PRACTICE MANAGEMENT GUIDELINES FOR PROPHYLACTIC ANTIBIOTIC USE IN TUBE THORACOSTOMY FOR TRAUMATIC HEMOPNEUMOTHORAX: EAST PRACTICE MANAGEMENT GUIDELINES WORK GROUP

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I. Statement of the problem

Chest injury is a common problem in patients sustaining blunt or penetrating trauma. Thoracic wounds account for 20 to 25% of all trauma deaths (16,000) annually.[1] Only 10 to 15% of all chest wounds require thoracotomy, whereas the remaining 85% can be managed with a closed tube thoracostomy. A major morbidity associated with this therapeutic device is empyema. The role of Aprophylactic@ antibiotics in reducing the incidence of this complication is controversial.

The value of antibiotic prophylaxis for elective and urgent operations in surgical practice has been validated by many studies.[2,3] For injured patients, the purpose and optimal duration of antibiotic use are less clear because there is no opportunity to administer the agent before bacterial contamination occurs. Antibiotics administered in this setting have been used traditionally for early presumptive therapy and thus are not truly prophylactic. The goal of this preventive therapy is the same as that of prophylaxis: to reduce the incidence of infectious complications following a therapeutic intervention. Reasonable assumptions about the microorganisms most often encountered are used to guide the selection of antimicrobial agents.

The primary goal of prophylactic antibiotic use in injured patients requiring tube thoracostomy is to reduce the incidence of empyema and its associated morbidity. A secondary goal may be a reduction of bacterial pneumonia, but the literature is difficult to interpret because of the variability in criteria used to make this diagnosis. An additional area of confusion in interpreting the results of various studies is the lack of clarity regarding pneumonia as a primary or secondary endpoint of prophylaxis. The primary benefit must be significant because of the risk of emergence of resistant organisms with excessive use of antimicrobials. A major variable that confounds analysis is the setting and conditions under which the tube is inserted i.e., prehospital, the emergency room, intensive care unit, operating room.[4] The incidence of empyema may also be affected by thoracostomy tube insertion by non-surgeon physicians. These factors are not mentioned in extant studies evaluating the role of prophylactic antibiotics with tube thoracostomy. Two other very important variables that have not been addressed appropriately in the literature are the choice of antimicrobial agent and the duration of therapy. Ideally, antibiotics with a narrow spectrum of activity focused against the most common organisms for a brief duration would help reduce the risk of resistance and, potentially, overall hospital costs.

II. Process

A. Identification of references

The recommended guidelines for prophylactic (preventive) antibiotic use for trauma patients requiring a chest tube are evidence-based. A MEDLINE search for the past 20 years (1977-1997) was performed. The following subject words were used for the query: antibiotic prophylaxis; chest tubes; human; drainage; tube thoracostomy; infection; empyema; and bacterial infection-prevention and control. This search

identified 44 references in the English language. The bibliographies of each article were searched for additional references not identified by the original MEDLINE query. Letters to the editor, case reports, and review articles were excluded from further evaluation. Eleven articles were identified for inclusion in the evidentiary review; nine were prospective series and two were meta-analyses. The articles were reviewed by four trauma surgeons and pharmaceutical outcome researchers with interest in pharmacokinetics and health care economics who collaborated to produce these guidelines.

B. Quality of the references

The references were classified by the methodology established by the Agency for Health Care Policy and Research (AHCPR) of the U.S. Department of Health and Human Services. Additional criteria and specifications taken from a tool described by Oxman et al.[5] were used for Class I articles. Thus, the classifications were:

Class I: Prospective, Randomized, Double-Blinded Study
Class II: Prospective, Randomized, Non-Blinded Trial
Class III: Retrospective Series of Patients or Meta-analysis

The evidentiary table contains 11 articles that were reviewed for these recommendations.

III. Recommendations (For isolated chest trauma)

A. Level I

There are insufficient data to support a Level I recommendation as a standard of care.

B. Level II

There are insufficient data to suggest prophylactic antibiotics reduce the incidence of empyema.

C. Level III

There are sufficient Class I and II data to recommend prophylactic antibiotic use in patients receiving tube thoracostomy following chest trauma. A first generation cephalosporin should be used for no longer than 24 hours. The data suggest there may be a reduction in the incidence of pneumonia but not empyema in trauma patients receiving prophylactic antibiotics when a tube thoracostomy is placed.

IV. Scientific Foundation

A. Historical background

Intrapleural infection received considerable attention as a complication of penetrating chest trauma in World War II.[6] This problem continued to concern wartime surgeons during the Vietnam conflict despite the availability of antibiotics.[7] The incidence of empyema following chest injury has varied according to whether the reports originated from civilian or battlefield experience. During the pre-antibiotic era from 1922 to 1935, the reported incidence of empyema from Emory University was 2%. At the same institution, when all patients received antibiotics, the incidence of empyema from 1948 to 1958 was 3%. Two World War II studies, in which most patients received either penicillin or sulfonamides, reported an incidence of empyema ranging from 5 to 9.7%.[8,9] During the Korean war, Valle noted that undrained hemothoraces became infected in 26% of cases.[10] Fortunately, 80% of the patients recovered with thoracentesis and antibiotics.[10] In contrast, Conn et al. and Smythe et al. reported a much lower infection rate of 1.6 to 2.1% in civilian practice when patients were treated with needle aspirations and antibiotics.[11,12] During the Vietnam war, Virgilio noted that empyemas occurred in 1.6% of patients treated with penicillin and streptomycin plus tube thoracostomy.[13] A similar incidence of 0.5 to 1.5% was reported at the Martin Luther King Hospital in Los Angeles in two separate reports without routine antibiotic use.[14,15]

Posttraumatic empyema is a significant problem in both blunt and penetrating chest injuries. Potential etiologies include (1) iatrogenic infection of the pleural space as during chest tube placement, (2) direct infection resulting from penetrating injuries of the thoracic cavity, (3) secondary infection of the pleural cavity from associated intra-abdominal organ injuries with diaphragmatic disruption, (4) secondary infection of an undrained or inadequately drained hemothoraces , (5) hematogenous or lymphatic spread of subdiaphragmatic infection to the pleural space, and (6) parapneumonic empyema resulting from posttraumatic pneumonia, pulmonary contusion, or acute respiratory distress syndrome (ARDS).

The organisms responsible for the infection vary according to the mechanism of contamination. When related to chest tube insertion, empyema typically will culture gram-positive *Staphylococcus aureus* or *Streptococcus* species.[15,16] Secondary contamination from pneumonic processes or other routes of spread often involve gram-negative or mixed bacterial pathogens.

The development of empyema increases patient morbidity, mortality, hospital length of stay, and the cost of the cure. Efforts to reduce the incidence of this complication will impact on morbidity and perhaps mortality. One possible interventional use of prophylactic antibiotics in patients requiring tube thoracostomy is for traumatic hemothorax or pneumothorax. However, this terminology is a misnomer in trauma patients. By definition, prophylactic antibiotic regimens achieve a pre-inoculation

serum and tissue-drug concentration before bacterial contamination, an impossibility in a trauma patient. Thus, antibiotic administration in the immediate post-injury period is more correctly considered presumptive therapy.

B. Risk Factors for complications with tube thoracostomy after chest injury.

1. Mechanism of Injury

Chest trauma occurs as a result of penetrating or blunt injury. Cant et al. described the utility of first-generation cephalosporins in victims of thoracic stab wounds requiring tube thoracostomies.[16] This is the only study that controlled patient enrollment by the mechanism of injury. They defined empyema as a need for thoracotomy, although they did not culture for pathogens. They did show a significant reduction in the need for thoracotomy in those individuals receiving prophylactic antibiotics compared to placebo (0% versus 9%). However, of the five placebo-treated cases diagnosed with empyema, one developed as a result of underlying pneumonia and the other was an infected, retained hemothorax. Taking this into account, the adjusted incidence of empyema was 5% (3/56). The diagnosis of pneumonia was made only by the presence of a positive sputum culture. There was a significantly lower incidence of positive cultures in the group receiving antibiotics (12% versus 34%), and a significantly greater hospital length of stay and cost in the placebo group.

Three other studies evaluated the role of antibiotics in individuals with penetrating chest wounds.[17-19] Only one was a double-blinded, randomized, prospective study,[17] while the other two were randomized but not blinded.[18,19] Most patients in these three studies had received stab wounds (n=276), and only 67 were injured by firearms. The double-blinded study concluded that antibiotics reduced the incidence of empyema.[17] The two randomized, open-label studies did not identify any benefit with the use of antibiotics.[18,19] The other studies[20-24] did not control for mechanism of injury, however, most of the patients in these studies sustained penetrating thoracic injuries. In one study, the specific mechanism of injury for the study population could not be determined.[23] Two reports included patients with spontaneous pneumothorax[20,21] (25% and 43% of the study cohort), which is irrelevant to trauma. These Class I and II studies do not support prophylactic antibiotics as a standard of care for reducing the incidence of empyema or pneumonia in patients sustaining penetrating thoracic wounds.

2. Antimicrobial Agents

Only two studies utilized a first-generation cephalosporin in their study design,[16,23] while the remainder used various antibiotics delivered via different routes. None of the studies evaluated the pharmacokinetics of the

antimicrobials in the trauma patient. Grover et al. utilized clindamycin in a suboptimal dosage.[17] Doxycycline,[18] cefoxitin,[22] and ampicillin[19] have less-than-ideal Staphylococcal coverage. Four studies used appropriate agents and dosing.[16,20,21,24] Brunner et al. utilized cefazolin, however, in an excessive dose.[23]

The duration of antibiotic use for prophylaxis is usually confined to 24 hours. Only one study limited antimicrobial use to 24 hours.[6] In Demetriades study, all patients received a single intravenous dose of ampicillin prior to tube insertions.[19] One group did not receive any additional doses while the other group continued to receive oral ampicillin. There was no difference in the rate of septic complications. All other reports continued the agent being studied until the chest tube was removed[17-19,23,24] or for an additional 12 to 48 hours after it was removed.[20-22] For those receiving antibiotic prophylaxis until the tube was removed, the number of days of intubation ranged from 3 to 6.5 days with an average of 4.7 days. Cant et al. reported no empyema in individuals who received cefazolin for 24 hours compared to a 5% incidence in the placebo group.[16] This is the only study using a 24-hour duration of antibiotic prophylaxis that demonstrated a reduction in empyema for patients with stab wounds to the chest.

3. Pneumonia/Empyema

The Centers for Disease Control and Prevention have clearly defined criteria for the diagnosis of pneumonia and empyema which have evolved during the past two decades. These include clinical signs of sepsis and positive cultures for a pathogen. Only three studies in this review had conforming definitions of these infectious complications,[20,22,24] while the remainder had various, non-standard definitions of pneumonia and empyema. Brunner et al. described two patients who underwent thoracotomy for entrapped lung but were culture-negative, which does not necessarily rule out empyema.[23] Nichols et al. described three control patients with empyema. Only one required decortication, and the other two were drained with placement of an additional chest tube. A fourth case of empyema was associated with a pneumonia (suggesting a parapneumonic empyema unrelated to the chest tube).[24]

Two studies described an empyema in one patient each with retained hemothorax and a persistent pneumothorax.[18,21] Grover et al. described six patients with empyema, only four of whom required formal thoracotomy.[17] One of these four patients had a necrotizing pneumonia, suggesting a parapneumonic process. The lack of a standardized definition of empyema in the various studies suggests the true incidence of chest tube-associated empyema may be less than that actually stated in the literature. It also raises a question of the real incidence of empyema in the control groups. Nonetheless, the overall empyema rate for the control group patients included in this review

was 6.8% (29/427) compared to 0.5% (2/431) in patients receiving preventive antibiotics. Most of the control patients were subsequently treated unnecessarily.

Because of the small number of patients in individual series, two meta-analyses have been performed.[25,26] Each concluded that prophylactic antibiotics made a significant impact on the incidence of empyema. Both analyses assumed that the study populations were similar when no objective information was supplied to support this assumption. The authors reported that all six studies met clinical combinability criteria without describing the specific criteria. The various antibiotics used in the studies over the 15-year period raises a question of comparative treatment regimens similar enough to draw any valid conclusions. These concerns, coupled with the multiple concerns in the above discussions, raise questions about the conclusions from the meta-analyses papers.

4. Cost

Cost is a major concern in the current health care market. Only Nichols et al.[24] and Cant et al.[16] performed a cost analysis. Nichols et al. claimed that prophylactic antibiotics resulted in a 0.9 day reduction in length of hospital stay. At the time of that study, the wholesale cost for 1 gm cefonicid was $26.10. The treated patients received an average of 5 doses of that agent. The daily hospital cost quoted was $688 in government-run institutions and $820 in private, for-profit facilities. They concluded that there was a potential direct medical cost offset of $488 to $607 per patient excluding the cost of drug administration. Thus, depending on the amount of direct cost for a specific antibiotic and the duration of prophylaxis, there may be a net increase in direct medical cost associated with prophylactic antibiotic treatment. When indirect costs are included there are overall cost savings; however this may be negligible. In summary, there are inadequate data to support any recommendations on cost analysis for prophylactic antibiotics.

C. Evidentiary Table

Eleven articles were utilized to formulate the guidelines for prophylactic antibiotic use in trauma patients with a tube thoracostomy. The data in the evidentiary table are listed alphabetically by class and include 4 Class I articles, 5 Class II, and 2 Class III meta-analyses. The following data were retrieved and reported from each article: (1) antibiotic utilized; (2) number of patients in each study group; (3) duration of prophylaxis in days; (4) incidence of pneumonia; and (5) incidence of empyema. Mechanism of injury was also determined but not shown in the table. Patients requiring tube thoracostomy for spontaneous pneumothorax were deleted from the patient populations reported in the table.[20,21]

V. Summary

Multiple factors contribute to the development of posttraumatic empyema. These factors include, the conditions under which the tube is inserted (emergent or urgent), the mechanism of injury, retained hemothorax, and ventilator care. The incidence of empyema in placebo groups ranges between 0% and 18%. The administration of antibiotics for longer than 24 hours did not appear to significantly reduce this risk compared with a shorter duration, although the numbers in each series were small. Most reports found a significant reduction in pneumonitis when patients received prolonged prophylactic antibiotics. This use of antibiotics might possibly be better described as presumptive therapy rather than prophylactic.

VI. Future Investigation

Further clinical evaluation is required due to the paucity of literature evaluating the role of prophylactic antibiotics in trauma patients receiving a tube thoracostomy for chest trauma. Well-designed, multi-institutional trials with double-blinded design need to be performed. These studies should control for the setting and conditions in which the tube is being inserted as well as the training of the physician performing the procedure. At greatest risk is the patient who is in shock in the emergency room. The intensive care unit and operating room should allow adequate time for strict, sterile technique and minimized risk of iatrogenic contamination during insertion. Future studies should also control for time from administration until time of insertion, duration of prophylaxis, and mechanism of injury.

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PROPHYLACTIC ANTIBIOTICS IN TRAUMA PATIENTS WITH TUBE THORACOSTOMY: EVIDENTIARY TABLE

First Author	Year	Reference	Class	Antibiotic	# Pts.	Duration	Pneumonia	Empyema
Grover FL	1977	Prophylactic antibiotics in the treatment of penetrating chest wounds: A prospective double-blinded study. *J Thorac Cardiovasc Surg 74:528-536*	I	Clindamycin Placebo	38 37	1-5 days N/A	10.5% 35.1%	2.6% 16%
Stone HH	1981	Cefamandole for prophylaxis against infection in closed tube thoracostomy. *J Trauma 21:975-977*	I	Placebo Cefamandole	43 40	48 hours after CT d/ced	12% 0%	4.7% 2.5%
Cant PJ	1993	Antibiotic prophylaxis is indicated for chest stab wounds requiring closed tube thoracostomy. *Br J Surg 80:464-466*	I	Cefazolin Placebo	57 56	24 hours	12% 34%	0% 9%
Nichols RL	1994	Preventive antibiotic usage in traumatic thoracic injuries requiring closed tube thoracostomy. *Chest 106:1493-1498*	I	Cefonicid Placebo	63 56	Until CT removed	0% 5%	0% 5%
LeBlanc KA	1985	Prophylactic antibiotics and closed tube thoracostomy. *Surg Gynecol Obstet 160:259-263*	II	Cephapirin Placebo	26 26	24 hours after CT d/ced	3.8% 3.8%	0% 3.8%
Mandal AK	1985	Prophylactic antibiotics andno antibiotics compared in penetrating chest trauma. *J Trauma 25:639-643*	II	Doxycycline Placebo	40 40	Until CT removed	0% 2.5%	0% 0%
LoCurto JJ Jr	1986	Tube thoracostomy and trauma--Antibiotics or not? *J Trauma 26:1067-1072*	II	Placebo Cefoxitin	28 30	12 hours after CT d/ced	14% 3%	18% 0%
Brunner RG	1990	The role of antibiotic therapy in the prevention of empyema in patients with an isolated chest injury (ISS 9-10): A prospective study. *J Trauma 30:1148-1154*	II	No antibiotics Cefazolin	46 44	Until CT removed	6.5% 2.3%	13% 0%
Demetriades D	1991	Antibiotic prophylaxis in penetrating injuries of the chest. *Ann R Coll Surg Engl 73:348-351*	II	Ampicillin IV prior to tube insertion	95 93	Pre-tube insertion Oral until CT d/ced	3.1% 2.1%	0% 1.1%

First Author	Year	Reference	Class	Conclusions
Evans JT	1995	Meta-analysis of antibiotics in tube thoracostomy. *Am Surg 61:215-219*	III	Meta-analysis performed of 6 randomized studies. Outcomes evaluated included empyema, effusion, pneumonia, wound infection, tracheitis, Concluded: Antibiotics should be used and maximize therapy for *Staphylococcus aureus.*
Fallon WF Jr	1992	Prophylactic antibiotics for the prevention of infectious complications including empyema following tube thoracostomy for trauma: Results of meta-analysis. *J Trauma 33:110-117*	III	Meta-analysis of same 6 studies as Evans et al. Only evaluated 4 studies which used first or second generation cephalosporins. Determined impact on early empyema and other infectious complications. Concluded: Antibiotic prophylaxis with broadspectrum first generation cephalosporin may reduce the potential infectious complications including empyema that are associated with tube thoracostomy.