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Perioperative Antibiotics in Thoracic Surgery

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Definition of Surgical Site Infection

In 1992, the Surgical Wound Infection Task Force redefined surgical infections as surgical site infections (SSI), involving infection of the incision or organs/spaces manipulated during a operative intervention[1]. Remote infections, not including bloodstream infections related to a SSI, are not included in the definition of SSI[1]. This task force split the categorization of SSIs into superficial incisional, deep incisional, and organ/space SSI (Table 1). SSIs need to manifest within 30 days of the operation, unless an implant was involved, in which case the time frame for deep incisional and organ/space SSIs is increased to 1 year. Superficial SSIs are confined to the skin and subcutaneous tissue, deep incisional SSIs involves deeper soft tissues such as fascial planes and muscle layers, and organ/space SSIs include any anatomic location, excluding incisional area, that was manipulated during an operation. An exception to these SSI classifications occurs when an organ/space infection communicates with the skin and drains along the incision site, as this is considered an incisional complication, and defined as a deep incisional SSI. Of note, the strict definition of a surgical site infection does not include “remote” postoperative infections such as pneumonia after a non-thoracic surgery or a urinary tract infection after a non-urologic procedure.

History of Surgical Antibiotic Prophylaxis

After the development of anesthetic techniques in the mid-nineteenth century, the surgeon was poised to expand the range and complexity of operative procedures that could safely be performed. However, the complications resulting from infection related to such intervention lead to continued difficulty with postoperative morbidity and mortality and severely limited the scope of disease processes that could be treated surgically. The work on antiseptic

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principles at the end of the nineteenth century was pivotal in regards to surgical site infection control and modern-day antibiotic prophylaxis. Ignaz Semmelweis was the first to realize the impact of handwashing on postoperative complications, noting that puerperal fever was three fold higher in patients treated by physicians who participated in autopsies of patients who died from the same cause. Based on this finding, he mandated that physicians wash their hands in chlorine prior to patient interaction, decreasing mortality from 9% to 1.5%[2]. Louis Pasteur later demonstrated that infectious diseases are attributable to microbes, and developed techniques for sterilization. His work laid the groundwork for Joseph Lister, the father of antisepsis, who in 1867 utilized carbolic acid to dress wounds and decrease the incidence of infection and perioperative mortality. Other notable scientists, such as Robert Koch and William Osler, contributed to surgical site infection treatment through techniques to isolate the infectious organisms. Their work led to the understanding that the host inflammatory response to infection can also lead to morbidity. All of these advances helped in understanding antisepsis and the role of microbial organisms in infection, paving the road to the discovery of prophylactic antibiotics[3].

In 1928, Sir Alexander Fleming discovered the first effective antimicrobial. He left a petri dish of bacteria uncovered during vacation, and upon his return, he noted that *Staphylococcus* did not grow in or around a mold colony. Realizing the potential of this mold, he discovered penicillin. Following this, multiple other antibiotics were developed, and used for prophylaxis during operative intervention in the 1950s. The clinical trials at that time demonstrated no difference with antibiotic use, but their study design included multiple flaws, including lack of randomization, inappropriate antibiotic use, and inappropriate timing of prophylaxis. More recent randomized controlled trials have shown perioperative antibiotics to be advantageous for prevention of surgical site infections (Table 2)[4-7].

Practice Patterns of Surgical Prophylaxis in Thoracic Surgery

Evidence Based Indications for Prophylaxis for Lung Resection

Efficacy of Perioperative Antibiotics—There have been multiple prospective randomized control trials regarding perioperative antibiotics for non-cardiac thoracic surgery, but unfortunately unlike the case for cardiac surgery,[8] no official guidelines exist. One of the earliest studies was performed was in 1977 by Kvale, et al[9]. It was a randomized, prospective double-blind study in patients undergoing pulmonary surgery, comparing cefazolin 500mg intramuscularly (IM), starting upon arrival to the operating room, followed by cefazolin 500mg IM every 6 hours then oral cephalexin 500mg when the patient was tolerating a diet for a total of 5 days versus placebo treatment. The results of this study showed a statistically significant difference in peri-operative infection with a 50% infection rate (17 of 34 patients) in the control group versus 19% in the perioperative antibiotic group (8 of 43 pts). This pivotal trial initiated the now common practice of using perioperative cephalosporin prophylaxis in thoracic surgery.

The subsequent two randomized trials, however, contradicted the findings of Kvale and colleagues, creating confusion and putting into doubt the role of antibiotic prophylaxis in pulmonary resection. Truesdale et al[10] treated patients with cephaloxin 1g IM in the operating room prior to pulmonary resection, followed by 2g intravenously (IV) every 6 hours for a total 48 hours or a placebo dosed in a similar fashion. Their data demonstrated a 17.2 % (5 of 29 pts) infection rate in those receiving a placebo and a 17.8% (5 of 28 pts) rate of postoperative infection in those receiving antibiotics. A similar trial performed at the Johns Hopkins medical center[11] also did not demonstrate a difference in the rate of perioperative wound infection between patients receiving 2g IV cephalothin vs. placebo prior to and 6 hours post pulmonary surgery. They reported no statistical difference, but did not give a number for the wound infections.

Following these two trials, all subsequent studies reported an advantage to using perioperative antibiotics swaying the clinicians toward antibiotic prophylaxix. In Toronto, Ilves et al[12] randomized patient with esophageal or pulmonary surgery to cephalothin 2g IV in the operating room followed by 2g IV 4 hours later versus placebo. The results showed 23.7 % (22 of 93) patients had wound infections in the placebo group, compared to 5.9% (7 of 118 pts) in the treatment group. They also demonstrated a non-statistically significant decrease in the postoperative pneumonia and empyema with prophylactic antibiotics. In 1982, Frimoldt-Moller et al compared Penicillin G 5 million international units (IU) IV prior to surgery and every 6 hours for a total of 5 doses versus placebo[13]. Placebo resulted in a 19.1% (9 of 47 pts) wound infection, while the use of prophylactic antibiotics led to a 4.4% (2 of 45 pts) infection rate. Aznar and collegues[14] revisited this topic in 1991. They designed another prospective, randomized, double blind trial comparing cefazolin 1g IV 30 minutes prior to surgery versus placebo. This trial, performed over a decade after the previous five studies, supported the data in Kvale, Ilves, and Frimoldt-Moller's trials, with a statistically significant decrease in wound infection from 14% (8 of 57 pts) in the placebo group versus 1.5% (1 of 70 pts) with perioperative antibiotics. Additionally there was a decrease in empyema (14% vs 7%) and pneumonia (9% vs 4%) in the treatment arm. Thus, despite the small number of randomized clinical trials and initial conflicting data, the majority of trials support the use of perioperative antibiotics in non-cardiac thoracic surgery with a decrease in surgical site infection post- operatively. No consistent data, however, is available to demonstrate an effect of perioperative antibiotics on the rate of postoperative pneumonia or empyema.

Duration of Perioperative Antibiotics—Multiple studies have shown the efficacy of single-dose prophylactic antibiotics in other surgical procedures[15-18], but few such trials have been conducted for pulmonary surgery. Olak et al[19] performed the first prospective study looking at the appropriate course of perioperative antibiotics in 1991. Patients were randomized to cefazolin 1g IV prior to induction of anesthesia or cefazolin 1g IV at induction and every 8 hours for a total of 6 doses. This study showed no difference in surgical site infections, including wound infection, pneumonia, or empyema between the two arms. Subsequently, Wertzel et al[20] randomized patients undergoing pulmonary resection to ampicillin/sulbactam 3g at induction only versus 3g at induction and every 8 hours for a total of 3 doses. Again, no difference was present between the single and multi-dose antibiotic regimens. Other studies, including Aznar et al[14], looked at single dose perioperative antibiotics versus placebo, and showed a significant decrease in surgical site infections, supporting the efficacy of single dose antibiotics for pulmonary surgery.

One randomized controlled study, conducted by Bernard et al in 1994[21], supported the longer use of perioperative antibiotics, randomizing patients to cefuroxime 1.5g IV prior to surgery and 2 hours later versus the same regimen plus doses every 6 hours postoperatively for 48 hours. His data showed no change in superficial wound infections, but demonstrated a decreased incidence in empyema, from 15.6% with two doses down to 6% in the 48 hours treatment. However, this data is skewed as seven patients in the two-dose group developed broncho-pleural fistulas, compared to two patients in the 48-hour group, with broncho-pleural fistula most likely related to surgical technique. It is thus likely that the fistula was the cause for the increased incidence of infection in the two-dose group, decreasing the validity of this study's findings.

Though a limited number of randomized controlled trials have investigated the appropriate duration of perioperative antibiotics for pulmonary surgery, based on these data we can conclude that a single dose of antibiotics prior to incision is effective at decreasing the incidence of surgical site infections. This conclusion is supported by the expansive number

of trials in cardiac surgery that also demonstrate the efficacy of perioperative antibiotics with a single dose of antibiotics is as effective as up to 48 hours of prophylaxis[8].

Selection of Perioperative Antibiotics—The choice of prophylactic antibiotics is based upon the most common pathogens likely to result in SSI, which heavily depends on the operative procedure[22]. In pulmonary surgery bacteria from normal skin and respiratory flora are the common cause of SSIs. This consists of *Staphylococcus Aureus,* coagulase negative staphylococci, *Streptococcus Pneumoniae*, and gram-negative bacilli,[23,24] with *S. Aureus* being the most commonly identified pathogen. Cephalosporins provide adequate coverage over these organisms and are a good class of antibiotics for infection prophylaxis in pulmonary surgery. Though cephalosporins differ in their spectrum of coverage based on generation (first-generation through fourth-generation cephalosporins are currently available with increased coverage of gram-negative bacteria with increasing generation of drug) differ in their coverage of bacteria, clinical trials have been unable to demonstrate a difference with regard to surgical site infection[25,26].

Only one randomized controlled trial compared the use of first versus third generation cephalosporins, and was designed to elucidate the effect of third-generation cephalosporins' increased activity against gram-negative bacilli on perioperative complications. Turna et al[26] randomized patients to a first generation cephalosporin (cephalexin 1.5g IV) prior to surgery then every 12 hours versus a third generation cephalosporin (cefepime 1g IV) prior to surgery then every 24 hours for a total of 48 hours for each group. Their results indicated no difference in SSIs postoperatively between the two groups, supporting the usage of first-generation cephalosporins given their decreased cost and better coverage against gram-positive organisms. This lack of difference between the cephalosporin classes is supported by multiple trials regarding SSI prevention in cardiac surgery[25].

Conclusion—Therefore first-generation cephalosporins, such as cefazolin, which have good coverage for the most common pulmonary surgical site infections, are an appropriate choice for prophylactic antibiotic therapy. The appropriate dosage for cefazolin is 1-2g IV prior to incision[27]. If the patient has a history of methicillin-resistant *S. Aureus* or a penicillin allergy, than vancomycin 1g IV can be used in place of cefazolin.

Evidence Based Indications for Prophylaxis for Esophageal Surgery

Efficacy of Perioperative Antibiotics—The use of perioperative antibiotics in esophageal and gastro-duodenal procedures is based on multiple randomized controlled trials, all of which overwhelmingly demonstrate a benefit from the use of perioperative antibiotic regimens. Since esophageal resections commonly involve gastroduodenal manipulation for conduit formation, our field relies significantly on data acquired by general surgeons for antibiotics in gastric surgeries to determine appropriate prophylaxis of esophageal surgery. Stone et al conducted one of the first large randomized controlled trials in 1976[22]. They enrolled 400 patients undergoing elective gastric, biliary, and colonic surgery, and randomized them to 4 groups with cefazolin 1g IV given: a) 8 to 12 hours prior to surgery, b) 1 hour prior, c) 1 to 4 hours postoperatively, or d) never. The gastric arm had 96 patients, with a 5% (1 of 22 patients) superficial surgical site infection rate 8-12 hours prior, 4% (1 of 27 patients) 1 hour prior, 17% (4 of 24 patients) 1-4 hours postoperatively, and 22% (5 of 23 patients) if no antibiotics were given. These data demonstrate the efficacy of perioperative antibiotics, and the necessity of giving the antibiotics prior to incision. Additionally, there was a decrease in organ/space SSIs as demonstrated by a decrease from 9% rate of peritoneal sepsis in the no treatment group to 4% in the 8-12 hour and 1-hour preoperative groups.

Subsequent studies, such as that of Lewis et al in 1982[28] and Nichols et al[29], confirm the role of antimicrobial prophylaxis in decreasing SSIs. Lewis et al randomized patients to receiving perioperative cefamandole versus placebo in elective and emergent gastric procedures, and noted a decrease in the infection rate from 28% (8 of 28 pts) to 3% (1 of 32 pts)[28]. Nichols et al also randomized patients to cefamandole versus placebo for high risk, elective gastro-duodenal procedures. The placebo group had a 35% (7 of 20 pts) rate of infection compared with 5% (1 of 19 pts) in the treatment arm[29].

Rotman et al held a large randomized controlled trial that investigated the use of preoperative cefazolin or cefotaxime 1g every 8 hours for 3 doses versus placebo for abdominal operations, enrolling greater than 3000 patients[30]. They studied the effect of perioperative antibiotics on clean, clean-contaminated, and contaminated resections (see Table 3)[31,32] as well as on patient with risk factors that predispose them to wound infections, such as diabetes, steroid use, ascites, etc. There was a statistically significant decrease incidence in infection across all groups between placebo and cefazolin, with a global reduction in postoperative wound abscesses from 5% to 2%. Cefotaxime had comparable rates as cefazolin. A decrease was noted in all four groups, with a decrease from 4% to 1% in patients with clean-contaminated operations and 9% to 5% reduction in high-risk patients, again supporting the use of antimicrobials prior to abdominal surgery[30].

Due to the strong evidence provided by randomized clinical trials, perioperative antibiotic therapy with esophageal, gastric, and duodenal surgeries are indicated to decrease the incidence of surgical site infection.

Duration of Perioperative Antibiotics—Many studies have focused on the duration of antibiotics for abdominal surgery, with some specific to gastric surgery. In 1976, Stone et al published a randomized trial of 220 patient undergoing gastric, biliary, and colonic surgery to cefamandole 1g IM 1 hour prior to surgery, 1g IV intraoperatively, and 1g IV in the recovery room, followed by either placebo or cefamandole 1g IM every 6 hours for 5 days. The gastric surgery arm demonstrated a 0% infection in rate in the 25 patients with short course antibiotic regimen and the 29 patients with the five-day antibiotic regimen, demonstrating no indication for prolonged perioperative antibiotics[33]. They further evaluated this by looking at patients undergoing emergent laparotomy in patients with abdominal trauma resulting in peritoneal contamination, and again demonstrated that there was no gain in prolonged antibiotic therapy for both superficial site infections (8% and 10%, respectively) and deep/organ space infections (4% versus 5%, respectively).[33]

These findings were corroborated when Lewis et al in 1991 studied the efficacy of a single perioperative antibiotic dose of intravenous cefotaxime versus a short postoperative course. Both groups demonstrated no incidence of superficial surgical site infection but a 3% incidence of a subphrenic abscess after anastamotic leak in both the single dose and short antibiotic course (1 of 26 pts and 1 of 27 pts, respectively), supporting the use of a single dose of antibiotics[34].

Based on these randomized trials, and others looking at the efficacy or single dose prophylaxis for abdominal surgery[15-18], we conclude that a short course of perioperative antibiotics, and perhaps even a single dose of preoperative antibiotics, is successful at decreasing the occurrence of surgical site infections associated with esophageal and gastro-duodenal surgery. Thus, as described in Table 4, based on the best available data antibiotic prophylaxis for general thoracic surgery in our institution, both pulmonary and esophageal, includes only a short course of perioperative antibiotics.

Selection of Perioperative Antibiotics—The most common pathogens present in surgical site infections for esophageal, gastric, and duodenal resection are enteric gram-negative bacilli, streptococci, and oropharyngeal anaerobes[16,22,24,35,36]. Given this spectrum of pathogens, cephalosporins again are an adequate class of antimicrobials for prophylaxis of postoperative infections. Most studies have evaluated first-, second- and third-generation cephalosporins as perioperative antibiotics for gastroduodenal resection. The 1979 Stone et al study also compared short course cefamandole, a second-generation cephalosporin, to cephaloridine, a first-generation cephalosporin, which no significant difference in wound infections for gastric surgeries[33]. The Lewis et al and Nichols et al studies both demonstrated that cefamandole was effective at significantly decreasing surgical site infections in high-risk patients[28,29]. The Rotman et al study showed no significant difference between patients treated with cefazolin versus cefotaxime, with cefazolin having the statistically significant decrease in overall infection when compared to placebo[30]. Therefore no differences have been shown between each generation of cephalosporins on changing SSI rate for upper gastrointestinal surgeries.

The use of cefazolin, which has good coverage against gram-positive cocci and enteric gram-negative organisms, as a prophylactic antibiotic for esophageal, gastric, and duodenal resections is the most efficacious in light of a low anaerobic burden. The appropriate dosage is 1-2g IV prior to incision,[27] and vancomycin 1g IV if the patient has a history of methicillin-resistant *S. Aureus* or a penicillin allergy. For patients with a high anaerobic burden, such as may occur after esophageal perforation or Boerhaeve's syndrome, the use of a fourth-generation cephalosporin such as cefepime, which has greater anaerobic coverage, would likely prove to be more efficacious, though no current study has evaluated this hypothesis.

Evidence Based Indications for Lung Transplantation

Perioperative antibiotic prophylaxis after lung transplantation is extremely important as infection and bronchiolitis are the major causes of death in the first five years after transplantation[37]. This high rate of infectious complications is due to many factors, including immunosuppression, decreased mucociliary action, and continuous exposure to the outside environment and pathogens[38]. However, no standardized regimen or guidelines exist regarding the choice of perioperative antibiotic or antifungal therapy[38,39].

Bacterial infections are the most common post-transplantation and pathogens are usually gram-negative rods such as *Psuedomonas* and *B. cepacia*[38]. Thus, an antipsuedomonal antibiotic with gram-negative bacilli coverage, such as cefepime, is appropriate for perioperative prophylaxis. *Staphylococcus* infections are also common post-operatively. Given the increased risk of methicillin-resistant *S. aureus*, vancomycin is also routinely used in conjunction with a cephalosporin. These antibiotics are given for 7-10 days post-transplantation and then discontinued unless the patient has a clinical indication for continued antibiotic therapy[40,41]. The routine use of trimethoprim-sulfamethoxazole for *P. carinii*, described later, is also adequate prophylaxis against development of rare bacterial infections, such as *Legionella*, *Listeria*, and *Nocardia*[38].

Viral infections, most notably with cytomegalovirus (CMV), are the second most frequent source of infection in lung transplantation. CMV infections generally occur in the first four months after transplant, and are most common in seronegative recipients (i.e. those who have never been infected with the virus and thus have not developed protective antibodies) that receive CMV positive lungs, or in patients who are seropositive but require increase immunosuppression to prevent rejection[42]. Common antiviral agents used in the post-opertaive period are ganciclovir, acyclovir, and valganciclovir. One randomized trial compared the efficacy of acyclovir to ganciclovir in prevention of CMV, using ganciclovir

for the first three weeks, then either acyclovir 800mg four times a day or ganciclovir 5mg five times a week. At 90 days, the rate of CMV shedding or pneumonitis was 50% with acyclovir versus 15% with ganciclovir. Additionally, the acyclovir group had a greater rate (54%) of obliterative bronchiolitis, as a sequelae of CMV infection, compared to ganciclovir (17%)[43]. Thus ganciclovir is the preferred method of viral prophylaxis, compared to acyclovir. The efficacy of valganciclovir versus ganciclovir in lung transplant patients has not been extensively studied. No prophylaxis is indicated for seronegative donor and recipients. For seropositive recipients, with seropositive or seronegative donors, CMV PCR can be monitored, and prophylaxis can be instituted if the infection is detected. Many institutions also choose to have universal prophylaxis is this subset of patients. With seronegative recipients and seropositive donors, prophylaxis is instituted with either IV ganciclovir or PO valganciclovir. Other viral infections, such as herpes simplex, also used to be prevalent, but since the routine use of antivirals in the postoperative period, their incidence has rapidly decreased[44].

Fungal infections are less common than bacterial infections, accounting for 10-14% of post-transplant infections, but have a much higher mortality compared to bacterial infections[38]. The most common fungal pathogens are *Candida* and *Aspergillosis*, which generally occur within the first months after transplant[38]. Most *Candida* species and *Aspergillosis* are sensitive to fluconazole, but the more resistant strains require treatment with amphotericin B[45-47]. In 1997, Reichenspurner and collegues published a thorough retrospective review demonstrating that amphotericin B significantly decreased the rate of invasive fungal infections post transplantation, from 20% to 8%[47]. Later, Minari performed a similar retrospective review of their patients focusing on itraconazole prophylaxis versus no prophylaxis, and found that 4.9% (4 of 81 pts) in the treated group developed aspergillosis, compared to 18.2% (16 of 88 pts) without treatment[48].

Voriconazole has also been compared to fluconazole and itraconazole, with a decreased incidence of invasive Aspergillosis, but increased hepatotoxicity and other side effects[49]. No other studies have directly compared amphotericin B versus the azoles, so no conclusions can be drawn except that all decrease the rate of postoperative fungal infections. *Pneumocystic carinii* is also a fungal infection that presents in the first 6 months after transplantation and occurred in up to 70% of patients prior to prophylactic regimens[40]. Current prophylaxis involves trimethoprimsulfamethoxazole, which has significantly decreased the incidence of *P. carinii* infection. If patients cannot tolerate TMP-SMX, then dapsone and aerosolized pentamadine are appropriate alternatives as well[38].

Special consideration applies to cystic fibrosis patients undergoing lung transplantation. Due to prolonged exposure to antibiotics, they have increased proclivity to multi-drug resistant *Psuedomonas*. It has been shown that inhaled aminoglycosides, specifically inhaled colistin or tobramycin, decreases psuedomonal colonization[50,51]. Additionally, use of aerosolized colistin in patients with cystic fibrosis leads promotes an increase in psuedomonal sensitivity from multi-drug resistant *Pseudomonas*[52]. Thus inhaled colistin, in addition to cefepime, is now routinely used in patients with cystic fibrosis whose pulmonary isolates demonstrate drug resistant *Psuedomonas*. This has directly led to an increase in survival from lung transplantation.

Overall, there is a generalized lack of randomized trials regarding appropriate perioperative antimicrobial therapy for lung transplantation. However, due to many retrospective studies that have evaluated post-transplantation infections and the specific pathogens involved, a generalized guideline for antimicrobial use in lung transplantation can be established. Given the prevalence of gram-negative bacilli and methicillin resistant *S. aureus* infections we routinely use perioperative cefepime and vancomycin in patients transplanted for non-

suppurative diseases . In those with cystic fibrosis inhaled colistin should be added. Ganciclovir should be used for CMV prophylaxis, while amphotericin B, itraconazole or voriconazole can be used for prevention of *Candida* and *Aspergillosis*. Trimethoprim-sulfamethoxazole is routinely used for prevention of *P. carinii*.

Evidence Based Indications for Empyema

Empyema, or infection of the pleural space, is a sequelae of pneumonia and subsequential parapneumonic effusion that develops into frank pus[53]. Frequently these are managed by drainage with thoracostomy tubes or surgical drainage, in addition to perioperative antibiotics[35]. Gram positive aerobes are the most common organisms, including *S. aureus* and *S. milleri*[54]. Additionally, gram negative aerobes, such as *Escherichia coli*, *Pseudomonas*, *Haemophilus influenzae*, and *Klebsiella*, are common, and occasionally in the presence of anaerobic orgarnisms in empyemas[54,55]. Anaerobes can be the sole isolate from empyemas in roughly 14% of cases, with a greater insidious onset[53]. Most of these organisms are resistant to penicillin, but beta-lactams are appropriate for psuedomonal and *S. milleri* infections. Both penicillin and cephalosporins penetrate the pleural space, while aminoglycosides do not and may not be effective for empyemas[56,57]. For community acquired infections, *Pneumococcus*, *Staphylococcus aureus*, and *Haemophilus influenzae* are the most common organisms, and a cephalosporin as well as a beta-lactamase inhibitor or metronidazole are appropriate due to frequent penicillin resistant aerobes and anaerobes[53,58]. Clindamycin alone will also adequately cover these common organisms[58]. Hospital acquired empyemas are generally due to nosocomial infections or trauma, so antibiotics should cover gram positive and negative aerobes and anaerobes, such as with piperacillin-tazobactam, meropenem, or third-generation cephalosporins[53,56]. There is no current recommended duration of antibiotic therapy as the mainstay for the treatment of the infected pleural space is surgical drainage, but prolonged antibiotic treatment for roughly 3 weeks is appropriate based on clinical experience[53]. For possible appropriate perioperative antibiotic regimens, see table 4.

Conclusion

No official guidelines exist for perioperative antibiotic use in non-cardiac thoracic surgery. Despite the original conflicting data and few randomized trials for prophylaxis in pulmonary resections, there is strong evidence supporting the use of perioperative antibiotic, specifically cefazolin 1-2g IV prior to incision, then every 8 hours for a total of 1 to 3 doses. Regarding esophageal resection, strong data exists supporting the use of cefazolin 1-2g IV prior to incision then every 8 hours for a total of 1 to 3 doses. However, despite lack of trials, we also suggest changing the antibiotic to cefepime 1g IV prior to incision then every 12 hours for 1 to 3 doses in patients that are at risk for high anaerobic burden (due to perforation for example), as cefepime has better anaerobic coverage. If patients have a history of MRSA or a penicillin allergy, vancomycin 1g IV should be substituted for cefazolin preoperatively and every 12 hours for a total of 1 to 3 doses. Lung transplant recipients that are at high risk for gram-negative bacilli (specifically pseudomonal), MRSA, CMV, *Candida, Aspergillosis*, and *P. carinii*, prophylaxis with cefepime, vancomycin, ganciclovir, antifungals, and trimethoprim-sulfamethoxazole is warranted. Antifungal therapy can consist of amphotericin B, itraconazole, or voriconazole. If patients are allergice to sulfa, dapsone and inhaled pentamadine can be substituted. Cystic fibrosis patients require extra prophylaxis with inhaled colistin due to their increased colonization with multidrug resistant *Psuedomonas*. Perioperative antibiotic treatment for empyema should be based on cultures and sensitivities. However, if those are not available, multiple IV and oral (PO) options exist for management of community acquired and hospital acquired pneumonia with subsequential empyema (Table 4).

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Table 1

Surgical Site Infections

	Tissue Involved	Timeframe	Symptoms
Incisional SSI			
Superficial	Skin and subcutaneous tissue	Within 30 days of surgery	One of: -Purulent discharge -Organism cultured from fluid or tissue -Pain, tenderness, swelling, erythema AND opened by surgeon -Diagnosis by surgeon or attending physician
Deep	Deep soft tissue (ex: fascial plane, muscles)	Within 30 days of surgery OR 1 year with implant	One of: -Purulent discharge -Spontaneous dehiscence OR opened by surgeon with fever or pain -Evidence on direct examination or radiology -Diagnosis by surgeon or attending physician
Organ/Space SSI*			
	Any anatomy manipulated during surgery other than incision	Within 30 days of surgery OR 1 year with implant	One of: -Purulent discharge from organ space -Organism cultured from fluid or tissue -Evidence on direct examination or radiology -Diagnosis by surgeon or attending physician

* Note: If an organ/space infection communicates with the skin and drains along the incision, this is considered an deep incisional SSI

Table 2

Pivotal Randomized Control Trials for Perioperative Antibiotic Use

Trial (year)	Surgical Field	Antibiotic Regimen	Antibiotic Group Infection Rate	Control Group Infection Rate	p value
Bernard et al[4] (1964)	Gastrointestinal surgery	Penicillin G/Methcillin/Chloramphenicol vs. placebo (given pre-, intra-, and post-op)	8% (5/66 patients)	27% (21/79 patients)	$p < 0.005$
Brown et al[5] (1969)	Gastrointestinal, head and neck, hernias, skin and soft tissue surgery	Cephaloridine vs. placebo (given pre-op then every 8 hours for 5-10 doses)	6.7% (6/90 patients)	22.8% (21/92 patients)	$p < 0.01$
Allen et al[6] (1972)	Gynecologic procedures	Cephalothin vs. placebo (given pre-, intra-, and post-op for 5 days)	14.1% (12/85 patients)	41.0% (34/83 patients)	$p < 0.001$
Boyd et al[7] (1973)	Hip fractures	Nafcillin vs. placebo (given pre-, intra-, and post-op)	0.8% (1/135 patients)	4.8% (7/145 patients)	$p = 0.041$

Table 3

Surgical Wound Classification

	Definition[31]	Wound Infection Rate[32]
Clean	-No inflammation -No break in sterile technique -Genitourinary or biliary tract can be entered if no infected urine or bile -Gastrointestinal or respiratory tract are not entered *transection of appendix or cystic duct without acute infection is considered clean	2.1%
Clean-Contaminated	-Minor break in sterile technique -Genitourinary or biliary tract entered with infected urine or bile -Gastrointestinal or respiratory tract entered without gross spillage	3.3%
Contaminated	-Major break in sterile technique (ex: cardiac massage) -Acute inflammation without presence of pus -Gastrointestinal tract gross spillage -Traumatic wound, fresh from relatively clean source	6.4%
Dirty	-Pus -Perforated viscus -Traumatic wound, old or dirty source	7.1%

Table 4

Perioperative Antimicrobial Recommendations for Thoracic Surgery

	Common Pathogens	Antibiotic Regimen
Pulmonary Resections	-*Staphylococcus Aureus*, -Coagulase negative staphylococci -*Streptococcus Pneumoniae* -Gram-negative bacilli	-Cefazolin 1 g IV preoperatively, with a total of 1-3 doses every 8 hours. -If penicillin allergic, vancomycin 1 g IV preoperatively, with a total of 1-3 doses every 12 hours
Esophageal Surgeries	-Enteric gram-negative bacilli -Streptococci -Oropharyngeal anaerobes	-Cefazolin 1g IV preoperatively, with a total of 1-3 doses every 8 hours. -If penicillin allergic, vancomycin 1g IV preoperatively, with a total of 1-3 doses every 12 hours -If high anaerobic burden likely, cefepime 1g IV preoperatively, with a total of 1-3 doses every 12 hours
Lung Transplantation	-Psuedomonas -B Cepacia -Gram negative bacilli -Methicillin resistant *Staphylococcus Aureus* -Cytomegalovirus -*Candida* -*Aspergillosis* -*P. Carinii*	-Cefepime 1g IV preoperatively, with a 7-10 day course (based on the empiric experience of Washington University in St. Louis). -For cystic fibrosis patients, sensitivities are sent and for multidrug resistant Psuedomonas, inhaled colistin should be added perioperatively. -Vancomycin 1g IV preoperatively, with a 7-10 day course (based on the empiric experience of Washington University in St. Louis) -For seropositive recipients, valganciclovir 900mg PO daily or ganciclovir 5mg IV five times per week while CMV PCR positive (based on the empiric experience of Washington University in St. Louis) -For seronegative recipients with seropositive donors, valcyte 900mg PO daily for 6 months (based on the empiric experience of Washington University in St. Louis) OR ganciclovir 5mg IV five times per week or 1g PO TID for 6 months -Amphotericin B, itraconazole, or voriconazole for 1 year -Trimethoprim-Sulfamethoxazole prophylaxis 3x per week -For sulfa allergies, dapsone and inhaled pentamadine can be used.
Empyema	-*S. aureus* -*S. milleri* -*Escherichia coli* -*Pseudomonas* -*Haemophilus influenzae*, -*Klebsiella* -Anaerobes	Antibiotics should be based on culture and sensitivity from empyema. If not available, the following regimens are appropriate for 3 weeks. Community Acquired (all are acceptable periop abx) -Cefuroxime 500mg IV TID + metronidazole 500mg PO or 400mg IV TID -Penicillin 1g QID + metronidazole 500mg PO or 400mg IV TID -Meropenem 1g TIC + metronidazole 500mg PO or 400mg IV TID -Augmentin 875/125mg PO TID -Amoxicillin 1g PO TID + metronidazole 400mg PO TID -Clindamycin 300 mg PO QID Hospital Acquired (all are acceptable periop abx) -Piperacillin-tazobactam 4.5g IV QID -Ceftazidime 2g IV TID -Meropenem 1g IV TID ± metronidazole 500mg IV TID or 400mg PO TID.