Department of Cardiothoracic Surgery
Helsinki University Central Hospital

and

Division of Infectious Diseases, Department of Medicine
Helsinki University Central Hospital

and

Department of Surgery, Jorvi Hospital
Helsinki University Central Hospital
University of Helsinki
Finland

MEDIASTINITIS AFTER CARDIAC SURGERY

Anne Eklund

Academic Dissertation

To be publicly discussed, with the permission of the Medical Faculty of the University of Helsinki, in the Auditorium of Jorvi Hospital, Helsinki University Central Hospital, Turuntie 150, Espoo, on May 12th, 2006, at 12 noon.

Supervised by Docent Matti Valtonen
Department of Medicine, University of Helsinki
Helsinki, Finland

Docent Kalervo Werkkala
Department of Cardiothoracic Surgery, University of Helsinki
Helsinki, Finland

Reviewed by Professor Jukka Nikoskelainen
Department of Medicine, University of Turku
Turku, Finland

Docent Arto Rantala
Department of Surgery, University of Turku
Turku, Finland

Opponent Professor Matti Tarkka
Department of Surgery, University of Tampere
Tampere, Finland

Publisher Hospital District of Helsinki and Uusimaa
HUCH, Jorvi Hospital
Turuntie 150 • FI–02740 Espoo • Finland
tel +358 9 8611 • telefax +358 9 861 5900
http://www.hus.fi/jorvi • firstname.surname@hus.fi

ISSN 1459-1383
ISBN 952-99495-6-1 (paperback)
ISBN 952-10-3084-4 (PDF)

http://www.hus.fi/jorvi/julkaisut • http://ethesis.helsinki.fi

Helsinki University Printing House
Helsinki 2006

To Tatu, Jenni and Jari-Pekka

CONTENTS

ABSTRACT

Background

Mediastinitis as a complication after cardiac surgery is rare but disastrous, increasing hospital stay, hospital costs, morbidity, and mortality. It occurs in 1–3 % of patients after median sternotomy. Studies on risk factors exist, but the results are conflicting. The aims of this study were to determine the risk factors in the Finnish population and to investigate new ways of preventing mediastinitis.

Patients and methods

The subject pool comprised patients undergoing sternotomy or thoracotomy during cardiovascular surgery with cardiopulmonary bypass between 1990 and 1999. Most surgeries entailed coronary artery bypass grafting (CABG). First, we assessed operating room air contamination monitoring by comparing the bacteriological technique with continuous particle counting in low level contamination achieved by ultraclean garment options in 66 CABG operations. Second, we examined surgical glove perforations and changes in bacterial flora of surgeons' fingertips in 116 open-heart procedures. Third, the effect of a gentamicin-collagen sponge on preventing surgical site infections (SSIs) was studied in a randomized controlled study with 557 participants. Finally, incidence, outcome, and risk factors of mediastinitis were evaluated in patients operated on during 1990–1999. Data were recorded prospectively in an operating room log, hospital discharge register, and the hospital's cardiothoracic unit register. Cases of mediastinitis were identified from the hospital infection register, and patients' charts were reviewed.

Main results

With the alternative garment and textile system (cotton group and clean air suit group), the air counts fell from 25 colony-forming units (CFU)/m^3 to 7 CFU/m^3. Contamination of the sternal wound was reduced by 46 % and that of the leg wound by >90 %. When an air particle level ≤50 particles/m^3 is reached, the bacterial air contamination is of the magnitude of that of orthopedic hip operations. The staff must during the entire operation adjust their activity to air asepsis.

Glove perforations occurred in the majority of heart operations. In only 17 % of operations were both gloves unpunctured. Frequency of glove perforations and bacteria counts on hands were found to increase with duration of surgery.

In the randomized study with local gentamicin-collagen sponge prophylaxis, SSI occurred in 11 of 272 patients (4.0 %) in the study group and in 16 of 270 patients (5.9 %) in the control group. This difference was not statistically significant. There were three cases of mediastinitis (1.1 %) in the study group and five (1.9 %) in the control group.

We identified 120/10 713 cases of postoperative mediastinitis (1.1 %) over the 10-year period. During the study period, the patient population grew significantly older, the proportion of women and patients with an American Society of Anesthesiologists (ASA) score >3 increased significantly. In multivariate logistic regression analysis, the only significant predictor for mediastinitis was obesity.

Conclusions

Continuous particle monitoring is a good intraoperative method to control air con-

tamination related to theater staff behavior during operations. When a glove puncture is detected, both gloves should be changed. Before donning a new pair of gloves, renewed disinfection of hands will help to keep bacterial counts lower, particularly towards the end of a long operation. A gentamicin-collagen sponge may have beneficial effects on prevention of SSI, but further research is needed. The prevalence of mediastinitis is not diminishing. Changes in the populations at risk, with, for example, the increasing proportion of overweight patients, reinforce the importance of surveillance and pose a challenge in focusing preventive measures.

LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications, referred to in the text by Roman numerals I to IV:

I. Verkkala K, Eklund A, Ojajärvi J, Tiittanen L, Hoborn J, Mäkelä P. The conventionally ventilated operating theatre and air contamination control during cardiac surgery – bacteriological and particulate matter control garment options for low level contamination. Eur J Cardiothorac Surg 1998; 14: 206–10.

II. Eklund AM, Ojajärvi J, Laitinen K, Valtonen M, Werkkala KA. Glove punctures and postoperative skin flora of hands in cardiac surgery. Ann Thorac Surg 2002; 74: 149–53.

III. Eklund AM, Valtonen M, Werkkala KA. Prophylaxis of sternal wound infections with gentamicin-collagen implant: randomized controlled study in cardiac surgery. J Hosp Infect 2005; 59: 108–12.

IV. Eklund AM, Lyytikäinen O, Klemets P, Huotari K, Anttila V-J, Werkkala KA, Valtonen M. Mediastinitis following over 10,000 cardiac surgical procedures. (Submitted).

These articles have been reproduced with the kind permission of their copyright holders. Some unpublished material has also been presented.

ABBREVIATIONS

ASA	American Society of Anesthesiologists
BITA	bilateral internal thoracic artery
BMI	body mass index
CABG	coronary artery bypass grafting
CDC	Centers for Disease Control and Prevention
CFU	colony-forming unit
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
EF	left ventricular ejection fraction
ICU	intensive care unit
ITA	internal thoracic artery
IV	intravenous
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant *Staphylococcus aureus*
MRSE	methicillin-resistant *Staphylococcus epidermidis*
NNIS	National Nosocomial Infections Surveillance
NYHA	New York Heart Association
OR	odds ratio
SENIC	Study on the Efficacy of Nosocomial Infection Control
SSI	surgical site infection

1 INTRODUCTION

Modern surgical practices have reduced the rate of wound infections markedly. However, no reduction has occurred in infection rates during the late 20th century, despite further developments in surgical techniques and antimicrobial prophylaxis. Surgical patients tend to be sicker and to undergo more complex operations. Surgical site infections (SSIs) have enormous clinical and financial implications. Higher infection rates translate into higher morbidity and mortality as well as higher costs to the hospital, patient, and society as a whole.

Mediastinitis after cardiac surgery is a very serious complication, which raises hospital costs, suffering, and mortality. Fortunately, mediastinitis is rare, occurring in only 1–3 % of patients (Loop et al. 1990; Higgins et al. 1992; Farinas et al. 1995; Milano et al. 1995; Valla et al. 1996; Ståhle et al. 1997; DiPiro et al. 1998) (Tables 1 and 2).

Although cardiologists are able to treat more patients with coronary artery disease, the affected population is becoming increasingly older. Moreover, coronary artery bypass grafting (CABG) surgery remains necessary and may even be on the rise. Furthermore, patients undergoing cardiac surgery are sicker than they were a few years ago, which has resulted in an increase in the number of postoperative complications (Quaini et al. 1995). Thus, every effort to understand the etiology and reduce the incidence of SSIs is justified.

Prevention of SSIs requires antisepsis, asepsis, perioperative antimicrobial prophylaxis, good surgical technique, preoperative identification of patients at risk, and additional individualized preventive measures. Various risk factors for mediastinitis have been suggested in numerous large studies. These include obesity, diabetes mellitus, smoking, use of bilateral internal thoracic artery as graft material, prolonged mechanical ventilation, and reoperation of the chest. However, study results are often conflicting. Research designs vary, with some being retrospective and others prospective, study populations are often small, wound infection definitions are different, and superficial wound infections are sometimes included. These inconsistencies make it difficult to compare findings. Risk factors for SSIs after cardiac surgery have been studied in the Finnish population (Vuorisalo et al. 1998), but they may not be the same for mediastinitis (Olsen et al. 2002), which has not been investigated in this context in Finland. Performing this risk factor study on our Finnish population thus was warranted.

As an SSI is one of the most feared complications after cardiac surgery, keeping the operating room contamination at the lowest possible level is essential. Two separate studies of cardiac operations have shown that improving the surgical environment, refining surgical and operating room protocols, and increasing the awareness of the dangers of infection among personnel can reduce the infection rate (Ferrazzi et al. 1986; Rao et al. 2004). The operating room environment has been widely investigated concerning scrub suits, surgical attire and drapes, patient skin preparation, preoperative hand antisepsis, glove perforations, and ventilation, but little is known about the operating room air contamination control or the impact of glove perforations on the bacterial flora on a surgeon's hands.

The beneficial effect of antimicrobial prophylaxis on wound infections was already demonstrated in the 1960s (Burke 1961; Polk and Lopez-Mayor 1969; Stone et al. 1976). Today, it is clear that antimicrobial prophylaxis is essential in cardiac surgery, reducing the risk of SSIs by a factor of five (Kreter and

Table 1. Risk factors for mediastinitis in selected large studies.

First Author	Year	N	Mediastinitis rate %	Age	Gender	Obesity	Smoking	Diabetes	COPD	EF	Preop. hospital stay	Emergency	Redo	Operation/CPB time	Bilateral ITA	Hyperglycemia	Blood transfusions	Prolonged ventila-tion	Reoperation	Stay in ICU
Ottino	1987	2579	1.9	–	–			–			+	–	+	–			+	–	+	–
Hammermeister	1990	10634	1.6	–	–			+		–		–	–		–	–		–		
Loop	1990	6504	1.1	–	–	+	–	+		–			–	+	–		+	–	–	
Wouters	1994	1368	1.7				+	+							–			+	+	
Blanchard	1995	4137	0.1									+							+	
Farinas	1995	3645	0.9				+					+		+				+	+	+
Milano	1995	6459	1.3			+		–					+	+	–					
The Parisian	1996	1830	2.3	–	–	+		–			–	–	–	–	+			–	+	
Valla	1996	9814	1.0		+	+		+				+	+	+				+		
Antunes	1997	2512	2.3	–	–	+	–	+		–		–		–	+			–	–	
Muñoz	1997	3711	2.2	–	–			–	–		–	–	–	–				–	+	–
Ståhle	1997	13285	1.5	–	–			+							+				–	
Bitkover	1998	1935	2.1			+		–	+		–			–				–	–	
Abboud	2004	9136	0.5		–	+	+	–	–	–	–	–	–	–	–	+	–	–	–	–
Upton	2005	5176	1.2					+		+	+									

COPD = chronic obstructive pulmonary disease; EF = left ventricular ejection fraction; CPB = cardiopulmonary bypass; ITA = internal thoracic artery; ICU = intensive care unit

Woods 1992). Locally administered antibiotics have been used successfully to treat wound infections, but there is little experience on their use as prophylactic agents. For instance, local antimicrobial prophylaxis with gentamicin was not investigated in cardiac surgery before 2005.

Table 2. Incidence and mortality of mediastinitis in selected large series.

First Author	Year	Number of patients	Rate of Mediastinitis (%)	Mortality (%) 30-d	Mortality (%) 90-d
Loop	1990	6504	1.1	14	
Wouters	1994	1368	1.7	30	
Farinas	1995	3645	0.9	35	
Milano	1995	6459	1.3		12
Valla	1996	9814	1.0	39	
Muñoz	1997	3711	2.2	18	
Ståhle	1997	13285	1.5	4	
Bitkover	1998	1935	2.1	12	
Gårdlund	2002	9557	1.3		19
Abboud	2004	9136	0.5	23	
Fowler	2005	331429	0.9	17	

2 REVIEW OF THE LITERATURE

2.1 Surgical site infections

Surgical site infections are the most common nosocomial infection among surgical patients (Mangram et al. 1999). According to Centers for Disease Control and Prevention (CDC) definitions, they can be classified into three categories: superficial incisional SSIs (involving only skin and subcutaneous tissues), deep incisional SSIs (involving deep soft tissue), and organ/space SSIs (involving any part of the body other than the incision itself that is opened or manipulated during the operative procedure). The categories of SSI in open-heart surgery via sternotomy are presented in Figure 1. Furthermore, according to the CDC, mediastinitis must meet at least one of the following criteria: 1) positive bacterial culture from the mediastinal space, 2) evidence of mediastinitis during a surgery or histology, and 3) one of the following: fever (>38°C), chest pain, or sternal instability, and at least one of the following: purulent discharge from the mediastinal area, organisms cultured from blood or from the discharge of the mediastinal area, or mediastinal widening in radiology (Horan et al. 1992) (Table 3). In the literature, various terms for chest SSIs have been used, including sternal infection, deep sternal infection, and major infection. The inconsistent definitions make it difficult to compare results.

Several studies exist on incidence of SSI after cardiac surgery. Most have included mediastinitis or all types of SSI, with infection being poorly defined. In large retrospective studies dated before 2000, comprising over 33 000 patients, the mediastinitis rate varied between 1.0 % and 2.3 % (Ottino et al. 1987; Hammermeister et al. 1990; Loop et al. 1990; Milano et al. 1995; Valla et al. 1996) (Table 1). Three prospective works published after 2000 by Gårdlund et al. (2002), Lu et al. (2003), and Lepelletier et al. (2005) showed similar rates (0.7–1.4 %). In three case-control studies, the rates were 2.2 %, 2.1 %, and 0.5 % (Muñoz et al. 1997; Bitkover and Gårdlund 1998; Abboud et al. 2004).

Microbial contamination of the wound is necessary for infection to develop. The risk of SSI can be estimated by the following relationship (Cruse 1992):

$$\frac{\text{DOSE OF BACTERIAL CONTAMINATION} \times \text{VIRULENCE}}{\text{RESISTANCE OF THE HOST PATIENT}} = \text{RISK OF SSI}$$

Figure 1. Cross-section of thoracic wall depicting CDC classifications of surgical site infections (SSIs).

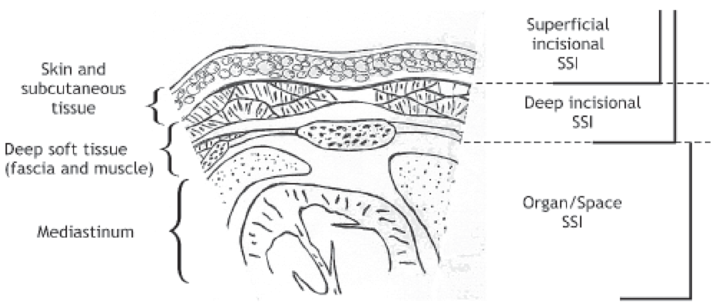


Table 3. Criteria for defining a surgical site infection (SSI) (Horan et al. 1992).

Superficial incisional SSI

Infection occurs within 30 days after the operation *and* infection involves only skin or subcutaneous tissue of the incision *and* at least *one* of the following:

1. Purulent drainage, with or without laboratory confirmation, from the superficial incision.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat *and* superficial incision is deliberately opened by surgeon, *unless* incision is culture-negative.
4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.

Deep incisional SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation *and* infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision *and* at least *one* of the following:

1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38 °C), localized pain, or tenderness, unless site is culture-negative.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

Organ/Space SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation *and* infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation *and* at least *one* of the following:

1. Purulent drainage from a drain that is placed through a stab wound into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

The pathogens involved in SSIs after cardiac surgery are mainly *Staphylococcus epidermidis* and *Staphylococcus aureus* (The Parisian Mediastinitis Study Group 1996; Tegnell et al. 2000; Sharma et al. 2004). Coagulase-negative staphylococci have recently become the most important pathogen, especially in deep incisional or organ/space SSIs (Tegnell et al. 2000). The finding that methicillin-resistant *S. aureus* strains (MRSA) have become more common is worrisome. In a recent report from New Zealand, 13 % of the *S. aureus* isolated in poststernotomy mediastinitis was methicillin-resistant (Upton et al. 2005). In another report from Australia (comprising 4474 patients), 32 % of organisms isolated from sternal wounds were MRSA strains (Harrington et al. 2004). This presents new challenges for prevention and treatment of these infections.

The clinical picture of mediastinitis varies from fulminant septic infection to vague clinical symptoms. El Oakley and Wright (1996) have presented a classification of mediastinitis as follows: type I mediastinitis presents within 2 weeks after operation in the absence of risk factors (e.g. diabetes, obesity, and use of immunosuppressive agents); type II mediastinitis presents at 2–6 weeks after operation in the absence of risk factors; type III mediastinitis comprises types I and II in the presence of risk factors; type IV mediastinitis includes types I–III after a failed therapeutic surgical intervention; and type V presents for the first time more than 6 weeks after operation and is characterized by chronic smoldering osteomyelitis with draining sinus tracts, leading to necrotic areas of bone or costal cartilages.

Treatment of mediastinitis varies from simple prolonged antibiotic therapy to complete sternectomy combined with a major plastic procedure. Antibiotic therapy alone is occasionally sufficient, but surgical intervention is usually required. The most common technique entails wound debridement, primary sternal closure, and closed mediastinal catheter irrigation. Types IV and V may be treated by wound debridement, sternectomy, excision of exposed costal cartilage if necessary, and muscle or omental flap repair (El Oakley and Wright, 1996).

Bitkover and colleagues (2000) studied the sources of coagulase-negative staphylococci in sternal wounds during operations done in an ultraclean environment, and found that bacteria in the sternal wound originated from patients' skin and from the surgical team. For the majority of SSIs, the source of pathogens is patients themselves (Altemeier and Culbertson 1968; Haas et al. 2005). In patients who have a prosthesis implanted during surgery, the pathogens can derive from a distant focus of infection (Slaughter et al. 1973; Edwards 1976; Valentine et al. 1986; Stuesse et al. 1995). The pathogens may also come from exogenous sources, including surgical team members, operating room air, tools, instruments, and materials brought to the sterile field during surgery (Whyte et al. 1982; Verkkala et al. 1990; Tammelin et al. 2001a).

2.2 Risk factors for mediastinitis

In the early 1980s, the Study on the Efficacy of Nosocomial Infection Control (SENIC) identified three risk factors in addition to wound class: location of operation, duration of operation, and patient clinical status (Haley et al. 1985). The National Nosocomial Infections Surveillance (NNIS) study reduced these four risk factors to three: wound classification, length of operation >T hours (where T is the approximate 75^{th} percentile of the duration of the specific operation), and American Society of Anesthesiologists (ASA) score >2 (Culver et al. 1991; Mangram et al. 1999). Both risk assessments integrate three determinants of infection: bacteria (wound class), local environment (duration), and systemic host defense (patient health status). However, the SENIC and NNIS assessments do not integrate other known risk variables, such as smoking, tissue oxygen tension, glucose control, shock, and maintenance of normothermia. In cardiac surgery, these risk indices yield little information since the wounds are always clean (wound class I) and the patient's ASA score is almost always 3 or worse. Consequently, the most important issue is the duration of the operation. The Northern New England Cardiovascular Disease Study Group has calculated a score not only for risk for mortality and cerebrovascular accident but also for mediastinitis in isolated CABG surgery. In this mediastinitis score, the patient receives 2 points when left ventricular ejection fraction (EF) <40 %, 1.5 points for urgent surgery, 3.5 points for emergency surgery, 1.5 points for diabetes, 2.5 points for dialysis or creatinine ≥2 mg/dl, 3.5 points for chronic obstructive pulmonary disease (COPD), 2.5 points for obesity (body mass index (BMI) 31–36 kg/m^2) and 3.5 points for severe obesity (BMI ≥37 kg/m^2). Perioperative risk for mediastinitis is 0 % with score 0, 1.1 % with score 4, 3 % with score 7, and ≥6.5 % with score 10 (Eagle et al. 1999).

Knowledge of risk factors may enable targeted preventive measures. Reviewing previous risk factor studies (Table 1), there is no doubt that obesity predisposes not only to sternal superficial incisional SSI but also to mediastinitis. It has been a significant risk factor in many well-conducted large studies (Loop et al. 1990; Milano et al. 1995; The Parisian Mediastinitis Study Group, 1996; Valla et al. 1996; Antunes et al. 1997; Bitkover and Gårdlund 1998; Abboud et al. 2004; Harrington et al. 2004; Fowler et al. 2005). Nevertheless, in some studies obesity was not investigated (Ottino et al. 1987; Hammermeister et al. 1990; Muñoz et al. 1997; Ståhle et al. 1997), and in one study (Wouters et al. 1994) it was not a significant risk factor; however the study population was small, comprising only 23 cases of mediastinitis. The evidence is therefore strong for obesity's influence on mediastinitis. Overweight is associated with type II diabetes mellitus. As a known possible risk factor for infections, diabetes has been included in nearly every risk factor study. Diabetes has been verified to be a predictor of mediastinitis in many reports (Loop et al. 1990; Wouters et al. 1994; Valla et al. 1996; Antunes et al. 1997; Ståhle et al. 1997; Trick et al. 2000; Lu et al. 2003; Harrington et al. 2004; Fowler et al. 2005). However, in several others, it has not been a significant risk factor (Grossi et al. 1985; Farinas et al. 1995; Milano et al. 1995; The Parisian Mediastinitis Study Group, 1996; Muñoz et al. 1997; Bitkover and Gårdlund 1998; Abboud et al. 2004). Recently, more information has been uncovered about diabetes. Furnary et al. (1999) showed that perioperative continuous intravenous insulin infusion lowers the incidence of mediastinitis in diabetic patients. In Trick and colleagues' study in 2000, diabetes mellitus with a perioperative blood glucose level of 200 mg/dl or more was demonstrated to be an independent risk factor for mediastinitis. Furthermore, in another study, diabetes and postoperative hyperglycemia were independently associated with SSIs (sternal and leg) among cardiothoracic surgery patients, and 6 % of patients had undiagnosed diabetes (Latham et al. 2001).

The internal thoracic artery (ITA) as graft material has proven superior, but use of both thoracic arteries has increased infectious complications. In the large subject pool of Grover et al. (1994) (14 172 patients), bilateral ITA (BITA) use was associated with an increase in mediastinitis. This is consistent with several studies (Loop et al. 1990; Grossi et al. 1991; The Parisian Mediastinitis Study Group 1996; Antunes et al. 1997). In some reports, however, use of BITA was not found to be a risk factor for mediastinitis (Wouters et al. 1994; Abboud et al. 2004). In Lu's study, BITA was a significant risk factor for superficial incisional SSI but not for deep incisional or organ/space SSI (Lu et al. 2003). This risk factor was impossible to evaluate in some studies due to small subject population (Bitkover and Gårdlund 1998), and in other reports it was not investigated (Ottino et al. 1987; Blanchard et al. 1995; Muñoz et al. 1997). Even though BITA was not a predictor of mediastinitis in Loop's study, combined with diabetes, the risk increased fivefold (Loop et al. 1990). In recent reports, however, skeletonization of both ITAs significantly decreased the risk compared with harvesting in a pedicled fashion (De Paulis et al. 2005). In diabetics, no difference was observed in incidence of mediastinitis among patients receiving a single ITA or a double skeletonized ITA (Matsa et al. 2001; Peterson et al. 2003; De Paulis et al. 2005). Although one might speculate that use of BITA would be ill-advised when operating on the elderly, bilateral skeletonized ITA has been reported to carry relatively low morbidity and mortality also in patients over 70 years (Kramer et al. 2000).

While old age has been confirmed to be a risk factor for SSIs in certain types of surgeries, many studies in cardiac surgery show that age does not compromise sternal SSIs (Ottino et al. 1987; Hammermeister et al. 1990; Loop et al. 1990; The Parisian Mediastinitis Study Group 1996; Antunes et al. 1997; Muñoz et al. 1997; Ståhle et al. 1997). Moreover, old age may not be a risk factor for SSI in some other types of operative procedures. Kaye et al. (2005) found that age was a strong predictor of SSI until the age of 65 years, but beyond this age a decreased risk of SSI was observed.

S. aureus causes 25 % of nosocomial infections. From 20 % to 30 % of the population carries this pathogen in the nares (Perl and Golub 1998). Carriers are at higher risk for SSIs (Perl and Golub 1998), also after cardiac surgery (Kluytmans et al. 1995). *S. aureus* can be eradicated effectively from the nares with mupirocin ointment. One study showed a decrease in SSI rate in cardiothoracic surgery when mupirocin was applied preoperatively to nares. However, the patients were compared with previous surgical patients (historical controls), and thus, there might also be other reasons for the reduction in SSI rate (Kluytmans et al. 1996). In a prospective randomized study with 4030 patients, mupirocin did not lower the rate of *S. aureus* SSIs (Perl et al. 2002). Screening of nasal carriers thus far is not recommended.

Additional risk factors can be found in the literature. Smoking delays primary wound healing and may increase the risk of SSI. In a large prospective study, cigarette smoking was an independent risk factor for SSIs following cardiac surgery (Abboud et al. 2004). However, most large studies have not investigated this relationship, perhaps because information about smoking habits is not often reliable. Occasionally, other risk factors, such as previous heart surgery, preoperative hospital stay, emergency operation, prolonged mechanical ventilation, reoperation, blood transfusions, and COPD, are significant in different studies (Table 1). Overall, the results are conflicting and confusing. Many studies are retrospective, the subject populations are small, wound infection definitions vary, and superficial incisional SSIs are included, all of which makes it difficult to compare findings.

2.3 Operating room practices

Several possibilities exist on how to influence the infection risk in the operating room. Informing the surgeons of their respective wound infection rates leads to a reduction in infection risk through better aseptic operative techniques and improved teamwork (Mangram et al. 1999). Although a preoperative antiseptic shower reduces the microbial colony count on the patient's skin, no evidence has emerged that it lowers the infection rate (Ayliffe et al. 1983; Lynch et al. 1992). Shaving the hair from the incision site, especially the night before surgery, increases the infection risk. Instead, hair should be clipped just prior to surgery (Cruse and Foord 1973; Geelhoed et al. 1983; Woodhead et al. 2002) or perhaps not clipped at all (Mishriki et al. 1990; The Parisian Mediastinitis Study Group 1996).

Thin, transparent plastic adhesive incise drapes reduce wound contamination, but microbial counts beneath the drape reach normal levels within three hours. Iodophor-impregnated incise drape eliminates skin colonization for three hours (Johnston et al. 1987), but there is no evidence that it lowers the incidence of SSI.

Some other practices have been shown to reduce infection rates. Dramatic reductions in SSI rates have been achieved through careful avoidance of hypothermia (Kurz et al. 1996; Melling et al. 2001). However, in cardiac surgery, hypothermia is often necessary and cannot be avoided. Excessive temperatures are also deleterious. Evidence suggests that among diabetics a peak core body temperature of >37.9 °C during cardiopulmonary bypass is a significant risk factor for mediastinitis (Groom et al. 2004). Supplemental oxygen administration (FiO_2 >80 %) may decrease infection rates in colorectal surgery (Greif et al. 2000; Belda et al. 2005).

2.4 Air asepsis

The purpose of achieving particle-free air (i.e. "ultraclean air") is logical in heart surgery where operations are long, numerous people are present in the operating theater, and the consequences of infection are often serious (Gnann and Dismukes 1983; Sarr et al. 1984). In 1972, Sir John Charnley published the results for 5800 total hip replacements performed under ultraclean air technology without prophylactic antibiotics. Incidence of deep wound infection fell from 7 % to 0.5 % (Charnley 1972). At the same time, prophylactic antibiotics were introduced, proving to be the single most effective measure in reducing incidence of SSI in 30 years.

Low bacterial contamination of the air has been shown to have an additional effect of preventing infections in orthopedic surgery. This may be achieved by ventilation, special clothing, and high standards for staff hygiene (Lidwell et al. 1982). Particles can originate from people, equipment, and surface shedding. Airflow design within a clean space is used as an aid to remove contamination from these internal sources. The proposed maximum level of air contamination for orthopedic surgery is ≤ 10 colony-forming units (CFU)/m^3 measured 30 cm above the wound (Whyte et al. 1983). A direct correlation between air contamination and wound infection has been shown in hip operations (Lidwell et al. 1982).

To obtain a clean environment in a surgical theater, particular attention must be paid to airflow pattern control and removal of particles and microorganisms from the space. The operating room doors must be kept closed except for the passage of equipment, personnel, and patients, and personnel traffic should be minimized because the air contamination level is directly proportional to the number of people moving in and out of the room (Ayliffe 1991). Operating theaters should be maintained at positive-pressure ventilation with respect to corridors and adjacent areas (Lidwell 1986; Mangram et al. 1999; The American Institute of Architects and The Facilities Guidelines Institute 2001). In a conventionally ventilated operating theater, a minimum of 15 total air changes, three of which are fresh air, should occur per hour (Clark et al. 1985; Nichols 1992; The American Institute of Architects and The Facilities Guidelines Institute 2001). All recirculated and fresh air should be filtered through the appropriate filters, providing at least 90 % efficiency (dust-spot testing) (Babb et al. 1995). Moreover, air should be introduced at the ceiling and exhausted near the floor (Laufman 1986; Lidwell 1986; The American Institute of Architects and The Facilities Guidelines Institute 2001). Ultraviolet (UV) light is not recommended since it has not been shown to prevent SSIs (Collis and Steinhaus 1976; Lidwell et al. 1982; Taylor et al. 1995).

Traditionally, ultraclean air has been achieved with the help of ventilation systems. Laminar airflow is designed to move particle-free air over the aseptic operating field, sweeping away particles in its path. In a laminar airflow system, recirculated air is usually passed through a high-efficiency particulate air (HEPA) filter (Hambraeus 1988; Friberg 1998). Laminar airflow has been suggested as an additional measure to reduce SSI risk in certain operations (e.g. some cardiac surgeries, neurosurgery, implant surgery theaters, and transplant units), and it is used widely in many centers even though its effect on reducing infections is controversial (Lidwell et al. 1987).

Most of the studies examining the efficacy of ultraclean air have done this only in conjunction with orthopedic operations, and some have shown ultraclean air to be effective (Howorth 1985; Gruenberg et al. 2004). A large study of 8000 orthopedic implant operations revealed that ultraclean air and antimicrobial prophylaxis both reduce incidence of SSIs, but the latter was more beneficial (Lidwell et al. 1987). In a recent study, wound contamination in laminar flow and standard operating theaters was compared, and no significant difference was found (Clarke et al. 2005).

For an efficient laminar airflow system, the filter ceiling must be sufficiently large, covering the whole aseptic working area, including instrumentation. Disadvantages are that the system is expensive, and opening doors and movement of personnel disturb the airflow. This system is best utilized in operations that demand the highest cleanliness (e.g. transplant surgery, prosthesis implantation, or surgery on immunosuppressive patients), but its benefit is realized only if the hygiene of personnel is strict, the scrub team wears special exhaust suits, and the doors of the operating theater are kept closed (Knobben et al. 2006).

Another means of lowering the number of airborne bacteria to reach the wound is the use of special scrub suits or gowns. Earlier studies, both in the laboratory and during surgery, have shown that specially designed working clothes, a polypropylene coverall, worn by all present in the theater, keep the level of microbial contamination in theater air during orthopedic surgeries low (Blomgren et al. 1983; Whyte et al. 1983; Bergman et al. 1985). Also in cardiac surgery, the use of a combined system of disposable gowns, drapes, and staff clean air suits reduces bacterial air contamination (Verkkala et al. 1990). However, wearing special scrub suits (tightly woven and cuffs at the wrists and ankles) did not influence the air counts or wound contamination with methicillin-resistant *S. epidermidis* (MRSE). With regard to *S. aureus*, a significantly lower air count was identified, but no effect was observed for wound contamination rates (Tammelin et al. 2001a, 2001b). If a laminar ventilation system was used in combination with body exhaust gowns, the contamination of the operative field could be brought to a very low level (Blomgren et al. 1983).

A healthy individual disperses thousands of bacteria-carrying skin particles per minute during walking. The airborne particles contaminate wounds directly by sedimentation or indirectly by first settling on instruments or other items that are then brought into contact with the wound. Various air sampling methods, e.g. slit samplers, filter samplers, and sedimentation plates, have been used to monitor microbial contamination (Table 4). These techniques are, however, awkward to perform, and the results are only available several days after the operation. Particulate contamination, on the other hand, may be

Table 4. Measurement principles for airborne microorganisms.

Method	Function
Volumetric method	
Impaction	Air with microorganisms is sucked through a slit or hole with such high speed that the microorganisms strike an agar surface and are trapped (and grow on it when incubated)
Centrifugal	Air with microorganisms is sucked axially by a fan blade and then moved radially at such high speed that particles hit the inside wall of the fan chamber and are trapped on agar (and grow when incubated)
Filtering	Air with microorganisms is sucked through a filter and microorganisms are trapped on a membrane filter and then transferred to a nutrient agar surface and incubated
Settle plate method	
Sedimentation	Microorganisms in the air are allowed to settle, over a specified time, on a dish containing nutrient agar medium, which is then incubated

readily and continuously monitored on the spot via computerized electronic equipment (Seal and Clark 1990). A prerequisite for using this technique is, however, the maintenance of very low particle counts. No agreement exists regarding tolerable levels of particles in operating rooms or the most suitable method for air monitoring. Evaluation of air quality can be performed by microbiological sampling or particle counting. The relationship between these two methods has rarely been examined. In a recent study, particle counting and microbiological sampling of air did not correlate, and the authors concluded that replacing microbiological sampling with particle counting for routine evaluation of microbiological contamination in conventionally ventilated operating rooms is not warranted (Landrin et al. 2005). However, the operating rooms were empty, and the results might have been different had there been people shedding infectious particles to the air.

2.5 Perforations in surgical gloves

One possible contamination route in the operating room environment is a perforated glove. The purpose of surgical gloves is to create a barrier between the operating staff and the patient, thereby protecting both from microbial infections. In unused surgical gloves, the puncture rate varies between 1.4 % and 5.5 % (Russell et al. 1966; Paulssen et al. 1988; Albin et al. 1992). Today, the industry standard for holes is an acceptance quality (AQL) of 1.5 % according to the EU directives. During operations high perforation rates (26–40 %) have been described in heart surgery (Berg et al. 1987; Wong et al. 1993; Driever et al. 2001). In other types of surgical procedures, the glove perforation rate varies from 10 % to 50 % (Maffulli et al. 1989; Jensen et al. 1997; Hollaus et al. 1999; Naver and Gottrup 2000; Laine and Aarnio 2001). Double gloving is considered to provide an additional barrier and to further reduce the risk of contamination. This has been confirmed in many studies (Jensen et al. 1997; Caillot et al. 1999; Naver and Gottrup 2000; Laine and Aarnio 2001). The 2002 Cochrane review also concluded that wearing double gloves significantly reduced perforations of the innermost glove (Tanner and Parkinson 2002).

Protecting healthcare workers from infectious diseases such as hepatitis B, hepatitis C, and acquired immunodeficiency syndrome (AIDS) has become more important in recent years. Open-heart procedures carry a high risk of puncture injury and frequent exposure to blood, increasing the risk of the surgical team acquiring viral infections from the patient (Kjaergard et al. 1992). Alternatively, some reports have indicated that surgeons may transmit hepatitis B or C to patients (Esteban et al. 1996; Harpaz et al. 1996).

Most punctures are not noticed by operating staff when donning the gloves (Berg et al. 1987; Naver and Gottrup 2000; Laine and Aarnio 2001). Avoidance of glove perforations and in their event quick detection are therefore of the utmost importance during surgery. How large a hole must be to allow microorganisms to enter or exit a glove is unknown. Small pinholes might be safe because they often close immediately and may even go undetected in the water test. Large holes are, however, a risk factor for both the patient and the operator.

Well-controlled studies with accurate methods investigating the effects of glove punctures on operating room asepsis are rare. Christensen and coworkers (1995) showed that 36 % of surgeons' fingertips after cardiothoracic operations were contaminated with Gram-positive bacteria. Similar results were obtained in 40 open-heart operations, with 50 % of surgeons' and scrub nurses' hands having significant amounts of skin recolonization at the end of surgery (Berg et al. 1987). In the 1980s, Dodds and coworkers investigated the significance of surgical glove perforation. They reported that glove perforation did not influence bacterial counts on surgeons' hands and concluded that after standard preoperative hand preparation glove perforations are of no clinical significance to the patient

(Dodds et al. 1988). However, the study was conducted in general surgery, where operation times are shorter than in heart surgery.

2.6 Antimicrobial prophylaxis

The recommended antimicrobial agents for cardiothoracic operations include cefazolin and cefuroxime (Page et al. 1993; Gilbert et al. 2005). For patients allergic to beta-lactam agents, vancomycin or clindamycin is appropriate (Mangram et al. 1999). The use of vancomycin is not generally recommended, however, because of the risk of development of vancomycin-resistant enterococci. Long prophylaxis has showed no benefit over short prophylaxis (Niederhäuser et al. 1997). Prolonged use of prophylactic agents is associated with the emergence of resistant bacterial strains and other infections (Harbarth et al. 2000). The consensus of the National Surgical Infection Prevention Project was that the infusion of the first antimicrobial dose should begin within 60 min (vancomycin 120 min) before surgical incision and that prophylactic antimicrobial agents should be discontinued within 24 h of the end of surgery (Bratzler et al. 2004). The drug should be given in an adequate dose based on patient's BMI, and the administration should be repeated intraoperatively if the operation continues two half-lives after the first dose to ensure sufficient antimicrobial levels until wound closure (Forse et al. 1989). Although the effectiveness of prophylactic antimicrobials in preventing SSIs has been shown, their use is often suboptimal. In a recent study by Bratzler and coworkers (2005), an antimicrobial dose was administered to 56 % of patients within 60 min before incision, 79 % of patients received regimens that were limited to recommended agents, and antimicrobial prophylaxis was discontinued within 24 h of surgery ending for only 41 % of patients.

Despite the development of techniques and effective antimicrobial prophylaxis in cardiac surgery, there is room for additional prophylaxis because deep infections exist and multiresistant bacteria have become more common. Local antibiotics have been widely used in bone and soft tissue infections (Ipsen et al. 1991; Jorgensen et al. 1991; Stemberger et al. 1997). As prophylactic agents, they have been used successfully in bone cement in total joint arthoplasty (McQueen et al. 1990; Engesaeter et al. 2003). Notwithstanding the possible benefits of antibiotic-impregnated bone cement in joint arthroplasty, its use is controversial and no established guidelines for this application exist (Bratzler et al. 2004).

In colorectal surgery, the use of a gentamicin sponge accomplished a significant reduction in postoperative wound infection rate and hospital stay (Rutten and Nijhuis 1997). In cardiac surgery, local antibiotics have not been widely used (Cyba-Altunbay and Hamann 1993; Leyh et al. 1999), but one prospective controlled randomized study where topical vancomycin was applied during wound closure after median sternotomy showed a significant reduction in sternal wound infections (Vander Salm et al. 1989). Topical vancomycin may, however, encourage the emergence of vancomycin-resistant pathogens. Therefore, some antimicrobial agent other than vancomycin that prevents mediastinitis would be a good addition in heart surgery. For treatment of patients with mediastinitis, the gentamicin-collagen sponge has been shown to be effective. One report describes mediastinitis being successfully treated with sternum refixation and a gentamicin-collagen sponge (Leyh et al. 1999). The advantages of local gentamicin are that it does not impair renal function, the risk of developing resistant pathogens is small, and it has the capacity to kill bacteria by inhibiting protein synthesis. It is also capable of destabilizing bilayered membranes of bacteria (Kadurugamuwa and Beveridge 1997). Systemically administered, gentamicin may be toxic, but when administered locally, even at very high concentrations the serum concentrations remain well below toxic levels. Gentamicin is effective against *S. epidermidis*; with local gentamicin, even resistant isolates were inhibited (Stemberger et al. 1997).

3 AIMS OF THE STUDY

The objectives of this study were to evaluate the risk factors for mediastinitis in the Finnish population and to explore ways of preventing this complication after cardiac surgery. Specific aims were as follows:

1. to compare the usefulness of a conventional bacteriological technique with that of particle counting under low level air contamination during open-heart operations.
2. to determine how often surgical gloves are punctured in cardiac procedures and to examine the correlation between glove punctures and bacterial counts on fingertips after surgery.
3. to assess a local gentamicin sponge in the prevention of surgical site infections in coronary artery bypass grafting surgery.
4. to determine the incidence and outcome of and risk factors for mediastinitis in a single-center patient population over a ten-year period.

4 MATERIALS AND METHODS

4.1 Patients

This project was carried out at the Department of Cardiothoracic Surgery, Helsinki University Central Hospital. The study population consisted of patients undergoing sternotomy or thoracotomy during cardiovascular surgery with cardiopulmonary bypass between 1990 and 1999. Most surgeries entailed CABG. In Studies I and III, only CABG operations were included.

Patient data were gathered prospectively in Studies I–III and retrospectively in Study IV regarding cases of mediastinitis. For each patient, the following information was prospectively recorded in the hospital discharge registry and operating room log: age, gender, operation code, wound class, ASA score, and duration of operation; the NNIS risk index was calculated from the last three. In the hospital's Cardiothoracic Surgery Unit register, the recorded data comprised BMI, New York Heart Association (NYHA) class, EF, preoperative hospitalization, urgency of the operation (elective, urgent, emergency), perfusion time, use of ITA, length of postoperative stay in the intensive care unit (ICU), hospital stay, transfer to other hospitals, and mortality. No major changes in surgical techniques occurred during this time span. Between 1990 and 1996, the antibiotic prophylaxis was two doses of intravenous (IV) vancomycin (1 g and 500 mg) in 6 h. From 1997, CABG patients received antibiotic prophylaxis in two doses of IV cefuroxime 1.5 g in 6 h. Patients who had undergone valve reconstruction or were hospitalized at least three days preoperatively also received IV vancomycin 500 mg on two occasions. Between July 1998 and September 1999, the 272 patients undergoing CABG surgery also received local gentamicin prophylaxis (Study III).

4.2 Clothing and draping (Study I)

This study included 66 adult patients who underwent open, elective coronary artery bypass surgery. The mean patient age was 55 (range 30–73) years. Preoperative whole body shower wash with 4 % chlorhexidine emulsion was performed three times on consecutive days preoperatively by all patients. Preoperative skin preparation was done three times in the operating theater with 0.5 % chlorhexidine in 80 % v/v ethyl alcohol. The operations were carried out via a median sternotomy incision. All operations were carried out in the same conventionally ventilated operating theater with twenty changes of air per hour. The operating team consisted of 10 ± 1 persons: always the same surgeon and mainly the same staff. Traffic inside the theater and connecting with the outside was minimized. The patients were randomly allocated to two different systems of patient draping and staff clothing: 1. Clean air suit group, where all personnel working in the operating theater wore polypropylene clean air suits, and the operating team also used nonwoven operating gowns reinforced with plastic film in the front and lower parts of the sleeves (Mölnlycke Health Care AB, S-43581, Mölnlycke, Sweden). The patients were covered with plastic foil-laminated impermeable drapes with self-adhesive edges; 2. Cotton group, where the operating theater personnel wore cotton shirts, trousers, and conventional cotton operating gowns. The patient was covered with cotton drapes. Head covers and masks in both groups were disposable types. Operating gloves were consistently changed by the surgeon when the sternum had been opened. In all operations, the patient draping was supplemented by incision foil (Steridrape®, 3M, St. Paul, MN, USA).

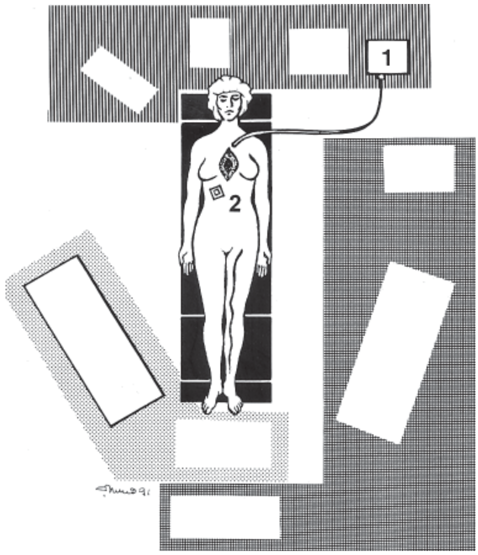
4.3 Bacteriological sampling (Study I)

At 17 randomly selected operations in the two groups, 300-l volumetric air samples were taken at the time of incision plus 1 and 2 h later from 30 cm above the sternal wound. A Sartorius filter sampler was used (Sartorius GmbH, Göttingen, Germany) with a capacity of 30 l/min and equipped with 3 mm pore size gelatine filters. The filters were transferred immediately after sampling to blood agar plates for incubation aerobically for 48 h at 37 °C. The colonies were then counted and typed using conventional clinical bacteriological techniques.

Approximately 3 h after the incision, three pieces of sterile polyvinylalcohol (PVA) foam (Mölnlycke Health Care AB, S-43581, Mölnlycke, Sweden), 4 × 7.5 cm, were placed against the sternal wound surface; two pieces on the wall of the wound and one piece on the surface of the heart. Two pads were also placed against the inguinal wound (done for saphenous vein harvesting) surface. The pads were allowed to absorb to saturation and then separately put into Ringer's solution supplemented with a ß-lactamase inactivator (Oxoid SR 113, Oxoid, Basingstoke, UK). They were immediately transported to the laboratory to be treated in a Stomacher homogenizer (Seward Laboratories, London, UK). The eluates were spread onto blood agar plates, which were incubated at 37 °C for 48 h, after which the colonies were counted and typed. Simultaneously with the wound sampling, the incision foil was sampled. A cardboard frame (aperture 50 cm^2) was placed onto the foil between the wound and the surgeon (Figure 2). The area in the aperture of the frame was rubbed with sterile lecithin–Tween solution (0.3 % and 2.0 %, respectively) on a sterile cotton swab. The specimen was placed in sterile 0.43 % saline. At the laboratory, the swabs were treated with the same technique as the wound pads.

Particles (≥5 µm) were counted by means of a Climet 0208A Particle Analyzer (Climet, Redlands, CA, USA) 30 cm above the wound for 4-min periods starting from the incision continually throughout the operation.

Figure 2. Layout of operating theater and position of investigation sites. 1, particle analyzer; 2, incision foil (Figure 1 from Study I).



4.4 Hand-washing and disinfection (Study II)

The study population comprised 23 participating surgeons in 116 consecutive open-heart procedures consisting mostly of CABG operations with cardiopulmonary bypass. Altogether 106 procedures were done via a median sternotomy incision. Preoperatively, the hands and arms were washed with liquid soap and water for 1 min and dried with disposable paper towels. The hands were then disinfected by rubbing alcoholic chlorhexidine (5 mg/ml chlorhexidine in 80 % ethanol) on the surfaces of the hands in a standardized manner for 2 min. The skin of the hands was kept wet during the time of rubbing, and additional solution was applied on the skin when necessary.

4.5 Bacteriological sampling (Study II)

Altogether 800 bacterial samples from the hands of surgeons were taken both after the preoperative hand-washing and disinfection, and postoperatively immediately after the removal of the gloves. The samples were taken by rubbing the fingertips for 1 min against the bottom of two Petri dishes, one for each hand, containing 10 ml of sterile physiologic saline solution with appropriate inactivators to neutralize possible remnants of the disinfectant. Thereafter, the samples were transferred into test tubes and brought immediately to the laboratory for incubation and analysis. After incubation, the colony-forming units of bacteria from the 1-ml aliquots of the sampling fluid and its tenfold dilutions were counted. Negative growth in 10 ml of fluid thus indicated the presence of less than 9 CFU of bacteria on the fingertips.

4.6 Testing of gloves (Study II)

A total of 200 pairs of gloves from 23 participating surgeons were checked for holes. The gloves were changed during the operation if the surgeon noticed a perforation in the glove. Their practice was to change only the damaged glove. The punctures reported by the surgeons during surgery were registered, and all gloves were analyzed for punctures. This was done according to European standard EN 455-1 by filling the gloves with one liter of water (European Committee for Standardisation 1993). Dripping of water was recorded as a puncture. Glove perforation with a diameter of more than 0.5 cm was defined as large. The sites of the punctures were also recorded. Three types of surgical gloves were used: Biogel® (Regent Hospital Products, Broxbourne, UK), Ansell Medical Gammex® (Ansell Medical, Surbiton, Surrey, UK), and Neutralon® (Johnson & Johnson Medical Inc., Arlington, TX, USA).

4.7 Gentamicin prophylaxis (Study III)

The study population comprised 557 patients who underwent elective CABG. Ten patients did not meet the inclusion criteria and five refused to participate, leaving 542 subjects (Figure 3). In all patients, the operative approach was through a median sternotomy with cardiopulmonary bypass. The patients were randomized to the gentamicin group or to the control group using sealed envelopes. All subjects in the gentamicin group gave their informed consent. Patients in this group received a 10 cm × 10 cm gentamicin-collagen implant (Gentacoll®, Schering-Plough, Espoo, Finland), which contains 130 mg of gentamicin and 280 mg of collagen, underneath their sternum before wound closure (Figure 4). The implant was cut into two or three strips before placement. The controls' sternums were closed in a routine manner with steel wires, without a gentamicin implant. All patients received routine IV

Figure 3. Formation of study groups (Figure 2 from Study III).

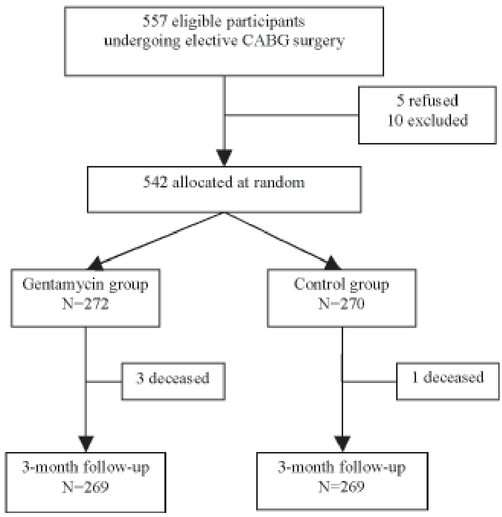
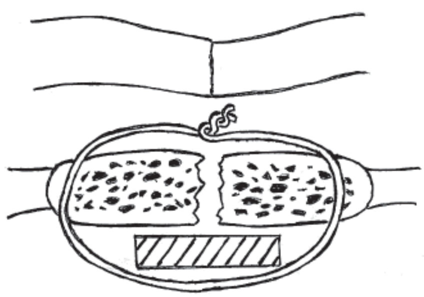


Figure 4. Cross-sectional view with gentamicin-collagen implant underneath sternum (implant shown as hatched area) (Figure 1 from Study III).



antimicrobial prophylaxis (cefuroxime or cefuroxime + vancomycin, section 4.1).

The following patient characteristics were recorded: age, sex, BMI, underlying disease, NYHA class, COPD, preoperative serum creatinine, EF, and preoperative hospitalization. The operative characteristics included antibiotic prophylactics, duration of surgery, types of bypass grafts used, number of bypasses, length of cardiopulmonary bypass, aortic cross-clamp time, mediastinal drain discharge, reoperation, duration of mechanical ventilation, blood transfusions, low output syndrome, stay in ICU, antibiotics administered, and postoperative C-reactive protein (CRP).

4.8 Cases of mediastinitis (Study IV)

Cases with possible mediastinitis were identified from the hospital infection registry and the hospital discharge registry. From the hospital infection registry, we also gathered all cases with SSI of the chest wound and positive blood cultures. The patients' charts were then reviewed and cases of mediastinitis were confirmed using CDC criteria (Table 3). Data collected in a retrospective chart review included antibiotic prophylaxis, microbiological diagnosis, radiological findings, treatment, and reoperations due to mediastinitis.

4.9 Surveillance of infections

For SSIs, we used the criteria published by the CDC. During the hospital stay, patients were monitored by cardiac surgeons daily for fever, wound discharge, and other evidence of wound infection. All patients were followed up for three months after discharge from hospital. Diagnosis of mediastinitis was made either by a cardiac surgeon or by an infection consultant based on clinical signs, results of wound and blood cultures and computed tomography, positive culture from mediastinal tissue, or clinical evidence of mediastinitis in surgery. The staff reported all nosocomial infections to the hospital infection registry, and infection control nurses confirmed these and entered them into the database.

4.10 Statistical methods

Data were analyzed using SPSS (Chicago, IL, USA) statistical software. Statistical evaluation of differences between the bacteriological and particulate contamination levels was performed by means of the Wilcoxon two-sample test (I). For assessment of differences in frequency of glove perforations, the uncorrected χ^2 test was used. For comparison of the length of operations, Student's t-test was used. The Cochran-Armitage trend test (StatXact 5.0, CYTEL Software Corporation, Cambridge, MA, USA) was used to compare bacterial distributions when gloves were intact, had small holes, or had large holes (II). In the gentamicin study, univariate analysis was performed using χ^2 tests for categoric variables and t-tests for continuous variables (III). In the risk factor study, univariate analyses for categoric variables were calculated with the χ^2 test or Fisher`s exact test, as appropriate, and for continuous variables with the Mann-Whitney U-test. Odds ratios (ORs) were used as an estimate of relative risk because the prevalence of SSI was low. Multivariate analysis was performed as forward step-wise logistic regression. Values of $P<0.05$ were considered to be significant.

5 RESULTS

5.1 Air contamination control in the operating room

With the alternative garment and textile system (cotton group and clean air suit group), air counts fell from 25 to 7 CFU/m^3 ($P<0.0038$). Contamination of the sternal wound was reduced by 46 % and that of the leg wound by >90 %. To give continuous contamination feedback throughout the operation to theater staff, particle counts ≥5 µm were monitored and visualized. Air particle counts decreased rapidly from 850 particles/m^3 and stabilized to approximately 50 particles/m^3 when the alternative clothing system (clean air suit group) was used ($P<0.001$) (Figure 5).

5.2 Glove perforations and postoperative skin flora of hands

5.2.1 Glove perforations

A total of 470 gloves were examined for holes. During operations, the surgeons had punctured and changed altogether 53 left-hand and 17 right-hand gloves. Of the 400 gloves removed at the end of operations, 154 were found to be punctured in a postoperative water test. Left-hand gloves were punctured more often (54 %, 136/253 gloves) than right-hand gloves (41 %, 88/217 gloves). At the end of the operation, holes were found more often in left-hand gloves (84 times) than in right-hand gloves (70 times). The majority of all punctures (50 %) were in the three first fingers of the left hand. Of large punctures, 73 % were located in the first two fingers of the gloves. The gloves of principal surgeons were found perforated at the end of operations more often (52 %, 100/192 gloves) than those of assistant surgeons (26 %, 54/208 gloves). The difference was statistically significant ($P<0.01$). With increasing duration of the operation, the frequency of glove perforations as well as the occurrence of large holes increased (Figure 6). In only 20 operations (17 %) were both gloves unpunctured. The chief surgeon had at least one glove perforated in 61 % of the operations.

Figure 5. Air particle counts during cardiac surgery in cotton and clean air suit clothing groups (Figure 2 from Study I).

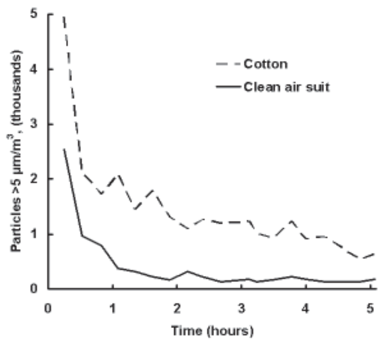
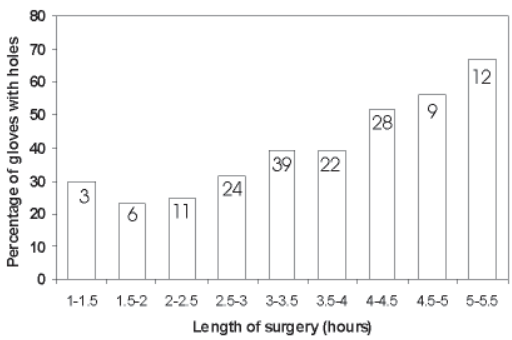


Figure 6. Rate of punctured gloves by duration of operation. The actual number of broken gloves in each group is shown in the respective column (Figure 1 from Study II).



5.2.2 Bacterial counts on surgeons' hands

After the preoperative disinfection of hands, bacterial counts were low. No colony counts were found in 84 % of hand samples, and in 95 % of samples the colony count was less than 10 CFU/ml. In samples taken from surgeons' hands immediately after the operation, the variation in bacterial counts was much wider; 36 % (144/400) of all samples showed no bacteria, and 54 % (216 hands) had bacterial counts between 0 and 9 CFU/ml. More than 1000 bacterial colonies per milliliter of sampling fluid were found in 6 % (23/400) of hand samples. The bacterial counts on hands increased with increasing operation time (P<0.05) (Figure 7).

5.3 Prophylaxis with local gentamicin

The two groups of patients were comparable with respect to preoperative and operative variables. Postoperative SSIs occurred in 11 of 272 patients (4.0 %) in the study group and in 16 of 270 patients (5.9 %) in the control group. This difference was not statistically significant (P=0.20). There were three cases of mediastinitis (1.1 %) in the study group and five (1.9 %) in the control group (P=0.47). No side-effects related to the gentamicin sponge were reported. Differences between the two groups were not statistically significant. Gram-positive organisms accounted for the majority of isolates in both groups. The pathogens cultivated from the sternal wounds or from blood in both groups were mainly *S. epidermidis* or other coagulase-negative staphylococci. The other pathogens cultured were *S. aureus*, Enterococcus spp., and other Streptococcus spp. (Table 5).

5.4 Incidence, outcome, and risk factors for mediastinitis

5.4.1 Study population and cases of mediastinitis

A total of 10 713 cardiovascular operations with cardiopulmonary bypass were performed during the study period, with 120 case-patients (1.1 %) identified as having mediastinitis. Table 6 shows the types of procedures and the rate of mediastinitis in each procedure. No trend towards an increase in annual incidence of mediastinitis was detected (range 0.8–1.5 % in 1990–1999, P=0.30) (Figure 8). During the study period, the patient population got significantly older (mean age 59.3–65.4 years, P<0.01), and the proportion of women increased significantly (from 25 % to 31 %, P<0.01), as did the proportion of patients with ASA >3 (from 10 % to 81 %, P<0.01). BMI was slightly higher in men than in women (26.8 vs. 27.0 kg/m², P<0.01).

Most of the 120 case-patients (83 %) were male, and the majority underwent CABG with left internal thoracic artery graft and

Figure 7. Colony counts on surgeons' hands (cfu/ml) at the end of the operation grouped by duration of surgery (Figure 2 from Study II).

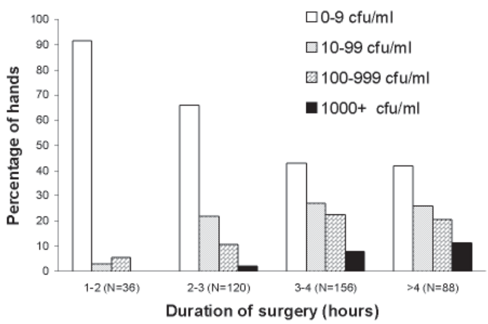
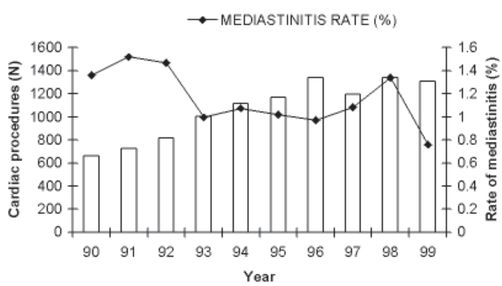


Figure 8. Number of patients undergoing cardiac procedures and annual incidence of mediastinitis (Figure 1 from Study IV).



vein grafts (83 %). The average postoperative hospital stay was 37 days. Diagnosis of mediastinitis was made a median of 12 (range 2–66) days after surgery. Table 7 shows the diagnostic criteria of mediastinitis. Case-patients had the following concomitant diseases: hypertension 61 (51 %), diabetes mellitus 25 (21 %), COPD 16 (13 %), and peripheral arterial disease 9 (7.5 %). Fifteen (13 %) had to be reoperated (most often due

Table 5. Numbers of sternal wound infections and types of pathogens cultured in each case of infection (Table III from Study III).

	Gentamicin group, N=272		Control group, N=270	
Infections	N	Pathogens cultured	N	Pathogens cultured
Superficial incisional SSI	6	*S. epidermidis* (3) None (3)	8	*S. epidermidis* (4) *E. faecalis* + *S. epidermidis* (1) None (3)
Deep incisional SSI	2	*S. epidermidis* (1) None (1)	2	*S. epidermidis* (2)
Sternum osteitis	0	–	1	*S. aureus* (1)
Mediastinitis	3	*S. epidermidis* (2) *S. aureus* (1)	5	*S. aureus* (1) *S. haemolyticus* + *S. epidermidis* + *E. faecalis* (1) None (3)
Total	11		16	

Table 6. Types of procedures and rates of mediastinitis (Table 1 from Study IV).

Procedure	Number	Mediastinitis cases	Rate
CABG	8540	100 (83 %)	1.2 %
Valve reconstruction	1662	14 (11.7 %)	0.8 %
CABG + valve surgery	457	3 (2.5 %)	0.7 %
Other*	16	3 (2.5 %)	0.2 %
Total	10675	120	1.1 %

CABG = coronary artery bypass grafting
**atrial/ventricular septal defect, arrhythmia surgery, procedures on ascending aorta, and left ventricular aneurysm*

Table 7. Presentation of signs and symptoms (CDC criteria) in patients with mediastinitis (N=120).

Criteria of mediastinitis	Number of patients
Positive bacterial culture from mediastinal space	57 (48 %)
Evidence of mediastinitis during surgery or histopathologic examination	81 (68 %)
Fever (>38°C), chest pain, or sternal instability	101 (84 %)
Purulent discharge from mediastinal area	64 (53 %)
Organisms cultured from blood or discharge from mediastinal area	86 (72 %)
Mediastinal widening on x-ray	77 (64 %)

to bleeding), 11 (9 %) had inotropic support for >48 h, 9 (8 %) had an intra-aortic balloon pump, 9 (8 %) underwent prolonged mechanical ventilation (>48 h), 5 (4 %) had low output syndrome, and 3 (3 %) underwent tracheostomy. For antibiotic prophylaxis, 74/120 case-patients (62 %) received vancomycin, 29/120 (24 %) cefuroxime, 13/120 (11 %) cefuroxime with vancomycin, and 3/120 (3 %) cephamandol. As for the 45 case-patients who received cephalosporin prophylaxis, 33/45 (73 %) received it within 60 (median 45, range 0–65) min before incision. Of the 74 case-patients who received only vancomycin, for 70/74 (95 %) this was within 120 min before incision; in 21/74 cases (28 %), the infusion started 0–30 min before incision.

5.4.2 Microbiology

Microorganisms were isolated from 109 case-patients (Table 8). For 3 case-patients, the cultures were negative, for 4, cultures were not taken, and for another 4 information was missing. Superficial or drain cultures accounted for 61 % of specimens, and invasive (mediastinal or blood) cultures for 39 %. In 66 case-patients, the mediastinitis was caused by one pathogen, and in 43, more than one. Gram-positives were isolated from 82 % cultures, and Gram-negatives from 16 %. The most commonly isolated pathogens were *S. epidermidis* (87 case-patients, 73 %) and *S. aureus* (28 case-patients, 23 %). Concomitant bacteremia was diagnosed in 24 cases (20 %) and was most often caused by *S. aureus*.

5.4.3 Treatment of mediastinitis

All case-patients received parenteral antibiotic treatment. Eighty-four case-patients (70 %) had surgery for mediastinitis; 17 (14 %) were operated on 2–5 times (42 operations altogether) (Table 9). The most

Table 8. Organisms isolated from 109 mediastinitis patients with at least one positive culture (Table 2 from Study IV).

	Site of isolation				
Organism	Wound N=109	Drains N=36	Mediastinum N=67	Blood N=24	All N=236
Gram-positive bacteria					
Staphylococcus epidermidis	52	15	34	7	108 (46 %)
Staphylococcus aureus	22	10	14	13	59 (25 %)
Propionibacterium	6	–	4	–	10 (4 %)
Enterococcus faecalis	3	–	3	1	7 (3 %)
Streptococcus viridans	3	–	–	–	3 (1 %)
Other Gram-positives	5	–	2	–	7 (3 %)
Gram-negative bacteria					
Klebsiella sp.	1	4	3	–	8 (3 %)
Acinetobacter sp.	3	2	2	–	7 (3 %)
Pseudomonas aeruginosa	3	3	–	–	6 (3 %)
Enterobacter sp.	1	1	1	1	4 (2 %)
E. coli	2	–	1	1	4 (2 %)
Serratia	2	–	–	1	3 (1 %)
Stenotrophomonas maltophila	2	–	1	–	3 (1 %)
Other Gram-negatives	2	–	–	–	2 (1 %)
Mycoplasma hominis	2	1	2	–	5 (2 %)

common procedure entailed debridement, sternal refixation, and closed mediastinal catheter irrigation (67/109). In 26 cases, the operative procedure included omentoplasty or pectoral myoplasty. Of the case-patients, 36 had no surgery for treatment of mediastinitis because the sternum was stable, and the diagnosis was made by clinical signs, computer tomography, and bacterial cultures. Comparing case-patients who underwent surgery for mediastinitis (N=84) with those who did not (N=36), the proportion in which *S. aureus* was isolated was significantly higher in the surgery group (26 % vs. 18 %, P=0.025). No difference appeared between these two groups with regard to when mediastinitis was diagnosed or the existence of concomitant bacteremia.

5.4.4 Risk factors and outcome

The operating room log showed the rate of mediastinitis to be zero in patients with ASA score 1–2 (0/91) and highest in those with ASA score 5 (2/25, 8.0 %). It was, however, higher in patients with score 3 (19/1294, 1.5 %) than in those with score 4 (88/8644, 1.0 %). The mediastinitis rate was not significantly higher in patients with an NNIS risk index score ≥2 than in those with a score <2 (1.2 % vs. 1.0 %, P=0.38).

Characteristics of patients with and without mediastinitis are shown in Table 10. The rate of mediastinitis was higher in males than in females (1.2 % vs. 0.7 %, P<0.01), and while mediastinitis patients were no older than non-mediastinitis patients, they did have a higher BMI. Their operation times also tended to be longer. In the three BMI categories of <25, 25–30, and >30 kg/m², the mediastinitis rates were 0.5 %, 1.0 %, and 1.8 %, respectively. Of the variables entered into multivariate logistic regression analysis (age, sex, BMI, operation year, perfusion time, type of procedure), only BMI was an independent risk factor (OR 1.1, 95 % CI 1.05–1.15, P<0.01). With mediastinitis, hospital stay was significantly longer, and more patients were transferred to other hospitals. The 30-day mortality did not differ between patients with and without mediastinitis, nor did one-year all-cause mortality (Table 10).

Table 9. Treatment of mediastinitis in case-patients (N=120) classified into five types according to El Oakley and Wright (1996).

Classification of mediastinitis	Number	Treatment: No surgery	Treatment: Refixation of sternum and closed catheter irrigation	Treatment: Omento-plasty/ myo-plasty	Treatment: Other (revision, debride-ment, drainage, sternec-tomy)	Poor out-come (MODS, death)
Type I (presenting within 2 weeks)	23 (19 %)	5	18	–	–	1
Type II (presenting at 2–6 weeks)	15 (13 %)	5	7*	1	2	–
Type III (types I–II in the presence of risk factors)	60 (50 %)	24	29†	4	3	3
Type IV (mediastinitis requiring two or more operations)	17 (14 %)	–	13	17	12	4
Type V (presenting >6 weeks after operation)	5 (4 %)	2	–	1	2	1

*MODS = multiple organ dysfunction syndrome. * In 1 case combined with pectoral myoplasty. † In 2 cases combined with pectoral myoplasty*

Table 10. Characteristics of patients with and without mediastinitis (mean ± SD) (Table 3 from Study IV).

Variables	Mediastinitis N=115	No mediastinitis N=10598	P
Preoperative characteristics			
Age (years)	61.3 ± 9.2	62.5 ± 10.8	0.127
Male gender	95 (83 %)	7570 (71 %)	0.008
BMI (kg/m2)	29 ± 5	27 ± 4	<0.001
NYHA III–IV	48 (76 %)	4529 (75 %)	0.805
Ejection fraction (%)	54 ± 15	54 ± 15	0.784
Preoperative hospitalization (days)	1.8 ± 1.2	1.8 ± 2.3	0.245
Intraoperative characteristics			
Urgent surgery	6 (5.2 %)	732 (6.9 %)	0.477
Perfusion time (min)	100 ± 37	101 ± 43	0.774
Operation time (min)	220 ± 65	214 ± 64	0.306
Bilateral ITA	6 (5.2 %)	691 (6.5 %)	0.573
Postoperative stay in ICU	2.6 ± 3.5	2.1 ± 4.7	0.274
Postoperative characteristics			
Days hospitalized after surgery	22 ± 17	9 ± 5	<0.001
Transferred to another hospital	34 (38 %)	2232 (26 %)	0.010
30-day mortality	1 (0.9 %)	168 (1.6 %)	0.540
1-year mortality	10 (8.7 %)	629 (5.9 %)	0.214

BMI = body mass index; NYHA = New York Heart Association; ITA = internal thoracic artery; ICU = intensive care unit.

6 DISCUSSION

The objectives of this thesis were to investigate ways of preventing SSI after cardiac surgery and to evaluate incidence and risk factors for poststernotomy mediastinitis. Mediastinitis as a complication following cardiac surgery is rare, but disastrous. It increases hospital costs, causes suffering to patients, and prolongs hospital stay markedly. Because SSIs are most often sequelae from contamination during surgery, examining the operating room environment to keep the contamination level as low as possible is warranted. This is why we have studied air contamination monitoring, glove perforations, and fingertip bacteria. Local antibiotic prophylaxis seems to be a sensible means of preventing SSIs after cardiac surgery and is also economically sound, since the treatment of mediastinitis is extremely expensive. Performing studies in cardiothoracic surgery where the infection rate is very low is challenging, time-consuming, and demands large study populations to get significant results. Changes in the population at risk, with, for example, the increasing prevalence of overweight patients, reinforce the importance of surveillance and pose a continuous challenge in focusing preventive measures.

6.1 Incidence and mortality of mediastinitis

The rate of mediastinitis that we detected (1.1 %) is in line with that of other large studies performed since the 1980s (Table 1). The risk was slightly higher in CABG procedures (1.2 %) than in valvular surgery (0.8 %).

Less than 1 % of our patients with mediastinitis died within one month of cardiac surgery, and 9 % died within one year. Mortality did not differ between patients with and without mediastinitis. The treatment of mediastinitis is thus efficient, and although quite expensive, worth the cost. Increased early mortality has been associated with mediastinitis (Loop et al. 1990; Valla et al. 1996; Gårdlund et al. 2002; Fowler et al. 2005), but a few studies also show increased long-term mortality (Milano et al. 1995; Braxton et al. 2000; Lu et al. 2003; Toumpoulis et al. 2005). Such differences may be related to the causative microbes. In two studies with mortality rates of 30 % and 40 %, the pathogens involved were mainly *S. aureus* and *P. aeruginosa* (Ottino et al. 1987; Wouters et al. 1994), while mediastinitis caused predominantly by coagulase-negative staphylococci showed low mortality (2–4 %) (Antunes et al. 1997; Ståhle et al. 1997; Bitkover and Gårdlund 1998). Among our mediastinitis patients, the most commonly isolated pathogen was *S. epidermidis* and then *S. aureus*. Pathogens involved in SSIs after cardiac surgery are usually *S. epidermidis* and *S. aureus* (The Parisian Mediastinitis Study Group 1996; Tegnell et al. 2000; Sharma et al. 2004). Coagulase-negative staphylococci have recently become an important pathogen, especially in deep infections (Tegnell et al. 2000).

6.2 Preventive methods

6.2.1 Air contamination control

The seriousness of postoperative infections and the increased susceptibility of patients undergoing cardiac surgery increase the demand on operating theater asepsis to prevent even low infecting doses of bacteria from reaching the wound. Evidence of the prophylactic effects of different aseptic measures in different operations is limited, with the most data found for orthopedic endoprosthetic operations. Whyte et al. (1982) have shown that a considerable amount of organisms carried by air reach the wound after sedimentation onto a sterile field. They also presented a model to clarify the patterns of transfer.

Figure 5 shows that use of the clean air suit system results in a significantly lower level of air particle counts at the beginning of the operation. A low level of total particles and corresponding bacteria carrying particle count offer an important possibility for individual operation air contamination follow-up.

When the level of air contamination is high, a poor correlation has been demonstrated between the number of particles sized 5–7 μm and microbial contamination (Seal and Clark 1990). Low particle counts ≥5 μm should allow indirect estimations of air bacteria carrying particle counts during the entire operation. The low level of particle counts, when achieved, would also mean a low level of particles carrying bacteria. As part of total air particles size is ≥5 μm, the bacteria carrying particles demonstrate less than 20 %. The low air contamination was achieved even in an ordinary ventilated theater when individual team members used clean air suits in combination with impermeable patient drapes. When air particle level ≤ 50 particles/m^3 is reached, the bacterial air contamination is of the order of that of orthopedic hip operations. The staff must during the entire operation adjust their activity to air asepsis.

Verkkala and coworkers (1990) have reported earlier on the effect of experimental conditions on air cleanliness. Even if the air contamination here is low (25.2 CFU/m^3), the effect of the clean air suit system is clear (7.0 CFU/m^3). The difference then corresponds well with the lower degree of contamination observed on the incision foil, in the sternal wound, and in the leg wound. The highest reduction was found on the incision foil, probably owing to both reduced sedimentation and a better barrier effect against the patient's own skin bacteria via contact transfer. The important result of this study is that when low levels of operative air contamination were achieved, continuous on-line air contamination information to the operating team throughout the operations could be generated.

6.2.2 Glove perforations

Contamination of the wound can happen through perforated surgical gloves; the frequency of these perforations is quite high. Studies conducted during surgical procedures have demonstrated glove perforation rates ranging from 10 % in ophthalmologic surgery to 50 % in general surgery (Nakazawa et al. 1984; Brough et al. 1988; Dodds et al. 1988; Albin et al. 1992; Chapman and Duff 1993). Greater than 50 % leak rates have been reported for cardiovascular, orthopedic, and abdominal surgeries (Albin et al. 1992). The puncture rate depends on the type of surgery and the skill of the surgeon. The risk of glove tears in orthopedic surgery may be especially high because of sharp instruments and jagged bone fragments. The risk of glove perforation increases with the length of the surgery. Three studies report glove perforations increasing by an additional 10 % for procedures lasting more than 1 h (Gani et al. 1990; Laine and Aarnio 2001, 2004). This is in line with our finding of more punctures occurring with longer operations (II). In operations lasting over 5 h, 67 % of gloves were perforated, and the fingertips of the surgeons were contaminated with large numbers of bacteria. This combination can be dangerous to the patient regarding wound asepsis.

It is common practice to change a glove when it is punctured. However, the difficulty is that surgeons may not notice the tear. In our study, the surgeons noticed glove holes and subsequently changed the glove 70 times during operations. However, the gloves removed after operations were often punctured; in 154 of 400 gloves, holes were detected in the water test. The surgeons detected only 45 % of these punctures (70 of the 154 punctured gloves). In previous studies, the detection rates of tears have varied from 3 % to 30 % (Berg et al. 1987; Chapman and Duff 1993; Laine and Aarnio

2001). When the double-gloving system is used, the detection rate is 87 % (Laine and Aarnio 2001). Left-hand gloves were punctured more often than right-hand gloves. Half of the holes were found in the first three fingers of the left-hand glove. Of large punctures, 73 % were located in the first two glove fingers. This is hardly surprising, nor is the finding that the gloves of principal surgeons were perforated more often than those of assistant surgeons. The latter finding is in agreement with the study of Whyte et al. (1991), in which the glove puncture rate for surgeons was 47 % and for assistant surgeons 22 %.

It is worrisome that despite the development of glove materials, gloves were found unpunctured in only 17 % of all operations, and the chief surgeon had at least one perforated glove in 61 % of operations. Glove holes were rated as large in 46 % of cases. It seems logical to assume that such a high glove breakage rate would considerably increase the infection risk. Our study does not, however, support this assumption because the glove holes did not seem to have a straightforward relationship with infection rates. Today, the skin of the patient is diligently disinfected, in Europe most often with efficient alcoholic preparations, the patients receive preoperative antibiotic prophylaxis, and the surgery is elective, whenever possible. The infection is a consequence of multiple causative factors, with the bacteria from the surgeon's hands being only one of these. Patients' sternal skin has been shown to be the main source for wound contamination with epidemic MRSE bacteria (Tammelin et al. 2001b). The same bacteria on the hands of the operating staff were not a risk factor for their occurrence in the wound at the end of the operation. This is consistent with statements from two other studies that glove punctures did not increase the risk for postoperative wound infection (Cruse and Foord 1980) or wound contamination (Whyte et al. 1991). Dodds found glove perforations in 35 % of operations and concluded that after standard preoperative hand preparation, glove perforations are of no clinical significance to the patient, and that protection of the surgeon is the main indication for a per operative change of damaged gloves. However, the operations in that study were general surgery and the operation times were shorter than in heart surgery (Dodds et al. 1988). We were not surprised that we were unable to confirm the correlation between glove perforations and elevated infection risk. The development of a wound infection is a complex and multifactorial issue, and our subject pool was not sufficiently large to thoroughly study various factors predisposing to SSIs. Although we were not able to prove increased infection risk, we did confirm that bacterial counts on hands increased with increasing length of the operation. The glove puncture rate also increased.

If preoperative hand disinfection is done properly and for sufficiently long, modern disinfection techniques efficiently reduce bacterial counts on hands. Some microbes may remain on the skin, but wearing surgical gloves probably prevents their escape into the wound. In our study, more than half of the hands were recolonized at the end of the operation, probably because of bacteria multiplying in the crypts of sebaceous glands and hair follicles. We found that some doctors had no or scant bacteria on their hands either before or after the operation, while the postoperative bacterial counts of others were quite high. This is likely due to personal skin problems, such as dermatitis, dry skin, or small scratches. In addition, in long and complex procedures, surgeons may injure their skin when making sutures. These small wounds may potentially become the source for small amounts of serum and extracellular fluid being released under the glove and, in case of leakage, may become a possible route for microbes to be transferred from the surgeon to the patient, or vice versa.

Since bacteria on the skin of the hands increase with time, it is not unreasonable to suggest that when gloves are changed because of a tear, the hands should also be disinfected before donning new gloves. Also, as glove holes tend to go undetected, changing both gloves when one glove is torn should be the practice of choice.

6.2.3 Prophylaxis with local gentamicin sponge

In our prospective, randomized study with a gentamicin-collagen implant (III), no significant difference was found between infection rates of the two groups. At the very least, we can say that locally administered gentamicin did not increase the SSI rate, which was 4 % in the gentamicin group and 6 % in the control group. The occurrence of mediastinitis was also slightly lower in the study group (1.1 % vs. 1.9 %). This kind of prophylaxis has not been investigated before the year 2005. Friberg et al. (2005) have recently published a prospective, randomized trial using prophylactic gentamicin-collagen sponges between sternal edges in 2000 cases undergoing open-heart surgery. The incidence of SSI was significantly reduced, from 9 % to 4.3 %, but in the case of osteitis or mediastinitis (3.3 % vs. 2.3 %), the difference was not statistically significant. Here, we can see a possibility of reducing SSIs, but further research related to mediastinitis is needed.

The gentamicin-collagen implant was very safe. Neither allergic reactions nor impairment in renal function occurred. We did not, however, determine plasma levels and drainage fluid levels of gentamicin in this study. With the gentamicin sponge, high local gentamicin levels (>300 mg/l) for 36 h have been detected in mediastinal effusions (Leyh et al. 1999; Friberg et al. 2003). The minimum inhibitory concentration (MIC) of gentamicin is 4 mg/l. The local peak levels of gentamicin are 75–200 times higher than the MIC (Leyh et al. 1999). We do not know how long gentamicin remains in mediastinal tissue, but release is dependent on the local blood flow. High bactericidal gentamicin levels are detected even 36 h after surgery (Leyh et al. 1999). Since many risk factors for infection have been identified, targeting additional measures to the patients at highest risk is advisable. Local antimicrobial agents, such as the gentamicin-collagen sponge, may be most beneficial in high-risk patients. If the gentamicin-collagen implant also prevents SSIs in larger studies, it would be cost-effective to use gentamicin-collagen implants in every CABG patient since the treatment of mediastinitis is extremely expensive.

6.3 Risk factors for mediastinitis

Results regarding risk factors for SSIs in other large studies are confusing. The data are mostly from the 1980s and 1990s (Table 1). Only a few studies are more recent. The studies are long-term, up to 15 years. Several shorter studies, which have smaller populations, multicenter studies, or case-control studies have also been published. Some research concentrates only on mediastinitis and some on all sternal infections. In most studies, data have been entered prospectively in registers, but the collection of infection data is retrospective. A few completely prospective studies and some case-control studies are also available. They often focus on different risk factors, depending on what data have been collected in registers. The definitions of infections may vary. Even diagnosing mediastinitis can be difficult.

The only predictive factor found for mediastinitis here was obesity. Obesity has previously been shown to predispose not only to superficial sternal infection but also to mediastinitis (Loop et al. 1990; Milano et al. 1995; The Parisian Mediastinitis Study Group 1996; Valla et al. 1996; Antunes et al. 1997; Bitkover et al. 1998, Abboud et al. 2004; Harrington et al. 2004; Fowler et al. 2005). Our rate of mediastinitis was almost three times as high in patients with BMI >30 kg/m² as in those with BMI <25 kg/m². Similarly, in a French study, the rate of mediastinitis was 5.6 % with BMI ≥30 kg/m², compared with 2.0 % with BMI < 30 kg/m² (The Parisian Mediastinitis Study Group 1996). The increased risk for mediastinitis in obese patients may be related to such factors as technical difficulties during surgery, prolonged operation time, increased bleeding, and ineffective prophylactic antibiotic dose (Milano et al. 1995). Overweight is also associated with type II diabetes mellitus and metabolic syndrome. Several groups have observed an increased risk for mediastinitis among diabetics undergoing cardiac surgery (Loop et al. 1990; Wouters et al. 1994; Valla et al. 1996; Antunes et al. 1997; Ståhle et al. 1997; Trick et al. 2000; Lu et al. 2003; Harrington et al. 2004; Fowler et al. 2005). Of our mediastinitis patients, 21 % had diagnosed diabetes. Due to incomplete documentation in postdischarge diagnoses and the cardiothoracic register, and lack of systematic information on peri- or postoperative glucose levels we could not, however, evaluate diabetes as a risk factor. More recent studies show that undiagnosed diabetes and postoperative hyperglycemia are also associated with development of SSIs, and that perioperative continuous intravenous insulin infusion can lower the incidence of deep sternal infection in diabetic patients during cardiac surgery (Furnary et al. 1999; Trick et al. 2000; Latham et al. 2001), a finding with important practical implications for prevention. These results were not available during our study period.

This study represents our single-center experience over a 10-year period. The limitations of this study are associated with its long time span and the changes that have occurred during this period. Cardiac surgery increased until 1999, and then started to decrease due to more active cardiologists. The annual number of cardiac operations doubled from 636 in 1990 to 1339 in 1999. Changes in technique and patient population over time, such as the increased number of older and sicker patients, may have an impact on the results. Equipment and techniques have developed, but the CABG procedure has basically remained the same. More radial arteries as grafts are used than at the beginning of the 1990s. No changes have taken place in operating room practices, except in antibiotic prophylaxis. Treating perioperative hyperglycemia with insulin infusion is probably more common today.

Looking at the whole population as one entity is also controversial. In our opinion, there are several kinds of mediastinitis. They can be due to contamination during surgery, hematogenous spread from other focuses or infection spreading from subcutaneous tissue to the mediastinal space. Fragmentation of the sternum can lead to mediastinitis if sawing is oblique or the patient's coughing breaks the sternum. Mediastinitis can vary from mild to severe. El Oakley and Wright (1996) have classified mediastinitis into five types according to time of diagnosis, risk factors, and number of reoperations (Table 9). This classification was supported by our subject pool, mediastinitis types I–II being less severe and having better outcome than types III–V. Gårdlund and colleagues (2002) suggested three types of mediastinitis; the first type associated with obesity, COPD, and sternal dehiscence typically caused by *S. epidermidis*, the second type following perioperative contamination and often caused by *S. aureus*, and the third type caused by infections at other sites by Gram-negative rods. The results of our study support the assumption that mediastinitis has various etiologic factors since we found only obesity to be a predisposing factor.

Essentially, all of our patients with mediastinitis (99 %) received antimicrobial prophylaxis, but there is still room for improvement, especially in its timing. Of patients who received prophylaxis, 13 % did not receive it within 60 min (120 min for vancomycin) before incision. Previous studies have demonstrated that timing is critical for effective prophylaxis, with current guidelines recommending dosing within 60 min before incision (Bratzler et al. 2004). More than half of our patients received only vancomycin, most likely to cover methicillin-resistant coagulase-negative staphylococci. We found that vancomycin infusion was often initiated rather close to incision and that the dose might have been insufficient, especially in obese patients (Forse et al. 1989). Data available in our operating room log included no information on type and timing of antimicrobial prophylaxis, so these could not be studied as risk factors.

Risk for mediastinitis did not increase directly with ASA and NNIS risk scores. Roy et al. (2000) also showed that duration of the procedure was the only component of the NNIS index that stratified patients undergoing cardiothoracic operations by risk for SSI. Their study, however, included all SSIs, not only mediastinitis.

CABG has been verified as a risk factor for infection (The Parisian Mediastinitis Study Group 1996; Muñoz et al. 1997; Ståhle et al. 1997), probably due to using ITA as bypass graft material, compromising sternal blood flow (Seyfer et al. 1988; Carrier et al. 1992). Harvesting both ITAs, in particular, has been shown to increase infection rates (Grover et al. 1994; Antunes et al. 1997; De Paulis et al. 2005). However, if ITAs were harvested skeletonized, no increase in infection risk occurred (De Paulis et al. 2005). Diabetes was not a predictor of deep sternal wound infection in patients receiving bilateral skeletonized ITA (Matsa et al. 2001; Peterson et al. 2003; Lev-Ran et al. 2004; De Paulis et al. 2005). In our patients who developed mediastinitis, we had used both ITAs rarely (5 %), and the proportions between patients with and without mediastinitis did not differ.

Our patient population undergoing cardiac surgery during the last decade had changed substantially. This was most likely due to an increasing number of patients having nonoperative cardiac procedures instead of CABG. Christakis et al. (1989) found incidence of CABG-associated morbidity and mortality to increase in parallel with the number of elderly patients, patients with previous CABG procedures, and patients undergoing urgent operations. We did not observe similar trends, although our patients had become significantly older and an increasing proportion had an ASA score of 3 or 4. In addition, the proportion of females had increased. This can in part explain our findings since risk for mediastinitis was lower in females. Previously, either gender has been a risk factor for SSI after cardiac surgery, depending on the site and type of SSI (Roy 1998). Our male patients had a slightly higher BMI, but gender was not an independent risk factor in multivariate analysis. Age has been verified as a risk factor for SSIs in many types of surgeries (Scott et al. 2001, Kaye et al. 2005). However, several cardiac surgery studies have shown that age does not predispose to sternal infections (Ottino et al. 1987; Hammermeister et al. 1990; Loop et al. 1990; The Parisian Mediastinitis Study Group 1996; Antunes et al. 1997; Muñoz et al. 1997; Ståhle et al. 1997), which is consistent with our findings.

Our study was based on a retrospective chart review, and to evaluate incidence and potential risk factors, we utilized data uploaded from four separate in-hospital databases: the hospital discharge register, hospital infection register, operating room log, and a register kept by cardiothoracic surgeons. Linkage of several databases at the patient level was problematic, and only a limited number of variables could be included in our final analysis. For example, in addition to diabetes and blood glucose levels, several other known risk factors for infection, such as tobacco or concurrent corticosteroid use, could not be investigated.

Our results indicate that the rate of mediastinitis is not decreasing. Changes in the population at risk, with, for example, an increasing prevalence of overweight patients, reinforce the importance of surveillance and pose a continuous challenge in focusing preventive measures. Planning and selection of data fields included and compulsory in different hospital information systems require research of potential infection control interventions for more efficient disease prevention.

6.4 Summary

We found obesity to be an independent predictor of mediastinitis in our large subject pool comprising over 10 000 patients. Moreover, we showed that a clean air suit results in low theater air contamination and low exogenous contamination of the operating wound. Continuous particle monitoring proved to be a good intraoperative method to control air contamination. Frequent glove perforations were found to form a possible contamination route because of exponentially multiplying bacteria on surgeons' fingertips. We presented a local antimicrobial prophylaxis which may be beneficial when performing sternotomy on high-risk patients.

Despite modern surgical techniques and our knowledge of the pathogenesis of SSIs and the use of perioperative antibiotic prophylaxis, the incidence of SSIs has not decreased, but has remained at the same level (IV). More effective preventive methods are thus needed and will likely become even more important in the future due to older and sicker patients, the population becoming increasingly obese, type II diabetes becoming more common, and the emergence of resistant bacteria. Every possible prevention method must be considered and those proven to be efficient taken into practice. Patients coming to surgery should be encouraged to lose weight and stop smoking before surgery. Bacterial contamination must be kept as low as possible via preoperative preparation of the patient, including proper timing of hair removal and careful skin preparation with topical antiseptics. Adequate dosing and optimal timing of antimicrobial prophylaxis must be considered. Local antibiotics can also be used. Airborne contamination should be minimized by effective ventilation in the operating room and by use of impermeable scrub suits by staff. Strict aseptic hygiene during operations together with minimal traffic in and out of the operating room is mandatory. Maintaining homeostasis during operations is critical, including perioperative control of blood glucose. The use of 80 % oxygen should also be considered. Finally, surveillance of SSIs, with reports of surgeon-specific SSI rates, is warranted.

7 CONCLUSIONS

On the basis of Studies I–IV, the following conclusions can be drawn:

1. In a conventionally ventilated operating theater, the use of clean air suits and impermeable patient clothing effectively reduces dispersal of organisms from the operating team, resulting in low theater air contamination and low exogenous contamination of operating wounds. Continuous particle monitoring is a good intraoperative method to control air contamination related to theater staff behavior during individual operations. This method increases the possibilities of studying the theaters, technical designs, materials, and methods with a view towards lower contamination levels, and also enables the evaluation of larger groups of patients regarding the risk for wound infection.
2. Glove perforations occur in the majority of heart operations. The frequency of glove perforations and bacterial counts on hands increase with operation time. When a puncture is detected, both gloves should be changed. Before donning a new pair of gloves, renewed disinfection of hands will help to keep bacterial counts low, particularly towards the end of a long operation.
3. The gentamicin-collagen sponge can safely be used as antimicrobial prophylaxis in CABG surgery, with slightly less SSIs occurring in the gentamicin group. The sponge may have beneficial effects on the prevention of SSIs after cardiac surgery, but our series was too small to allow any firm conclusions to be made.
4. The rate of mediastinitis is not decreasing. The main predictive factor found for mediastinitis was obesity. Mortality did not differ between patients with and without mediastinitis. Changes in the population at risk, with, for example, an increasing prevalence of overweight patients, reinforce the importance of surveillance and pose continuous challenges in focusing preventive measures.

8 ACKNOWLEDGMENTS

This project was carried out at the Department of Cardiothoracic Surgery and at the Department of Medicine, Division of Infectious Diseases, Helsinki University Central Hospital in 1997–2001. Data analysis and preparation of the manuscipts were done while I was employed at Jorvi Hospital.

Many people are owed a debt of thanks for their help with this work. First of all, I wish to thank Professors Severi Mattila and Ari Harjula for giving me the opportunity to carry out these studies.

My sincere thanks go to my supervisor Docent Kalervo Werkkala for initiating this work, for providing ideas on the topic, for a positive attitude, and for support. I greatly admire his skills as a cardiac surgeon and his enthusiasm and his optimism.

I owe my deepest gratitude to the late Docent Matti Valtonen, my supervisor, who guided me in the world of surgical infections, encouraged me, and remained interested in this project even when I went to work in another hospital. He was an excellent clinician. His help was crucial in getting this work finished; I am sorry that he could not see the dissertation and that he is no longer with us. His expertise and warm personality are missed.

The official reviewers, Docent Arto Rantala and Professor Jukka Nikoskelainen are gratefully acknowledged for their constructive criticism of this manuscript; their comments greatly improved its final form.

I owe my sincere thanks to the co-authors of the published manuscripts for their important contributions. My deepest gratitude is due to Docent Outi Lyytikäinen for introducing me to scientific writing. She always found time to revise manuscripts, even when she had her hands full with the bird flu. Special thanks are due to Juhani Ojajärvi for his contribution in the study of glove perforations. His vast knowledge of hospital hygiene is impressive. In addition, I would like to thank Peter Klemets for going through tremendous amounts of patient records to locate cases of mediastinitis, and Kaisa Huotari for valuable help with statistical analysis.

I am indebted to my colleagues at the Department of Cardiothoracic Surgery for participating in the studies by rubbing their fingertips in Petri dishes before and after surgical procedures, and placing gentamicin sponges under sternums. Without their help, this work could not have been done.

I am also very grateful to colleagues at Jorvi Hospital, in particular, Jorma Nieminen, the Surgeon-in-Chief, who made it possible to complete this thesis by giving me time off work for writing.

Carol Ann Pelli is thanked for excellent language editing, and Jari Simonen for handling the lay-out of this thesis. Special thanks are due to Sari Karesvuori and Eila Karonen for their help in organizing practical matters related to the dissertation.

My heartfelt thanks go to my late mother and my father for love, trust, a positive attitude, and interest always in my work.

This work is dedicated to three people who have consistently supported me and whom I love very much: my husband Jari-Pekka, my daughter Jenni, and my son Tatu. They live in my heart.

This study was financially supported by Helsinki University Central Hospital, the Finnish Society of Angiology, the Finnish Society for Hospital Infection Control, SSL Healthcare / Regent Medical, Schering-Plough Corporation, and the Jorvi Hospital Scientific Foundation.

Vantaa, April 2006
Anne Eklund

9 REFERENCES

Abboud CS, Wey SB, Baltar VT. Risk factors for mediastinitis after cardiac surgery. Ann Thorac Surg 2004; 77: 676–83.

Albin MS, Bunegin L, Duke ES, Ritter RR, Page CP. Anatomy of a defective barrier: Sequential glove leak detection in a surgical and dental environment. Crit Care Med 1992; 20: 170–84.

Altemeier WA, Culbertson WR. Surgical infection. In: Moyer CA, Rhoads JE, Allen JG, Harkins HN, eds. Surgery, principles and practice, 3rd ed. Philadelphia: JB Lippincott; 1965. p. 51–77.

The American Institute of Architects and The Facilities Guidelines Institute. Guidelines for design and construction of hospital and health care facilities, 2001. Washington, DC: American Institute of Architects Press, 2001.

Antunes PE, Bernardo JE, Eugénio L, de Oliveira JF, Antunes MJ. Mediastinitis after aorto-coronary bypass surgery. Eur J Cardiothorac Surg 1997; 12: 443–9.

Ayliffe GA, Noy MF, Babb JR, Davies JG, Jackson J. A comparison of pre-operative bathing with chlorhexidine-detergent and non-medicated soap in the prevention of wound infection. J Hosp Infect 1983; 4: 237–44.

Ayliffe GA. Role of the environment of the operating suite in surgical wound infection. Rev Infect Dis 1991; 13(Suppl): S800–4.

Babb JR, Lynam P, Ayliffe GA. Risk of airborne transmission in an operating theatre containing four ultraclean air units. J Hosp Infect 1995; 31: 159–68.

Belda FJ, Aguilera L, Garcia de la Asuncion J, Alberti J, Vicente R, Ferrandiz L, Rodriguez R, Company R, Sessler DI, Aguilar G, Botello SG, Orti R; Spanish Reduccion de la Tasa de Infeccion Quirurgica Group. Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. JAMA 2005; 294: 2035–42.

Berg GA, Kirk AJ, Bain WH. Punctured surgical gloves and bacterial re-colonisation of hands during open heart surgery: Implications for prosthetic valve replacement. Br J Clin Pract 1987; 41: 903–6.

Bergman BR, Hoborn J, Nachemson AL. Patient draping and staff clothing in the operating theatre. A microbiological study. Scand J Infect Dis 1985; 17: 421–6.

Bitkover CY, Gårdlund B. Mediastinitis after cardiovascular operations: A case-control study of risk factors. Ann Thorac Surg 1998; 65: 36–40.

Bitkover CY, Marcusson E, Ransjö U. Spread of coagulase-negative staphylococci during cardiac operations in a modern operating room. Ann Thorac Surg 2000; 69: 1110–5.

Blanchard A, Hurni M, Ruchat P, Stumpe F, Fischer A, Sadeghi H. Incidence of deep and superficial sternal infection after open heart surgery. A ten years retrospective study from 1981–1991. Eur J Cardiothorac Surg 1995; 9: 153–7.

Blomgren G, Hambraeus A, Malmborg A-S. The influence of the total body exhaust suit on air and wound contamination in elective hipoperations. J Hosp Infect 1983; 4: 257–68.

Bratzler DW, Houck PM, Richards C, Steele L, Dellinger EP, Fry DE, Wright C, Ma A, Carr K, Red L. Use of antimicrobial prophylaxis for major surgery: baseline results from the National Surgical Infection Prevention Project. Arch Surg 2005; 140: 174–82.

Bratzler DW, Houck PM, the Surgical Infection Prevention Guidelines Writers Workgroup. Antimicrobial prophylaxis for surgery: An advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis 2004; 38: 1706–15.

Braxton JH, Marrin CA, McGrath PD, Ross CS, Morton JR, Norotsky M, Charlesworth DC, Lahey SJ, Clough RA, O'Connor GT. Mediastinitis and long-term survival after coronary artery bypass graft surgery. Northern New England Cardiovascular Disease Study Group. Ann Thorac Surg 2000; 70: 2004–7.

Brough SJ, Hunt TM, Barrie WW. Surgical glove perforations. Br J Surg 1988; 75: 317.

Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. Surgery 1961; 50: 161–8.

Caillot J-L, Côte C, Abidi H, Fabry J. Electronic evaluation of the value of double gloving. Br J Surg 1999; 86: 1387–90.

Carrier M, Grégoire J, Tronc F, Cartier R, Leclerc Y, Pelletier L-C. Effect of internal mammary artery dissection on sternal vascularization. Ann Thorac Surg 1992; 53: 115–9.

Chapman S, Duff P. Frequency of glove perforations and subsequent blood contact in association with selected obstetric surgical procedures. Am J Obstet Gynecol 1993; 168: 1354–7.

Charnley J. Postoperative infection after total hip replacement with special reference to air contamination in the operating room. Clin Orthop Relat Res 1972; 87: 167–87.

Christakis GT, Ivanov J, Weisel RD, Birnbaum PL, David TE, Salerno TA. The changing pattern of coronary artery bypass surgery. Circulation 1989; 80: I151–61.

Christensen JB, Andersen BM, Thomassen SM, Johansen O, Lie M. The effects of 'in-use' surgical handwashing on the pre- and postoperative fingertip flora during cardiothoracic and orthopaedic surgery. J Hosp Infect 1995; 30: 283–93.

Clark RP, Reed PJ, Seal DV, Stephenson ML. Ventilation conditions and air-borne bacteria and particles in operating theatres: proposed safe economies. J Hyg (Lond) 1985; 95: 325–35.

Clarke MT, Lee PT, Roberts CP, Gray J, Keene GS, Rushton N. Wound contamination during primary THR detected by polymerase chain reaction. J Bone Joint Surg (Br) 2005; 87-B(Suppl III): B227.

Collis DK, Steinhaus K. Total hip replacement without deep infection in a standard operating room. J Bone Joint Surg Am 1976; 58: 446–50.

Cruse PJ, Foord R. A five-year prospective study of 23,649 surgical wounds. Arch Surg 1973; 107: 206–10.

Cruse PJ, Foord R. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. Surg Clin North Am 1980; 60: 27–40.

Cruse PJ. Surgical wound infection. In: Wonsiewicz MJ, ed. Infectious diseases. Philadelphia: W.B. Saunders Co; 1992. p. 758–64.

Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG, Banerjee SN, Edwards JR, Tolson JS, Henderson TS, Hughes JM, and National Nosocomial Infections Surveillance System. Surgical wound infection rates by wound class, operative procedure, and patient risk index. Am J Med 1991; 91(Suppl 3B): 152S–7S.

Cyba-Altunbay S, Hamann H. Perioperative Infektionsprophylaxe bei gefässthoraxchirurgischen Eingriffen im infizierten Gewebe. Chirurgische Praxis 1993; 46: 89–97.

De Paulis R, de Notaris S, Scaffa R, Nardella S, Zeitani J, Del Giudice C, De Peppo AP, Tomai F, Chiariello L. The effect of bilateral internal thoracic artery harvesting on superficial and deep sternal infection: The role of skeletonization. J Thorac Cardiovasc Surg 2005; 129: 536–43.

DiPiro JT, Martindale RG, Bakst A, Vacani PF, Watson P, Miller MT. Infection in surgical patients: Effects on mortality, hospitalization, and postdischarge care. Am J Health Syst Pharm 1998; 55: 777–81.

Dodds RD, Guy PJ, Peacock AM, Duffy SR, Barker SG, Thomas MH. Surgical glove perforation. Br J Surg 1988; 75: 966–8.

Driever R, Beie M, Schmitz E, Holland M, Knapp M, Reifschneider HJ, Hoffman F, Vetter HO. Surgical glove perforation in cardiac sugery. Thorac Cardiovasc Surg 2001; 49: 328–30.

Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, Gott JP, Herrmann HC, Marlow RA, Nugent WC, O'Connor GT, Orszulak TA, Rieselbach RE, Winters WL, Yusuf S, Gibbons RJ, Alpert JS, Eagle KA, Garson A Jr, Gregoratos G, Russell RO, Smith SC Jr. ACC/AHA guidelines for coronary artery bypass graft surgery. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1991 guidelines for coronary artery bypass graft surgery). Circulation 1999; 100: 1464–80.

Edwards LD. The epidemiology of 2056 remote site infections and 1966 surgical wound infections occurring in 1865 patients: a four year study of 40,923 operations at Rush-Presbyterian-St. Luke's Hospital, Chicago. Ann Surg 1976; 184: 758–66.

El Oakley RM, Wright JE. Postoperative mediastinitis: classification and management. Ann Thorac Surg 1996; 61: 1030–6.

Engesaeter LB, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0–14 years in the Norwegian Arthroplasty Register. Acta Orthop Scand 2003; 74: 644–51.

Esteban JI, Gómez J, Martell M, Cabot B, Quer J, Camps J, González A, Otero T, Moya A, Esteban R, Guardia J. Transmission of hepatitis C virus by a cardiac surgeon. N Engl J Med 1996; 334: 555–60.

European Committee for Standardisation. EN 455-1: 1993 E. Medical gloves for single use. Pars 1: requirements and testing for freedom from holes. British standard institute, Milton Keynes, England.

Farinas MC, Gald Peralta F, Bernal JM, Rabasa JM, Revuelta JM, Gonzalez-Macias J. Suppurative mediastinitis after open-heart surgery: a case-control study covering a seven-year period in Santander, Spain. Clin Infect Dis 1995; 20: 272–9.

Ferrazzi P, Allen R, Crupi G, Reyes I, Parenzan L, Maisonnet M. Reduction of infection after cardiac surgery: a clinical trial. Ann Thorac Surg 1986; 42: 321–5.

Forse RA, Karam B, MacLean LD, Christou NV. Antibiotic prophylaxis for surgery in morbidly obese patients. Surgery 1989; 106: 750–6.

Fowler VG Jr, O'Brien SM, Muhlbaier LH, Corey GR, Ferguson TB, Peterson ED. Clinical predictors of major infections after cardiac surgery. Circulation 2005; 112(Suppl): I358–65.

Friberg B. Ultraclean laminar airflow ORs. AORN J 1998; 67: 841–51.

Friberg Ö, Jones I, Sjöberg L, Söderquist B, Vikerfors T, Källman J. Antibiotic concentrations in serum and wound fluid after local gentamicin or intravenous dicloxacillin prophylaxis in cardiac surgery. Scand J Infect Dis 2003; 35: 251–4.

Friberg Ö, Svedjeholm R, Söderquist B, Granfeldt H, Vikerfors T, Källman J. Local gentamicin reduces sternal wound infections after cardiac surgery: A randomized controlled trial. Ann Thorac Surg 2005; 79: 153–61.

Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. Ann Thorac Surg 1999; 67: 352–60.

Gani JS, Anseline PF, Bissett RL. Efficacy of double versus single gloving in protecting the operating team. ANZ J Surg 1990; 60: 171–5.

Gårdlund B, Bitkover CY, Vaage J. Postoperative mediastinitis in cardiac surgery – microbiology and pathogenesis. Eur J Cardiothorac Surg 2002; 21: 825–30.

Geelhoed GW, Sharpe K, Simon GL. A comparative study of surgical skin preparation methods. Surg Gynel Obstet 1983; 157: 265–8.

Gilbert DN, Moellering RC, Eliopoulos GM, Sande MA. The Sanford Guide to Antimicrobial Therapy 2005 (35th ed.). Hyde Park, Vermont: Antimicrobial Therapy, Inc; 2005. p. 123–124.

Gnann JW, Dismukes WE. Prosthetic valve endocarditis: an overview. Herz 1983; 8: 320–31.

Greif R, Akça O, Horn E-P, Kurz A, Sessler DI. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. N Engl J Med 2000; 342: 161–7.

Groom RC, Rassias AJ, Cormack JE, DeFoe GR, DioDato C, Krumholz CK, Forest RJ, Pieroni JW, O'Connor B, Warren CS, Olmstead EM, Ross CS, O'Connor GT, Northern New England Cardiovascular Disease Study Group. Highest core temperature during cardiopulmonary bypass and rate of mediastinitis. Perfusion 2004; 19: 119–25.

Grossi EA, Culliford AT, Krieger KH, Kloth D, Press R, Baumann FG, Spencer FC. A survey of 77 major infectious complications of median sternotomy: a review of 7,949 consecutive operative procedures. Ann Thorac Surg 1985; 40: 214–23.

Grossi EA, Esposito R, Harris LJ, Crooke GA, Galloway AC, Colvin SB, Culliforf AT, Baumann FG, Yao K, Spencer FC. Sternal wound infections and use of internal mammary artery grafts. J Thorac Cardiovasc Surg 1991; 102: 342–6.

Grover FL, Johnson RR, Marshall G, Hammermeister KE. Impact of mammary grafts on coronary bypass operative mortality and morbidity. Department of Veterans Affairs Cardiac Surgeons. Ann Thorac Surg 1994; 57: 559–68.

Gruenberg MF, Campaner GL, Sola CA, Ortolan EG. Ultraclean air for prevention of postoperative infection after posterior spinal fusion with instrumentation: a comparison between surgeries performed with and without a vertical exponential filtered air-flow system. Spine 2004; 29: 2330–4.

Haas JP, Evans AM, Preston KE, Larson EL. Risk factors for surgical site infection after cardiac surgery: The role of endogenous flora. Heart Lung 2005; 34: 108–14.

Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM. Identifying patients at high risk of surgical wound infection. A simple multivariate index of patient susceptibility and wound contamination. Am J Epidemiol 1985; 121: 206–15.

Hambraeus A. Aerobiology in the operating room – a review. J Hosp Infect 1988; 11(Suppl): A68–76.

Hammermeister KE, Burchfiel C, Johnson R, Grover FL. Identification of patients at greatest risk for developing major complications at cardiac surgery. Circulation 1990; 82(Suppl): IV380–9.

Harbarth S, Samore MH, Lichtenberg D, Carmeli Y. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. Circulation 2000; 101: 2916–21.

Harpaz R, Von Seidlein L, Averhoff FM, Tormey MP, Sinha SD, Kotsopoulou K, Lambert SB, Robertson BH, Cherry JD, Shapiro CN. Transmission of hepatitis B virus to multiple patients from a surgeon without evidence of inadequate infection control. N Engl J Med 1996; 334: 549–54.

Harrington G, Russo P, Spelman D, Borrell S, Watson K, Barr W, Martin R, Edmonds D, Cocks J, Greenbough J, Lowe J, Randle L, Castell J, Browne E, Bellis K, Aberline M. Surgical-site infection rates and risk factor analysis in coronary artery bypass graft surgery. Infect Control Hosp Epidemiol 2004; 25: 472–6.

Higgins TL, Estafanous FG, Loop FD, Beck GJ, Blum JM, Paranandi L. Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients. JAMA 1992; 267: 2344–8.

Hollaus PH, Lax F, Janakiev D, Wurnig PN, Pridun NS. Glove perforation rate in open lung surgery. Eur J Cardiothorac Surg 1999; 15: 461–4.

Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol 1992; 13: 606–8.

Howorth FH. Prevention of airborne infection during surgery. Lancet 1985; 16: 386–8.

Ipsen T, Jorgensen PS, Damholt V, Torholm C. Gentamicin-collagen sponge for local applications; 10 cases of chronic osteomyelitis followed for 1 year. Acta Orthop Scand 1991; 6: 592–4.

Jensen SL, Kristensen B, Fabrin K. Double gloving as self protection in abdominal surgery. Eur J Surg 1997; 163: 163–7.

Johnston DH, Fairclough JA, Brown EM, Morris R. Rate of bacterial recolonization of the skin after preparation: four methods compared. Br J Surg 1987; 74: 64.

Jorgensen LG, Sorensen TS, Lorentzen JE. Clinical and pharmacokinetic evaluation of gentamicin containing collagen in groin wound infections after vascular reconstruction. Eur J Vasc Surg 1991; 5: 87–91.

Kadurugamuwa JL, Beveridge TJ. Natural release of virulence factors in membrane vesicles by Pseudomonas aeruginosa and the effect of aminoglycoside antibiotics on their release. J Antimicrob Chemother 1997; 40: 615–21.

Kaye KS, Schmit K, Pieper C, Sloane R, Caughlan KF, Sexton DJ, Schmader KE. The effect of increasing age on the risk of surgical site infection. J Infect Dis 2005; 191: 1056–62.

Kjaergard HK, Thiis J, Wiinberg N. Accidental injuries and blood exposure to cardiothoracic surgical teams. Eur J Cardiothorac Surg 1992; 6: 215–7.

Kluytmans JA, Mouton JW, Ijzerman EP, Vandenbroucke-Grauls cm, Maat AW, Wagenvoort JH, Verbrugh HA. Nasal carriage of Staphylococcus aureus as a major risk factor for wound infections after cardiac surgery. J Infect Dis 1995; 171: 216–9.

Kluytmans JA, Mouton JW, VandenBergh MF, Manders MJ, Maat AP, Wagenvoort JH, Michel MF, Verbrugh HA. Reduction of surgical-site infections in cardiothoracic surgery by elimination of nasal carriage of Staphylococcus aureus. Infect Control Hosp Epidemiol 1996; 17: 780–5.

Knobben BA, van Horn JR, van der Mei HC, Busscher HJ. Evaluation of measures to decrease intra-operative bacterial contamination in orthopaedic implant surgery. J Hosp Infect 2006; 62: 174–80.

Kramer A, Matsa M, Paz Y, Locker C, Pevni D, Gurevitch J, Shapira I, Lev-Ran O, Mohr R. Bilateral skeletonized internal thoracic artery grafting in 303 patients seventy years and older. J Thorac Cardiovasc Surg 2000; 120: 290–7.

Kreter B, Woods M. Antibiotic prophylaxis for cardiothoracic operations. Meta-analysis of thirty years of clinical trials. J Thorac Cardiovasc Surg 1992; 104: 590–9.

Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996; 334: 1209–15.

Laine T, Aarnio P. Glove perforation in orthopaedic and trauma surgery. A comparison between single, double indicator gloving and double gloving with two regular gloves. J Bone Joint Surg Br 2004; 86: 898–900.

Laine T, Aarnio P. How often does glove perforation occur in surgery? Comparison between single gloves and a double-gloving system. Am J Surg 2001; 181: 564–6.

Landrin A, Bissery A, Kac G, Monitoring air sampling in operating theatres: can particle counting replace microbiological sampling? J Hosp Infect 2005; 61: 27–9.

Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. Infect Control Hosp Epidemiol 2001; 22: 607–12.

Laufman H. The operating room. In: Bennett JV, Brachman PS, eds. Hospital Infections. 2nd ed. Boston, MA: Little, Brown and Company,1986: 315–23.

Lepelletier D, Perron S, Bizouarn P, Caillon J, Drugeon H, Michaud JL, Duveau D. Surgical-site infection after cardiac surgery: incidence, microbiology, and risk factors. Infect Control Hosp Epidemiol 2005; 26: 466–72.

Lev-Ran O, Mohr R, Pevni D, Nesher N, Weissman Y, Loberman D, Uretzky G. Bilateral internal thoracic artery grafting in diabetic patients: short-term and long-term results of a 515-patient series. J Thorac Cardiovasc Surg 2004; 127: 1145–50.

Leyh RG, Bartels C, Sievers H-H. Adjuvant treatment of deep sternal wound infection with collagenous gentamycin. Ann Thorac Surg 1999; 68: 1648–51.

Lidwell OM, Elson RA, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Ultraclean air and antibiotics for prevention of postoperative infection. A multicenter study of 8,052 joint replacement operations. Acta Orthop Scand 1987; 58: 4–13.

Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement. Br Med J 1982; 285: 10–4.

Lidwell OM. Clean air at operation and subsequent sepsis in the joint. Clin Orthop Relat Res 1986; 211: 91–102.

Loop FD, Lytle BW, Cosgrove DM, Mahfood S, McHenry MC, Goormastic M, Stewart RW, Golding LA, Taylor PC. Sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care. Ann Thorac Surg 1990; 49: 179–86.

Lu JC, Grayson AD, Jha P, Srinivasan AK, Fabri BM. Risk factors for sternal wound infection and mid-term survival following coronary artery bypass surgery. Eur J Cardiothorac Surg 2003; 23: 943–9.

Lynch W, Davey PG, Malek M, Byrne DJ, Napier A. Cost-effectiveness analysis of the use of chlorhexidine detergent in preoperative whole-body disinfection in wound infection prophylaxis. J Hosp Infect 1992; 21: 179–91.

Maffulli N, Capasso G, Testa V. Glove perforation in elective orthopedic surgery. Acta Orthop Scand 1989; 60: 565–6.

Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR, Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999; 20: 250–80.

Matsa M, Paz Y, Gurevitch J, Shapira I, Kramer A, Pevny D, Mohr R. Bilateral skeletonized internal thoracic artery grafts in patients with diabetes mellitus. J Thorac Cardiovasc Surg 2001; 121: 668–74.

McQueen MM, Hughes SP, May P, Verity L. Cefuroxime in total joint arthroplasty. Intravenous or in bone cement. J Arthroplasty 1990; 5: 169–72.

Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. Lancet 2001; 358: 876–80.

Milano CA, Kesler K, Archibald N, Sexton DJ, Jones RH. Mediastinitis after coronary artery bypass graft surgery. Risk factors and long-term survival. Circulation 1995; 92: 2245–51.

Mishriki SF, Law DJ, Jeffery PJ. Factors affecting the incidence of postoperative wound infection. J Hosp Infect 1990; 16: 223–30.

Muñoz P, Menasalvas A, Bernaldo de Quirós JC, Desco M, Vallejo JL, Bouza E. Postsurgical mediastinitis: A case-control study. Clin Infect Dis 1997; 25: 1060–4.

Nakazawa M, Sato K, Mizuno K. Incidence of perforations in rubber gloves during ophthalmic surgery. Ophthalmic Surg 1984; 15: 236–40.

Naver LP, Gottrup F. Incidence of glove perforations in gastrointestinal surgery and the protective effect of double gloves: a prospective, randomised controlled study. Eur J Surg 2000; 166: 293–5.

Nichols RL. The operating room. In: Bennett JV, Brachman PS, eds. Hospital infections. 3rd ed. Boston, MA: Little, Brown and Company, 1992: 461–73.

Niederhäuser U, Vogt M, Vogt P, Genoni M, Künzli A, Turina MI. Cardiac surgery in a high-risk group of patients: is prolonged postoperative antibiotic prophylaxis effective? J Thorac Cardiovasc Surg 1997; 114: 162–8.

Olsen MA, Lock-Buckley P, Hopkins D, Polish LB, Sundt TM, Fraser VJ. The risk factors for deep and superficial chest surgical-site infections after coronary artery bypass graft surgery are different. J Thorac Cardiovasc Surg 2002; 124: 136–45.

Ottino G, De Paulis R, Pansini S, Rocca G, Tallone MV, Comoglio C, Costa P, Orzan F, Morea M. Major sternal wound infection after open-heart surgery: a multivariate analysis of risk factors in 2,579 consecutive operative procedures. Ann Thorac Surg 1987; 44: 173–9.

Page CP, Bohnen JM, Fletcher JR, McManus AT, Solomkin JS, Wittman DH. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. Arch Surg 1993; 128: 79–88.

The Parisian Mediastinitis Study Group. Risk factors for deep sternal wound infection after sternotomy: a prospective, multicenter study. J Thorac Cardiovasc Surg 1996; 111: 1200–7.

Paulssen J, Eidem T, Kristiansen R. Perforations in surgeons' gloves. J Hosp Infect 1988; 11: 82–5.

Perl TM, Cullen JJ, Wenzel RP, Zimmerman MB, Pfaller MA, Sheppard D, Twombley J, French PP, Herwaldt LA. Mupirocin and the risk of Staphylococcus aureus study team. Intranasal mupirocin to prevent postoperative Staphylococcus aureus infections. N Engl J Med 2002; 346: 1871–7.

Perl TM, Golub JE. New approaches to reduce Staphylococcus aureus nosocomial infection rates: treating S. aureus nasal carriage. Ann Pharmacother 1998; 32: S7–16.

Peterson MD, Borger MA, Rao V, Peniston cm, Feindel cm. Skeletonization of bilateral internal thoracic artery grafts lowers the risk of sternal infection in patients with diabetes. J Thorac Cardiovasc Surg 2003; 126: 1314–9.

Polk HC Jr, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. Surgery 1969; 66: 97–103.

Quaini E, Colombo T, Russo C, Vitali E, Pellegrini A. Hospital morbidity and mortality after myocardial revascularisation surgery: current changes in risk factors. Eur J Cardiothorac Surg 1995; 9: 275–82.

Rao N, Schilling D, Rice J, Ridenour M, Mook W, Santa E. Prevention of postoperative mediastinitis: a clinical process improvement model. J Healthc Qual 2004; 26: 22–7.

Roy MC, Herwaldt LA, Embrey R, Kuhns K, Wenzel RP, Perl TM. Does the Centers for Disease Control's NNIS system risk index stratify patients undergoing cardiothoracic operations by their risk of surgical-site infection? Infect Control Hosp Epidemiol 2000; 21: 186–90.

Roy MC. Surgical-site infections after coronary artery bypass graft surgery: discriminating site-specific risk factors to improve prevention efforts. Infect Control Hosp Epidemiol 1998; 19: 229–33.

Russell TR, Roque FE, Miller FA. A new method for detection of the leaky glove. Arch Surg 1966; 93: 245–9.

Rutten HJ, Nijhuis PH. Prevention of wound infection in elective colorectal surgery by local application of a gentamicin-containing collagen sponge. Eur J Surg 1997; 578(Suppl): 31–5.

Sarr MG, Gott VL, Townsend TR. Mediastinal infection after cardiac surgery. Ann Thorac Surg 1984; 38: 415–23.

Scott JD, Forrest A, Feuerstein S, Fitzpatrick P, Schentag JJ. Factors associated with postoperative infection. Infect Control Hosp Epidemiol 2001; 22: 347–51.

Seal DV, Clark RP. Electronic particle counting for evaluating the quality of air in operating theatres: a potential basis for standards? J Appl Bacteriol 1990; 68: 225–30.

Seyfer AE, Shriver CD, Miller TR, Graeber GM. Sternal blood flow after median sternotomy and mobilization of the internal mammary arteries. Surgery 1988; 104: 899–904.

Sharma M, Berriel-Cass D, Baran J Jr. Sternal surgical-site infection following coronary artery bypass graft: prevalence, microbiology, and complications during a 42-month period. Infect Control Hosp Epidemiol 2004; 25: 468–71.

Slaughter L, Morris JE, Starr A. Prosthetic valvular endocarditis. A 12-year review. Circulation 1973; 47: 1319–26.

Ståhle E, Tammelin A, Bergström R, Hambreus A, Nyström SO, Hansson HE. Sternal wound complications – incidence, microbiology and risk factors. Eur J Cardiothorac Surg 1997; 11: 1146–53.

Stemberger A, Grimm H, Bader F, Rahn HD, Ascherl R. Local treatment of bone and soft tissue infections with the collagen-gentamicin sponge. Eur J Surg 1997; 578(Suppl): 17–26.

Stone HH, Hooper CA, Kolb LD, Geheber CE, Dawkins EJ. Antibiotic prophylaxis in gastric, biliary and colonic surgery. Ann Surg 1976; 184: 443–52.

Stuesse DC, Robinson JH, Durzinsky DS. A late sternal wound infection caused by hematogenous spread of bacteria. Chest 1995; 108: 1742–3.

Tammelin A, Hambraeus A, Ståhle E. Routes and sources of Staphylococcus aureus transmitted to the surgical wound during cardiothoracic surgery: possibility of preventing wound contamination by use of special scrub suits. Infect Control Hosp Epidemiol 2001a; 22: 338–46.

Tammelin A, Hambraeus A, Ståhle E. Source and route of methicillin-resistant Staphylococcus epidermidis transmitted to the surgical wound during cardio-thoracic surgery. Possibility of preventing wound contamination by use of special scrub suits. J Hosp Infect 2001b; 47: 266–76.

Tanner J, Parkinson H. Double gloving to reduce surgical cross-infection. The Cochrane Database of Systematic Reviews 2002, Issue 3. Art No.: CD003087. DOI: 10.1002/14651858.CD003087.

Taylor GJ, Bannister GC, Leeming JP. Wound disinfection with ultraviolet radiation. J Hosp Infect 1995; 30: 85–93.

Tegnell A, Arén C, Öhman L. Coagulase-negative staphylococci and sternal infections after cardiac operation. Ann Thorac Surg 2000; 69: 1104–9.

Toumpoulis IK, Anagnostopoulos CE, DeRose JJ, Swistel DG. The impact of deep sternal wound infection on long-term survival after coronary artery bypass grafting. Chest 2005; 127: 464–71.

Trick WE, Scheckler WE, Tokars JI, Jones KC, Reppen ML, Smith EM, Jarvis WR. Modifiable risk factors associated with deep sternal site infection after coronary artery bypass grafting. J Thorac Cardiovasc Surg 2000; 119: 108–14.

Upton A, Roberts SA, Milsom P, Morris AJ. Staphylococcal post-sternotomy mediastinitis: five year audit. ANZ J Surg 2005; 75: 198–203.

Valentine RJ, Weigelt JA, Dryer D, Rodgers C. Effect of remote infections on clean wound infection rates. Am J Infect Control 1986; 14: 64–7.

Valla J, Corbineau H, Langanay T, Sevray B, Felix C, Sellin M, Le Couls H, Leguerrier A, Rioux C, Logeais Y. Mediastinitis after cardiac surgery. A

10-year evaluation (1985–1995). Ann Cardiol Angeiol 1996; 45: 369–76.

Vander Salm TJ, Okike ON, Pasque MK, Pezzella AT, Lew R, Traina V, Mathieu R. Reduction of sternal infection by application of topical vancomycin. J Thorac Cardiovasc Surg 1989; 98: 618–22.

Verkkala K, Mäkelä P, Ojajärvi J, Tiittanen L, Hoborn J. Air contamination in open heart surgery with disposable coveralls, gowns and drapes. Ann Thorac Surg 1990; 50: 757–60.

Vuorisalo S, Haukipuro K, Pokela R, Syrjälä H. Risk features for surgical-site infections in coronary artery bypass surgery. Infect Control Hosp Epidemiol 1998; 19: 240–7.

Whyte W, Hambraeus A, Laurell G, Hoborn J. The relative importance of routes and sources of wound contamination during general surgery. I. Non-airborne. J Hosp Infect 1991; 18: 93–107.

Whyte W, Hodgson R, Tinkler J. The importance of airborne bacterial contamination of wounds. J Hosp Infect 1982; 3: 123–35.

Whyte W, Lidwell OM, Lowbury EJ, Blowers R. Suggested bacteriological standards for air in ultraclean operating rooms. J Hosp Infect 1983; 4: 133–9.

Wong PS, Young VK, Youhana A, Wright JE. Surgical glove punctures during cardiac operations. Ann Thorac Surg 1993; 56: 108–10.

Woodhead K, Taylor EW, Bannister G, Chesworth T, Hoffman P, Humphreys H. Behaviours and rituals in the operating theatre. A report from the Hospital Infection Society Working Party on Infection Control in Operating Theatres. J Hosp Infect 2002; 51: 241–55.

Wouters R, Wellens F, Vanermen H, De Geest R, Degrieck I, De Meerleer F. Sternitis and mediastinitis after coronary artery bypass grafting. Analysis of risk factors. Tex Heart Inst J 1994; 21: 183–8.