moving single or several loops of dilated small intestine):

Loops small bowel remain unchanged in position for 24 to 36 hours, and is referred to as the persistent loop sign. It suggests the death of a segment of intestine.

vi) X-ray contrast studies:

Performed infrequently in NEC due to rsk of intestinal obstruction and perforation.

Indications for contrast studies:

For diagnosis of NEC in premature, to differentiate NEC from other diseases, and in patients in whom the diagnosis of NEC has been in question.

Contrast studies are done in later phase of NEC to identify stricture or obstruction of the intestine.

Contrast studies findings:

Ulcers in the intestinal lining, spasm and a thickened bowel wall, narrowing of the intestine, and air in the bowel wall.

vii) Ultrasound:

Plain x-rays are all that is required for diagnosis, though ultrasound is used in some. Portal venous gas shows as bright white spots or lines within the liver.

Air in the wall of the intestine can be identified occasionally by a ultrasound.

Ultrasound is most helpful to detect ascites.

C. Confirmatory diagnosis:

The above clinical setting combined with physical examination and x-ray findings should be used to established the diagnosis of NEC.

12.3.5 Treatment

Conservative:

In the absence of intestinal death or perforation, the initial Rx of NEC is without an operation. 80% of NEC is managed by (NG) suction, intravenous fluids, and IV antibiotics.

1) Nasogastric (NG) suction:

↓ Gas in the stomach and intestines by applying suction to the tube.

2) Intravenous fluids:

Maintains fluid balance and effective circulating volume.

A normal blood pressure must be maintained to continue to have blood flow to the intestine and diminish the risk of further intestinal damage.

Electrolytes and blood acid-base status should be maintained at normal levels.

Intravenous nutrition should be initiated as soon as it is practical to do so.

3) Antibiotic therapy:

♣ Most important part of care is antibiotic therapy and antibiotics used vary according to the typical bacteria in each hospital.

Most common usage is combination of three antibiotics:

I.e., ampicillin with gentamicin, flagyl / or clindamycin, and vancomycin.

In some ICUs cefotaxime and vancomycin are used.

The antifungal agents are added for candida infections.

12.3.6 Monitoring the Course of NEC

i) Continue NG suction until complete recovery of intestinal function (often takes 10-14 days).

ii) Perform frequent physical examination, x-rays of the abdomen, and platelet and white blood cell counts.

iii) Perform arteial blood gas: oxygen satuaration, carbon dioxide, and pH.

iv) Antibiotics are continued for 10-14 days in severe cases.

If there are no ongoing or progressive signs of intestinal necrosis, administer small quantities of dilute formula (usually 10-14 days after intestinal rest). Oral feedings are advanced if they are tolerated.

12.3.7 Surgery of NEC and Indications

A. Persistent or progressive signs of infection (i.e., deteriorating heart or lung function, often in conjunction with a falling platelet count).

B. X-Ray evidence of intestinal perforation (pneumoperitoneum) or dead intestine. ♣ Not all with intestinal perforation have air in the abdomen. Pneumoperitoneum generally requires an operation, especially if patient is getting sicker.

C. Progressive deterioration on physical exam:

I.e., increasingly distended abdomen, abdominal mass, and/or redness of the abdominal wall.

D. X-Ray evidence of:

* a) Fixed enlarged (dilated) loop of intestine.

● b) Fluid in the abdomen.

♠ c) Portal vein gas.

* Fixed loop of a dilated intestine for more than 24 hours strongly suggests intestinal death.

* It is an accurate estimate of intestinal death and is seen in approximately 60% of dead intestines.

● If ascitic fluid is confirmed by ultrasound, 20% to 40% of patients have a dead intestine.

● On examination of a needle sampled fluid, if bacteria are found or the fluid is green or brown in color an intestinal perforation is likely.

♠ 85% of patients with portal vein gas require an operation, and all of these patients have dead intestine at the time of the operation.

E. Reduction of 50% in platelet count after initiation of NEC treatment is a strong index of continuing infection and need for an operation.

F. Persistent acid production (metabolic acidosis).

♣ None of above findings by themselves indicate that dead or perforated bowel is present. Probably best sign of dead intestine is continuing low platelet count despite platelet transfusions. Optimal time for an operation is just at the time of intestinal death or perforation.

1. The goals of surgical intervention:

i) Remove dead or dying intestine, and bring ends of the resected intestine out onto the abdominal wall without a primary anastamosis.

ii) If the remaining intestinal length is of concern, suspicious areas of the intestines may be left intact, and a second look operation is performed after 24 hours.

iii) If the entire intestine is dead, no intervention is indicated.

2. Alternative surgical strategies:

These are applicable in small neonates with NEC, especially if:

i) Perforation of the intestine is diagnosed. In such an instance, place a drain into the abdomen via an incision in the right lower abdomen.

ii) If clinical deterioration continues on observation, perform laprotomy and if a short segment of necrotic intestine is present, excise the segment with primary anastamosis.

12.3.8 Treatment Results and Complications of NEC

The survival rate is 65-70%.

Widespread infection and prematurity are causes of mortality.

Complications:

i) Intestinal (postoperative) fistulas.

ii) Necrosis of exteriorized loop of intestine.

iii) Intestinal strictures:

Most patients have just one stricture, but multiple strictures may occur.

11% to 35% of NEC develops strictures.

The most common site is the large intestine (70%), followed by the ileum (15%).

Of colonic strictures, 60% involve the left side of the colon.

Perform a dye study of the colon and downstream intestine before the ileal stoma closure.

In conservatively treated NEC, > 50% of colonic strictures present with intestinal obstruction.

12.3.9 Long-Term Outcomes of NEC

25% to 30% of survivors have some form of impairment on long-term such as short gut syndrome, inability to tolerate feeds, and need for a long-term hyper alimentation. The more advanced the NEC, the more the problems are with growth and development.