Chylothorax
A review of the literature and report of 3 cases

P. B. HESSELING, H. HOFFMAN

Summary
The applied anatomy of the thoracic duct, the physiology of chyle and the pathogenesis and management of chylothorax are briefly reviewed. Three cases of chylothorax in children (1 neonate, 1 infant who had undergone cardiac surgery and 1 child with lymphocytic lymphoma) are presented.

Chylothorax is an accumulation of chyle in the pleural cavity. According to Brescia, it was first described by Bartololet in 1633, and Quincke reported the first case of traumatic chylothorax in 1875. By 1944, 105 cases had been recorded. Large series of cases were reported by Bower in 1964 and Macfarlane and Holman in 1972.

Embryology and anatomy
Lymph vessels develop during the 9th week of fetal life. During the 14th week they form wide lymph trunks in the connective tissue through the tissue planes of least resistance, which divide the parenchyma of the lung into distinct lobules. By the 20th week this lobulation is less distinctive, the connective tissue increases, and the lymph vessels become thinner in relation to the parenchyma of the lung.

Van Pernis studied the thoracic duct in 1081 cadavers. The duct arises from the cisterna chyli, which overlies the anterior surface of the 2nd lumbar vertebra and lies posterior to and to the right of the aorta. The duct then ascends through the aortic hiatus on the anterior surface of the vertebral bodies between the aorta and azygos vein. Between the 7th and 5th thoracic vertebrae it crosses to the left and ascends behind the arch of the aorta and subclavian artery into the base of the neck, where it empties at or near this junction of the left subclavian and internal jugular veins. The duct is always a single structure between T8 and T5. The thoracic duct receives all the lymph of the body surface of the 2nd lumbar vertebra and lies posterior to and to the right of the aorta. The duct then ascends through the aortic hiatus on the anterior surface of the vertebral bodies between the aorta and azygos vein. Between the 7th and 5th thoracic vertebrae it crosses to the left and ascends behind the arch of the aorta and subclavian artery into the base of the neck, where it empties at or near this junction of the left subclavian and internal jugular veins. The duct is always a single structure between T8 and T5. The thoracic duct receives all the lymph of the body except that from the right hemithorax, right upper limb and right side of the head and neck. Lymph from the parietal pleura reaches the thoracic duct via posterior intercostal lymphatics, the right bronchomediastinal trunk and other lymphaticovenous anastomoses between the thoracic duct system and the azygos, intercostal and lumbar veins.

Physiology
Both the volume and rate of flow of chyle may vary enormously under different physiological conditions. In adults a flow rate of 14 - 110 ml/h has been measured. The thoracic duct pressure at the height of maximum flow is 10 - 28 cm H2O. The normal daily volume is 1500 - 2400 ml. In cirrhotic patients as much as 8 litres of chyle may pass through the duct daily. In 3 children aged 3 months, 5 years and 14 years respectively a flow of 37 - 56 ml/kg/d was recorded during 14 days of continuous pleural drainage. Strauss documented a total chyle loss of 80 litres in one patient. The flow of chyle depends on intra-abdominal and intrathoracic pressure changes, adjacent arterial pulsations and smooth-muscle contractions of the thoracic duct wall. A meal containing fat provides the maximum increase in the flow of chyle. Water taken by mouth can increase the flow of chyle by 20%, and an ordinary hospital meal can cause a threefold increase in flow.

The characteristics and composition of chyle are set out in Table I. Prolonged loss of chyle results in severe nutritional depletion and loss of water and electrolytes, leading to the death of the patient. Lymphopenia may develop. Severe metabolic acidosis has been reported in an infant, and hypoprothrombinemia with a bleeding tendency may result. Correct management requires the meticulous replacement of all the lost components.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>0.4 - 6.8 x 10^9/l</th>
<th>0.05 - 0.6 x 10^9/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milky appearance</td>
<td>Sterile</td>
<td></td>
</tr>
<tr>
<td>pH 7.4 - 7.8</td>
<td>Fat globules staining with Sudan III</td>
<td></td>
</tr>
<tr>
<td>Specific gravity 1 012</td>
<td>Lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Sterile</td>
<td>Erythrocytes</td>
<td></td>
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<tr>
<td>Fat globules staining with Sudan III</td>
<td>Total protein</td>
<td></td>
</tr>
<tr>
<td>Sterile</td>
<td>Albumin</td>
<td></td>
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<tr>
<td>Fibrinogen</td>
<td>Globulin</td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td>Triglycerides</td>
<td></td>
</tr>
<tr>
<td>Electrolytes similar to plasma values</td>
<td>Cholesterol</td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td>Sugar</td>
<td></td>
</tr>
<tr>
<td>Triglycerides — plasma value</td>
<td>Urea</td>
<td></td>
</tr>
<tr>
<td>Cholesterol — plasma value</td>
<td>Electrolytes</td>
<td></td>
</tr>
<tr>
<td>Sugar 2.7 - 11.1 mmol/l</td>
<td>Electrolytes — similar to plasma values</td>
<td></td>
</tr>
<tr>
<td>Urea 1.4 - 3.0 mmol/l</td>
<td>Fat-soluble vitamins present</td>
<td></td>
</tr>
<tr>
<td>Electrolytes — similar to plasma values</td>
<td>Pancreatic exocrine enzymes present</td>
<td></td>
</tr>
</tbody>
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Aetiology and pathogenesis

Rupture of the thoracic duct. Rupture of the thoracic duct causes chyle to accumulate in the posterior mediastinum. This so-called chyloma (which may be noticeable on radiographic examination) finally ruptures the mediastinal pleura, usually on the right side, at the base of the pulmonary ligament. Damage above T6 results in a left-sided effusion and damage below T6 in a right-sided effusion. Surgical damage to the thoracic duct accounts for a quarter of all cases of chylothorax. The thoracic duct is particularly vulnerable during surgical mobilization of the aorta, left subclavian artery and oesophagus. Chylothorax has, however, been documented following almost every known thoracic operation. It may also follow median sternotomy for intracardiac heart surgery. The incidence following cardiovascular surgery varies between 0,24% and 0,5%. Penetrating injuries to the thoracic duct may be caused by gunshot or stab wounds, oesophageal dilatation and even translumbar aortography. Non-penetrating injuries to the thoracic duct may follow sudden hyperextension of the spine, fracture of vertebrae or ribs, blast and crush injuries and severe bouts of coughing or vomiting. An aortic aneurysm may compress or erode the thoracic duct.

Lymphatic obstruction. There may be a reflux of chyle following extensive intrathoracic lymphatic obstruction. The reflux occurs via the left postero intercostal lymphatics to the parietal pleura and via the bronchomediastinal trunk to the visceral pleura. Obstruction may follow thrombosis of the superior vena cava, left subclavian or left innominate vein or infections such as tuberculosis, mediastinitis, paravertebral abscesses and filariasis. Amyloidosis may cause bilateral chylous effusions. Abnormal lymph vessels. Abnormalities of lymphatic drainage with chylous thorax occur in congenital lymphangiectasis, Noonan’s syndrome and pulmonary lymphangiomyomatosis. Tumours. Secondary malignant disease accounts for more than half of cases of chylothorax; it has been reported in association with lymphoma, sarcoma, carcinoma, seminoma, teratoma and neuroblastoma. Primary malignant tumours of the pleura may be associated with chylous effusion arising from multiple fistulas so that the lung appears to weep chyle. Benign cysts and lymphangiomata of the thoracic duct may cause chylothorax.

Transdiaphragmatic movement of chyle. Chylous ascites is illustrated by chylothorax in one-third to one-half of cases. Radio-isolated albumin and carbon particles can pass from the peritoneal to the pleural space, probably via a diaphragmatic communication or communicating lymphatics. The presence of a diaphragmatic defect was confirmed by the appearance of pneumothorax within a hydrothorax after induction of pneumoperitoneum in 5 patients. Acute hydrothorax has been reported during periportal dissection. Obstruction of the thoracic duct near the cisterna chyli by lymphoma has resulted in chylous ascites and chylothorax, both of which disappeared following abdominal irradiation.

Neonatal chylothorax. Spontaneous neonatal chylothorax, although rare, is the most common cause of pleural effusion in the first few days of life. It may be associated with Down syndrome and maternal polyhydramnios. Other causes of neonatal chylothorax include damage to the thoracic duct from abdominal irradiation, aortic and venous thrombosis, and infection.

Management

Chylothorax should be confirmed by means of biochemical investigations. Cholesterol pleural (pseudochylothorax) effusions occur in association with tuberculosis, rheumatoid arthritis and other inflammatory conditions. The pseudochylothorax contains no triglycerides and less protein and cholesterol than chyle. It may contain many cells, has a specific gravity of less than 1012, and does not stain after ingestion of a lipophilic dye.

Chylothorax is best managed when the exact cause and the pathogenesis are known. Bipedal lymphangiography will demonstrate the site of leakage or obstruction.

Management should always be conservative at the onset. Only when a large flow of chyle persists for more than 2 - 3 weeks or if clinical or biochemical evidence points to a decline in the nutritional status of the patient should surgical procedures be considered.

Conservative management

Modern hyperalimentation techniques combined with the meticulous replacement of water and electrolytes can to a large extent prevent the serious metabolic consequences of prolonged loss of chyle. If the patient is given nothing by mouth the flow of chyle will be reduced. The substitution of dietary fat with medium-chain triglycerides (which are absorbed directly into the portal venous system) may cause a drastic reduction in chyle flow. An elemental diet may have a similar effect in neonatal chylothorax.

Adequate drainage of the pleural space prevents cardiorespiratory embarrassment, and a fully expanded lung may block the thoracic duct and promote pleural symphysis. Flow from the chylous fistula will cease with obliteration of the pleuromediastinal space. Repeated thoracocentesis or continuous tube drainage (using a large-bore siliconized chest tube to prevent obstruction due to the gelatinous disposition of chyle) with negative pressure may be used. The mode of choice depends on the rate of leakage.

Chyle removed by thoracocentesis has been returned orally, per rectum, by intratracheal infusion and intravenously in an attempt to maintain nutrition. Intravenous infusion of chyle has, however, been associated with sudden death.

Surgical management

Transthoracic ligation of the thoracic duct was first performed by Lampson. Because the duct is always a single structure between T8 and T12, a right-sided thoracotomy can be performed for duct ligation if other factors indicating a left-sided approach are absent. The appropriate side of approach is obvious. The establishment of pleural symphysis to stop leakage of chyle is best managed when the exact cause and the pathogenesis are known. Bipedal lymphangiography will demonstrate the site of leakage or obstruction.

Low thoracic duct ligation, at the level of the diaphragm, has been successfully performed regardless of the site of chylothorax.

The administration of 250 ml of double cream or olive oil through a nasogastric tube 4 hours before the operation will cause a tenfold increase in the flow of chyle, facilitating identification of the site of leakage.

Plural symphysis

The establishment of plural symphysis to stop leakage of chyle is indicated when medical treatment fails and surgical treatment is ineffective or impossible. Iodinized talc sprinkled over the lung surface or the instillation of sterile talc (USP) (10 g suspended in 250 ml saline) through a thoracostomy tube have been successfully used to achieve pleural symphysis and cure chylothorax. The intrapleural instillation of sterile broth, azochloramide, hypertonic glucose, nitrogen mustard and pleurectomy have been tried with little success.

Radiotherapy

Radiotherapy to the mediastinum or abdomen has been used with success in patients in whom lymphoma was the primary disease.
Specific conditions

Neonatal chylothorax

Neonatal chylothorax may present at birth as respiratory distress. The infant should be given nothing by mouth, and intravenous hyperalimentation should be started after 3 days. The majority of cases respond well to thoracocentesis. Medium-chain triglycerides are of doubtful value. Continuous thoracostomy tube drainage with negative pressure is indicated when more than 3 thoracocenteses have been performed. Ligation of the duct is seldom required. It should be borne in mind that a chylous effusion in the neonate is initially serous and assumes its typical chylous appearance only after milk feeds have commenced.

Chylothorax following cardiovascular surgery

This condition was treated successfully with multiple thoracocentesis in 11 out of 13 patients. Persistent severe loss of chyle may, however, necessitate thoracic duct ligation. The initial volume of chyle aspirated bears no correlation to the duration or severity of the subsequent course of the chylothorax.

Non-traumatic chylothorax

Management is conservative. Radiotherapy followed by chemotherapy is indicated when the chylothorax is secondary to lymphomatous disease in the abdominal or thoracic cavity. Talc pleurodesis may be tried when prolonged chyle loss causes problems and the patient’s condition or the nature of the basic disease does not allow for ligation of the thoracic duct.

Complications

The severe nutritional and metabolic complications that may result in death in the poorly managed patient have been mentioned. Pneumothorax and haemothorax may occur secondary to thoracocentesis. Chyle loculations caused by intrapleural adhesions may lead to pulmonary constriction as a result of chylofibrosis, necessitating decortication.

Prognosis

The mortality rate for traumatic chylothorax was 48% before the first successful transthoracic ligation of the thoracic duct was carried out by Lampson in 1948. This declined to 10% in 1955. Neonatal chylothorax was associated with mortality rates of 23% in the series of Yancy and Spock and 15% in the series reported by Brodman.

In non-traumatic chylothorax the underlying disease determines the eventual outcome.

Case reports

Case 1

A 5-year-old boy was referred from a rural hospital with an abdominal tumour. Lymphocytic lymphoma was diagnosed on open biopsy. On admission the child was cachectic, with both weight and height below the 3rd percentile for age. Generalized lymphadenopathy was present. A huge nodular tumour almost filled the abdominal cavity, and bilateral pleural effusions were present. The haemoglobin concentration was 8 g/dl, the white cell count 12 x 10^9/l and the erythrocyte sedimentation rate 13 mm/1st h.

A chest radiograph showed mediastinal lymphadenopathy. Aspiration of the pleural cavity yielded 300 ml of straw-coloured fluid on the left side and 400 ml on the right side; the protein content of the fluid was 39 g/l and the lymphocyte count was 2 160 x 10^9/l. Five days later another 700 ml of straw-coloured fluid was aspirated from both pleural cavities.

Chemotherapy consisting of weekly intravenous daunomycin and vincristine and daily oral prednisolone was instituted. Three weeks later the pleural effusions had disappeared but the abdominal tumour showed no signs of regression. Chemotherapy was changed to the CHOP regimen consisting of cyclophosphamide, vincristine, adriamycin and prednisolone.

Three days later severe respiratory distress developed owing to a massive left-sided pleural effusion. Pleural aspiration yielded 600 ml of chylous fluids. Venous blood was collected simultaneously (Table II). The chylothorax and abdominal mass showed little response to 1 000 rad administered to the abdomen over 14 days.

During the next 2 months another three pleural aspirations were performed to relieve dyspnoea, yielding a total of 2 000 ml of chyle. The patient developed disseminated lymphoma and died 20 weeks after admission. Autopsy was not performed.

<table>
<thead>
<tr>
<th>TABLE II. BIOCHEMICAL ANALYSIS OF CHYLE AND SERUM</th>
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<tbody>
<tr>
<td><strong>Chyle</strong></td>
</tr>
<tr>
<td>Total protein (g/l)</td>
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<tr>
<td>Albumin (g/l)</td>
</tr>
<tr>
<td>Globulin (g/l)</td>
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<tr>
<td>Triglycerides (mmol/l)</td>
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<tr>
<td>Cholesterol (mmol/l)</td>
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<td>Free fatty acids (mmol/l)</td>
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Case 2

A premature female infant with a birth weight of 1 610 g and gestational age of 34 weeks was born by unassisted vaginal delivery. The Apgar rating was 10 after 1/2 and 10 minutes. The baby was observed in an incubator and nasogastric tube feeds were commenced 4 hours after birth. Respiratory distress developed on the 2nd day and there were clinical and radiological signs of a right-sided pleural effusion. A pleural aspiration relieved the respiratory distress and yielded 30 ml of chylous fluid with a specific gravity of 1 015 and a protein content of 40 g/l. On the 3rd day a bulging fontanelle was noted. Meningitis was confirmed by lumbar puncture and *Escherichia coli* was cultured from the cerebrospinal fluid. Gentamicin and penicillin were administered, but the infant died 12 hours later. Permission for autopsy was refused.

Case 3

A 4-month-old girl presented with cardiac failure caused by a patent ductus arteriosus which was part of a congenital rubella syndrome. Other abnormalities were hepatosplenomegaly, deafness and a cataract.

The patent duct was ligated through a left thoracotomy. On the 1st postoperative day the baby became dyspnoeic. Investigation revealed a large left-sided pleural effusion which yielded chyle on aspiration. During the following 24 hours 500 ml of chyle drained through an indwelling tube.

Surgical exploration revealed chylous leakage near the origin of the left subclavian artery. The thoracic duct was ligated and the infant made an uneventful recovery.
News and Comment/Nuus en Kommentaar

Primary biliary cirrhosis

Primary biliary cirrhosis is a progressive fatal disease of unknown origin but in some way related to an immunological assault on the intrahepatic bile ducts, resulting ultimately in cirrhosis. Two papers in The Lancet (1981, 1, 1275 and 1278) discussed its pathogenesis, clinical pattern and treatment. Epstein et al. from the Royal Free Hospital, London, again reported on their trial of n-penicillamine at a dose of 600 mg daily in the treatment of this disease. In this randomized trial 55 patients received penicillamine and 32 placebo. Drug reactions developed in 16 patients on penicillamine and all deaths occurred in patients with liver disease in histological stage 3 or stage 4. Out of 37 penicillamine-treated patients 5 died and out of 23 placebo patients 10 died. However, the improvement in survival with treatment only became evident after 18 months. The mechanism of action of penicillamine appears to be related not only to its copper-chelating effect but also to its immunological and antifibrotic action. It is noteworthy, however, that penicillamine did not retard the histological progression towards the fibrotic or cirrhotic phase of the disease.

James et al. from Newcastle upon Tyne discussed the clinical spectrum of primary biliary cirrhosis on the basis of 93 patients, of whom almost one-half had no symptoms of liver disease when the disease was diagnosed; in many of these serum antimitochondrial antibody was detected during immunological screening for other diseases. They do not believe that treatment with n-penicillamine for a period of less than 2 years in a series of 40 patients materially altered the life expectancy of the group as a whole or of the early or symptomatic groups taken separately. On the basis of their experience with this group of 93 patients they believe that there may be many symptom-free cases of early primary biliary cirrhosis in the community, and they note the frequent association of this with other auto-immune diseases such as thyroid disease and rheumatoid or collagen diseases. It may well be that in many of these patients the symptoms never develop despite grossly abnormal liver histology. To treat these patients by any but innocuous means is not justified.

Die gebruik van naloksoon by skisofreniëse psigose en maniese syndrome

Verskillende peptyd met 'n morfinagtige werkende (endorfiene), ook twee pentapeptide (mentionies- en leusien-endorfiene) en drie langer peptide (β-endorfiene) is uit ekstrakte van die hipofise en harsings (enkefaliene) en drie langer peptiede (endorfiene) en drie langer peptide. Drug reactions developed in 16 patients on penicillamine and all deaths occurred in patients with liver disease in histological stage 3 or stage 4. Out of 37 penicillamine-treated patients 5 died and out of 23 placebo patients 10 died. However, the improvement in survival with treatment only became evident after 18 months. The mechanism of action of penicillamine appears to be related not only to its copper-chelating effect but also to its immunological and antifibrotic action. It is noteworthy, however, that penicillamine did not retard the histological progression towards the fibrotic or cirrhotic phase of the disease.

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