*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*
*e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 9 Ver. I (Sep. 2015), PP 83-89*
*www.iosrjournals.org*

# Management and treatment of pleural effusion and empyema

[1]Murtaza Mustafa, [2]AFM.Saleh, [3]RK.Muniandy,
[4]MS.Rahman.SS.Husain,
*[1,2,3,4]Faculty of Medicine and Health Sciences, University Malaysia Sabah,Kota Kinabalu,Sabah, Malaysia.*

***Abstract:*** *Approximately 1.5 million patients are diagnosed with pleural effusion each year in the United States. Clinical manifestations of pleural effusion include dyspnea, pleuritic chest pain, cough, fever, fever, chills and weight loss and depending on the underlying disease. Diagnostic tools include chest radiograph, ultrasound, and computed tomography {CT).Ultrasound guided pigtail catheters as the initial draining method is strongly suggested. Light and Rodriguez treatment for pleural effusion and empyema is useful. The American College of Chest Physicians panel grouped management of pleural effusion into six categories: no drainage, therapeutic thoracentesis, tube thoracostomy be, fibrinolytic therapy, video- assisted thorcoscopy (VATS) and open surgery. Uncomplicated effusions (category1or 2) generally resolve with antibiotics alone. Drainage is recommended for management of patients in category 3 or 4.Therapeutic thoracentesis and tube thoracotomy is insufficient for managing patients in category 3 or 4.Fibrinolytic drugs, VATS, and surgery are better choices in these patients. High mortality inpleural effusions is due to mismanagement. Antibiotics of choice in pleural effusions are penicillin's, cephalosporins, clindamycin, metronidazole, vancomycin, and quinolones.*
*Aminoglycosides have poor penetration in the pleural space, and should not be used alone to treat gram-negative empyema's.*
***Keywords:*** *Pleural effusion, Empyema, Thoracentesis, and Treatment*

## I. Introduction.

Pleural effusion (parapneumonic effusion-PPE) is an accumulation of fluid in the pleural space that is classified as transudate according to its composition and underlying pathophysiology.Empyema is defined by purulent fluid collection in the pleural space, which is most commonly caused by pneumonia [1].Approximately 1.5 million patients are diagnosed with pleural effusion each year in the United States[2].Parapneumonic effusions occur in 20 to 40 % of patients are hospitalized with pneumonia. The mortality rate in patients with in parapneumonic effusion is higher than in patients with pneumonia without a parapneumoniceffusion [3].Some of the excess mortality is due to mismanagement of the parapneumoniceffusion[3].Infections of the pleural space most commonly follow pneumonia, amounting for 40% to 60% of all empyema's. Thoracotomy is the next most common precursor of empyema,accounting for 20% and trauma accounts for 4% to 10%[4,5].Frequently isolated pathogens in PPE include:*Streptococcus pneumoniae* accounted for 60% to 70%,*Staphylococcus aureus* for 10% to 15%,Anaerobes present in 25% to 76% ofempyema's[6,7,8].*Legionella* can be isolated from PPE, tuberculous effusions are common in many parts of the world[9,10].Pleural effusion is divided into transudate and exudate based on Light's criteria. In transudate, fluid accumulates in the pleural space due to increased hydrostatic pressure or decreased oncotic pressure across the intact capillary beds of pleural membranes[11,12].However in exudate, the capillary beds themselves are diseased and its increased permeability results in fluid leak intothe pleural space[13].The symptoms of pleural effusion(PE) include dyspnea, pleuritic chest pain,cough, fever, chills, and weight loss. Clinical manifestations of PE are largely dependent on the underlying disease[14].The goal in management of PE is to provide symptomatic relief by removing fluid from the pleural space and allow the treatment of underlying disease[14].Chest radiograph, ultrasound, computed tomography(CT) are the diagnostic tools[15].Thoracentesis to be performed when there is at least 10mm of PE on the lateral decubitus film[16] Characteristics of patients that indicate invasive procedure will be necessary for its resolution include: effusion occupying more than 50% of the hemi thorax or one that loculated;a positive Gram stain or culture of PE; and a purulent PE that has a pH below 7.20 or a glucose below 60,or has a lactic acid dehydrogenase(LDH) level of more than three times the upper normal limit for serum[3].The treatment of PE by Light and Rodriguez's classification and treatment scheme [16]. The paper reviews the management and treatment of PE and Empyema.

## II. Pathogenesis

When PE develop without pleural inflammation, factors that can be identified include increased hydrostatic pressure and decreased oncoticpressure, and alterations in lymphatic drainage[12].In the noninflamed state, the pleural space contains a small amount of transudative pleural fluid with a low concentration of protein and 1000 to 5000 cells/mm, primarily lymphocytes,macrophages,and mesothelial cells,

neutrophils usually are usually absent[17,12].In addition, infected pleural fluid is deficient in the opsonins and complement necessary for optimal phagocytic function, and the low pH and hypoxia in infected pleural fluid further impair neutrophil function[12].

With pleural inflammation, the interaction of bacteria, liposaccharide (LPS), cytokines, and chemokines lead to changes in pleural permeability. The initial events during pleural inflammation are mediated via response of stimulated pleural mesothelial cells(PMCs).Bacterial cell wall products bind to PMCs and stimulate production of interleukin(IL)-I,IL-8,epithelial neutrophil-activating protein(ENA)-78,tumor necrosis factor(TNF)-α,and platelet –activating factor. Invitriol-I,TNF-α and LPSs have been shown to release IL-8,although levels to TNF-alpha and IL-1 in pleural fluid did not correlate with IL-8 production[18].The primary role of PMCs is coordinating and facilitating the permeability and recruitment of neutrophils and mononuclear phagocytes.PMCs are also capable of phagocytosis and release of nitric oxide (N0)[19].

Jonjic and colleagues have studied the capability of PMC to express adhesion molecules and chemoattractant cytokines, two basic mechanisms in the regulation of neutrophil recruitment [20].PMCs were able to express the chemotactic cytokines IL-8 and monocyte chemoattractant protein 1(ICAM-1) and vascular adhesion and molecule 1(VCAM-1),and that these are functionally important in interacting with mononuclear phagocytes. The regulated expression of adhesion molecules and chemostaticcytokines by PMCs is important in inflammation and immune mediation.The interaction between CD11 and CD18 intergins expressed on neutrophils and 1CAM-1 can lead adhesion of neutrophils to the surface of the implicated cell.Expression of these adhesive glycoproteins by PMCs enhances the recruitment of neutrophils and mononuclear cells into pleural space[20].

Pleural fluid from patients who develop PPE has been found to be chemotactic to neutrophils when compared with pleural fluid collected from patients with other diagnoses [21].Studies have found a positive correlation between IL-8 levels and the number of neutrophils in pleural fluid. Broaddus and associates have reported that anti-IL-8 antibodies decrease chemotactic activity in empyema fluid [21].Antony and co-workers have shown elevated IL-8 levels in both PPE and empyema fluid when compared with PPE secondary to other diseases.IL-8 levels were higher in empyema fluid than in PPE.They also found a significant correlation betweenIL-8 levels and the total number of neutrophils in pleural fluid. Chemotactic activity for neutrophils was increased in empyema fluid but decreased with the addition of IL-8 neutralizing serum[22].

ENA-78 is a CXC chemokine that has been shown to be present in high amounts in PPE.For early PPE,ENA-78 is the dominant chemokine responsible for neutrophil chemotaxis.In the later stages of the development of empyema,Il-8 becomes the dominant chemokine[22].Although the pleural space is normally fibrinolytic ,parapneumonic fluid has also been shown to have increased procoagulant activity and also depressed fibrinolytic activity that favors fibrin deposition in the pleural space. The deposition of fibrin and increased activity of fibroblasts leads to a thick pleural peel characteristics of the later stages seen in empyema. Animal model data have suggested that this final phase of organization is driven by mediators such as transforming growth factor(TGF) β and platelet- derived growth factor(PDGF)[23].However, if pneumonia is associated with a PPE is treated promptly with appropriate antimicrobial agent, the cellular and cytokine mediators of inflammation are aborted. Resolution of uncomplicated PPE leaves the pleura essentially normal, without clinically significant fibrosis [19].

In contrast to common pyogenic bacteria, when the pleura is infected with mycobacteria, pleural mesothelial cells release-C-chemokines, which recruit mononuclear cells to the pleural space[24].This is facilitated by adhesion molecule-1 expressed by pleural mesothelial cells[25]. Th1 cytokines are also increased in tuberculous pleural fluid, which has been shown to regulate expression of C-C chemokines [26].

## III. Contributory factors

Frequently associated contributory factors in transudate pleural effusion include:[27]

- Congestive heart failure
- Liver cirrhosis
- Hyperproteinemia
- Nephrotic syndrome
- Acute atelectasis
- Myxedema
- Peritoneal dialysis
- Meigs syndrome
- Obstructive uropathy
- End-stage kidney disease

Pulmonary embolism was once thought to be associated with transudate effusions but have been recently shown to be exudative [28].

Exudative pleural effusion once identified, need additional evaluation to determine the cause of excess fluid, and pleural fluid amylase, glucose, pH and cell counts are obtained[27].Conditions associated with exudative pleural effusions include post-surgery,malignancy, infection, trauma, pulmonaryinfarction, pulmonaryembolism, autoimmunedisorders, pancreatitis, ruptured esophagus, rheumatoidpleurisy, drug induced Lupus and tuberculosis [27].

## IV. Etiological agents

Microbiology of empyema has changed dramatically in the last 50 years. In the preantibioticera,*Streptococcus pneumonia* accounted for 60 % to 70% of cases,*Streptococcuspyogenes* for 10% to 15% of cases, and *Staphylococcus aureus* for 5% to 10% of cases[6].*S.pneumoniae* more recently accounts for only 5 % to 10% of and many infections are mixed, with anaerobes in 25 % to 76 % of empyema's as sole organisms or in combination with other anaerobic or facultative organisms [8,9].Bartlett and Finegold found that pleural empyema was caused by aerobic bacteria in 24 % ,anaerobic bacteria in 35 %,and both aerobic and anaerobic bacteria in 41% of medical service patients without prior antibiotic therapy or surgical procedures[29].The most common anaerobes isolated include the *Bacteroidesfragilis* group, prevotellaspecies,*Fusobacteriumnucleatum*,and what was then called a *Peptostreptococcus* and would likely now be identified as*Finegoldia*.A 1990 study suggested that anaerobic infection may occur in 25% to 33% of children with empyema[30].

Several recent studies have reported a shift from traditional pathogens to the *Streptococcus anginosus* group(formerly termed *Streptococcus milleri*) in community acquired disease, especially in patients with comorbidities.In a large study from Canada, the*streptococcus anginosus*(*S..anginosus,S.intermedius* and *S.constellatus*) was recovered in 50% of proven empyemas in patients with community acquired pneumonia;50% had a coexisting condition[8].

Predisposing factors are most important in predicting the most likely pathogens. Pneumonia continues to be the most frequent predisposing factor in development of empyemas[6].In otherwise healthy adults with pneumonia, the most common bacteria causing pleural empyema are *S.aureus,S.pneumoniae or S.pyogenes*[4].The incidence of PPE in hospitalized patients is estimated to be 40%[31].*Although S.pneumoniae* is the most common cause of community acquired pneumonia empyema has occurred in only 1% to 2 % of cases of pneumococcal pneumonia compared with 10 % to 18 % in the preantibiotic era[32].

Most cases of *S.aureus* empyema result from *S.aureus*pneumonia,which is most often seen in older hospitalized patients with underlying medical problems.*S.aureus*is an uncommon cause of pneumonia in otherwise healthy adults, except during an influenza outbreaks [33.34].*S.aureus* has a tendency to cause cavitation,with resultant with resultant secondary lung abscesses. Empyema can be seen in 10% to 24 % of adults with *S.aureus*pneumonia [33].In children, multiple thin –walled cavities or abscesses or pneumatocelesdevelop with *S.aureus*pneumonia. Empyema develop in as many as 50% of children[35].Several reports have linked influenza-related complications with *S.aureus* necrotizing pneumonia and empyema[36].Most recently,10 cases of severe community acquired MRSA pneumonia in children associated with influenza were reported from Lousiana and Georgia with 60% mortality.Allisolates were positive for Panton-Valentine leukococidin(PVL) toxin genes and were designated USA300-0114[37].

Factors predisposing to aspiration, such as altered mental status, alcoholism,and periodontal disease, is common in patients with anaerobic infection of the pleura. Many of these cases tend to be polymicrobial.In addition to anaerobes, viridians group streptococci, aerobic gram-negative bacilli, ad occasionally *S.aureus* have been recovered[19].Pleuropulmonaryactinomycosis can result from aspiration. These patients exhibit a chronic pulmonary infection with chest wall involvement or draining sinus tractswith sulfur granules, or both. Up to 50% of pulmonaryactinomycosishas pleural involvement [38].

*Legionella* can be isolated from parapneumoniceffusions.These effusions tend to be small and usually do not progress into empyema [39].In many parts of the world, tuberculosis effusions are common, and they can be secondary to a primary infection or occur as a reactivation of tuberculosis [40, 41].Although fungal infections of the pleural space are uncommon in the normal host, there has been an increase in fungal empyema and most are caused by *Candida*species. *Candida* empyema has been reported as complication of surgery, a result of esophageal rupture a sub diaphragmaticinfection, and being spread hematogenously.Many of these infections are polymicrobial [42].

Amebic liver abscess is associated with pleural involvement in up to 15% to 20% of cases. Two mechanisms have been identified. First in amebic abscess can irritate the diaphragm,producing a sympathetic pleural effusion. Second complex pleural effusion can develop when amebic liver abscess ruptures into the pleural space through the diaphragm [19].

Immunocompromised patients have higher frequency of empyema caused by fungi and gram-negative bacilli [5].Organ transplantation recipients and patients with acquired immunodeficiency syndrome (AIDS) may reactivate pleural foci of mycobacterial or fungal infection, but they rarely present with empyema without

disseminated disease. Unsuccessful resection of cavitarycoccidioidomycosis or aspergillosis may be complicated by empyema and bronchopleural fistula from that organism [43,].*Nocardia* infections occur more frequently in patients with underlying conditions, such as organ transplantation, malignancy diabetes mellitus, AIDS, and long-term use of steroids. Pleural effusions can develop in up to 50% of patients with nocardiosis[44].

**Noninfectious causes** should be considered in the differential diagnosis in patients who present with pleural effusions and fever. Pulmonary embolism is commonly overlooked as a cause of pleural effusion. It is estimated that between 30% to 50% of patients with pulmonary emboli have an associated pleural effusion[45].Patients with acute pancreatitis who develop a pleural effusion tend to have more severe disease[46].Approximately 5% of patients with rheumatoid arthritis have pleural effusion, and 20% present with pleuritic chest pain[47].Patients with systemic lupus erythematosus 40% develop a pleural effusion at some point in the course of disease[48].Finally, the pericardiectomy or myocardial infarction patients may present with pleural disease[49,50].The symptoms typically appears about 3 weeks after the injury and is characterized by fever and chest pain. Pleural effusion can be demonstrated in more than 50% of cases [51].

## V. Clinical symptoms

The pleural response to microbial invasion can be divided into three stages. The initial, or exudative, stage is characterized by collection of thin free- flowing fluid with low number of neutrophils,pH higher than 7.2,lactate dehydrogenase(LDH) levels less than 1000IU/L,glucose levels higher than 60mg/dl, and negative culture. The second stage, a fibropurulent,stage is characterized by increasing number of neutrophils and fibrin deposition over the pleura, with tendency to loculate.Pleural glucose levels and pH fall and LDH levels increases. In the final organization, stage, fibroblast formation and scarring produce a pleural peel that encases and traps the lung [52].The clinical presentation varies with the underlying disease the microbiology and host factors [19].Patients with bacterial pneumonia usually present with fever, shortness of breath, productive cough, and chest pain. Patients with anaerobic pleuropulmonary infection exhibit a more indolent course and weight loss, fever chronic cough. A history of aspiration is often obtained and poor oral hygiene is often evident [19].

Esophageal rupture or perforation, and subdiaphragmatic rupture of a liver abscess or sub diaphragmatic abscess frequently present with acute pain, fever and respiratory distress [19].The physical examination reveals decreased breath sounds, dullnessto percussion, and crackles over the affected area. Chronic empyema's may erode the chest wall and present with a spontaneous draining abscess termed empyema necessitates. Anemia and leukocytosis are nonspecific findings [19].

## VI. Diagnosis and management

Pleural effusion is usually diagnosed on the basis of medical history and physical examination, and confirmed by chest X-rays-.Once the accumulated fluid is more than 300 ml, there are usually detectable clinical signs in the patient, such as decreased movement of chest on the affected side, stony dullness to percussion over fluid, diminished breath sounds on the affected side, decreased vocal resonance and fremitus (though this is an inconsistent and unreliable sign),and pleural rub. A systematic review(2009) published as part of Rational Clinical Examination Series in the Journal of American Medical Association (JAMA) showed that dullness to conventional percussion was most accurate for diagnosing pleural effusion(summary positive likelihood ration,8.7;95 % confidence interval(2.2-33.8),while the absence of reduced tactile vocal fremitus made pleural effusion less likely(negative likelihood ration,0.21;95 % confidence interval,0.12-0.37)[53].

**Imaging**.A pleural effusion will show up as an area of whiteness on a standard posteroanterior X-rays [54].Normally the space between the two layers of lung, the visceral pleura and the parietal pleura cannot be seen. A pleural effusion infiltrates the space between these layers. Because the pleural effusion has a density similar to body fluid or water, it can be seen on radiographs. Since the effusion has larger density than rest of the lung, it will gravitate towards the lower portions of the pleural cavity. The pleural effusion behaves according to basic fluids dynamics, conforming to the shape of the lung and chest cavity. If the pleural cavity contains both air and fluid then the fluid will have a" fluid level" that is horizontal instead of conforming to the lung space. Chest radiographs acquired in the lateral decubitus position (with patient lying on his side) are more sensitive and can pick up as little as 50 ml of fluid. At least 300 ml of fluid must be present before upright chest films can pick up signs of pleural effusion (e.g. Blunted costophrenic angles)[55].

Ultrasound is widely available, it enables bedside studies, is fast and cost less than computed tomography (CT) or magnetic resonance imaging (MRI).Ultrasound is particularly useful for detecting small amounts of pleural fluid, for guiding diagnostic throracentesis, and for pleural drainage. For most patients, the chest CT has emerged as the imaging study of the choice. It is more accurate in distinguishing lung abscess from empyema than the conventional radiograph. Stark and colleagues have reported plural separation, adjacent lung compression, and wall characteristics to the most reliable signs for distinguishing empyema from lung abscess [56].The role of IMR in the evaluation of pleural effusion is limited. It may be a useful alternative when IV

contrast required to complete the CT imaging is contraindicated for patient. MRI can detect pleural effusions, pleural tumors, and chest wall invasion. In some cases, it may be useful for distinguishing, hemorrhagic effusions from other causes [57].

**Thoracentesis**.Once a pleural effusion is diagnosed, the cause must be determined. Pleural fluid is drawn out of the pleural space in a process called thoracentesis,and it should be done in almost all patients who have pleural fluid that is ≥ 10 mm in thickness on CT, ultrasonography, or lateral decubitus X-rays and that is new or of uncertain etiology. In general, only patients who do not require thoracentesis are those who have heart failure with symmetric pleural effusions and no chest pain or fever; in these patients, diuresis can be tried, and thoracentesis avoided unless effusions persist for ≥ 3 days. In thoracentesis,a needle is inserted through the back of the chest wall in sixth, seventh or eighth intercostal space on the maxillary line, into the pleural space[58].

**Diagnostic workup**.Fluid may be evaluated for the diagnostic test include chemical composition including protein, lactate dehydrogenase (LDH), albumin, amylase, pH, and glucose, Gram stain and culture to identify bacterial infections, cell count and differential count,cytopathology to rule out cancer cells, but also identify infecting organisms, and other tests as suggested by the clinical situation-lipids, fungal culture, viral culture, specific immunoglobulins[58].

**Management**.Theprinciples of empyema management are to control infection, minimize, morbidity and hospitalization and maximize maximum lung function include 1) **Adequate drainage**.Because pus in the pleural cavity represents infection in a closed space.**Drainage is always necessary**.Only rarely is adequate drainage achieved by daily thoracentesis.Usually fluid is too thick or loculated,and image guided chest tube drainage is necessary. If there is poor response in the first 24 hours and the patient is stable then instillation over 2 to 3 days of intrapleural thrombolytic may be tried. Repeat imaging studies should be followed to assure complete drainage and a reduction in the cavity size. When this fails, early surgical intervention is indicated [59].2)Video-assisted thoracoscopy(VATS) may help break down loculations,provide for through irrigation, allow visual placement of drainage tubes, and may obviate the need for thoracotomy.Even with careful patient selection,10% to 20% of VATS procedures need to be converted to thoracotomy[59].Liu and colleagues strongly suggest that ultrasound- guided pigtail catheters be considered as the initial draining method for a variety of pleural diseases[60].

## VII. Treatment

Therapeutic options for a pleural effusion depend on the type or stage of the effusion. Light and Rodriguez have proposed a classification and treatment for PPE and empyema[16].It is based on amount of fluid, gross and chemical characteristics of the pleuralfluid, and whether or not fluid was loculated.The American College of Chest Physicians published an evidence-based consensus guideline on the medical and surgical treatment of PPE[61,Id,74].Three variables- pleural space anatomy, pleural fluid microbiology, and pleural fluid chemistries, were used to categorized patients into four risk levels for poor outcome 1(very low risk),2(low risk),3,(moderate risk),and 4 (high risk).The panel grouped management of pleural effusion into six categories: no drainage, therapeutic thoracentesis, tubethoracostomy,fibrinolytic therapy, video assisted thoracoscopic surgery(VATS),and open surgery. Fibrinolytic approach requires tube thoracostomy for administration of drug, and VATS requires tube thoracostomy after the procedure. Uncomplicated effusions (category 1 or 2) generally resolve with antibiotics alone. Drainage is recommended for management of patients in category 3 or 4.On the basis of a literature review, therapeutic thoracentesis and tube thoracostomy appear to be insufficient for managing most patients in category 3 or 4.Fibrinolytic drugs,VATS,and surgery are better choices for these patients[61].

Many antimicrobial agents can adequately penetrate into infected pleural fluid to exceed the minimal inhibitory concentration (MIC) of most common organisms; these include penicillin's, cephalosporins, clindamycin, metronidazole, vancomycin, and quinolones. Aminoglycosides are less capable of entering the pleural space and have decreased activity in an acidic anaerobic environment [62].Thus, it is best that aminoglycosides not to be used alone to treat gram-negative empyema's [63].

## VIII. Conclusion

High morality is due to mismanagement of parapneumonic effusion.Therapeutic thoracentesis and tube thoracotomy appear to be insufficient for managing most patients in category three and category four.Fibrinolytic drugs, video-assisted thoracoscopy(VATS), and surgery are best options for these patients.

## References

[1]. HyeonYu.Management of Pleural Effusion,Empyema,and Lung abscess.SeminInterventRadiol.2011;29{1):75-86.
[2]. Light RW.Pleural Diseases.4th ed.Philadelphia:Lippincott William & Wilkins;2001.
[3]. Light RW.Parapnrumonic Effusions and Empyema.Proccedings of Am Thorac Soc.2006;3(1):75-80.
[4]. Light RW.Parapneumonic effusions and empyema.In Light RW,ed.Pleural Diseases.3rd ed..Baltimore:Williams& Wilkins;1995;129-153.

[5]. Smith JA,MullerworthMH,WestlakeGW,etal.Empyemathoracis:A 14 years' experience in a teaching center. AnnThorac Surg.1991;51:39-42.
[6]. Finland M,Barnes MW.Changing ecology of acute bacterial empyema: Occurrence and mortality at Boston City Hospital during 12 selected years from 1935-1972.J Infect Dis.1978;137:274-91.
[7]. Ahmed RA,MarrieTJ,HuangJQ.Thoracic empyema in patients with community acquired pneumonia.Am J Med.2006;119:877-83.
[8]. MaskellNA,BattS,HedleyEJ,etal.The bacteriology of pleural infection by genetic and standard methods and its mortality significance. Am J RespirCrit Care Med.2006;174:817-824.
[9]. Kim KW,GooJM,LeeJM,etal.Chest computed tomographic findings and clinical features of Legionella pneumonia.JComput Assist Tomgy.2007;31:950-55.
[10]. Mlika-CabanneN,BraunerM,MugusiF,etal.Radiographic abnormalities in tuberculosis and risk of coexisting human immunodeficiency virus infection. Am J RespirCrit Care.1995;152:786-93.
[11]. Light RW,McgregorMI,LuchsingerPC,etal.Pleural effusions: the diagnostic separation of transudate and exudates. Ann Intern Med.1972;77(4):507-513.
[12]. John SA. State of the art: The pleura.Am Rev Respir Dis.1988;138(1):184-234.
[13]. Miller EJ,Idell S.Interleukin-8:An important neutrophil chemotaxin in some cases of exudative pleural effusions .Exp Lung Res.1993;19:589-601.
[14]. Chung J,PerrotMD.Pleuraleffusion and empyema thoracic.In:BopeET,Rakel Kellerman RD,editors,Conn's current Therapy 2010,Is ted. Philadelphia: Saunders/ Elsevier;2010.pp.263-65.
[15]. BressEL,FrancisIR,GlazerGM,etal.Bolus contrast medium enhancement for distinguishing pleural from parenchymal lung disease: CT features.JComput AssistTomogr.1987;11(3):436-40.
[16]. Light RW,RodriguezRM.Management of parapneumoniceffusions.Clin ChestMed.1998;19:373-82.
[17]. AlfagemeJ,MunozJ,PenaN,etal.Empyema of the thorax in adults: biology, microbiology findings and management.Chest.1993;103:839-43.
[18]. Miller EJ,Idell S.Interleukin-8:An important neutrophil chemotaxin in some cases of exudative pleural effusion. Exp Lung Res.1993;19:589-601.
[19]. SeptimusJE.Pleural effusion and empyema. In:Mandell Douglas and Bennett'sPrinciples and Practice of Infectious Diseases,7th ed. MandellGL,BennettJE,Dolin R(editors).Churchill Livingstone Elsevier,2010.pp.917-24.
[20]. JonjicN,PeriG,BernasconiS,etal.Expression of adhesion molecules and chemotactic cytokines in cultured human mesothelial cells. J Exp Med. 1992; 176: 1165-74.
[21]. Antony VB,GodbeySW,KunkelSL,et al.Recruitment of inflammatory cells to the pleural space: chemotactic cytokines,IL-8 and monocyte chemotactic peptide-1 in human pleural fluids' Immunol.1993;151:7216-23
[22]. Broaddus VC,HebertCA,VitangcolRV,et al.Interleukin-8 is a major neutrophil chemotactic factor in pleural liquid of patients with empyema. Am Rev Respir Dis.1992;146:825-30.
[23]. SasseSA,JadusMR,KukesGD,Pleural transforming growth factor-beta-1correlates with pleural fibrosis in experimental empyema.Am J RespirCrit CareMed. 2003;168:700-705.
[24]. Mohammad KA, NasreenN,WardMJ,et al.Mycobacterium mediated chemokine expression in pleural mesothelial cells.Role of C-C chemokines in tuberculous pleurisy.J Infect Dis.1998;178:1450-56.
[25]. NasreenN, Mohammaed KA, Ward MJ,etal.Mycobacterium induced transmesothelial migration of monocytes into pleural space. Role of intracellular molecule-1 in tuberculous pleurisy. J Infect Dis.1999;180:1616-23.
[26]. Zhang M,GatelyMK,WangE,etal.Interleukin 12 at the site of disease in tuberculosis.JClin Infect.1994;93:1733-39.
[27]. Galaganetal.Color Atlas of Body Fluids.CAP Press, Northfield, 2006.
[28]. PorcelJM,LightRW.Pleural effusions due to pulmonary embolism. Curropinpulm Med.2008;14(4):337-42.
[29]. BartletJG,FinegoldSM.Anaerobic infections of the lung and pleural space.Am RevRepir Dis.1974;110:56-77.
[30]. Brook J.Microbiology of empyema in children.Pediatrics.1990:85:722-726.
[31]. Light RW,GirardWM,JenkinsonSG,etal.Parapneumoniceffusions.Am JMed.1980;69:507-12.
[32]. TaryleDA,PottsDE,SahnSA.The incidence and clinical correlates of parapneumonic effusions in pneumococcal pneumonia.Chest.1978;74:170-73.
[33]. Kaye MG,FoxMJ,BartletJG,etal.The clinical spectrum of Staphylococcus aureus pulmonary infection.Chest.1990;97:788-92.
[34]. Schwarzman SW,AdlerJL,SullivanRFJ,etal.Bacterial pneumonia during Hong Kong influenza epidemic of 1969-1969.Arch Intern Med.1971;127:1037-41.
[35]. BukinghamSC,King MD, Miller MJ.Incidence and etiology of complicated parapneumonic effusions in children.1996 to 2001.Pediatr Infect Dis J.2003;22:499-504.
[36]. Hageman JC,Uyeki TM, Francis JS,etal.Severe community acquired pneumonia due to Staphylococcus aureus,2003-04 influenza season. Emerg Infect Dis.2006;12:894-99.
[37]. Centers for Disease Control and Prevention.Severe methicillin resistant Staphylococcus aureus community acquired pneumonia associated with influenza-Louisiana and Georgia, December 2006- January 2007.MMWR.Morb Mortal Wkly Rep. 2007;56:325-29.
[38]. Flynn MW,FelsonR,The roentgen manifestation of thoracic actinomycosis.Am J Roentgenol Radium TherNucl Mol.1970;110:707-716.
[39]. Kim KW, Goo JM,LeeHJ,et al. Chest computed tomographic findings and clinical features of Legionella pneumonia.JComput Assist Tomogr.2007;31:950-55.
[40]. MlikaCabanneN,Brauner M, MugusiJ,etal.Radiographic abnormalities in tuberculosis and risk of coexisting human immunodeficiency virus infection. Am J RespirCrit Care Med.1995;152:786-793.
[41]. MoudgilH,SridharG,LeitchAG.Reactivationdisease:The commonest form of tuberculous pleural effusion in Edinburgh,1980-1991.Respir Med.1994;88:301-304.
[42]. KoSC,ChenKY,HsuchPR,etal.Fungal empyema thoracic An Emerging entity.Chest.2000;117:1622-1678.
[43]. Wex R, UttaE,DrozdzW.Surgical treatment of pulmonary and pleuropulmonaryAspergillusdisease.ThoracCardiovasc Surg.1993;41:64-71.
[44]. Lerner PJ.Nocardiosis.Clin Infect Dis.1996;22:891-905.
[45]. Stein PD, Henry JW.Clinical characteristics of patients with acute pulmonary embolism stratified according to their presenting syndromes.Chest.1997;112:974-79.
[46]. LankischPG,DRogeM,BecherR.Pleuraleffusion:A new negative prognostic parameter for acute pancreatitis.Am J Gastroenterol.1994;89:1849-51.
[47]. Walker WC,WrightV.Rheumatoidpleuritic.Am Rheum Dis.1967;26:467-74.

[48]. Good JT,Jr,KingTF,AntonyVB,etal.Lupuspleuritic:Clinical features and pleural fluid characteristics with special reference to pleural fluid antinuclear antibodies. Chest.1983;84:714-18
[49]. Light RW,RogersJT,ChengDS,etal.Large pleural effusions occurring after coronary artery bypass grafting.Am Intern Med.1999;130:891-96.
[50]. Dressler W. The post myocardial infarction syndrome. Arch Intern Med.1959;103:28-42.
[51]. StelznerTJ,KingTFJr,AntonyVB,et al.The pleuropulmonarymanifestations of post cardiac injury syndrome.Chest.1983;84:383-87.
[52]. Andrews NC,ParkerEF,Shaw RP, et al.Management of nontuberculous empyema.Am Rev Respir Dis.1962;85:935-36.
[53]. Wong CL,Holroyd-LeduceJ,StrausSE.Does this patient have a pleural effusion? JAMA .2009;301(3):309-17.
[54]. Corneet al.(2002).Chest X-rays Made Easy. Churchill Livingstone.ISBN 0-443-07008-3.
[55]. Squire L F,Novelline RA.(2004).Squire's fundamentals of radiology. Cambridge: Havard University Press.pp.132-3.ISBN 0-67401279-8.
[56]. Stark DD,FederleMr,GoodmanPC,et al.Differentiating lung abscess and empyema.Radiography and computed tomography.AJR Am JRoentgenol. 1983; 141:163-67.
[57]. GamsuG,SostmanD.Magnetic resonance imaging of the thorax.Am Rev Respir Dis.1989;139:254-74.
[58]. Light RW.Pleural Effusion..Merk Manual of for Health Care Professionals. Merck Sharp &DohmeCorp.Retrieved 21 August 2013.
[59]. Heffner JE.Infection of the pleural space.Clin Chest Med.1999;20:607-22.
[60]. Liu YH,LiangSJ,TuCY,etal.Ultrasound-guided pigtail catheters for drainage of various pleural diseases.Am J Emerg Med.2010;28(8):915-21.
[61]. ColiceGL,CurtisA,DeslauriersJ,etal.Medical and surgical treatment of parapneumoniceffusions:An evidence based guideline.Chest.2000;118:1158-71.
[62]. TeixeriaLR.Antibiotic levels in empyema pleural fluid.Chest.2000;117:1734-39.
[63]. Bryant RE,SalmonCJ.Pleuralempyema.Clin Infect Dis.1996;22:747-762;quiz763-744.