Institution: University College London

Unit of Assessment: 1 - Clinical Medicine

Title of case study: Improved management of empyema in children

1. Summary of the impact

The management of childhood pleural empyema has been standardised and improved as a direct result of research at the UCL Institute of Child Health (ICH). Pioneering trials demonstrated the clinical equivalence of chest drain insertion with fibrinolytic installation compared to video-assisted thoracoscopic surgery as a primary intervention. Chest X-ray and ultrasound scanning were shown to provide enough information and it was established that chest CT scanning had no role in the routine management of empyema. International guidelines have been modified to reflect this, reducing paediatric exposure to unnecessary general anaesthesia, invasive surgery and ionising radiation. Cost savings are estimated to be £1.5 million/year in the UK alone.

2. Underpinning research

Empyema is a significant cause of childhood morbidity which occurs in 1 in 150 children hospitalised with pneumonia. Many treatment options are available for the management of empyema, including antibiotics alone or in combination with thoracocentesis, chest-drain insertion, chest drain and fibrinolytics, mini-thoracotomy, open decortication, and video-assisted thoracoscopic surgery. However, treatment is not standardised and prior to our research, patient care was dependent on local practice and physician preference. Guidelines issued by the British Thoracic Society in 2005 on the management of pleural infection in children highlighted the lack of standardisation and the fact that there was little evidence to inform the best management approach.

Between 2002 and 2008, Dr Samatha Sonnappa (Clinical Research Fellow, Portex Respiratory Unit) and Professor Adam Jaffe (then Senior Lecturer in Respiratory Research) conducted the first randomised study to prospectively compare two standard treatments. These were percutaneous chest drain insertion together with intrapleural urokinase instillation and primary video-assisted thoracoscopic surgery (VATS), which is a more invasive approach. The aim was to determine the primary intervention of choice by assessing the length of post-intervention hospital stay. Secondary end points were number of chest drain days, total hospital stay, failure rate, radiological outcome at six months and total treatment costs. The study revealed that there were no differences in clinical outcomes between intrapleural urokinase and primary VATS. There was no significant difference in the length of hospital stay after the intervention, the total length of hospital stay, failure rate or radiological outcome at six months post-intervention **[1]**. The study also showed that percutaneous chest drain insertion with intrapleural urokinase was cost saving, being approximately £1,500 lower than primary VATS (£6,084 vs £7,586, $p< 0.001$) **[1]**.

Furthermore, the research showed that chest CT scanning did provide additional clinically relevant information to chest ultrasound scans and chest X-rays, neither altering management decisions nor predicting clinical outcome. It was shown to have a limited role in complex, non-resolving cases or when other pathology was suspected, but the study demonstrated that it should not be used as routine **[2]** – a particularly relevant finding, given a number of recent studies which have raised concerns about potential cancer risk after exposure to radiation in childhood

In further work, a retrospective review of V/Q scans of children originally recruited as part of the study, confirmed that these scans did not provide additional information to functional assessment in a clinically well child following empyema **[3]**.

3. References to the research

[1] Sonnappa S, Cohen G, Owens C, van Doorn C, Cairns J, Stanojevic S, Elliott M, Jaffe A.

Comparison of urokinase and video-assisted thoracoscopic surgery for treatment of childhood empyema. Am J Respir Crit Care Med. 2006 Jul 15;174(2):221-7. http://dx.doi.org/10.1164/rccm.200601-027OC

[2] Jaffe A, Calder A D, Owens C M, Stanojevic S, Sonnappa S. The role of routine computed tomography in paediatric pleural empyema. Thorax. 2008 Oct;63(10):897-902. http://dx.doi.org/10.1136/thx.2007.094250

[3] Mew RC, Biassoni L, Jaffe A, Sonnappa S. Ventilation perfusion scans in children treated for empyema. Thorax. 2009 Mar;64(3):273. http://dx.doi.org/10.1136/thx.2008.107516

4. Details of the impact

Empyema is a complication of pneumonia which causes significant morbidity, with prolonged hospitalisations and multiple invasive procedures. The incidence of paediatric empyema has risen dramatically over the last decade, both in the UK and around the world **[a]**.

Prior to the research described above, significant variance in the management of paediatric empyema existed. Treatment was dependent on institutional and practitioner preference, with concern over both the state of the evidence base and a lack of standardised practice. This was acknowledged in the British Thoracic Society Guidelines for the Management of Pleural Infection in Children (2005) which said that "*in the UK there is little consensus over management among respiratory paediatricians and thoracic surgeons*" **[b]**.

Through the demonstration by Sonnappa and Jaffe of clinical equivalence between chest drain insertion with fibrinolytic instillation and video-assisted thoracoscopic surgery, a clinical consensus favouring the former has emerged. Supported by subsequent randomised trials in the US, chest drain use is now established in international guidelines as first-line management of empyema. Furthermore, it is now widely accepted that routine CT chest scanning should not be performed in the management of children with empyema, thus reducing exposure to harmful radiation.

Impact on international guidelines

The Thoracic Society of Australia and New Zealand reference our studies in their recommendations on: the use of daily X-rays, drainage of pleural fluid and use of VQ scans **[c]**. Clinical practice guidelines issued by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America on the management of community-acquired pneumonia in infants and children, referencing both our study and the subsequent US study, recommend: "*Both chest thoracostomy tube drainage with the addition of fibrinolytic agents and VATS have been demonstrated to be effective methods of treatment. The choice of drainage procedure depends on local expertise*" **[d]**. The Canadian Paediatric Society also refers to our research in their guidelines which state that "*Although there is still ongoing controversy and a need for additional randomized trials, the best evidence suggests that either VATS, early thoracotomy or small-bore percutaneous chest tube placement with instillation of fibrinolytics (CTWF) results in the best outcomes as measured by hospital length of stay. CTWF may be the most cost-effective choice*" **[e]**.

Impact on hospital practice

Many hospitals in the UK and abroad have adopted our research finding in drafting their local guidelines for managing empyema in children. Guidelines from United Bristol Healthcare NHS Trust state that "*Video-assisted thoracoscopic surgery (VATS) may be an appropriate alternative to thoracotomy. Early VATS, as a primary procedure, does not appear to offer benefit over a chest drain and urokinase, but is routinely used in some centres and in the US*" **[f]**.

Furthermore, guidelines from the Children's Mercy City Hospital in Kansas, USA recommend that "*Utilization of VATS or chest tube with fibrinolytic agents have been shown to decrease morbidity compared to chest tube alone with evidence suggests that treatment with VATS or chest tube plus*

fibrinolysis decreases the duration of fever and hospital length of stay" **[g]**.

Our study is also referenced in the Children's Health Clinical Guideline for Empyema provided by Auckland City Hospital, New Zealand **[h]**.

Benefits to patients

This shift in practice has reduced exposure to the potential harms of general anaesthesia and invasive surgery along with the associated psychological stress to both paediatric patients and their parents/carers. Furthermore, the use of CT scans itself carries significant morbidity. Various studies have indicated an increased risk of cancer developing later in life for those who have undergone CT scanning. An Australian study, published in 2013, found that cancer incidence was increased by 24% in patients exposed to a CT scan when aged 0-19 years, compared with the incidence in the unexposed **[i]**. Thus our demonstration that routine CT scanning is clinically unnecessary means that through the use of plain chest X-rays and ultrasound scans for confirming a diagnosis of empyema, children are exposed to much lower doses of ionising radiation, reducing the risk of future malignancies.

Economic benefits

A 2008 US study used our data as the basis for their estimations of cost-effectiveness and concluded that "*On the basis of the best available data, chest tube with instillation of fibrinolytics is the most cost-effective strategy for treating pediatric empyema*" **[j]**.

5. Sources to corroborate the impact

[a] The national programme for enhanced pneumococcal surveillance of complicated pneumococcal pneumonia and empyema in UK children, http://research.ncl.ac.uk/bces-modelling/biologicalclinicalandenvironmentalsystems/thenationalprogrammeforenhancedpneumococcal/ and see for example, studies from the US and Scotland:

- Li ST, Tancredi DJ. Empyema hospitalizations increased in US children despite pneumococcal conjugate vaccine. Pediatrics. 2010 Jan;125(1):26-33. http://dx.doi.org/10.1542/peds.2009-0184.

- Roxburgh CS, Youngson GG, Townend JA, Turner SW. Trends in pneumonia and empyema in Scottish children in the past 25 years. Arch Dis Child. 2008 Apr;93(4):316-8. http://dx.doi.org/10.1136/adc.2007.126540

[b] Balfour-Lynn IM, Abrahamson E, Cohen G, Hartley J, King S, Parikh D, Spencer D, Thomson AH, Urquhart D; Paediatric Pleural Diseases Subcommittee of the BTS Standards of Care Committee. BTS guidelines for the management of pleural infection in children. Thorax. 2005 Feb;60 Suppl 1:i1-21. http://dx.doi.org/10.1136/thx.2004.030676

[c] Strachan RE, Jaffé A; Thoracic Society of Australia and New Zealand. Recommendations for managing paediatric empyema thoracis. Med J Aust. 2011 Jul 18;195(2):95. http://www.thoracic.org.au/professional-information/position-papers-guidelines/paediatric-empyema/.

[d] Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, Kaplan SL, Mace SE, McCracken GH Jr, Moore MR, St Peter SD, Stockwell JA, Swanson JT, Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76. http://dx.doi.org/10.1093/cid/cir531

[e] Canadian Paediatric Society Guidelines https://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=4&ved=0CFAQFjAD&url

=https%3A%2F%2Fonlinereview.cps.ca%2Fpapers%2Fcomplicated-pneumonia-empyema%2Fprint_ready.pdf&ei=cJuEUsXNCYGc0AXFpYCYDQ&usg=AFQjCNGs-9DRcJew8DuQpP7KA8igNAFnNQ&sig2=3IygBSipeQTFCkHslc6lKA&bvm=bv.56343320,d.d2k

[f] United Bristol Healthcare NHS Trust Hospital Guidelines http://www.bristolpaedresp.org.uk/Guidelines/Empyema%20guidelines.pdf

[g] Children's Mercy Kansas City Hospital – Management of Effusion Empyema

[h] Starship Children's Health Clinical Guideline Auckland – Empyema http://www.adhb.govt.nz/starshipclinicalguidelines/_Documents/Empyema.pdf

[i] Mathews JD, Forsythe AV, Brady Z, Butler MW, Goergen SK, Byrnes GB, Giles GG, Wallace AB, Anderson PR, Guiver TA, McGale P, Cain TM, Dowty JG, Bickerstaffe AC, Darby SC. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. BMJ. 2013 May 21;346:f2360. http://dx.doi.org/10.1136/bmj.f2360.

[j] Cohen E, Weinstein M, Fisman DN. Cost-effectiveness of competing strategies for the treatment of pediatric empyema. Pediatrics. 2008 May;121(5):e1250-7. http://dx.doi.org/10.1542/peds.2007-1886.