INTRODUCTION — Prior to the development of modern cardiovascular surgery, most cases of mediastinitis arose from either esophageal perforation or from contiguous spread of odontogenic or retropharyngeal infections. Rarely, primary infections of the mediastinum developed as a result of penetrating trauma or hematogenous spread of infection. However, in modern practice, most cases of mediastinitis are a postoperative complication of cardiovascular or other thoracic surgical procedures.

The medical management of sternal wound infection will be reviewed here. The surgical management of sternal wound complications is discussed in detail separately. (See "Surgical management of sternal wound complications").

PATHOGENESIS — The pathogenesis of postoperative mediastinitis is complex and multifactorial. The most important factor is intraoperative wound contamination. Such contamination probably occurs in virtually all patients during the long time interval that large sternotomy wounds are open during cardiac surgery. It is therefore likely that the degree and type of contamination interact with host factors, such as the adequacy of local blood supply, nutrition, and immunologic status, to result in infection in small numbers of patients even if meticulous care is exercised by the surgical team.

A number of other preoperative and operative factors occasionally play a role in the pathogenesis of postoperative mediastinitis. These include preoperative skin colonization with potentially pathogenic or highly resistant organisms, disruption of the blood supply to the sternum during surgery, tissue trauma due to electrocautery, and early postoperative wound disruption (eg, from coughing).

Microbiology — The majority of patients with postoperative mediastinitis have monomicrobial infections. In two reviews with a total of 350 patients with postoperative mediastinitis, 290 (83 percent) had a single pathogen isolated from their mediastinum or blood [1,2].

Virtually any organism can cause mediastinitis. In a prospective review of 316 patients with mediastinitis occurring less than 30 days after sternotomy, the most common microorganisms isolated were methicillin-susceptible Staphylococcus aureus (MSSA) (45 percent), methicillin-resistant S. aureus (MRSA) (16 percent), gram-negative bacilli (17 percent), coagulase-negative staphylococci (13 percent), and streptococci (5 percent) [2].

Postoperative mediastinitis due to MSSA appears to occur more often in the setting of preoperative nasal MSSA colonization, whereas postoperative mediastinitis due to MRSA appears to occur via nosocomial transmission between patients. This was illustrated in a study of 17 cases of mediastinitis observed among 1432 cardiac surgery patients [3]. Among the nine cases due to MSSA, seven had an identical isolate in preoperative nasal and surgical site cultures (as demonstrated by pulsed field gel electrophoresis [PFGE]). Among the eight cases due to MRSA, none had an identical isolate by PFGE, and the same MRSA clone was implicated in all of these cases.

Rarely, postoperative mediastinitis is due to unusual organisms such as fungi [4,5], Legionella [6], Mycoplasma hominis [7], or Nocardia [8] and even Mycobacterium tuberculosis [9]. (See "Candida infections of the abdomen and thorax", section on 'Mediastinitis'.)

INCIDENCE — The incidence of postoperative mediastinitis ranges from 0.4 to 5 percent, with the incidence in most centers being between 1 and 2 percent [1,10-12]. However, the risk may be considerably higher in certain subsets of patients. As an example, the rates have ranged from 2.5 to 7.5 percent in patients undergoing heart transplantation [13], and may be higher if cardiac assist devices are used [14].

In October 2008, the Centers for Medicare Services (CMS) in the United States implemented a policy that eliminated reimbursement for mediastinitis following coronary artery bypass surgery. An analysis of billing data following 638,739 CABG procedures in over 1200 United States hospitals from 2006 to 2010 showed that this
Policy change was associated with a decline in billing claims for mediastinitis in the post policy implementation period [15]. However, data on rates of mediastinitis reported to the National Patient Safety Network remained unchanged during the two intervals. These findings suggest that CMS payment penalties resulted in significant changes in coding for mediastinitis as a complication of cardiac surgery but had no significant effect in the actual risk of infection.

**Risk factors** — The following risk factors for postoperative sternal wound infection have been described [11,16-36]:

In adults:
- Diabetes or perioperative hyperglycemia
- Obesity
- Peripheral artery disease
- Tobacco use
- Prior cardiac surgery
- Mobilization of the internal mammary arteries
- Prolonged surgical procedure (greater than five hours)
- Return to the operating room within four days postoperatively (eg, control bleeding)
- Prolonged postoperative intensive care

There is no consensus as to which risk factors are most important and whether the individual risk factors listed above are independent predictors of an increased risk of postoperative mediastinitis. It is likely that all or many of the above risk factors for infection may be clinically important in selected patients, especially when two or more are present. The risk factors for sternal wound infection in adults are discussed in further detail separately. (See "Surgical management of sternal wound complications", section on 'Risk factors for sternal wound complications'.)

In children:
- Age <1 year [37]
- Male gender [12]

Pediatric risk factors for mediastinitis following cardiac surgery were described in two case control studies. One compared 43 children with postoperative mediastinitis to 184 uninfected controls [38]. Risk of postoperative mediastinitis was significantly increased in patients with a known or suspected genetic syndrome, American Society of Anesthesiologists (ASA) score >3, and presence of intracardiac pacing wires for >3 days (odds ratio 4.5, 3.4, and 15.8 respectively). In the other study involving 72 cases of SSI and 144 controls, independent risk factors for a SSI included age <1 and postoperative exposure to >2 red blood cell transfusions [37].

Furthermore, other traditional risk factors for surgical site infection may also be important [10,39]. (See "Antimicrobial prophylaxis for prevention of surgical site infection in adults", section on 'Cardiac surgery'.)

**Risk indices** — Several risk indices for sternal wound infections following cardiac surgery have been described [16,17,28,40,41]. A preoperative scoring system based on a 3-point scale evaluated in a cohort of 4987 patients may be the most useful for predicting the risk of postoperative mediastinitis [28]. In this study, points were assigned for diabetes (1 point), a body mass index (BMI) >29 but <35 kg/m2 (1 point) and a BMI of 35 kg/m2 or greater (2 points). Each point in the scoring system approximately doubled the risk for postoperative surgical-site infection. Subsequent validation of this risk index was noted in a separate study of 269 cases of surgical site infections after coronary artery bypass surgery [41].

**CLINICAL FEATURES** — Postoperative mediastinitis may follow a fulminant or subacute clinical course. Virtually all patients have fever, tachycardia, chest pain or sternal instability, signs of sternal wound infection, or purulent discharge from the mediastinal area. In one study, for example, sternal wound drainage and/or cellulitis were present in 29 of 34 patients (85 percent) with postoperative mediastinitis [1]. Other local findings that may be seen include crepitation and edema of the chest wall, and Hamman's sign (a crunching sound that is synchronous with the heart beat and heard by chest auscultation). Although signs of sternal wound infection can precede or follow the
recognition of mediastinitis, fever and systemic symptoms appear first in most patients. (See "Surgical management of sternal wound complications", section on 'Wound assessment'.)

Bacteremia is common in postoperative mediastinitis, occurring in 57 percent of patients with postoperative mediastinitis in one report [25]. In another series, mediastinitis was the underlying cause of bacteremia in 16 of 27 patients with positive blood cultures in the early postoperative period [42]. Bacteremia may precede or follow the recognition of mediastinitis. Because bacteremia may be the first sign of postoperative mediastinitis, the possibility of mediastinitis should be considered carefully during the evaluation of all bacteremic patients following cardiac or thoracic surgery.

**Incubation period** — The majority of patients with postoperative mediastinitis show evidence of infection within 14 days of surgery; however, the onset may be delayed for months. In one report, for example, the incubation period ranged from 3 to 417 days after surgery; however, the median time of onset was seven days and began within two weeks in two-thirds of patients [25]. Similar findings were noted in another series in which the onset of infection occurred more than one month after surgery in only 4 of 34 cases [1].

**Laboratory and radiologic features** — Almost all patients with postoperative mediastinitis have leukocytosis, but this is a nonspecific finding. Mediastinal widening on chest X-ray, which is a radiologic hallmark of non-postoperative mediastinitis, is rarely seen in patients with mediastinitis following cardiac surgery. Other abnormalities that are rarely seen are air fluid levels in the mediastinum or subcutaneous tissue, and mediastinal air on lateral chest radiographs. However, the last finding is of no utility in patients who are evaluated immediately after surgery.

Computed tomography (CT) is better than plain radiography in demonstrating the two hallmark findings of mediastinitis:

- Localized mediastinal fluid
- Pneumomediastinum

These findings have increasing diagnostic significance with increasing time after surgery [43].

**DIAGNOSIS** — The diagnosis of postoperative mediastinitis is generally easy in patients who develop their infection within several weeks of surgery. Such patients usually manifest the characteristic clinical pattern of fever, leukocytosis, and sternal instability and/or sternal wound drainage, which may contain bubbles. The diagnosis is virtually assured when these findings occur in the presence of bacteremia or systemic symptoms such as fever, chills, and/or signs of sepsis. Typically, such patients are taken immediately to surgery, where the diagnosis can be established definitively by the finding of pus in the mediastinum.

The diagnosis may be more difficult to establish in patients with fever and leukocytosis but no signs of sternal wound infection or drainage. In the majority of such patients, sternal wound infection becomes evident within a few days.

Another potential difficulty is distinguishing between superficial sternal wound infection and sternal wound infection associated with mediastinitis. As a general rule, patients with mediastinitis have signs of systemic infection such as fever, chills, and, as noted above, bacteremia in more than one-half of cases [25].

CT scan and/or subxiphoid aspiration may be useful in patients with systemic symptoms or bacteremia in the absence of sternal wound suppuration and in those with subacute symptoms. The later imaging is performed after surgery, the more likely the findings are to be diagnostically useful. In one study, for example, CT had a sensitivity of 100 percent but a specificity of only 33 percent for postoperative mediastinitis if performed before the postoperative day 14; however, both the specificity and sensitivity were 100 percent when CT scan was performed later [43].

One group reported on experience using sternal puncture to diagnose postoperative mediastinitis in patients with prior median sternotomies [44]. A 21 gauge needle was placed through the margins of the prior sternotomy site and an aspirate was performed at an approximate depth of one centimeter. If the initial aspirate did not obtain fluid, aspirates were repeated at two other portions of the sternal wound. This approach yielded the same organism as was subsequently found during a later debridement in all 23 mediastinitis patients; cultures and Gram stain of
aspirates were negative in 24 of 26 patients without mediastinitis. Although this report suggests that sternal puncture is safe and reliable, the sensitivity, specificity, and safety of this technique require validation by others.

Another study examined the utility of blood cultures in diagnosing postoperative mediastinitis in a large number of patients undergoing open heart surgery via a median sternotomy [45]. In this cohort of 5500 patients, the detection of S. aureus bacteremia had a likelihood ratio (LR) of 25 for the presence of mediastinitis (95 percent CI, 14.7-44.4). Forty-six of 60 patients (77 percent) who had bacteremia due to S. aureus within 90 days of cardiac surgery developed mediastinitis due to the same organism. Curiously, bacteremia due to other organisms did not have the same prognostic significance: only 15 of 126 patients (12 percent) with non-S. aureus bacteremia developed mediastinitis (LR 1.0; 95 percent CI, 0.6-1.7). Patients with negative blood cultures were significantly less likely to have mediastinitis (LR 0.45; 95 percent CI, 0.35-0.58).

Cultures of epicardial pacing wires may be of some utility in patients who present with early-onset postoperative mediastinitis. In one report, such cultures had a sensitivity of 75 percent and a specificity of 83 percent [46]. Although the positive predictive value of a single culture was only 12 percent, the negative predictive value of an individual culture was 99 percent. When S. aureus was isolated from such cultures, the specificity, sensitivity, and positive predictive value were even higher. In my experience, however, these cultures are rarely practical because pacing wires have often been removed by the time mediastinitis manifests or because the diagnosis is obvious from the typical clinical findings.

**TREATMENT** — Treatment of mediastinitis requires a combination of surgical debridement and antimicrobial therapy.

**Surgical management** — Surgical debridement is the mainstay of therapy for postoperative mediastinitis followed by an immediate closure, or an interval of open wound care followed by delayed primary or flap closure [5,10]. The surgical management of sternal wound complications is discussed separately. (See "Surgical management of sternal wound complications").

For patients who have an open sternal wound following debridement for post-sternotomy mediastinitis, negative pressure wound therapy, or vacuum-assisted closure (VAC), is commonly used prior to subsequent delayed pectoral flap or omental flap repair. In a systematic review of studies that evaluated the outcome of negative pressure wound therapy compared to other wound management strategies for post-sternotomy mediastinitis, most studies observed that negative pressure wound therapy was associated with clinical benefits, such as decreased hospital stay, decreased rates of reinfection, and in a few studies, decreased early mortality [47]. The comparable efficacy of this modality versus conventional treatment (debridement followed by delayed closure with open dressings or immediate closure with closed irrigation) was also evaluated in a separate retrospective study of 90 patients who developed mediastinitis after coronary artery bypass surgery [48]. Negative pressure wound therapy was associated with a lower ninety day mortality (8.5 versus 23.2 percent with conventional treatment) and higher overall one-year survival (91.5 versus 76.7 percent). These results should be interpreted with caution, however, as all these studies are observational (and predominantly retrospective), and there was substantial variability in the actual wound management strategies used for comparison.

The management of the open sternal wound, including the use of negative pressure wound therapy or open dressings, is discussed separately. (See "Surgical management of sternal wound complications", section on 'Management of the open sternum'.)

**Antimicrobial therapy** — Systemic antimicrobial therapy should be instituted as soon the diagnosis of mediastinitis is established or suspected and after blood cultures have been obtained. Initial empiric therapy should consist of broad coverage against gram-positive cocci and gram-negative bacilli. In hospitals such as ours in which there is a substantial incidence of methicillin-resistant staphylococci, we typically use a regimen consisting of intravenous vancomycin plus a third generation cephalosporin (eg, ceftazidime or cefotaxime), a quinolone (such as ciprofloxacin), or an aminoglycoside. The regimen should be adjusted as soon as the results of cultures of blood and mediastinal or deep sternal wound drainage are available.

In general, most favor 2 to 3 weeks of antibiotic therapy following sternal resection and a pectoral flap. If sternal debridement has been performed without resection, or if there is residual rib or sternal bone following surgery that
may be a site of residual infection, 4 to 6 weeks of antimicrobial therapy may be required (see "Overview of osteomyelitis in adults").

PREVENTION — The issue of antibiotic prophylaxis to prevent surgical site infections such as postoperative mediastinitis is discussed in detail separately. (See "Antimicrobial prophylaxis for prevention of surgical site infection in adults", section on 'Cardiac surgery' and "Adjunctive measures for prevention of surgical site infection in adults", section on 'S. aureus decolonization'.)

Summarized briefly:

● Routine antimicrobial prophylaxis should be administered within 60 minutes before the initial incision. There are conflicting recommendations for repeat dosing during and shortly after the completion of surgery.

● The usual drugs of choice are intravenous cefazolin (1 g if less than 80 kg and 2 g if more than 80 kg) or cefuroxime (1.5 g). Intravenous vancomycin (1 g [10 to 15 mg/kg]) is preferred if the patient is previously colonized with MRSA or is allergic to penicillins or cephalosporins, or if surgery is performed in a hospital in which MRSA and/or coagulase-negative staphylococci are a common cause of postoperative infection.

The antimicrobial regimen may need to be expanded in patients who have cardiac conditions associated with the highest risk of infective endocarditis. (See "Antimicrobial prophylaxis for bacterial endocarditis").

● Nasopharyngeal and oropharyngeal decontamination with chlorhexidine gluconate nasal ointment may reduce deep surgical site infections as well as lower respiratory tract infections in patients undergoing elective cardiac surgery [49].

The use of gentamicin-collagen sponges does not appear to reduce the 90-day sternal wound infection rate among patients with diabetes and/or high body mass index [50].

Technical factors that are important for preventing sternal wound infection include appropriate choice of sternal wiring (or suture) technique with proper alignment of the sternal edges and meticulous hemostasis that avoids the excessive use of electrocautery. These issues are discussed further separately. (See "Surgical management of sternal wound complications", section on 'Sternal closure'.)

PROGNOSIS — The mortality rate in postoperative mediastinitis is between 12 and 50 percent in most contemporary series [1,2,10,12,18,51]. In one study including 83 patients with mediastinitis, the mortality during the first 90 days after surgery was 12 percent (compared with 6 percent for 6376 patients without mediastinitis) [18]. In addition, the interval mortality between one and two years after surgery remained higher in the patients with mediastinitis (8 versus 2 percent). Another study suggested that the risk of death following mediastinitis remains higher than in uninfected controls for up to 10 years (49 versus 71 percent) [12]. The majority of deaths in both groups was attributed to cardiac causes, but the proportion of cardiac deaths was higher in patients who had mediastinitis [12].

A prospective study of 316 consecutive cases of postoperative mediastinitis identified patient risk factors for intensive care unit mortality [2]. Independent risk factors present on admission were age greater than 70 years, operation other than coronary artery bypass grafting alone, severity of the underlying medical condition (McCabe class 2/3), APACHE II score, and organ failure. After introducing day three variables into the logistic regression model, the additional independent risk factors for death were mechanical ventilation still required on day three and persistently positive blood cultures.

Another study of 183 patients with postoperative mediastinitis found that death occurred in 51 patients (33 percent); median time to death in those who died was 37 days [52]. Independent predictors of death included:

● Delay >3 days in sternal closure after debridement (Hazard Ratio [HR] 6.3)
● Age >65 (HR 2.3)
● Stay in ICU before sternal debridement (HR 5.6)
● Serum creatinine >2 mg/dL before debridement (HR 2.5)
● Infection due to MRSA (HR 2.1)
● Treatment with antibiotics with in vitro activity against the infecting pathogen within 7 days of debridement was associated with decreased mortality risk (HR 0.4)
Mortality is higher among patients with MRSA than MSSA infection [53-55]. This was illustrated in a series of 41 patients with mediastinitis; 15 with MRSA and 26 with MSSA [53]. MRSA mortality rates were higher than MSSA mortality rates at one month (40 versus 15 percent), one year (48 versus 21 percent) and three years (74 versus 21 percent). However, these results should be interpreted with caution since the underlying characteristics of patients with MRSA infections are often substantially different from those of typical patients who acquire infections due to MSSA.

Postoperative mediastinitis is also associated with substantial morbidity. The length of stay for affected patients is increased by 38 to 51 days and the total cost of care by two- to threefold compared with control patients [11].

**SUMMARY AND RECOMMENDATIONS**

- Most contemporary cases of mediastinitis occur as a postoperative complication of thoracic surgical procedures. The majority of infections are caused by a single organism. Although a wide array of bacterial, mycobacterial, and fungal organisms can cause mediastinitis, Staphylococcus aureus is the most commonly isolated pathogen. (See 'Introduction' above and 'Microbiology' above.)

- In adults, risk factors for the development of postoperative mediastinitis include diabetes mellitus, obesity, peripheral arterial disease, tobacco use, a history of prior cardiac surgery, and surgical complications. (See 'Risk factors' above.)

- The vast majority of patients with postoperative mediastinitis present with fever or other signs of sepsis, chest pain or sternal instability, signs of sternal wound infection, or purulent discharge. Bacteremia is common. The infection typically manifests within two weeks following the surgery, although the onset of symptoms can occasionally occur months later. Hallmark findings on computed tomography are localized mediastinal fluid and a pneumomediastinum. (See 'Clinical features' above.)

- The diagnosis is made clinically in a patient presenting with signs and symptoms consistent with postoperative mediastinitis. Computed tomography is more useful in supporting the diagnosis when performed later than two weeks postoperatively. Finding pus in the mediastinum during subsequent surgical debridement can confirm the clinical diagnosis. (See 'Diagnosis' above.)

- The treatment of mediastinitis involves a combination of antimicrobial therapy and surgical debridement with either immediate or delayed closure. An empiric antimicrobial regimen should include broad coverage against both gram-positive cocci (including methicillin-resistant S. aureus, if institutionally prevalent) and gram-negative bacilli and can later be adjusted based on culture and susceptibility data. The duration of therapy generally ranges from two to six weeks and depends on the extent of surgical debridement performed. (See 'Treatment' above.)

- Strategies to prevent postoperative mediastinitis include perioperative antibiotics, naso- and oropharyngeal chlorhexidine decontamination, and surgical techniques that ensure alignment of sternal edges and meticulous hemostasis. Mediastinitis is associated with an excess postoperative mortality that can persist for years following the procedure. (See 'Prevention' above and 'Prognosis' above.)

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**REFERENCES**


