

# Is Streptokinase Fibrinolysis the Best Treatment for Empyema in Pediatric Patients? And Must We Tap Every Cirrhotic Patient with Bilateral Pleural Effusion?

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From the 5th century BC, empyema has been diagnosed in both adults and children. Empyema is defined as pus in the pleural space due to infection. There are multifactorial underlying causes, but the majority of cases are post-bacterial pneumonia or due to direct infection of the chest. Despite advances in antibiotics development and improvement of minimal invasive therapeutics, empyema is still associated with significant morbidity and mortality [1]. Management guidelines were published by the British Thoracic Society in 2003 for adults [2] and 2005 for children [3] and were reviewed in 2010 [4].

The question whether all patients with empyema should undergo medical thoracostomy before proceeding to video-assisted thoracoscopic surgery for both acute and chronic empyemas has been the subject of debate in the literature for the last 20 years and continues to be.

In this issue of *IMAJ*, Levy Faber et al. [5] review their experience treating 75 children suffering from empyema. They implemented intrapleural streptokinase washing instead of surgical treatment for stage II pediatric empyema and present the success rates compared to the historical surgical approach, namely, reduced stay in the pediatric intensive care unit

as well as shorter overall hospitalization duration. In a study in 1949, Tillett and Sherry [6] reported the use of a mixture of streptokinase and streptodornase for intrapleural fibrinolysis. Purified streptokinase was available in the 1960s, resulting in an improved safety profile [7]. Due to concerns about the antigenicity of streptokinase, urokinase was introduced in 1987 and became the most frequently used agent for fibrinolysis. Yao and co-researchers [8] demonstrated the safety and efficacy of streptokinase pleural fibrinolysis in a pediatric population. Levy Faber and co-authors [5] concluded that streptokinase pleural fibrinolysis could obviate the need for surgery in most cases. The authors stress that the attempt be made early on, when complicated parapneumonic effusion is first diagnosed.

Treatment of empyema can be summarized as appropriate antibiotic therapy combined with medical or surgical drainage of the pleural space, management of any underlying factors, with early use of intrapleural streptokinase or urokinase. Such treatment can obviate the need for surgery in most cases of empyema, leaving the complicated chronic disease cases for surgery.

In the spectrum of pleural infectious disease, not much attention is paid to spontaneous bacterial empyema, defined as the spontaneous infection of the pleural fluid, which represents a distinct complication of hepatic hydrothorax. The pathogenesis of SBEM remains unclear. It

might occur as a result of a direct bacterial spread from the peritoneal cavity. Therefore, a high index of suspicion is essential for the diagnosis of SBEM, as advised by Nitzan et al. in this issue of *IMAJ* [10], in their case report of a cirrhotic patient with bilateral pleural effusion and a positive culture from the pleural fluid. Moreover, SBEM may occur even in the absence of ascites. In such cases, a transient bacteremia that infects the pleural space could be the underlying pathogenetic mechanism. The causative microorganisms in most cases of SBEM are *Escherichia coli*, *Streptococcus* species, *Enterococcus* and *Klebsiella* [9]. Nitzan et al. [10] present a patient with alcoholic liver cirrhosis as well as ascites and hydrothorax in whom two positive cultures of *Pneumococcus pneumoniae* were obtained. SBEM is rarely diagnosed because thoracocentesis is not routinely performed in cirrhotic patients with hepatic hydrothorax. Therefore, the authors stress the need for awareness regarding early thoracocentesis. Conventional cultures are not sufficiently sensitive for the diagnosis of SBEM. Therefore, inoculation of 10 ml of the pleural fluid into a TSB (tryptic soya broth) [11] blood culture bottle at bedside is advisable since it contains an opsonin inhibitor that protects bacteria from further complement- or phagocyte-mediated killing [12].

Chen et al. [13] found that 56% of 26 SBEM episodes were associated with spontaneous bacterial peritonitis and 31% had bacteremia. The incidence of

SBEM = spontaneous bacterial empyema

SBEM was 2% in 862 cirrhotic patients and 13% in 132 with hydrothorax. They thus concluded that lower serum albumin, prolonged prothrombin time, and lower pleural fluid protein are associated with the presence of SBEM in cirrhotic patients with hydrothorax.

Since SBEM is a frequent complication in cirrhotic patients with hydrothorax and almost half the cases of SBEM are not associated with spontaneous bacterial peritonitis, a diagnostic thoracentesis should be performed in cirrhotic patients with pleural effusion when infection is suspected or clinical deterioration occurs. A chest tube is not even necessary in patients with positive pleural fluid culture. Culture performed by inoculating 10 ml of the fluid into a blood culture bottle at the bedside is a more sensitive method and should be considered.

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**References**

1. Lee SF, Lawrence D, Booth H, Morris-Jones S, Macrae B, Zumla A. Thoracic empyema: current opinions in medical and surgical management [Editorial Review]. *Curr Opin Pulmonary Med* 2010; 16: 194-200.
2. British Thoracic Society (BTS) Standards of Care Committee. BTS guidelines for the management of pleural disease. *Thorax* 2003; 58 (Suppl II): ii1-59.
3. Balfour-Lynn IM, Abrahamson E, Cohen G, et al., on behalf of the Paediatric Pleural Diseases Subcommittee of the British Thoracic Society (BTS) Standards of Care Committee. BTS guidelines for the management of pleural infection in children. *Thorax* 2005; 60 (Suppl I): i1-21.
4. Davies HE, Davies RJ, Davies CW; BTS Pleural Disease Guideline Group. Management of pleural infection in adults: British Thoracic Society Pleural Disease Guideline 2010. *Thorax* 2010; 65 (Suppl 2): ii41-53.
5. Levy-Farber D, Anson Best L, Orlovsky M, Lapidot M, Reuven N, Kremer R. Streptokinase fibrinolysis protocol: the advantages of a non-operative treatment for stage II pediatric empyema patients. *IMAJ Isr Med Assoc J* 2012; 14: 157-61.
6. Tillet WS, Sherry S. The effect in patients of streptococcal fibrinolysin and streptococcal desoxyribonuclease on fibrinous, purulent, and sanguinous pleural exudations. *J Clin Invest* 1949; 28 (1): 173-90.
7. Bergh NP, Ekroth R, Larsson S, Nagy P. Intrapleural streptokinase in the treatment of haemothorax and empyema. *Scand J Thorac Cardiovasc Surg* 1977; 11: 265-8.
8. Yao CT, Wu JM, Liu CC, Wu MH, Chuang HY, Wang JN. Treatment of complicated parapneumonic pleural effusion with intrapleural streptokinase in children. *Chest* 2004; 125: 566-71.
9. Yakoob J, Abbas Z, Khan R, Hamid S, Awan S, Jafri W. Small intestinal bacterial overgrowth and lactose intolerance contribute to irritable bowel syndrome symptomatology in Pakistan. *Saudi J Gastroenterol* 2011; 17 (6): 371-5.
10. Nitzan O, Elias M, Raz R, Saliba WR. Spontaneous bacterial empyema caused by *Streptococcus pneumoniae*. *IMAJ Isr Med Assoc J* 2012; 14: 190-1.
11. Runyon BA, Umland ET, Merlin T. Inoculation of blood cultures with ascitic fluid. Improved detection of spontaneous bacterial peritonitis. *Arch Intern Med* 1987; 147: 73-5.
12. Xiol X, Castellvi JM, Guardiola J, et al. Spontaneous bacterial empyema in cirrhotic patients: a prospective study. *Hepatology* 1996; 23: 719-23.
13. Chen TA, Lo GH, Lai KH. Risk factors for spontaneous bacterial empyema in cirrhotic patients with hydrothorax. *J Chin Med Assoc* 2003; 66 (10): 579-86.