DOCTORAL THESIS

from
Division of Surgery, Center for Surgical Sciences, Karolinska Institutet,
Division of Medical Engineering, Department of Laboratory Medicine, Karolinska Institutet, and
Department of Cardiothoracic Surgery & Anesthesiology, Huddinge University Hospital

WOUND VENTILATION
A NEW CONCEPT FOR PREVENTION OF COMPLICATIONS IN CARDIAC SURGERY

Mikael Persson
M.Sc.

STOCKHOLM 2003
You cannot give people lasting help by doing for them what they should do themselves.
Abraham Lincoln

Perfection is something for the dead. Isn’t it imperfection that drives us forward?
Karin Boye

Right to criticize has the one who wants to help.
Abraham Lincoln
# CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>1</td>
</tr>
<tr>
<td>INCLUDED PAPERS</td>
<td>2</td>
</tr>
<tr>
<td>RELATED PUBLICATIONS</td>
<td>3</td>
</tr>
<tr>
<td>DEFINITIONS AND ABBREVIATIONS</td>
<td>4</td>
</tr>
<tr>
<td>DEFINITIONS</td>
<td>4</td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td>4</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>5</td>
</tr>
<tr>
<td>CARDIAC SURGERY – A BRIEF OVERVIEW</td>
<td>5</td>
</tr>
<tr>
<td>Background</td>
<td>5</td>
</tr>
<tr>
<td>A cardiac operation</td>
<td>5</td>
</tr>
<tr>
<td>Early postoperative management</td>
<td>9</td>
</tr>
<tr>
<td>COMPLICATIONS IN CARDIAC SURGERY</td>
<td>10</td>
</tr>
<tr>
<td>Air embolism and organ dysfunction or damage</td>
<td>10</td>
</tr>
<tr>
<td>Bacterial contamination and surgical wound infection</td>
<td>12</td>
</tr>
<tr>
<td>Wound desiccation and cardiac adhesions</td>
<td>14</td>
</tr>
<tr>
<td>WHY WOUND VENTILATION?</td>
<td>14</td>
</tr>
<tr>
<td>Prevention of air embolism</td>
<td>14</td>
</tr>
<tr>
<td>Prevention of bacterial contamination and growth</td>
<td>16</td>
</tr>
<tr>
<td>Prevention of wound desiccation</td>
<td>19</td>
</tr>
<tr>
<td>AIMS</td>
<td>20</td>
</tr>
<tr>
<td>MATERIALS AND METHODS</td>
<td>21</td>
</tr>
<tr>
<td>INSUFFLATION DEVICES</td>
<td>21</td>
</tr>
<tr>
<td>Conventional insufflation devices</td>
<td>21</td>
</tr>
<tr>
<td>The new gas-diffuser</td>
<td>21</td>
</tr>
<tr>
<td>EXPERIMENTAL SET-UP AND MEASUREMENTS</td>
<td>24</td>
</tr>
<tr>
<td>Study I</td>
<td>24</td>
</tr>
<tr>
<td>Study II</td>
<td>25</td>
</tr>
<tr>
<td>Study III</td>
<td>26</td>
</tr>
<tr>
<td>Study IV</td>
<td>27</td>
</tr>
<tr>
<td>Study V</td>
<td>27</td>
</tr>
<tr>
<td>Study VI</td>
<td>28</td>
</tr>
<tr>
<td>STATISTICAL METHODS</td>
<td>28</td>
</tr>
<tr>
<td>RESULTS</td>
<td>29</td>
</tr>
<tr>
<td>Study I</td>
<td>29</td>
</tr>
<tr>
<td>Study II</td>
<td>29</td>
</tr>
<tr>
<td>Study III</td>
<td>30</td>
</tr>
<tr>
<td>Study IV</td>
<td>31</td>
</tr>
<tr>
<td>Study V</td>
<td>31</td>
</tr>
<tr>
<td>Study VI</td>
<td>32</td>
</tr>
</tbody>
</table>
DISCUSSION

COMMENTS ON EXPERIMENTAL DESIGN
Assessment of air displacement
Assessment of airborne contamination
Assessment of antibacterial effects
Assessment of desiccation rate
Insufflation devices
CO₂ flows
Wound cavity models

COMMENTS ON EXPERIMENTAL RESULTS
Air displacement
Direct airborne contamination
Bacteriostatic effect of CO₂
Antibacterial effect of antiseptic CO₂ mix
Wound desiccation

CLINICAL IMPLICATIONS
The wound ventilator
Recommended use
Financial aspects
Environmental aspects
Clinical significance

CONCLUSIONS

ACKNOWLEDGEMENTS

PERSONAL
FINANCIAL

REFERENCES
Cardiac surgery through an open chest wound is a major operation both in size and duration. The wound’s exposure to ambient air implies considerable risks. 1) Air may enter the heart and great vessels and embolize to the brain or cardiac muscle where it may cause dysfunction or permanent damage. 2) The wound is exposed to airborne bacterial contamination, which may lead to postoperative wound infection. 3) The wound is subjected to desiccation, which may lead to serious adhesions and possible impairment of cardiac function.

Intraoperative wound ventilation with carbon dioxide (CO₂) might help to protect the patient against these risks. CO₂ is more soluble than air and thus less harmful to the human body. CO₂ is also heavier than air, which facilitates the establishment of a CO₂ atmosphere in the chest wound cavity. The present study investigated how the physical properties of CO₂ could be used to prevent or reduce complications in cardiac surgery.

The study shows that conventional insufflation devices, such as an open-ended tube, a tube with a gauze sponge at the end, or a multi-perforated catheter, cannot efficiently supply CO₂ to the wound. The flow velocities at which these devices supply gas are too high and the resulting turbulence mixes and dilutes the delivered CO₂ with ambient air. The net effect is a low degree of air displacement. Even more important, it also results in a much higher rate of direct airborne contamination and desiccation of the wound than what is the case without any CO₂ insufflation at all.

A new insufflation device, a gas-diffuser, was developed. The thesis shows that with this device a CO₂ atmosphere of more than 99% can be created in the cardiothoracic wound. At a continuous flow of 10 L/min, wound ventilation should thus significantly decrease the risk of air embolism. Furthermore, this type of wound ventilation may reduce the risk of postoperative wound infection in three different ways. In the first place, the laminar outflow of CO₂ from the wound opening withholds airborne contaminants from reaching the wound. Secondly, the bacteriostatic effect of CO₂ may decrease the growth rate of bacteria in the wound. Thirdly, the addition of a few vol. % of a gasified antiseptic agent to the CO₂ may decrease the number of bacteria in the wound or inhibit their growth even more. Finally, wound ventilation with humidified CO₂ should significantly reduce desiccation of sensitive wound tissue.

The present thesis indicates that intraoperative wound ventilation may be a simple and effective method to reduce the risk of several life-threatening complications in cardiac surgery as well as in other types of surgery. Future clinical studies will eventually reveal its clinical significance.

Keywords: Cardiac surgery, air embolism, airborne contamination, wound infection, desiccation, adhesion, carbon dioxide insufflation, antiseptic agent, ethanol, humidification

ISBN 91-7349-626-X
This thesis is based on the following papers that are referred to by their roman numerals:

I. **Persson M**, van der Linden J*
   De-airing of a cardiothoracic wound cavity model with carbon dioxide: theory and comparison of a gas-diffuser with conventional tubes

II. **Persson M***, Svenarud P, van der Linden J*
Which is the optimal device for carbon dioxide de-airing of the cardiothoracic wound and how should it be positioned?
*Journal of Cardiothoracic & Vascular Anesthesia* (Accepted for publication)

III. **Persson M***, van der Linden J*
Wound ventilation with carbon dioxide: a simple method to prevent direct airborne contamination during cardiac surgery?
(Submitted)

IV. **Persson M***, Svenarud P, Flock J-I, van der Linden J*
Carbon dioxide as a possible tool to inhibit bacterial growth in surgery
(Submitted)

V. **Persson M***, Flock J-I, van der Linden J*
Antiseptic wound ventilation with a gas-diffuser: a new intraoperative method to prevent surgical wound infection?
*Journal of Hospital Infection* 2003; 54:294-299

VI. **Persson M***, van der Linden J*
Can wound desiccation be averted during cardiac surgery? An experimental study
(Submitted)

* Corresponding author
The following related work was carried out during the period of this thesis.

- **Persson M**, Flock J-I, van der Linden J
  Wound antisepsis with gaseous alcohol

- Svenarud P, **Persson M**, van der Linden J
  Intermittent or continuous carbon dioxide insufflation for de-airing of the cardiothoracic wound cavity? An experimental study with a new gas-diffuser
  *Anesthesia & Analgesia* 2003; 96:321-7

- Svenarud P, **Persson M**, van der Linden J
  Efficiency of a gas-diffuser and influence of suction in carbon dioxide de-airing of a cardiothoracic wound cavity model

- van der Linden J, **Persson M**
  A gauze sponge cannot act as a gas diffuser in cardiac surgery when it gets wet

- **Persson M**, van der Linden J
  A simple system for intraoperative antiseptic wound ventilation
  *Journal of Hospital Infection* (Letter, in press)
DEFINITIONS AND ABBREVIATIONS

DEFINITIONS

Agar  Nutritious jelly on which bacteria can be cultivated.
Air embolism  Vessel obstruction caused by air bubbles.
Antiseptic  Agent used on living tissue to destroy or inhibit bacteria.
Bacterial colony  A visible spot, which bacteria form when multiplying on a culture medium.
Bactericidal  Capable of destroying bacteria.
Bacteriostatic  Inhibiting the growth or multiplication of bacteria.
Broth  Nutritious liquid in which bacteria can be cultivated.
Complete sternotomy  Division of the sternum into two halves.
De-airing  Removing air.
Diffusion  Mixing process due to microscopic molecular movements.
Disinfectant  Agent used on inanimate surfaces to destroy or inhibit bacteria.
Endothelium  Membrane of cells which covers the inner surface of vessels.
Epicardium  Tissue layer which covers the heart, outside the myocardium.
Incubation  The development of microorganisms or other cells in an appropriate media.
Infarction  Tissue death due to obstruction of vessel.
Inoculation  Introduction of microorganisms into a culture medium.
Intracardiac  Inside the heart cavities.
Intraoperative  During the operation.
Ischemia  Oxygen deficit in living tissue due to reduced blood supply.
Necrosis  Death of tissue, usually in individual cells, groups of cells or in small, localized areas.
Open-heart surgery  Surgery inside the heart which has been opened and emptied of blood.
Postoperative  After the operation.
Preoperative  Before the operation.
Turbulence  Mixing process due to macroscopic fluid movements.
Vancomycin  A highly effective antibiotic agent against cocci (a spherical bacterial cell).
Ventricular fibrillation  Fibrillatory twitching of the ventricular muscle, the impulses traversing the ventricle so rapidly that coordinated contractions of the heart cannot occur.

ABBREVIATIONS

CFU  Colony forming unit
CO₂  Carbon dioxide
CPB  Cardiopulmonary bypass
N₂  Nitrogen
O₂  Oxygen
PVC  Polyvinyl chloride
S. aureus  Staphylococcus aureus
INTRODUCTION

CARDIAC SURGERY with an open chest wound is a major operation associated with considerable risks. Large areas of internal tissue are exposed during several hours, and the blood circulation system is punctured at its most vulnerable location. Thus, there are risks of arterial air embolism, bacterial wound contamination, and wound desiccation. These problems may cause various postoperative complications. Supplying carbon dioxide (CO\(_2\)) to the cardiothoracic wound during surgery might help to protect the patient. The present thesis investigates how the physical properties of CO\(_2\) could be used in such “wound ventilation” to prevent complications in cardiac surgery.

CARDIAC SURGERY – A BRIEF OVERVIEW

Here follows a brief description of cardiac surgery and of a typical cardiac operation.\(^{1-3}\)

Background

Cardiopulmonary bypass (CPB) and the heart-lung machine were developed experimentally during and after the Second World War. In 1952, Dr Charles Hufnagel used the first artificial heart valve to correct aortic incompetence. The first successful operation done under CPB took place in 1953 when Dr John Gibbon repaired an atrial septal defect at the Jefferson Medical School in Philadelphia. Later in 1967, Dr Barnard in Cape Town performed the first successful cardiac transplant in a human, while Dr Norman Schumway at the Stanford University developed heart transplantation into a useful method. In 1982, Dr William DeVries at the University of Utah implanted the first artificial heart, named Jarvick 7 after its inventor Dr Robert Jarvick, in a human.

During the last 50 years, cardiac surgery with CPB has been developed from experimental surgery into an effective routine procedure. Today almost 1 million cardiac operations are carried out in the western world each year. About 200 000 of these operations are open-heart procedures, i.e. surgery inside the heart, whereas the majority are coronary bypass operations.

A cardiac operation

The operating room

Modern operating rooms are equipped with special ventilation systems that provide a laminar flow of clean, filtered air over the operating table. This inflow causes a slightly higher air pressure in the operating room than outside, which prevents introduction of non-filtered air into the operating room.

The area around the operating table is divided into two zones separated by a blanket. One is a sterile zone, the area at the operating table where the surgeon, surgical assistant and nurse
INTRODUCTION

stand. The other zone is a non-sterile area for anesthesiologists, nurses and technicians (Figure 1). Cardiac surgery is carried out under aseptic conditions, i.e. instruments, clothes, surgical material are sterile. All personnel in the operating room carry clean shirts and trousers, hoods, and surgical masks. The surgical team in the sterile zone also wear surgical gowns and gloves. Surgical clothes and blankets usually have a blue or green color in order to minimize the reflection of the bright operating light.

Preparations
After the patient has been cleaned and his/her chest has been shaved he/she is transported to the operating room. In the meantime nurses and the perfusionist have prepared the operating room by arranging the surgical instruments, mounting the anesthetic and monitoring equipment and the heart-lung machine. Before surgery takes place, the patient is anaesthesized, intubated, and the appropriate monitoring lines are inserted. The skin at the incision area is prepared with an antiseptic solution and draped with a plastic film to prevent bacterial contamination. Meanwhile the surgeon has cleaned his/her hands meticulously and finally washed them with an alcohol based antiseptic. When the surgeon enters the operating room a nurse helps him/her to put on the sterile surgical gown and gloves, and the operation can begin.

Surgical access to the heart
In cardiac surgery on adult patients the most favored approach to the heart is via a complete median sternotomy (Figure 2, left). The skin is incised about 20 cm along the midline through the subcutaneous tissue to the bone. Then the sternum is completely divided with a saw. After possible bleeding has been stopped via diathermy, a thermo-electric knife, the sternal edges are separated with a retractor (Figure 2, right). The surgeon

Figure 1: The surgeons are in the sterile zone (right), whereas the anesthetists and technicians are in the non-sterile zone (left).

Figure 2: The sternum is completely divided with a saw (left) and the edges are held apart with a retractor (right), exposing the right atrium (RA) and ventricle (RV), the pulmonary artery, the left ventricle (LV), and the aorta. (Reprinted with permission from BMJ Publishing Group.)
then sweeps aside the pleurae and opens the pericardium, i.e. the cardiac sac, which exposes the heart. At this stage, the right atrium and ventricle can be seen, whereas little can be seen of the left atrium and ventricle. The first part of the aorta is also visible. The ascending aorta arises from the left ventricle immediately distal to the aortic valve. The aorta passes upwards and forms the aortic arc as it curves to the patient's left side and continues as the descending aorta. The aortic branches in this first segment include the left and right coronary arteries, and those leading to the brain and arms.

**Cardiopulmonary bypass**

CPB is the method by which a patient’s circulation is supported during operations of the heart and great vessels. Before surgery of the heart, the heart-lung machine is connected to the patient via an aortic cannula and one or two venous cannulas on the right atrium depending on the type of operation. When full flow has been established in the cannulas the blood flow through the aorta is shut off with a cross clamp, which is attached distal to the coronary arteries.

The heart-lung machine, which consists of a number of different parts (Figure 3), takes over both the pumping action of the heart and the gas-exchange function of the lungs. This makes it possible for the surgeon to operate on a heart that is not moving and also enables him to perform surgery inside the heart. The blood circulation is maintained with a roller pump that squeezes blood through elastic tubing in a sweeping action. Such a pump also drives the coronary suction by which blood collections in the heart cavity are removed during surgery.

---

**Figure 3:** The heart-lung machine overtakes the functions of the heart and lungs during cardiac surgery. (Reprinted with permission from BMJ Publishing Group.)
This blood is led back to the CPB circuit in order to be reused. The oxygenator adds oxygen (O₂) and removes CO₂ from the blood. This gas exchange takes place through a gas permeable membrane that separates the blood from the gas flow. Before the blood is returned to the patient it is filtered to avoid transfusion of particulate debris and gas microemboli. In order to lower the patient’s metabolic rate and thus decrease the O₂ demand, the blood is usually cooled, which lowers the patient’s body temperature to about 30-34°C.

**Cardiac arrest and myocardial protection**
Although the heart-lung machine has taken over the pumping function of the heart it continues to beat spontaneously. To work successfully and accurately on the heart, it is usually necessary to arrest it. Thus, when the aortic cross clamp is in place, a high concentration of potassium is administered with crystalloid solution or blood to the heart via the coronary arteries. This arrests the heart in diastole leaving it still. The infused cardioplegic solution has a temperature below 10°C. This lowers the myocardial temperature to about 15°C and not only helps to keep the heart still, but also substantially reduces the metabolic rate in the heart.

**Closed heart surgery**
Coronary artery bypass grafting is the surgical method for revascularization of the myocardium. The decision for surgical intervention is based on clinical investigations such as coronary angiogram, electrocardiogram, and nuclear tests. Bypass surgery is a highly effective method to relieve subjective symptoms of ischaemia, such as tightness, choking, heaviness, and breathlessness. The idea of the procedure is to use grafts to bypass partly occluded coronary arteries to restore adequate blood supply distal to the vessel obstructions. The most commonly used graft is the long saphenous vein at the medial aspect of the leg. The graft is harvested at the same time as the chest is being opened. The vein branches are tied or clipped and the vein is then stored briefly in heparinized blood. It is also common to use the internal mammary (thoracic) artery as a graft, since it has the best long-term patency of all available grafts. Both internal mammary arteries can be used but sternal healing may then be comprised due to the limited blood supply.

**Open heart surgery**
Whereas the bulk of open-heart surgery consists of repair or replacement of heart valves, it also includes surgery on aortic aneurysm, cardiac tumors, and corrections of congenital anatomical lesions. Valve failure, usually the disability to adequately open or close, is most often the result of degenerative calcification or rheumatic fever, which causes leaflet thickening and subsequent calcification. Valve diseases are serious as they may cause severe heart failure or sudden death. Valve failure usually involves the mitralis and aortic valves, where the former is more amenable to surgical repair than the latter, which is almost invariably replaced. Artificial valves come in three groups, mechanical valves, xenograft valves from animals, and homograft valves from human cadavers or explanted hearts at transplantation.
INTRODUCTION

Transplantation
A small part of the cardiac patients with extensive pathologic changes in the heart undergo transplantation if they are so lucky as to receive a transplant. To qualify as a candidate for cardiac transplantation the patient not only has to have severe heart failure, but should also be free from other organ disease, evidence of malignancy, and overwhelming sepsis. Due to the extensiveness of the operation and the use of immunosuppressive treatment, cardiac transplantation is a procedure with higher risks than in coronary bypass and valve surgery.

End of operation
At the end of surgery of the heart or great vessels the patient is rewarmed, the aortic cross clamp is removed, and the heart is reperfused. Pacing wires may be placed at the epicardial surface of the heart to optimize weaning from CPB and to manage bradycardia in the early postoperative period. If sinus rhythm does not return spontaneously pacing may be necessary until satisfactory spontaneous rhythm returns. After the patient has been weaned from CPB and any blood left in the CPB circuit has been retransfused to the patient, the arterial cannula is removed. Drainage tubes are placed in the mediastinum, and if a pleural cavity has been opened a further drain may be necessary. At wound closure the pericardium is usually left open. After haemostasis has been secured the sternal retractor is removed and the sternum is closed with about 6-8 stainless steel wire loops. The sub- and intracutaneous layers of the incision are usually closed with an absorbable suture.

Early postoperative management
After the operation the patient is transported to the intensive care unit (ICU). The ICU has two main functions; simple postoperative recovery for most patients, and true intensive care for a few with complications. Patients in the ICU usually require intensive monitoring, respiratory assistance, analgesia, vasodilators, volume replacement, and diuretics.

During the initial hours after the operation the patient is usually ventilated, whereby his/her cardiovascular state is assessed and the possibility of excessive bleeding is eliminated. Thereafter the patient is allowed to wake up and breathe spontaneously. When full respiratory function is restored he/she is weaned from the ventilator and extubated. The patient’s cardiovascular variables are monitored including heart rate, arterial blood pressure, and central venous pressure. Also airway pressures and blood gases are checked. Monitoring the progress towards returning to normal body temperature is also an important element of the patient’s care.

The drainage tubes that were inserted at the end of the operation allow the blood that postoperatively collects within the pericardial space to drain, thus avoiding cardiac compression and tamponade. Moreover, the drains allow monitoring of the bleeding rate. Usually the drains are removed within 24-36 hours, and if there are no problems the patient is transferred to the ward for final recovery before discharge from the hospital. The sternum that was separated 10-15 cm during surgery usually heals within 2-3 months.
INTRODUCTION

COMPLICATIONS IN CARDIAC SURGERY
Cardiac surgery through an open chest wound is a major operation both in size and duration. The exposure of the surgical wound to ambient air implies several risks. Air may enter the heart and great vessels and embolize to the brain or cardiac muscle where it may cause dysfunction or permanent damage. The wound is exposed to airborne bacterial contamination, which may lead to wound infection. Moreover, the wound is subjected to desiccation, which may lead to serious adhesions and possible impairment of cardiac function.

Air embolism and organ dysfunction or damage
When the heart is opened and emptied of blood during open-heart surgery, ambient air is introduced into the cardiac chambers. At the end of the operation this intracardiac air may be mobilized and embolize cerebral and myocardial arterioles.4-8

Incidence
Diffuse cerebral injury that alters short-term memory and concentration is common after cardiac surgery. Via neuropsychological tests such complications may be identified in one third of all patients two months after the operation.1 Most symptoms are mild and patients usually recover completely, but a few have persisting severe disability. The incidence of stroke is higher in open-heart surgery since it involves the risk of embolization of debris and large amounts of air.1 However, intracardiac air is detected both in open (100%) and closed (11-53%) heart procedures.8,9

Pathophysiology
The main components of air, O2 and nitrogen (N2), dissolve poorly in blood and tissue.10,11 Whereas O2 can be carried by hemoglobin and consumed by cell respiration, N2 is physiologically inert and cannot be assimilated and absorbed that way. Intravascular air bubbles may obstruct blood vessels mechanically causing distal tissue ischemia, and cause endothelial damage, which indirectly may lead to permanent obstructions via the inflammatory response (Figure 4).4,12,13 Cerebral arterial gas embolism typically involves arterioles with inner diameters of 30-60µm.4 As the size of an intravascular air bubble slowly decreases it can occasionally dislodge, move downstream,14 and thus cause multiple damage.

Experimental animal studies have shown that arterial air embolization in the brain and the heart may not only cause cerebral and myocardial dysfunction, but may also lead to convulsions, infarctions, ventricular fibrillation and increased mortality.5,15-20 Even obstruction of cerebral arterioles by air microbubbles (25 µL) for less than 30 seconds may still disrupt brain function in rabbits.21,22 Moreover, recent clinical studies have demonstrated neuropsychological impairment after coronary bypass surgery as an effect of air microemboli during perfusionist interventions.23 Massive air embolism (> 20 mL) is an infrequent but well-documented risk of CPB.24,25
INTRODUCTION

When and where does intracardiac air occur?
Intracardiac air occurs in the form of micro-bubbles or as residual pooled air. The latter is most common in open-heart surgery where large amounts of air are introduced into the heart cavities and great vessels. Intracardiac air is frequently observed after termination of CPB in patients undergoing open-heart surgery in spite of the systematic use of available surgical de-airing techniques. In fact, new episodes of air bubbles are even noticed in the heart up to 20 minutes after weaning from CPB.6,8,9,23 The main cause seems to be air trapped in the highest parts of the heart and great vessels i.e. pulmonary veins, superior part of the left atrium, the left ventricular apex, the left atrial appendage and the right coronary sinus.7 The trapped air is only mobilized when the heart is ejecting blood, especially during and soon after weaning from CPB.6,8

Conventional de-airing techniques
Usual surgical measures to prevent air embolism during open-heart surgery include evacuation of trapped air (diagnosed by transesophageal echocardiography)8 by gravitation or aspiration, atrial venting, aortic vent suction, Trendelburg position - that is positioning the patient’s head below the horizontal plane by tilting the operating table - (without effect in a clinical trial),26 and ventricle emptying by compression.

De-airing with CO₂
It is also possible to replace the air in the wound cavity with CO₂ gas. The use of this de-airing method has been based on the fact that CO₂ is more soluble in human tissue and blood than air.10,11 Furthermore, positive results have been obtained in animal studies.5,16-20

Figure 4: An intravascular air bubble may obstruct blood flow directly by itself or indirectly through endothelial irritation (Reprinted4 with permission from Massachusetts Medical Society.)
INTRODUCTION

Bacterial contamination and surgical wound infection

Incidence
Surgical wound infection may ruin an otherwise successful operation, and is associated with extended hospital stay, extra costs, and high mortality rates. The incidence of deep chest wound infection after cardiac surgery usually ranges between 1% and 2%, and the mortality rate varies from 10% to 40%. A cardiothoracic wound infection may increase hospital costs with up to about US$10 000 and extend the patient’s hospital stay with up to about 25 days. Factors that influence the frequency of surgical wound infection include: use of ultra-clean air ventilation in the operating room, antibiotic prophylaxis, and duration of surgery.

Contamination
The most common cause of wound infection in cardiac surgery is *Staphylococcus aureus*, which belongs to the skin flora. The surgical wound may be contaminated by skin bacteria from the incision site and via autotransplanted tissue from other areas. However, skin bacteria may also spread into the environment with the shedding of loosely attached corneal cells with sizes of ≥5 µm. This form of contamination is very difficult to control. Despite the use of modern operating room ventilation airborne bacteria remain an important source for contamination of the open surgical wound. The well draped patient is not considered to contribute to the airborne wound contamination, but the surgical team is, since we all emit thousands of bacteria-carrying airborne particles every minute.

Direct airborne contamination results from the deposition of airborne particles directly into the wound, whereas during indirect contamination airborne bacteria settle on surfaces outside the wound and are then transferred into the wound via the surgeon’s hands or the surgical instruments. Over 90% of bacteria contaminating clean surgical wounds come from the ambient air, and a substantial part of these bacteria contaminate the wound directly. The importance of direct airborne contamination was already brought home some twenty years ago by Lidwell et al., who found the infection rate in joint replacements to correlate with the number of airborne bacteria near the wound. Later Friberg et al. showed that in the surgical area, air counts of airborne bacteria-carrying particles are strongly correlated with bacterial surface counts.

Ironically, the use of laminar ultra-clean airflow from the ceiling downward to the operating table may help to convey airborne particles from the surgical team into the operating field. It has been reported that when the surgeon leans over the wound in such an airflow, as he usually does (Figure 5), he increases the risk of airborne wound contamination 27-fold. Firstly, the airflow...
may release and transport bacteria-carrying particles from the surgeon’s head and neck downstream. Secondly, when the unidirectional airflow meets an obstruction (the surgeon) it breaks up into vortices on the leeward. In this region where the air is fairly stagnant airborne particles will deposit \(^{52}\) in the wound area, just as a snowdrift builds up on the leeward of a tree or a stone.

Given the disastrous consequences that a wound infection has in orthopedic surgery, it is not surprising that in the efforts to prevent it orthopedic surgeons have played a leading role. However, orthopedic surgery is not the only specialty that stands to gain by the combating of airborne infection. Cardiac surgery through an open chest wound is similarly exposed. It also involves the introduction of foreign material in the form of prosthetic devices and metal wires for fixation of the sternum. The use of internal thoracic artery grafts in coronary bypass surgery reduces the perfusion of the sternum, \(^{53}\) and is also an important risk factor for postoperative deep chest wound infection. \(^{29}\) Furthermore, many cardiac patients may already have an impaired tissue perfusion due to atherosclerosis or cardiac failure. On account of all this, combating airborne contamination should be regarded as a matter of high priority also in cardiac surgery. A case could even be made that direct airborne contamination is more important in cardiac than in orthopedic surgery, since the wound area that faces upwards is usually larger, \(^{46}\) operations usually also last for several hours, and there are fewer instruments lying around, which limits the role of indirect contamination.

**Conventional preventive measures**

Conventional measures to prevent wound infection include the maintenance of aseptic (sterile) conditions during surgery, e.g. use of sterile instruments, and antiseptic measures, e.g. preoperative skin cleaning at the incision site using alcohol. Moreover, antiseptic agents, such as povidone-iodine and chlorhexidine-gluconate, \(^{54,55}\) are sometimes applied directly to the open wound to reduce the bacterial load.

Operating room ventilation is a generally accepted method for the prevention of airborne contamination. Such a system usually provides a flow of ultra-clean air from the ceiling downward to the operating table where the airflow then curves horizontally outward (Figure 6). \(^{49}\) Thus, it is thought to supply the surgical area with clean air and then blow against any person or instrument that is approaching the table.

Antibiotics are effective and have been widely used for both prophylaxis and treatment of infection for many decades now. However, the increased use of antibiotics has led to an increased incidence of resistant bacteria. The emergence of methicillin-resistant *S. aureus* and
the recent identification of strains of *S. aureus* with resistance to vancomycin pose a significant public health threat.

**Wound desiccation and cardiac adhesions**

When the surgeon opens the thoracic cavity he abruptly exposes the cavity’s organs to a totally new environment, ambient air, which is characterized by lower temperature and, probably even more important, far lower humidity.56 Although the implications of this sudden change have so far not been studied very extensively it has become clear that desiccation during surgery leads to tissue damage,57 and the risk of such damage increases with time.58 In the presence of shed blood such damage may result in extensive adhesion formation,59 which apart from complicating re-operation can even lead to right ventricular dysfunction.60 The effect of desiccation is of special interest in cardiac surgery where turbulent gas exchange, i.e. convection, occurs not only as a result of standard operating room ventilation, but also because dry CO₂ is not infrequently insufflated for de-airing and to facilitate the suturing of coronary anastomoses. In animal experiments the latter procedure was found to cause severe endothelial damage, which could be alleviated by humidifying the gas.61 Since water loss from a surface is an energy requiring process, desiccation is also associated with a cooling effect. However, in conventional cardiac surgery with CPB this is not a problem since the temperature of the patient, in particular that of the heart itself, are intentionally lowered and controlled for organ protection.

**WHY WOUND VENTILATION?**

Wound ventilation with CO₂ during cardiac surgery may contribute to prevent the above complications. Here is a summary of the background that supports this assumption.

**Prevention of air embolism**

*Air displacement with CO₂*

The theoretical background for de-airing with CO₂ is simple. CO₂ is ≥ 25 times more soluble in tissue and blood than air.10,11 Thus, a CO₂ bubble in a blood vessel will be absorbed more quickly and do less harm than would an air bubble. Furthermore, CO₂ is 50% heavier than air, which facilitates the air displacement in the cardiothoracic wound cavity. The question remains unanswered at what concentration the presence of air will become a risk factor. One thing is clear though. When there is no air left in the wound, we can stop worrying about air embolism. Therefore the present work aimed at complete air displacement.

*New insufflation device*

Although de-airing with CO₂ has been used in open-heart surgery since the 1950’s,62 little attention has been paid to the question how CO₂ should be administered to accomplish effective displacement of air in the wound cavity. In order to gain acceptance by surgeons a CO₂ insufflation device should not hinder the surgeon in his work. Consequently, the commonly used device for CO₂ insufflation has been a thin open-ended tube, but some studies
INTRODUCTION

point to its inability to provide efficient air displacement. In a recent clinical study in open-heart surgery Martens et al. used an open-ended perfusion line with an inner diameter of 2 mm for CO$_2$ insufflation at a flow of 2 L/min. They did not find a difference in neuropsychological outcome, when CO$_2$ insufflation was applied in the cardiothoracic cavity compared with a control group without CO$_2$. Neither did they achieve efficient air displacement (mean air content 56%, range 14-92%), and they concluded: “For effective reduction of cerebral and coronary artery emboli, higher levels of CO$_2$ must be achieved in the operating field by more sophisticated means of application”.

A few modified insufflation devices have been suggested in order to make air displacement more efficient, e.g. a multi-perforated catheter placed at the bottom of the pericardial well, and a gauze sponge to divert the gas stream in front of a thin tube. However, the methods used to study the efficiency of these devices are questionable and they might have inherent properties that make them unsuitable as insufflation devices. The author and his main supervisor have developed a new instrument, a gas-diffuser. In the present study the gas-diffuser was compared with open-ended tubes of different diameters, a multi-perforated catheter, and a gauze sponge as to their ability to remove air from a cardiothoracic wound cavity. Ideally, an insufflation device should be kept as far away from the active surgical area as possible. Therefore, the effects of different positions of the devices were studied. Moreover, since a cardiothoracic wound usually contains fluid the devices were tested after exposure to liquid.

**Fluid mechanical aspects**

Earlier studies have not thoroughly investigated the technical aspects of air displacement with CO$_2$. First of all, when a cavity is insufflated with CO$_2$, air and CO$_2$ will spontaneously mix due to diffusion. Just as a temperature difference is the driving potential of heat transfer, a concentration difference is the driving potential of diffusion. The diffusion of a gas in a binary gas mixture can be described by Fick’s law, which in a simple one-dimensional form can be expressed as:

$$ J = \frac{D_{ab} \cdot A \cdot \Delta C}{L} \quad [mol/s] \quad (1) $$

where $J$ is the diffusion flow (can be converted to $[L/min]$) of one of the gases a and b, $D_{ab}$ the diffusion coefficient, $A$ the area through which diffusion occurs, $\Delta C$ the concentration difference between two points, $L$ the length between the two points. This means that the larger the area of a wound opening and the lower the air content in the wound cavity, the greater is the impact of diffusion. Thus, when aiming at efficient air displacement of the relatively large cardiothoracic wound, diffusion should be an important factor to consider.

This thesis investigated the influence of diffusion, CO$_2$ flow, and outflow velocity on air displacement. The latter was assumed to be related to the degree of turbulent gas movements in the wound.
Prevention of bacterial contamination and growth

The risk of wound infection after cardiac surgery increases with the duration of the operation. Furthermore, since it is during the operation that bacterial wound contamination occurs, it seems logical to apply new countermeasures intraoperatively. Wound ventilation is one of those pathways, and attacks the problem in three different ways.

Repel airborne bacteria

It has been estimated that as few as 10 bacteria carrying airborne particles are sufficient to cause deep surgical wound infection. This implies that preventing only a few airborne particles from reaching the surgical wound should be of clinical significance. Since the surgical team is the source of direct airborne contamination, the question arises if the ventilation flow should not be directed the other way round and emanate from the wound itself. When considering the role that wound ventilation might play in combating airborne infection, it should be kept in mind that when CO₂, which is heavier than air, is continuously supplied to a wound cavity, surplus CO₂ gas will flow out of it as shown in Figure 7. This continuous overflow of CO₂ from the wound opening might be able to repel and transport particles away from it and thus prevent direct airborne contamination.

The following theoretical reasoning supports this assumption. Stokes’ law describes the terminal settling velocity \( v_s \) of a spherical particle of uniform density that is falling in a fluid (gas or a liquid) due to gravity:

\[
v_s = \frac{d^2 \cdot g}{18 \mu} (\rho_{\text{particle}} - \rho_{\text{gas}}) \quad [\text{m/s}]
\]

where \( d \) is the diameter of the particle, \( g \) the acceleration due to gravity, \( \rho_{\text{particle}} \) and \( \rho_{\text{gas}} \) the density of the particle and gas, respectively, and \( \mu \) the dynamic viscosity of the gas.

Airborne bacteria are usually attached to larger particles, such as epithelial cells, respiratory droplets, and dried droplet nuclei. The latter particles are spherical, but skin scales do normally have a flattened shape with sizes of about 30×30×5μm. For reasons of mathematical convenience, these airborne particles may be considered as spheres with unit density that behave as the particles in question. The unit density of the equivalent particles is 1 g/cm³, which is the greatest expected particle density in this matter as it is the density of water. The mean equivalent diameter of airborne particles that carry pathogenic bacteria has been found to be 14 μm.
According to Stokes’ law, the settling velocity of such a particle in CO₂ (at 20°C) is 7 mm/s. Let us consider a cardiothoracic wound opening with an elliptic shape and a length and width of 20 and 12 cm, respectively, i.e. the measures used in experimental models in the present study. If we assume that the CO₂ flow out of the opening is uniformly directed upward, an airborne particle will be repelled and transported away from the wound when the upward velocity of the CO₂ is equal to or higher than the settling velocity of the particle. The required CO₂ flow (Φ) for this is given by multiplying the particle’s settling velocity (vₜ) with the area of the wound opening (A):

\[ Φ = vₜ \cdot A \cdot 60 \cdot 10^3 \quad [L/min] \]  

The area of the considered wound opening is 1.9 dm², which gives a required CO₂ flow of 8 L/min. Since usually flows of 2-10 L/min are used for de-airing purposes, a considerable reduction of direct airborne contamination will thus theoretically be possible.

The present study investigated how CO₂ insufflation with different devices and flows influences the rate of airborne contamination in a chest wound model.

**Bacteriostatic effect of CO₂**

For many years now CO₂ in high concentrations has been used in modified atmosphere packaging to prolong the shelf life of fresh food. Consequently, the inhibitory effects of CO₂ on bacterial growth has been most extensively studied in this field. The inhibitory effect has been found to be especially marked in fresh meat. As a result, the use of CO₂ as a preservative was introduced in shipments of beef to the UK, and already in 1938 60% of all beef from New Zealand to Britain was transported in this manner. The question arises why an antibacterial method that has proved to be so effective in the food industry has not been put to clinical use in surgery to prevent postoperative wound infection. One reason may be that intraoperative methods to expose an open surgical wound to 100% CO₂ have not yet been available.

Low levels of CO₂ may stimulate the growth of many micro-organisms, but in high concentrations CO₂ has an inhibiting effect on most organisms, both on aerobes and anaerobes. In general, the rate of bacterial multiplication decreases and the length of the lag phase increases with increasing levels of CO₂. Furthermore, the inhibitory effect of CO₂ increases as the temperature decreases. This has been explained by the increased solubility of CO₂ at lower temperatures, which increases the CO₂ concentration that the bacteria are subjected to.

Inhibition of bacterial growth with CO₂ is connected to two main mechanisms: suffocation and a specific CO₂-effect that acts directly on the bacterial cell. Decreased pH in the surrounding medium may, however, not be of primary importance since the permeability of cells to CO₂ probably results in a direct intracellular pH-change that is independent of the external pH. Up to 99% of CO₂ dissolved in water or unbuffered salt solution is actually in the physical form of CO₂, whereas only 1% is in the carbonic acid form including
bicarbonate and carbonate ions. The direct CO$_2$-effect is not yet completely understood. It seems to be a result of multiple actions on the bacterial cell; including altered rate of enzyme reactions, intracellular pH changes, reactions with amino acids, peptides, and proteins of the cell, increased fluidity and permeability of the cell membrane, alteration of the ion transport due to a charged cell membrane, structural changes of the cell membrane, and regulation of cell-surface components such as capsular polysaccharides.

This study investigated if the growth rate of *S. aureus* at body temperature could be decreased by exposure to 100% CO$_2$.

**Gaseous wound antisepsis**

If prevention of airborne contamination and the bacteriostatic effect of CO$_2$ would not be sufficient to prevent infection, wound ventilation provides a third possibility, which is to spic up the CO$_2$ by letting it carry a gaseous antisepic agent. The major advantages with gaseous wound antisepsis compared with methods involving liquids are: invisibility, total exposure, and uniform as well as controllable dosage.

If gaseous wound antisepsis is applied, the antiseptic agent will be delivered to the wound as an invisible gas of free molecules that will create a uniform molecular coating on the exposed surface. The wound will be completely exposed to the agent if the wound cavity is flooded with a carrier gas that is heavier than air. In gaseous form the agent will be present only as long as it is supplied to the wound and thus the dosage can be controlled. In contrast, in liquid form, even as a spray, the agent will be unequally distributed in the wound, and many hidden recesses will not be reached unless the wound is completely filled up. This would hinder surgery and the dose of the agent will be difficult to control.

Already in the mid-sixteenth century Paracelsus stated, "*All things are poison and nothing is without poison. Solely the dose determines that a thing is not a poison*". Direct topical application of an antiseptic agent to an open wound makes it possible to use agents that otherwise would be too toxic if delivered systemically. However, if the dose gets too high, local toxic effects may cause damage to the wound tissue, which paradoxically could favor wound infection. A liquid agent will always leave residuals in the wound, and even if the agent is diluted the residuals may become toxic because the duration of exposure cannot be controlled. In contrast, with the agent in gaseous form there will be no residuals. According to Avogadro's law, the number of molecules in a certain gas volume is constant. Thus, provided that the saturation of the gaseous agent in the carrier gas is controlled, the delivered dose will be easy to control, as it will only be determined by the exposure time. This allows for the use of non-diluted potent agents. Furthermore, in order to prevent a surgical wound infection the delivered dose may not necessarily have to be bactericidal. A smaller bacteriostatic dose may be sufficient.

The search for simple and effective antiseptic agents has been going on from the age of Galenus (131-201 A.D.), who recommended alcohol for wound treatment. The possibilities of finding a new agent are limited, since it has to be both effective and non-toxic, and since official requirements reduce the chances of acceptance for new substances. Thus, it is essential to work with established agents and try to obtain improvements by creating new combinations. Common antiseptic agents for open wounds are highly diluted solutions of
povidone-iodine and chlorhexidine-gluconate.\textsuperscript{54,55} However, if delivered in gaseous form an agent should be concentrated (100%), since the delivered amount is small and the higher the concentration the shorter the required exposure time.

The present study investigated the antibacterial effect on \textit{S. aureus} of CO\textsubscript{2} carrying gasified alcohol (ethanol).

\textbf{Prevention of wound desiccation}

The optimal way to protect wound tissue from desiccation during surgery is to enclose it in a plastic bag,\textsuperscript{56} thus providing it with a fully humidified gas environment. This is possible only with tissues that are easily externalized such as intestines during abdominal surgery. Furthermore, it cannot be done in areas where the surgery takes place. An alternative solution is to create a micro-atmosphere with high humidity and low convection in the open wound itself. Thus, the wound will be completely exposed to a humidified and invisible gas during surgery.

Desiccation of a surface results from superficial water loss, which occurs through diffusion and convective gas movements. The rate of water loss from a surface of a certain area can be expressed as:\textsuperscript{86}

\[
\sigma = \frac{m_a(x_s-x_a)}{A} \quad [kg/(m^2 \cdot s)]
\]

where \(m_a\) is the rate of air exchange above the surface, \(x_s\) the saturated water content in the gas close to the surface, \(x_a\) the water content in the ambient gas, and \(A\) the area of the considered surface.

The formula says that when the ambient gas is saturated with water no water loss can take place regardless of the gas movements above the surface, and wound ventilation with fully humidified CO\textsubscript{2} should thus theoretically eliminate desiccation. However, when the ambient gas is not saturated with water the gas exchange above a surface, i.e. the convection, will be the important factor in desiccation. Diffusion alone is a rather slow transfer process, but convection maximizes the evaporation by constantly exchanging the “humidified” gas close to the surface with “dry” ambient gas, i.e. the diffusion gradient is kept maximized. Thus, if it is not possible to saturate the CO\textsubscript{2}, avoiding convection in the open wound can still substantially reduce desiccation.

The present study investigated the humidity and the desiccation rates in a cardiothoracic wound cavity model without insufflation and during insufflation of dry and humidified CO\textsubscript{2} via different devices.
The aims of this thesis were to:

I-II. Identify an optimal method for de-airing of the cardiothoracic wound with CO₂.

   a) Develop a new device for efficient and practical supply of CO₂ to the chest wound cavity during cardiac surgery.
   b) Develop an experimental set-up, i.e. finding suitable instruments and building realistic test models, for assessment of air displacement with CO₂.
   c) Compare the efficiency of the developed insufflation device with other devices that have been suggested or used earlier.
   d) Analyze how insufflation flow, outflow velocity, and diffusion will affect air displacement in a chest wound cavity.
   e) Determine the importance of the position of an insufflation device.

III. Investigate how insufflation of CO₂ via different devices and flows influences the rate of direct airborne contamination in a cardiothoracic wound model.

IV. Investigate how CO₂ affects the growth rate of *S. aureus* at body temperature.

V. Investigate the antibacterial effect on *S. aureus* of CO₂ carrying a gasified antiseptic agent, alcohol (ethanol).

VI. Quantify and compare the desiccation rates with and without CO₂ insufflation via different devices, and to determine the influence of gas humidification.
MATERIALS AND METHODS

INSUFFLATION DEVICES

Figure 8 shows the orifice of the studied insufflation devices.

![Figure 8: The studied insufflation devices. From the left; an open-ended tube with an inner diameter of 2.5 mm and one with inner diameter ¼ inch, a multi-perforated drain catheter, and a 2.5-mm tube with a gauze sponge or the new gas-diffuser at the end.]

Conventional insufflation devices

The four conventional devices, from the left in Figure 8, were two different open-ended tubes with an inner diameter of 2.5 mm and ¼ inch (6.35 mm), respectively. They were made by cutting away the distal part of a gas-diffuser set. The third device was a multi-perforated silicone catheter with a length of 50 cm and an inner diameter of 3 mm. It had an open end and 20 elliptical holes, 3×5 mm wide, placed in a spiral around the distal 25 cm of the catheter. The catheter was attached to the distal end of the ¼ inch tube. The fourth conventional device consisted of a surgical gauze sponge attached in front of the 2.5-mm tube.

The new gas-diffuser

The gas-diffuser device is a sterile and disposable set (Figure 9), which consists of a PVC tube (a) with an inner diameter of ¼ inch (6.35 m), a gas filter (b), and a distal 2.5-mm tube (c) with a diffuser (e) at its end. The cylindrical diffuser (14×18 mm) is made of soft
polyurethane foam with open cells, and is attached to the thin tube via a circular PVC disc (d). See also Figure 8.

The gas-diffuser set is gray since that is the international color-code for medical CO₂ gas. The total length of the gas-diffuser set is 3.5 m. This is the same length as that of surgical suction devices that similarly reach from the surgical wound to a gas connection outside the sterile zone in the operating room.

**Gas line**
The wider tube (a) has a total length of 3.3 m and leads the gas with minimal flow resistance from the gas source in the non-sterile area of the operating room to the surgical area. The inner diameter of ¼ inch is a standard size in medical devices where similar gas flows are used.

**Gas filter**
The in-line particulate gas filter (b), with a pore size of 0.2 µm, is capable of removing bacteria and viruses from a gas. Medical gas is considered to be sterile. However, other parts such as tube connections may be contaminated. Thus, the filter is an extra safety measure to eliminate any risks of contamination via the insufflated gas.

**Distal thin tube**
The distal tube (c) has a small diameter in order to not interfere with the surgeon in the wound, and to be easy to bend. Its 15-cm long distal part contains a stainless steel wire, which makes it easy to fix the diffuser in a suitable position in the surgical area.

**Attachment disc**
The circular plastic disc (d) has several functions. Firstly, it provides a large bonding surface for the soft diffuser material, which is important to prevent the diffuser from coming loose and accidentally being left behind in the surgical wound. Secondly, it decreases the required size of the diffuser, which should be as small as possible. Direct attachment to the tube without the disc would have required a larger diffuser in order to obtain a sufficient bonding surface. Thirdly, the disc maintains the cylindrical shape of the diffuser, which is important for its function. Fourthly, if the diffuser has accidentally been soaked with blood the disc constitutes a good support when compressing the diffuser with a finger. Fifthly, the plastic disc, which is securely attached to the thin tube, prevents the steel wire from coming out at the distal end and cause accidental rupture of surgical gloves.
**Diffuser**

The diffuser (e) is the key part. A gas jet insufflated into the diffuser will be diverted into multiple directions via the tortuous paths inside the diffuser material. Hereby, the gas will be uniformly distributed to the larger diffuser surface and exit from there with greatly reduced velocity.

During the development of the gas-diffuser, sintered plastic was tested as a possible diffuser material. Diffusers of this material are used in various fields for dispersion and filtration of liquids and gases. Sintered plastic is a solid porous material that is made up of small plastic bodies with sizes from a few to several hundred microns. Its material structure is the inverse of that of plastic (polyurethane) foam with open cells. Thus, where there is material in the sintered plastic, there is empty space in the foam, and vice versa. The sintered plastic showed to be a fairly effective gas diffuser but it failed on one important point where the plastic foam was superior. When any part of the sintered plastic came into contact with a liquid (albumin, Figure 10) it failed to redistribute the gas to a clear part and thus rapidly created foam (Figure 11). This is not acceptable since the diffuser may come into contact with blood during surgery. Foam creation would be disturbing and might act as a potential source of gas emboli. By contrast, the plastic foam with open cells effectively redistributed the gas when in contact with the liquid, and hence no foam was created. Even when the orifice of the tube and most of the plastic foam were submerged, the gas could still escape through the small part left above the surface (Figure 12). The plastic foam had to be completely drowned before foam was created. This difference in diffuser characteristics is probably due to higher flow speeds from the micro-channels in the porous sintered plastic, which are narrower than those inside the plastic foam. Furthermore, due to its low density the plastic foam is buoyant while the sintered plastic is not. Another advantage of the plastic foam is that, thanks to its softness, it can be compressed to remove fluid.

---

**Figure 10:** The sintered plastic diffuser created foam immediately when coming into contact with the albumin.

**Figure 11:** A large amount of foam was rapidly produced.

**Figure 12:** Despite a CO₂ flow of 10 L/min the gas-diffuser did not produce foam, even when the tube’s orifice was positioned below the surface.
EXPERIMENTAL SET-UP AND MEASUREMENTS

Study I

Set-up

In order to analyze and solve the problem of inefficient CO₂ de-airing,¹⁰,⁶³,⁶⁴ the important variables had to be studied separately in a controlled set-up. Thus, the first approach in this project was an experimental study of air displacement with accurate and systematic measurements in a symmetric cardiothoracic wound model positioned in a non-ventilated room.

The air displacement efficiency of the CO₂ insufflation devices was tested in a cylindrical model with a diameter of 16 cm and a depth of 8 cm (Figure 13). The model was based on the maximal measures of the open chest wound cavity of five adults undergoing cardiac surgery through a complete median sternotomy. The mean depth of the studied cavities (average of cranial and caudal depths) during CPB with an empty heart was 7 cm (range 6.5-7.5 cm). The corresponding mean length (midline) and width of the wound opening were 19 cm (range 17-20 cm) and 10 cm (range 9-12 cm), respectively. A similar wound cavity model was used by Selman et al.⁶³

![Figure 13: Dimensions of the wound cavity model, and positions of the insufflation devices, and the horizontal measuring positions. Due to symmetry positions 6-8 were represented by measurements in positions 2-4.](image-url)
MATERIALS AND METHODS

Measurements
The air displacement efficiencies of the two open-ended tubes with different diameters and that of the gas-diffuser were studied. CO₂ flows of 2.5, 5, 7.5, and 10 L/min were used. Remaining air content was measured in a set of systematically distributed horizontal measuring positions (Figure 13) at every second cm below the opening. Ten values were recorded at each measuring point. The content of remaining air (\%\text{Air}) was analyzed by measuring the O₂ concentration according to the following formula:

\[
\%\text{Air} = \frac{\%\text{O}_2}{\%\text{O}_2(\text{ref})} \cdot 100
\]  

(5)

where %\text{O}_2 is the measured O₂ concentration and %\text{O}_2(\text{ref}) is the normal O₂ concentration in atmospheric air (20.95% near sea-level).\textsuperscript{87}

Study II

Torso measurements
The study of air displacement continued in a normally ventilated operating room for cardiac surgery. To reduce the number of measurements in patients, the greater part of the study was carried out in a full-scale torso (Figure 14), which was positioned on the operating table. The shape and size of the torso’s wound cavity were based on patient measurements during cardiac surgery (see study I).

CO₂ was insufflated into the wound cavity of the torso at 2.5, 5, 7.5, and 10 L/min with a multi-perforated catheter, and a 2.5-mm tube with either a gauze sponge or a gas-diffuser at its end. Their air displacement efficiency was tested when positioned at the level of the wound opening and inside the wound cavity, respectively, where they also were tested after exposure to fluid. The air content was measured at the upper level of the right atrium and repeated 10 times, by using the same method as in study I.

Figure 14: The torso model with a wound cavity and a silicone heart replica. The shape and measures of the wound cavity were based on in vivo measurements.
**MATERIALS AND METHODS**

**Patient measurements**
The device found most efficient in the torso measurements, the gas-diffuser, was further studied on 10 adult patients (six men and four women, median age 66.5 years, range 49-74) undergoing cardiac surgery with a complete sternotomy and during CPB when the heart was empty. The gas-diffuser was positioned inside the wound cavity as shown in Figure 15. CO₂ was supplied to the wound at a flow of 5 and 10 L/min, respectively. The air content was measured at the upper level of the right atrium and repeated 5 times in each patient.

The Institutional Ethical Committee approved the study, and informed consent was obtained from all patients.

**Study III**

**Set-up**
The degree of direct airborne contamination was studied at a part of our department facilities where people were walking to and fro. Airborne bacteria were sampled in a model of a chest wound cavity containing two standard 9-cm blood agar plates (Figure 16). The measures of the wound model were based on the maximal measurements of cardiac patients (study I). The model was elliptically shaped with a length, width, and depth of 20, 12, and 8 cm, respectively. A sterile insufflation device, a 2.5 mm open-ended tube or a gas-diffuser, was positioned at the acute end of the model with its orifice located approximately 2 cm inside the brim. The tube pointed towards the center of the model (Figure 16), a commonly used clinical position to achieve a central supply of CO₂, whereas the gas-diffuser, which produces a
multidirectional gas flow, was positioned at half the depth of the cavity pointing downwards. Since the open-ended tube was made by cutting away the diffuser of the gas-diffuser device, both insufflation devices included a 0.2\(\mu\)m bacterial filter, which prevented contamination of the wound model via the insufflated gas.

**Measurements**

Airborne contamination rates were studied in three experiments. Each experiment included one control model without insufflation and two competing models with insufflation via: 1) a thin open-ended tube and a gas-diffuser at a CO\(_2\) flow of 5 L/min, 2) a gas-diffuser with an air and a CO\(_2\) flow of 5 L/min, and 3) via a gas-diffuser at a CO\(_2\) flow of 5 and 10 L/min. After the experiment the agar plates were incubated at 37\(^\circ\)C for 48 hours, whereupon the number of colonies were counted.

**Study IV**

**Set-up**

*S. aureus* (Newman) inoculated on blood agar (5% horse blood) grew overnight at 37\(^\circ\)C. With a sterile inoculating loop bacteria from the colonies were transferred to the surface of 24 blood agar plates. The plates were divided into three groups, each with 8 plates, which were put in CO\(_2\) (100%), anaerobic gas (5% CO\(_2\), 10% hydrogen, 85% N\(_2\)), and air, respectively. In a second experiment the cultivated colonies were instead resuspended in phosphate-buffered saline to an optical density of 1.0 at 550 nanometer, of which 3 mL was added to a bottle containing 300 mL of brain-heart-infusion broth. CO\(_2\) or air was insufflated via a sterile pumice stone that was held immersed into the broth. In both experiments the samples were kept at 37\(^\circ\)C during the gas exposure.

**Measurements**

The blood agar plates were exposed to the different gases for 24 hours, whereupon a viable count of the colonies was made. The broth cultures were exposed to CO\(_2\) or air during 8 hours. After 0, 2, 4, 6, and 8 hours samples were taken and their optical density was measured. A viable count in number of colony forming units per mL (CFU/mL) was made on the 4 and 8-hour samples. The first experiment was repeated 8 times in a parallel set-up, whereas the second was repeated 8 times in a consecutive series. The culture medium’s pH was measured before and after the various gas exposures in both experiments.

**Study V**

**Set-up**

Different dilutions of *S. aureus* (Newman) were inoculated on standard blood agar plates (5% horse blood) and on sterile filter discs (diameter 6 mm). A plastic box, large enough to hold all agar plates and filter discs at the bottom and equipped with a sliding lid, was supplied with medical CO\(_2\) at a flow of 5 L/min. The gas-diffuser was used for the insufflation. The CO\(_2\) was humidified with deionized water, 70% ethanol, or 95% ethanol, using a bubble
MATERIALS AND METHODS

humidity. The humidifier was kept at room temperature in a heat regulated water bath in order to keep a stable degree of saturation throughout the 60-minute experiment.

Measurements
Agar plates were exposed during 0, 20, 40, and 60 minutes, respectively, and filter discs during 0, 5, 10, 15, 20, 40, and 60 minutes, respectively. After the exposure, the content of the filter discs were plated on blood agar plates to make a viable count. All plates were incubated overnight (18 hours) at 37°C, whereupon the number and size of the colonies were assessed. Twenty-four randomized experiments were carried out, i.e. eight repetitions per additive.

Study VI
Set-up
In a fully ventilated operating room the humidity and desiccation rate were studied in a cardiothoracic wound cavity model, which contained two standard blood agar plates (same as in study III, Figure 16). Dry and humidified CO2 was supplied to the model at 10 L/min via a ¼ inch open-ended tube or a gas-diffuser. Humidification was carried out as described in study V. The effects of insufflation were compared with a control without insufflation.

Measurements
First, room temperature and relative humidity inside the model were measured at steady state. Afterwards the two agar plates were weighed, without their lid, on a sensitive laboratory scale and placed into the wound model. The lids were then removed, and a timer started. Every five minutes the timer was stopped, the lids put back on the agar plates that were then removed from the model and quickly weighed again. This procedure was done while the gas was kept flowing, and was repeated six times in a row. Hence, the blood agar plates were subjected to desiccation for a total period of 30 minutes. In every experiment a fresh pair of room tempered agar plates were used. The five experiments, four types of insufflation and one control, were repeated ten times in a random order, which resulted in a series of 50 measurements.

STATISTICAL METHODS
Non-parametric data are presented as medians with quartiles or ranges, and Mann-Whitney U and Wilcoxon’s tests were used for pair wise comparisons. Normally distributed data are presented as means with standard deviations or ranges, and student’s t-test was used for pair wise comparisons. If data had suitable distribution characteristics analysis of variance (ANOVA) was applied, which included Bonferroni’s correction to account for multiple testing and post hoc tests for multiple comparisons. Otherwise a more conservative non-parametric analysis was chosen. Differences were considered statistically significant if $P < 0.05$. Data were analyzed with SPSS version 11.0 statistical program. Curve fitting by non-linear regression was carried out with NLREG version 5.3, whereas Microsoft Excel was used for linear regressions.
RESULTS

Study I

When tubes were used the mean air content was 18-96% at the studied CO₂ flows and depths of the cavity. Furthermore, both tubes produced a somewhat lower air content in the CO₂ jet, than at adjacent measuring positions (P < 0.01, Mann-Whitney U-test). With the gas-diffuser the mean air content inside the cavity (≤ 2 cm depth) was about 0.2% at CO₂ flows of 5-10 L/min. At 2.5 L/min the air content was significantly higher at all depths (P < 0.001). Three-, two-, and one-way ANOVA all revealed significant interaction of device, flow, and depth on air content (P < 0.001). There was an exponential relation between calculated outflow velocity and remaining air content in the wound model (Figure 17).

After discontinuation of CO₂ supply the diffusion rate decreased with time as the air content inside the cavity increased (Figure 18). Furthermore, the diffusion rate was found to be highest near the opening of the model. After 10 minutes the air content was almost 100% in the whole model.

Study II

All devices produced a much more efficient air displacement in the torso when they were positioned inside the wound cavity than when positioned at the level of the wound opening (P < 0.001, Figure 19). With one-way ANOVA the effect of device on air content was significant (P < 0.001). The following post hoc tests for multiple comparisons showed that all devices were significantly different from each other (P < 0.001). With two-way ANOVA comparing flows and devices the interaction device×flow was significant (P < 0.001). When exposed to fluid, the gauze sponge and the multi-perforated catheter immediately became inefficient,
whereas the gas-diffuser remained efficient (Figure 20). During surgery the gas-diffuser provided a median air content of 1.0% at 5 L/min, and 0.7% at 10 L/min (n.s.).

**Study III**

CO₂ insufflation at 5 L/min with an open-ended tube resulted in a contamination rate that was almost 4 times that of the control \( (P = 0.01) \), whereas with the gas-diffuser the contamination rate was lower \( (P = 0.01, \text{Figure } 21) \). With the tube the contamination rate was much higher on the agar plate that was exposed to the CO₂ jet than on the other plate \( (P = 0.01) \). With the gas-diffuser, air insufflation at 5 L/min markedly reduced the contamination rate compared with the control \( (P < 0.001) \), but was less protective than CO₂ insufflation at the same flow \( (P < 0.001) \). With both gases, the contamination rate was particularly low close to the gas-diffuser \( (P < 0.001) \). Increasing the CO₂ flow from 5 to 10 L/min reduced the average contamination rate in the model from 30% to 22% \( (P < 0.001) \) of the control (Figure 22).

---

**Figure 19:** Air displacement efficiency when the devices were positioned inside the torso’s wound cavity

**Figure 20:** Air displacement efficiency of the insufflation devices before and after they were exposed to fluid.

**Figure 21:** Contamination rate during CO₂ insufflation at 5 L/min with a tube and a gas-diffuser, relative that of a control (100%) without insufflation.

**Figure 22:** Contamination rate during CO₂ insufflation at 5 and 10 L/min with a gas-diffuser, relative that of a control (100%) without insufflation.
RESULTS

Study IV

On blood agar the number of bacteria per colony after 24 hours was about 100-fold lower in CO₂ than in anaerobic gas \((P = 0.001)\), and about 1000-fold lower than in air \((P = 0.001\), Figure 23). After the 24-hour exposure to air, anaerobic gas, and CO₂ the median surface pH on eight non-inoculated blood agar plates were 7.2, 7.2, and 6.8, respectively. Before gas exposure the median surface pH was 7.4 in all three groups.

In broth culture after 2 hours the number of bacteria, measured in optical density, was increased with air \((P < 0.001)\) but not with CO₂ \((P = 0.13\), Figure 24). After 4 hours the median number of CFU/mL was about 100-fold lower with CO₂ than with air \((P = 0.002)\). After 8 hours with air the median number of CFU/mL had increased about 100-fold \((P = 0.01)\). By contrast, with CO₂ after 8 hours there was no significant increase in the median number of CFU/mL \((P = 0.12)\), which was then about 1000-fold lower than with air \((P = 0.003)\). After 8 hours the broth culture’s optical density had increased from an initial zero-value to 1.2 with air but only to 0.01 with CO₂ \((P = 0.001)\). The median pH in the broth cultures were 7.3 before exposure to air and CO₂, and decreased to 6.3 and 6.5, respectively, after 8 hours.

![Figure 23: Number of bacteria per colony on inoculated blood agar plates, after incubation at 37°C for 24 hours in different gas environments.](image)

![Figure 24: Optical density of broth culture after 0 to 8 hours of bacterial growth at 37°C during continuous insufflation of air or CO₂.](image)

Study V

On filter discs, CO₂ carrying vapor from a 95% ethanol solution decreased the number of CFU:s after 5 minutes of exposure \((P = 0.04)\), and killed all bacteria within 10 to 15 minutes \((P < 0.001\), Figure 25). The bacterial colonies from the 10-min samples were smaller than those obtained from the unexposed samples \((p = 0.02)\). On exposed blood agar plates, the colony size decreased with exposure time, and no colonies were detected after 60 minutes of exposure \((P < 0.001\), Figure 26). Antiseptic gas derived from 70% ethanol solution was less effective than that derived from 95% ethanol \((P < 0.001)\). CO₂ humidified with water did not have a significant effect on number or size of the colonies. The exposed blood agar never became transparent, which was a rough indication that haemolysis did not occur.
Study VI

The humidity in the wound cavity model under the various experimental conditions all differed significantly ($P < 0.05$, Figure 27). The accumulated water loss (mg/cm$^2$) in the model increased almost linearly with time, irrespective of the humidity of the gas or the vehicle for its supply ($R^2 \geq 0.97$). Significant differences appeared between the five groups as to their desiccation rate, i.e. the inclination of the water loss curves ($P \leq 0.001$). Dry and humidified CO$_2$ insufflation via the open-ended tube resulted in much higher desiccation rates than the control (Figure 28). Insufflation of dry as well as humidified CO$_2$ caused a much higher desiccation rate on the distal plate than on the proximal one ($P = 0.005$). When insufflated via a gas-diffuser, dry CO$_2$ gave a slightly higher desiccation rate than that of the control, but humidified CO$_2$ lowered the rate in the model to $< 10\%$ of the control. With both dry and humidified CO$_2$ the desiccation rate was higher on the proximal plate than on the distal one ($P = 0.005$).
COMMENT ON EXPERIMENTAL DESIGN

Assessment of air displacement

Although air is a mixture of several gases, mainly N\textsubscript{2} (78\%) and O\textsubscript{2} (21\%), it acts as one gas at normal atmospheric pressure and temperature. Furthermore, Avogadro’s law states, “At constant pressure and temperature equal volumes of different gases contain equal amounts of gas molecules”. This means that for every five CO\textsubscript{2} molecules that are supplied to a cavity, five air molecules are displaced of which approximately four are N\textsubscript{2} molecules and one an O\textsubscript{2} molecule (Figure 29). Thus, when the content of one of the gases is measured, the content of the other gases is indirectly measured at the same time.

The facts that N\textsubscript{2} is the major constituent of air and is probably its most harmful component, are valid arguments in favor of direct measurement of the N\textsubscript{2} content instead of the O\textsubscript{2} content in the assessment of air displacement. However, N\textsubscript{2} is difficult to detect. The molecules have a very strong chemical bond, which makes N\textsubscript{2} a fairly inert gas. Moreover, the molecules are not dipoles and do not absorb energy from electromagnetic radiation in the infrared or ultraviolet range. Therefore, conventional chemical, magnetic, or optical sensor techniques cannot be used. Consequently, practical instruments are not available for intraoperative measurements. However, air displacement with CO\textsubscript{2} can be assessed by measuring the content of CO\textsubscript{2} or O\textsubscript{2}\textsuperscript{10,63} present in the wound.

The used O\textsubscript{2} instrument with a heated ceramic sensor can assess air displacement more accurately and faster than commonly used CO\textsubscript{2} sensors that utilize an optical infrared sensor technique to measure CO\textsubscript{2} concentrations up to 100\%. The O\textsubscript{2} sensor’s accuracy is 1\% of the measured value in the range 0.0001%-100\% O\textsubscript{2}, which means that the accuracy increases when the O\textsubscript{2} and the air content decreases. Moreover, the O\textsubscript{2} sensor requires only a 2 mL gas sample volume and has a response time of < 2 seconds, resulting in a sampling flow of < 0.06 L/min. This causes a low degree of interference with the experiments. Furthermore, the allowed thin sampling probe, only 1.5 mm thick, made it possible to measure the air content at exact positions, and also caused little interference with surgery during the patient measurements. In contrast, CO\textsubscript{2} sensors using the infrared technique usually have a constant...
accuracy of approximately \( \pm 2\% \) units CO\(_2\) over the entire range of measurement 0-100\% CO\(_2\), a larger required sampling volume, and a longer response time, usually > 10 seconds.

Both in the torso and in patients the air content was measured at the upper level of the right atrium, which is close to the atrial incision during mitral valve replacement. Measuring the air content at the bottom of the wound cavity, as reported by Webb et al.,\(^6\) may lead to an overestimation of the air displacement efficiency, since CO\(_2\) tends to accumulate at the lowest point, and since diffusion with air is less marked there.\(^8\)

**Assessment of airborne contamination**

Bacteriologic wound sampling methods, such as wound washout\(^{46,51}\) and the use of absorption swabs or pads,\(^44\) are not quantitative and will not differentiate between direct and indirect wound contamination.\(^46\) Sedimentation plates are used in vivo for assessment of direct airborne contamination close to the surgical wound. However, wound ventilation is based on insufflation of a gas into a wound cavity and the use of sedimentation plates inside the wound is impossible during surgery. The study did not include simulated surgery in a fully ventilated operating room since this would provide insufficiently low contamination rates on a 9-cm agar plate.\(^{43,52}\) Usually when assessing direct airborne contamination in the surgical field, several 14-cm agar plates are needed to obtain sufficient sensitivity.\(^{43,52}\) In order to increase the sensitivity of this settle plate sampling method, the experiment was carried out at a place outside the operating room where people were walking to and fro.\(^8\) The differences in contamination rates in the controls between the three experiments were therefore most probably due to differences in the number and activity of the people present in the facilities. Since paired comparisons were made throughout, and since the contamination rate was expressed as a percentage of the control (without insufflation), these variations were irrelevant. Furthermore, an experimental study with paired comparisons and the use of standardized symmetric wound models facilitated the detection of differences in contamination rates, and the comparison with theoretical predictions.

**Assessment of antibacterial effects**

In both study IV and V the bacterium *S. aureus* was studied since this pathogen is the most common cause of wound infection in cardiac surgery.\(^{28,31,34,36}\) There is an important difference between the two experiments that may need to be made clear. Study IV investigated the bacterial multiplication rates during growth in different environments, whereas study V investigated the decontamination and growth inactivation effects of a short gas exposure whereupon the samples were left to grow in optimal conditions, in air at 37\(^\circ\)C.

When the bacteriostatic effect of CO\(_2\) was studied (study IV), the relevant variables were kept constant. Thus, in contrast to earlier food related studies,\(^{74,77}\) the growth temperature was kept at body temperature and the CO\(_2\) concentration at 100\%. Since the microbial activity in a contaminated surgical wound is initially located at the surface there is a gas-solid interface that is being dealt with rather than a population dispersed in a liquid medium. Growth on blood agar, not used in food studies, may thus be more clinically relevant, but in order to analyze the outcome of that experiment the incubation time had to be long for the bacterial
colonies in the CO2 atmosphere to become visible. Growth in the broth cultures enabled study of shorter incubation times.

In study V gasified ethanol was used in an antiseptic CO2 mix. Ethanol is a potent antiseptic agent with well-known properties in the liquid form. Furthermore, since ethanol is available in high concentrations and is one of the most rapid acting of antiseptics, it was suitable for testing the potency of the present antiseptic method. Disinfectants, i.e. agents that are used on inanimate materials, must be tested on resting cells in the absence of nutrient compounds. However, laboratory experiments testing the efficacy of antiseptics should include controls for what is present in wounds, namely organic material. In the present study the antiseptic effect of gaseous ethanol was therefore evaluated both on filter discs and blood agar plates. Incubation overnight made it possible to study both decontamination and growth inactivation effects. The latter would have been more difficult to detect after longer incubation, since bacterial growth eventually recovers after an extended lag-phase. Decreased colony size was used as a simple indication of growth inhibition. Assuming that the size of the bacterial cells is constant, the number of bacteria in a colony directly determines the colony size.

**Assessment of desiccation rate**

Desiccation results from superficial water loss, described by Equation 4. The water loss from blood agar, which provides a wet surface like a fresh surgical wound, was quantified under different surgical conditions. Since the dimensions of the agar plate are known, its weight loss could easily be converted into water loss per cm² of exposed surface. As in study V, the humidifier was kept at room temperature and not higher, to prevent condensation in the gas delivery system and in the wound model. Condensation would have interfered with our measurements. The experiment was performed when the relative humidity was around 45% (control), which is about the middle of the normal range of variation (10-90%). Furthermore, water loss was measured during 30 minutes in order to ascertain whether the accumulated water loss was linear or not. The same period has also been used in earlier studies of desiccation.

**Insufflation devices**

The present study included the new gas-diffuser and conventional insufflation devices that have been reported. The conventional devices’ orifices were positioned and directed in the wound cavity according to recommendations when available. The position of the insufflation devices at the caudal end of the wound cavity was chosen for two reasons. Firstly, in open-heart surgery the CO2 insufflation device is usually positioned there since it causes little interference with surgery. Secondly, the caudal position made it possible to study whether effects varied with the distance from the device.
**DISCUSSION**

**CO₂ flows**

CO₂ flows higher than 10 L/min were not studied since only flows of 10 L/min or less have so far been reported for CO₂ de-airing in cardiac surgery. Furthermore, flows of ≥ 5 L/min were found to be sufficient for de-airing of a wound cavity model.

**Wound cavity models**

In order to obtain reliable estimates of the various effects of exposure to ambient air (study I-III and VI), the shape and size of the wound cavity models were based on the maximal measures in patients (study I).

**COMMENTS ON EXPERIMENTAL RESULTS**

**Air displacement**

*Open-ended tube*

CO₂ de-airing of a cardiothoracic wound cavity has to include the cannulation sites of the aorta and the incisions of the heart. However, since the maximal de-airing efficiency of tubes was found to be restricted to a small area in front of the CO₂ jet they cannot satisfy this requirement. The fact that the air content in the CO₂ jet was high even at close range may be explained by ambient air being sucked down with the jet, the so-called ejector effect. All in all, the open-ended could not produce efficient air displacement at any studied CO₂ flow.

*Multi-perforated catheter*

The multi-perforated catheter delivers CO₂ from multiple holes. Assuming that the outflow is more or less equally distributed over the various holes, their great number will substantially reduce outflow velocity and turbulence. However, when the catheter is curved the assumption is no longer valid. When CO₂ meets a curve in the multi-perforated catheter gas will tend to escape through the first holes in the outer side of the curve. The air content in the wound cavity increased with enhanced CO₂ flow, which points to increased turbulence. Moreover, a multi-perforated catheter or a commercial drain is designed to remove blood, which is almost always present at the bottom of the pericardial well. Once fluid enters the multi-perforated catheter its distal part will be blocked and inactivated leading to increased outflow velocities, turbulence, and air contents in the wound cavity (Figure 20).

*Gauze sponge*

The use of a gauze sponge presupposes the tortuous paths inside it to distribute the CO₂ gas uniformly over a much larger surface, thus reducing gas velocity. Because of their hydrophilic properties gauze sponges are used for absorption of fluids. When the gauze sponge gets wet, its structure collapses and its function as a diffuser is lost (Figure 20). Thus, during surgery an undetected absorption of fluid by the gauze sponge will within seconds lead to a significant rise in air content and thus a risk of air trapping. Since almost any surgical wound, and in particular the cardiothoracic wound, is wet, one would then have to measure the CO₂/air
content continuously in order to know when to exchange the gauze sponge. This is not practical.

**Gas-diffuser**
When positioned a few cm below the wound opening the gas-diffuser produced a higher degree of air displacement than all other devices (Figure 17 and 19). In terms of lowest median air content, the gas-diffuser was approximately 8 and 30 times more efficient than the dry gauze sponge and dry multi-perforated catheter, respectively, and 120 and 580 times more efficient than the ¼ inch and 2.5 mm open-ended tube, respectively.

The gas-diffuser remained efficient when exposed to liquid (Figure 20). Due to its elastic properties the diffuser foam does not collapse even when soaked, and as gas is blown through the diffuser, large parts of its cell structure will remain open. If the gas-diffuser gets partly covered with tissue or blood, which occurred frequently in our patient study, its function will not be affected. According to the law of least resistance the CO₂ gas will automatically be redirected inside the diffuser foam to exit through an open part (Figure 12).

Although the foam material of the gas-diffuser is hydrophobic, the foam may absorb and store a liquid if it is completely drowned and at the same time compressed, just as a car wash sponge would. However, if the gas-diffuser unexpectedly becomes soaked through, a short compression with the tip of a finger will evacuate the fluid and restore the function of the gas-diffuser. The same does not hold true for a wet gauze sponge due to its lack of hydrophobic and elastic properties.

**Diffusion**
In the present study the impact of diffusion on air displacement was only observable with the gas-diffuser and was only prominent at a CO₂ flow of 2.5 L/min with significantly increased air contents at all depths in the cavity. Higher CO₂ flows compensated for the CO₂ that diffused out of the cavity and for the air that correspondingly diffused into the cavity. Earlier studies have suggested a minimum required CO₂ flow between 2 to 5 L/min,⁵,¹⁰,⁶³ but the reason for this has hitherto not been explained.

The shallowest part of a cardiothoracic wound cavity is the anterior part of the aortic root, usually 3-4 cm below the wound edge in adult patients. However, our data imply that diffusion had a minimal effect on the de-airing already at a depth of 2 cm and deeper when CO₂ was supplied at a flow of ≥ 5 L/min.

**Turbulence**
The larger the dispersing area of the insufflation device, the lower is the outflow velocity. The dispersing area of the gas-diffuser corresponds to that of an open-ended tube with an inner diameter of 36 mm. This is more than 30 times greater than the inner cross-sectional area of the ¼ inch tube and more than 200 times greater than the inner cross-sectional area of the 2.5 mm tube.

The major cause of insufficient air displacement with tubes was consequently high velocities of the CO₂ jets and the turbulence that they produced in the wound cavity model. The same phenomenon occurs when one tries to fill a pail with water using a garden hose. Most of the water splashes out of the pail. By contrast, the pail is quickly filled if the hose is
DISCUSSION

provided with a multi-perforated nozzle resulting in a reduced outflow velocity. Figure 17 demonstrates how the air content in the cavity rapidly increased with increasing outflow velocity. Thus, only a slight increase in outflow velocity of the CO₂ gas has a destructive influence on the air displacement.

It was earlier thought possible that a laminar internal CO₂ flow in open-ended tubes would be a sufficient condition to avoid turbulence in the wound cavity and thus to obtain efficient air displacement. With the results from study I at hand (Figure 17) the hypothesis can be tested. The type of flow inside a tube is described by the dimensionless “Reynolds number” defined as:

\[
Re = \frac{w \cdot d}{\nu}
\]  

(6)

where \( w \) is the mean flow velocity inside the tube, \( d \) the inner diameter of the tube and \( \nu \) the kinematic viscosity of the gas. When Re is 2300 or lower the flow is laminar, and when Re is about 10 000 the flow has become fully turbulent in the tube. By inserting the inner diameter of the ¼ inch tube (6.35 \( \cdot \) 10⁻³ m), the kinematic viscosity of CO₂ (8 \( \cdot \) 10⁻⁶ m²/s), and a Reynolds number of 2300 into the above equation we find the flow velocity \( w \) to be 3 m/s. Thus, up to this internal flow velocity the flow is laminar in the ¼ inch tube. But in Figure 17 we see that this flow velocity corresponds to an unsatisfactory air displacement. This implies that although the CO₂ flow inside the tube is laminar the jet still causes turbulent gas mixing in the wound cavity model. Obviously, eliminating the internal turbulence in an open-ended tube is not a sufficient condition for efficient air displacement. Thus, that hypothesis can be rejected.

Direct airborne contamination

The open-ended tube substantially increased the rate of airborne contamination on the distal agar plate that was exposed to the CO₂ jet, where the contamination rate was almost 4 times that of the control (Figure 21). Most likely, the jet dragged ambient air down and ejected airborne particles onto the surface.

Insufflation of CO₂ provided a better protection than insufflation of air. Since CO₂ is not bactericidal in room temperature and atmospheric pressure, this difference is probably related to the greater density of CO₂. According to Stokes’ law (Equation 2) the greater density of CO₂ should only marginally decrease the settling velocity of airborne particles, i.e. increase their buoyancy. The different protective effects may thus be explained by different flow patterns. Due to its greater density, CO₂ acts like a liquid in the cavity.

Stokes’ law predicts that the airborne contamination rate will be reduced if the CO₂ flow is raised from 5 to 10 L/min (Equation 2 and 3). In the studied wound model the increased flow reduced the average contamination rate from 30% to 22% compared with the control (Figure 22). Thus, the relation between flow and contamination rate seems to be non-linear,
in such a manner that a further doubling of the flow will have less effect on the airborne contamination rate.

**Bacteriostatic effect of CO₂**

On blood agar the bacteria grow in colonies, whereas in broth culture all bacteria appear as single cells detached from each other. Despite this difference, both experiments showed that the bacterial growth rate in CO₂ was much lower than the aerobic growth rates. Figure 23 shows and confirms that the bacteriostatic effect of CO₂ is not only a result of O₂ deficit but also of a specific CO₂-effect, which in fact turned out to be the more important contribution. This difference between growth rates in CO₂ and anaerobic atmosphere, containing only 5% CO₂, also shows that the CO₂-effect is dependent on a high CO₂ concentration. As expected, the studied gases all caused only a slight and bacteriologically insignificant decrease in pH in the growth mediums. The results of this study indicate that CO₂ provides a significant bacteriostatic effect within the duration of most cardiac procedures (Figure 24).

**Antibacterial effect of antiseptic CO₂ mix**

The most important result of this experiment is that the small addition of an antiseptic agent to the CO₂ via simple bubble humidification is enough to create a bactericidal gas (Figure 25). This is even more surprising when realizing that only a fraction of the insufflated gas comes into contact with the exposed surface as a molecular layer.

Organic material may reduce the antimicrobial effect of a topically applied antiseptic by reacting with it or by diluting it. Obviously this also holds true for gaseous agents, since the bactericidal effect of gaseous ethanol on inoculated blood agar plates (Figure 26) was delayed compared with that on inoculated filter discs. With the chosen incubation time it cannot be excluded that some bacteria were not killed on the blood agar. Nevertheless, a pronounced inhibition of growth could be seen. The colony size decreased with increasing exposure time. The almost linear relationship between reduction in colony size and exposure time, and the influence of ethanol concentration, was probably a result of accumulation in the blood agar medium. In the clinical situation, the accumulation of a gaseous antiseptic will be most pronounced in parts of the wound that have little or no perfusion, e.g. necrotic and fat tissue. These parts are also most prone to infection. The observed growth inhibition may also have been due to a growth inactivation effect during the gas exposure, since the colony size decreased with exposure time also in the filter disc experiment where there was no organic material present.

**Wound desiccation**

This study showed that even with a relative humidity of 45% (Figure 27), exposure to the operating room ventilation alone causes substantial desiccation (Figure 28). The desiccation rate should vary with the relative humidity of air in the operating room and may also vary with its type of ventilation system. Insufflation of dry as well as humidified CO₂ via the open-ended tube increased the desiccation rate 2-3 times, and the increase was most marked in the
area directly exposed to the jet. Accordingly, it has been found that even humidified CO₂ causes endothelial damage during high-flow gas insufflation to facilitate the suturing of a precise coronary anastomosis.⁶¹ Conversely, although insufflation of dry CO₂ with the gas-diffuser produced almost zero humidity in the model, the rate of water loss was only slightly higher than the control without any insufflation. In fact, on the plate distal to the gas-diffuser the desiccation rate was significantly lower than in the control. The reason should be that the very low outflow velocities from the gas-diffuser reduce the turbulent convection,⁸⁸ see Equation 4. Furthermore, CO₂ is heavier than air and tends to gravitate towards the surface and covers it almost like a protective layer. This also explains the dramatic fall in the desiccation rate to about 1/10 of the control value when humidified CO₂ was delivered via a gas-diffuser. Again the CO₂ gravitates towards the surface but this time the gas-layer contains water. This effect should be independent of the relative humidity in the operating room air, because the gas-diffuser has been found able to provide almost complete air displacement in a cardiothoracic surgical wound.⁹² Since the relative humidity of a gas increases when its temperature decreases, the protective effect of humidified CO₂ may be slightly higher on colder tissue surfaces, such as the epicardium during CPB, and slightly lower on warmer.

**CLINICAL IMPLICATIONS**

**The wound ventilator**

The efficiency of wound ventilation partly depends on the individual efficiency of the wound ventilator’s components (Figure 30).

*Figure 30: A schematic picture of the wound ventilator and its different parts.*
**DISCUSSION**

**Ventilation gas**
As this study shows, CO₂ is unique in several aspects that make it suitable for wound ventilation. Admittedly, medical air delivered directly from the anesthetic central supply may be used to reduce airborne contamination and wound desiccation. However, this will probably be less effective than with CO₂ due to the lack of a density difference. Moreover, air cannot be used in cases when there is a risk of air embolism. Other gases may not come into question, and any mixture of gases probably has to be based on CO₂. For instance, use of O₂ would pose a fire or explosion hazard.

**Gas source**
Since CO₂ is so far not widely used in health care, it is usually delivered from mobile pressurized gas cylinders. The cylinders are equipped with pressure and flow regulators including a flowmeter, which usually is back-pressure compensated. This means that the flow is automatically kept constant even when a minor flow resistance occurs in the gas line distal to the flowmeter. Most clinicians use O₂ flowmeters since CO₂ flowmeters are rarely available. Due to the greater density of CO₂ the flow marker, usually a spherical float, should then be set at a flow that is approximately 10% higher than the CO₂ flow one aims at.

**Humidifier**
Since only dry CO₂ has so far been used for de-airing in open-heart surgery, no special device has been developed for gas humidification. The bubble humidifier used in this study is commonly employed for humidification of respiratory gases. It is a disposable, prefilled bottle that forms a closed sterile system and should also be suitable for intra-operative use.

In order to attain a constant and high degree of humidification with a bubble humidifier, it must be continuously heated. Since cold gas cannot carry as much water as does warm gas, cooling reduces the humidification efficiency. The cooling effect is due to two thermodynamic phenomena. Firstly, gas delivered from a pressurized system has a very low temperature as a result of its sudden expansion. Secondly, humidification is an evaporative process that requires energy and thus lowers the water temperature in the humidifier. Heating the humidifier in a water bath is suitable due to the good heat conduction of water. An advantage of bubble humidifiers in this respect is that the bubbling effectively stirs the humidification agent, which contributes to efficient heating. Keeping the humidifier at room temperature gave CO₂ a relative humidity of about 75%. Heating above room temperature may cause condensation in the gas line, which would require a heated gas line or a water trap close to the wound. None of these accessories are part of the present gas-diffuser device since it was originally designed for insufflation of dry CO₂. However, such components may well be used together with the gas-diffuser device. On the other hand, they may not be needed. Since the heart is actively cooled during CPB the relative humidity of supplied gas may increase automatically close to the tissue surface. Furthermore, if an antiseptic agent is used with an initial relative humidity close to 100%, toxic condensation may form on such cold surfaces. Thus, a saturation degree of 75% may be suitable after all.

Humidifiers that produce a mist, i.e. nebulizers, should not be used since they will cause condensation in the delivery system, and since an opaque mist in the wound will make
surgery more difficult. Furthermore, if an antiseptic agent is used, condensation and even micro-droplets from the mist may be toxic in the wound.

**Humidification agent**

Many different humidification agents may be considered for wound ventilation.\(^{57,95-97}\)

As for antiseptic wound ventilation, the present study showed that the antibacterial effect of gaseous ethanol is reduced in the presence of organic material. An even better effect may be expected from chlorhexidine-gluconate, since in its liquid form it has been shown to be effective also under those conditions.\(^{55}\) Furthermore, a mix of different antiseptic agents can be synergistic, which may prolong and widen the antimicrobial effect.\(^{85}\) For example, high concentrations of alcohol with 0.5% chlorhexidine are used for preoperative skin antisepsis, which then combine the rapid effect of alcohol with the residual effect of chlorhexidine. A combination of different agents can also reduce the concentration of the individual substances, which lower their toxicity without reducing the antimicrobial effect.\(^{85}\) Furthermore, it may well be that a bactericidal effect is not necessary for the prevention of wound infection, especially since airborne contamination is reduced. Increasing the bacteriostatic effect of CO\(_2\) with an antiseptic component may be sufficient.

For prevention of wound desiccation the natural humidification agent is water. As stated above, disposable bubble humidifiers that are prefilled with sterile water are available. Other solutions, such as biocompatible polymer solutions, e.g. sodium hyaluronic acid and carboxymethyl cellulose,\(^{57,95}\) may show to be useful in wound ventilation for prevention of cardiac adhesions. However, it remains to be tested whether CO\(_2\) gas can carry substances made up of large and complex molecules.

It is not yet clear if a gaseified antiseptic such as ethanol may increase desiccation, as is the case with liquid ethanol, which dissolves lipids. Future research may lead to the development of a “perfect” mix of agents that combine antibacterial effects with prevention of desiccation. It should be kept in mind that, due to differences in volatility, the relative concentrations of agents in such a liquid mix may change as it is gasified in a bubble humidifier.

**Insufflation device**

Open-ended tubes should not be used for gas insufflation into a surgical wound due to the poor air displacement efficiency and the increased rates of direct airborne contamination and wound desiccation. A multi-perforated catheter and a gauze sponge are more effective as gas dispersers than a tube, but only as long as they are not exposed to a fluid. Conversely, with the gas-diffuser an almost 100% CO\(_2\) atmosphere can be maintained in a cardiothoracic wound cavity, both during wet and dry conditions, and will most likely contribute to reduce airborne contamination and desiccation during surgery.

**Recommended use**

Although the wound ventilator may be properly designed, it still has to be used correctly for wound ventilation to be effective.
**Position of the gas-diffuser**

A wound ventilator should provide total air displacement in the wound cavity without disturbing surgery.

The present study showed that CO\(_2\) must be delivered from within the cardiothoracic wound cavity in order to achieve a high degree of air displacement. Theoretically the air displacement should be more efficient the deeper down the orifice of the device is positioned. However, although the gas-diffuser can tolerate contact with fluid, the diffuser may become drowned in blood if positioned at the bottom of the wound cavity. Thus, a position at half the depth is suitable. If the gas-diffuser would accidentally become soaked, compressing it with a finger will remove the fluid and restore the gas-diffuser’s function.\(^{98}\)

There is limited space in the wound during cardiac surgery. Other surgical equipment, such as cannulas and aortic x-clamp, usually occupy the cranial side, where also the depth is often insufficient to prevent the orifice of the device from getting submerged in blood collections. The space along the sides near the sternal retractor is not suitable since it might have to be adjusted during the operation, and since the surgeon’s movements are often forceful when handling the heart with his hands and with compresses. By contrast, at the caudal part of the wound there is little surgical action and surgical equipment.

Thus, the gas-diffuser should be positioned at the caudal end of the wound, at about half the depth of the cavity.

**Flow**

External disturbances, including diffusion,\(^{88}\) convective air currents around the wound caused by the operating room ventilation,\(^ {99}\) surgical hand movements, and use of suction,\(^{100}\) may increase the air content in the wound unless compensated for with an increased inflow of CO\(_2\). In wound models and in patients a CO\(_2\) flow of 5 L/min sufficed to reach a high degree of de-airing (1% remaining air) during active surgery without use of suction. However, in a related paper the author and colleagues showed that the use of rough suction will deteriorate CO\(_2\) de-airing unless the CO\(_2\) flow is equal or higher than the suction rate.\(^{100}\) It was also found that a CO\(_2\) flow higher than 5 L/min is needed for rapid filling of the wound cavity with CO\(_2\),\(^ {99}\) which is of importance initially and if CO\(_2\) accidentally has been removed from the wound during surgery. Thus, a CO\(_2\) flow of 10 L/min is recommended for wound ventilation in conventional cardiac surgery.

Furthermore, the rate of direct airborne contamination was found to be lower at a CO\(_2\) flow of 10 L/min than at 5 L/min. It is probably difficult to reach a contamination rate of 0% even with moderately higher flows, since there may always be a fraction of larger airborne particles\(^ {39,71}\) that have much greater settling velocities than the upward gas velocity achieved. On the other hand, making the wound opening smaller with a surgical drape can theoretically further decrease the contamination rate, not only due to a smaller exposed area but also because of an increased upward gas velocity through the opening.

**Duration**

During open-heart surgery air may be trapped in the heart and the great vessels and may not be released until late after closure of the heart.\(^9\) It is important that these gas pockets are filled up by CO\(_2\) instead of air. This requires that CO\(_2\) is supplied from the first cardiac incision. If
the CO2 supply is discontinued the surrounding air will soon mix with CO2 in the wound cavity (Figure 18). Therefore CO2 should be supplied until the heart and great vessels are closed.

Not only prevention of air embolism, but most functions of wound ventilation require a continuous CO2 flow. The protection against direct airborne contamination is active as long as there is a CO2 flow. Moreover, the bacteriostatic and antiseptic effects, and the wound humidification are dependent on a fully developed CO2 atmosphere in the surgical wound. Since a bacterial population increases exponentially with time, the bacteriostatic effect of CO2 becomes more and more important the longer the operation lasts. Thus, especially long procedures should benefit from the inhibition of bacterial growth. Furthermore, fat tissue including subcutaneous fat is poorly perfused and thus prone to infection. However, fat tissue will quickly absorb large amounts of CO2 that will be stored because of the slow loss rate. Hence, this sensitive tissue will possibly also longer retain a bacteriostatic effect postoperatively. As for desiccation, the surgical wound is subjected to desiccation immediately after incision. Thus, wound ventilation should be applied as long as the chest wound is open. The addition of an active agent other than water, for humidification and/or antisepsis, may be applied throughout the operation or only temporarily after incision or before closure for coating of the inner wound surfaces.

All cardiac cases?
Wound ventilation with CO2 should be used in cardiac surgery when there is a risk of air embolism. This risk is admittedly higher in open heart surgery but not negligible during closed heart surgery such as coronary bypass, where intracardiac air has been detected in between 11% and 53% of cases. Currently, the incidence may be even higher due to the increased use of the single clamp technique in coronary bypass surgery. One could therefore speculate if wound ventilation should be applied in all cardiac cases, especially in view of the fact that other preventive effects could be gained from it simultaneously.

Financial aspects
The cost for medical CO2 at continuous supply with a flow of 10 L/min during 3 hours is about 15 US$ at our Hospital, and that of a disposable bubble humidifier (340 mL) is about 4 US$. The market price for the disposable gas-diffuser device has not yet been set.

Environmental aspects
Breathing air
Inhalation of high concentrations of CO2 may increase the breathing rate or even cause fainting-fits. However, due to the high density of CO2, surplus CO2 will drain away quickly from the surgical wound to the floor. The gas finally escapes via the extraction system as do anaesthetic gases. In a not yet published study the author and colleagues measured the CO2 concentration in cardiac patients, where CO2 was insufflated at a flow of 10 L/min via a gas-diffuser. At 10 cm above the wound opening the CO2 concentration was less than 1%.
Furthermore, CO₂ has been used for de-airing for almost 50 years now and there have not been any reports of such side-effects.

As for antiseptic wound ventilation, ethanol may be an attractive “non-toxic” agent in the view of the fact that the antiseptic gas is released into the open air. Moreover, the addition of a heavier component such as ethanol (C₂H₅OH) to CO₂ will theoretically expedite the draining away of the gas from the wound.

**Inflammability**

As a rule inflammable antiseptic agents such as alcohol are not used intraoperatively. During surgery such an agent may ignite by the use of thermo-electrical instruments like diathermy. In a pilot study the amount of 95% ethanol needed for 1 hour of CO₂ insufflation at 5 L/min (300L CO₂) was found to be about 20g, which is equal to about 3 vol.% of the insufflated gas mixture. Admittedly, this corresponds to the lower range of the explosion limit of ethanol in air, but for the mixture to inflame it must first be diluted with air. Any such dilution of the CO₂ will imply a corresponding dilution of the ethanol. Consequently, the vol.% of ethanol will always remain below the explosion limit in air. CO₂ is commonly used as a fire extinguisher as it is chemically stable and cannot support a fire, and since it efficiently excludes ambient air by gravity. Thus, flammability risks with ethanol in CO₂ can theoretically be ruled out.

**Discharge of greenhouse gas**

When considering a method that is based on continuous outflow of a greenhouse gas, such as CO₂, we need to understand to what extent this will contribute to the worldwide CO₂ discharge. Continuous wound ventilation during a 3-hour cardiac operation will use about 3 kg CO₂. This corresponds to the discharge from a regular car during a 15 minutes’ drive. It should also be noted that medical CO₂ (AGA AB, Sweden) is a recycled byproduct from beer, spirits, and fertilizer production.

**Clinical significance**

This thesis is based on experimental studies. Although they provide promising results, the clinical significance of wound ventilation can only be determined in clinical studies that show whether wound ventilation actually reduces the incidence and degree of postoperative cerebral and myocardial dysfunction, wound infection, and cardiac adhesion.
The study showed that an open-ended tube, a tube with a gauze sponge at the end, or a multi-perforated catheter cannot efficiently supply CO₂ to a cardiothoracic wound. These devices provide gas at too high velocities and the resulting turbulence mixes and dilutes the CO₂ in the wound with ambient air. This not only cause a low degree of air displacement, but also a much higher rate of direct airborne contamination and desiccation (even with humidified CO₂) of the open surgical wound than when CO₂ is not insufflated.

By contrast, CO₂ insufflation with the new gas-diffuser positioned below the wound edge will remove more than 99% of the air in the cardiothoracic wound cavity. At a continuous flow of 10 L/min, wound ventilation will thus significantly decrease the risk of air entering the heart and great vessels. Moreover, wound ventilation may help to reduce the risk of postoperative wound infection in three different ways. Firstly, the laminar outflow of CO₂ from the wound opening can reduce direct airborne contamination of the wound. Secondly, the bacteriostatic effect of CO₂ can decrease the growth rate of bacteria in the wound. Thirdly, a mix with a few vol.% of a gasified antiseptic agent may decrease the number of bacteria in the wound or inhibit their growth even more. Furthermore, wound ventilation with humidified CO₂ should significantly reduce desiccation of the exposed wound tissue.

This thesis has proposed intraoperative wound ventilation as a new concept for prevention of various complications in cardiac surgery. The method’s potential was explored in experimental studies. Future research may evaluate the clinical significance of wound ventilation and further adopt it for clinical use. The new possibilities of efficient wound ventilation may also have clinical implications in other surgical disciplines.
ACKNOWLEDGEMENTS

PERSONAL

I would like to express my deep gratitude to all persons that have helped me in this work.

♦ **Associate Professor Jan van der Linden**, my main supervisor. With your positive attitude it is difficult to fail. Whenever I had doubts about this work, one minute of conversation, if not less, was enough to turn sorrow into joy. I am still amazed by this phenomenon. No doubt we share a personal as well as a scientific curiosity and understanding, and due to our different academic backgrounds our collaboration has been fun and productive. **Marie van der Linden**, thank you for lending me your husband during these years.

♦ **Professor Håkan Elmqvist**, my assistant supervisor. Thanks for adopting me as a PhD student in the first place at the Division Medical Engineering, Karolinska Institute, and for offering help and resources whenever needed. I am most grateful that you gave me the scientific freedom I needed to be creative.

♦ **Associate Professor Dan Lindblom**, head of the Department of Cardiothoracic Surgery & Anesthesiology, Huddinge University Hospital. Your support and interest in my work has meant a lot to me. Thanks also for allowing me to acquaint myself with the clinical activity at the department.

♦ **Christer Persson, PhD**, my father. I owe you many thanks for your personal as well as your scientific and technical support and advice throughout this journey. I am also very grateful for your laborious and invaluable work with the final preparations of the gas-diffuser, including final design, documentation for certificates, and planning the manufacturing.

♦ **Professor em. Willem van der Linden**. Many thanks for editing most of the manuscripts, and for providing expert advice about surgery, scientific issues, and the English language.

♦ **Professor Jan-Ingmar Flock**. Thank you for being willing to listen to our “crazy“ ideas and help us investigate them in your lab at the Division of Clinical Bacteriology, Karolinska Institute. **Ingegerd Löfving Arvholm**, thanks for your assistance and positive attitude during the experiments in the same lab.

♦ **Göran Hedin, MD, PhD** and **Gerd Fessé** at the Division of Infection Control, Huddinge University Hospital. Thanks for your help and good advice.
**Peter Svenarud, MD** and **Per Bergman, MD.** Thanks for the collaboration, for being nice friends, and for sharing the same supervisor. For the reader’s knowledge, the three of us frequently found ourselves forming a queue outside as well as inside our supervisor’s office. It soon became almost a tradition to suggest him to mount a queue ticket device at the door.

**The personnel at the Department of Cardiothoracic Surgery & Anesthesiology.** Thank you all for the kind support.

**I thank all my colleagues at the Division of Medical Engineering, Karolinska Institutet for your friendship and support.** A special thanks goes to **Jan Bergholm** for your technical support in the workshop.

**Mattias Öhman, MSc.** In my opinion statisticians and scientists often seem to speak different languages. However, with your northern calmness, straightforward attitude, and great knowledge in mathematical statistics there has always been a clear communication and understanding for which I thank you.

**Anders Wikberg** at **Bonnier Education**, Stockholm, Sweden. Thanks for transforming my drawing of the wound ventilator into a pedagogical high-quality artwork.

**Lars-Gunnar Johansson** and **Stefan Holmström** at **DX Plastic AB**, Bredaryd, Sweden. Many thanks for the nice job of manufacturing the first gas-diffuser sets.

**Rickard Thorsén, MSc** at **Paper Pak AB**, Aneby, Sweden. Thanks for your co-operation regarding the packaging and sterilization of the gas-diffuser sets.

**Sture Randström** at **Centri AB**, Järfälla, Sweden. Thanks for giving me advice about construction of prostheses and the necessary material for building the torso model.

**Weng-Onn Lui, PhD.** Thanks for your friendship, all scientific advice and for giving me the opportunity to meet many other interesting scientists in your field. I also want to thank you for introducing me to the Asian kitchen to which I have almost developed an addiction. Finally, I hope that our regular badminton games on Saturday mornings will continue. During this period, they were something I really needed and enjoyed, despite the fact that I lost almost all the time.

**Tor-Leif Berglund.** I am grateful for your friendship, and for always have been willing to listen and discuss problems about my work. Your reasonable comments and ideas have helped me several times. I enjoyed our endless discussions over the phone and over the internet for that matter. “Discussion is the soul’s gym” as Richard Wiggins once put it, and I totally agree.
Acknowledgements

♦ Rickard Juntikka, Tech Lic. Thanks for the close friendship and for all the great moments on as well as off the golf course during this period. It has been interesting to discuss our similar but yet different situations as PhD students, you at KTH and me at KI.

♦ Markus Andersson. Thanks for the friendship and for being the mould for the plaster cast, which was used for the torso model’s outside shape. This difficult procedure that took place in my apartment was a priceless scene that I, and certainly you, will not forget.

♦ Lena-Kajsa Sidén, Tech Lic. Thanks for all the dinners and classical music events during this period. I enjoyed it immensely, and needed it too for that matter.

♦ Ruth Öslöf. I thank you for your close friendship the last few years. Your home is a church, and I think all your other regular guests agree on that point. You are a special person that I am grateful to know. I thank you for the intellectual and playful conversations we have had, for your support and guidance, and for all the musical experiences we have shared in your home as well as at the Royal Swedish Academy of Music.

♦ Last, but not least Ingrid and Christer Persson, my parents, as well as my brother Mattias Skielta, MD and his wife Anna Skielta. Thank you for your kind support and interest in my work. The family is what finally counts, since you always can count on the family.

Financial

This work was financially supported by the Karolinska Institute and Cardia Innovation AB. Dr Jan van der Linden and I have developed and patented the gas-diffuser and are two of several shareholders in Cardia Innovation AB, which owns the patents and produces the device.
REFERENCES

REFERENCES

REFERENCES


92. Persson M, Svenarud P, van der Linden J. Which is the optimal device for carbon dioxide de-airing of the cardiothoracic wound and how should it be positioned? J Cardiothorac Vasc Anesth (accepted for publication).


