Some aspects of infection surveillance in open-heart surgery

Citation for published version (APA):

Staal, M. J. (1983). *Some aspects of infection surveillance in open-heart surgery*. [Doctoral Thesis, Maastricht University]. Rijksuniversiteit Limburg. <https://doi.org/10.26481/dis.19830930ms>

Document status and date:

Published: 01/01/1983

DOI:

[10.26481/dis.19830930ms](https://doi.org/10.26481/dis.19830930ms)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

SOME ASPECTS OF INFECTION SURVEILLANCE
IN OPEN-HEART SURGERY

SOME ASPECTS OF INFECTION SURVEILLANCE IN OPEN-HEART SURGERY

PROEFSCHRIFT

ter verkrijging van de graad van doctor in de geneeskunde
aan de Rijksuniversiteit Limburg te Maastricht,
op gezag van de Rector Magnificus Prof. Dr. H. C. Hemker,
volgens besluit van het College van Dekanen
in het openbaar te verdedigen in de aula van de universiteit
op vrijdag 30 september 1983, des namiddags te vier uur

door

MICHAËL JOSEPHUS STAAL

geboren te Amsterdam

1983

DRUKKERIJ VAN DENDEREN B.V.
GRONINGEN

Promotores : Prof. Dr. C. P. A. van Boven
Prof. Dr. J. N. Homan van der Heide

Co-promotor : Drs. J. Dankert

Referenten : Prof. Dr. J. A. Flendrig
Prof. Dr. G. Kootstra
Dr. M. J. Haverkorn

Financial support by the Netherlands Heart Foundation for the publication of this thesis is gratefully acknowledged.

CONTENTS

Chapter I	Introduction.....	1
Chapter II	Patients, procedures, facilities, registration and occurrence of postoperative infections.....	11
Chapter III	Postoperative infections in open-heart surgery patients: relation between the causative microorganisms, the microorganisms isolated on admission and the microorganisms isolated from various indwelling devices.....	27
Chapter IV	Detection and treatment of <i>Staphylococcus aureus</i> carriage in relation to the occurrence of postoperative <i>Staphylococcus aureus</i> infections.....	55
Chapter V	Bacteriological surveillance of the extra corporeal circuit; relation between the microorganisms isolated and those involved in the occurrence of postoperative bacteraemia, septicaemia and/or early-onset bacterial endocarditis.....	75
Chapter VI	The significance of isolation of <i>Staphylococcus epidermidis</i> from blood cultures obtained from patients after open-heart surgery.....	93
Chapter VII	General discussion and conclusions.....	105
Chapter VIII	Summary.....	117
Chapter IX	Samenvatting.....	121
Dankbetuiging		127
Curriculum vitae.....		129

CHAPTER I

INTRODUCTION

1. OPEN-HEART SURGERY AND PREVENTION OF INFECTIONS

Open-heart surgery is one of the recent technological achievements of modern medicine. In addition to the risk of infection associated with any operative technique, cardiac surgery and especially open-heart surgery has created a new group of infectious complications: postoperative infective endocarditis. Since the report of Koiwai (1) of 12 cases with postoperative infective endocarditis in 1190 patients after closed and open-heart operations, our understanding of the biology, diagnosis, treatment and prevention of this infection has increased considerably. The majority of publications on infections after cardiac surgery deals with postoperative endocarditis. Only a relative small number of reports also pays attention to other infections associated with cardiac surgery.

Infections after cardiac surgery, a clean type of surgery, can be caused by so called "non pathogenic" microorganisms. These microorganisms constitute the endogenous microflora present on the skin and mucosa and are able to induce endocarditis after open-heart surgery (2).

There is a number of factors increasing the risk of acquiring infections after cardiac surgery: the extended use of prophylactic antibiotics (3-5), the presence of preoperative cardiac and extra-cardiac infections (6-8), the type of non-infective cardiac disease of the patient (9). Furthermore, it has been shown that patients with aortic valve disease have a higher risk of postoperative infection than patients with lesions of the other valves (10). The risk factors at operation may include the insertion of prosthetic material (11-13), the use of an extra corporeal circuit (14-17), the need for intravascular haemodynamic monitoring (18-22), the large number of persons present in the operating room (23) and the long duration of open-heart operations (24-26). Postoperative risk factors are mainly associated with intensive care treatment, such as the use of pressure transducers (18-22), intravascular catheters (20,27-32) and continued mechanical respiratory assistance (33-36).

In open-heart surgery, antibiotics are administered prior, during and after operation to prevent postoperative infections. The rationale for this prophylaxis has not been proven, but is felt to be necessary (37). Several antibiotics have been recommended, but the effectiveness of the different antibiotics is difficult to assess, because changes in operative technique and postoperative management will also affect the rate of infection (37).

Surveillance of infections which includes the registration of

occurrence of infections and the bacteriological monitoring of procedures performed, has been advocated for gaining insight into the transmission of microorganisms and the mechanisms involved in inducing the infections. Based on the results of the surveillance programme appropriate actions can be taken to reduce the occurrence of hospital associated infections (38).

The purpose of this study is to assess prospectively the efficacy of certain elements of the surveillance programme, as used in the first 18 months after starting cardiac surgery in the Catharina Hospital at Eindhoven, The Netherlands. Feasibility and cost-benefit analyses were not included in this study.

2. SCOPE OF THE STUDY

An inventory of the measure taken to maintain asepsis in the operating room and in the intensive care unit was made before open-heart surgery was initiated (Chapter II). Some measures were taken according to common practice while others were based on findings reported in the literature. Because only certain elements of the total programme were evaluated, the results obtained from the prospective registration of infections should be seen as an overall assessment of all the precautions taken (Chapter II). In a number of reports, routine preoperative bacteriological culturing has been performed without evaluation of its significance with respect to the occurrence of postoperative infections (39,40). Although a detailed bacteriological-epidemiological study was not performed, it was attempted by comparing the isolates from preoperative cultures with the isolates cultured from sites postoperatively shown to be infected, to assess the significance of such a routine culturing programme (Chapter III).

A feature often neglected in studies evaluating the efficacy of preventive measures is the accuracy of the sampling method used. The rate of *Staphylococcus aureus* carriage among patients and hospital personnel seems to be well known, but the detection of carriers is often based upon single sampling. In addition the persisting carriage of *Staph.aureus* in the microflora of the skin and mucous membranes has been questioned (41). In this study the accuracy of the sampling method and the constancy of *Staph.aureus* carriage in patients and hospital personnel is studied (Chapter IV). The effect of the application of nasal antimicrobial ointment in patient carriers on the occurrence of postoperative infections due to *Staph.aureus* was also

studied (Chapter IV). Contamination of open-heart surgery patients can occur from various sources in the hospital (42). We chose to investigate one of these sources, the extra corporeal circuit, because of the conflicting reports in the literature (23,43), concerning its significance as a cause of postoperative infections (Chapter V).

Intravascular infections due to *Staphylococcus epidermidis* in open-heart surgery patients are serious and life threatening. This microorganism, often considered as a harmless microorganism present on the human skin and in the hospital environment, is an important cause of infections in patients with intravascular catheters (44) and arteriovenous and cerebrospinal fluid shunts (44-46), and in orthopaedic surgery (45), vascular surgery (47) and open-heart surgery patients (45) after insertion of prosthetic material. However, the interpretation of *Staph.epidermidis* positive blood cultures taken from patients after open-heart surgery is often difficult due to the possibility of contamination. Differentiation of contaminated from true positive cultures due to bacteraemia or intravascular infections is based upon repeated isolation of this microorganism from a number of blood cultures taken within a certain time period. To get insight into the frequency of contamination during the collection and culturing of blood samples, in this study paired samples were postoperatively collected from open-heart surgery patients (Chapter VI).

REFERENCES

1. Koiwai, E.K. and Nahas, H.C. Subacute bacterial endocarditis following cardiac surgery. *Arch. Surg.* 73: 272, 1956.
2. Norenberg, R.G., Sethi, G.K., Scott, S.M. and Takaro, T. Opportunistic endocarditis following open-heart surgery. *Ann. Thorac. Surg.* 19: 592, 1975.
3. Lord, J.W., Jr., Imparato, A.M., Hackel, A.H. and Doyle, E.F. Endocarditis complicating open-heart surgery. *Circulation* 23: 489, 1961.
4. Goldman, D.A., Hopkins, C.C., Karchmer, A.W., Abel, R.M., Mc. Enany, M.T., Akins, C., Buckley, M.J. and Moellering, R.C., Jr. Cephalothin prophylaxis in cardiac valve surgery. A prospective double-blind comparison of two-day and six-day regimens. *J. Thorac. Cardiovasc. Surg.* 73: 470, 1977.
5. Penn, R.G., Sanders, W.E. and Sanders, C.C. Colonization of the oropharynx with gram-negative bacilli: A major antecedent to nosocomial pneumonia. *Am. J. Inf. Contr.* 9: 25, 1981.
6. Hughes, R.K. A method of improved anti-sepsis for open-heart surgery. *Ann. Thorac. Surg.* 2: 230, 1966.
7. Frater, R.W.M. and Santos, G.H. Sources of infection in open-heart surgery. *N.Y. State J. Med.* 74: 2386, 1974.
8. Dismukes, W.E. and Karchmer, A.W. The diagnosis of infected prosthetic heart valves: bacteremia versus endocarditis. In: R.J. Duma, ed. *Infections of prosthetic heart valves and vascular grafts*. Baltimore: University Park Press, 1977; 61.
9. Kaplan, E.L., Rich, H., Gersony, W., and Manning, J. A collaborative study of infective endocarditis in the 1970s. Emphasis on infections in patients who have undergone cardiovascular surgery. *Circulation* 59: 327, 1979.

CHAPTER II

PATIENTS, PROCEDURES, FACILITIES, REGISTRATION AND OCCURRENCE OF POSTOPERATIVE INFECTIONS

1. PATIENTS

From February 1978 to July 1979, 182 open-heart operations (table 1) were performed on 181 patients. One patient was re-admitted five months after a first aorto-coronary bypass graft (ACBG) operation. She was operated on a second time because of occlusion of the coronary bypass grafts. The data obtained during both admissions of this patient are used in this study as if obtained from two different patients.

Seven out of the 181 patients died. Four patients died on the day of operation: three after an ACBG operation, one after a mitral valve replacement operation. One patient died several days after the second operation from causes unrelated to infection. Two other patients died several weeks after their operation due to a septicaemia and an early-onset bacterial endocarditis respectively.

Therefore the study includes 181 patients of whom all were included in the pre-operative study whereas 178 of them were available for the postoperative follow-up.

The age and sex distribution of the 181 patients is shown in table 2. The mean age of the 138 male patients was 51 years (range: 15-68 years). The mean age of the 43 female patients was 46 years (range: 8-69 years). The modal age class of the whole population was 50-59 years.

The indication for surgery, the type of operation and the use of prosthetic material are indicated in table 3.

2. ARCHITECTURAL DESIGN AND FACILITIES OF THE DEPARTMENT

The department of cardiac surgery was functionally and architecturally fully integrated in a general hospital with 756 beds. This hospital was about five years old at the time of this study. Some structural alterations were made for the department of cardiac surgery.

2.1. GENERAL WARD

In a general ward with 43 beds, located on the seventh floor, patients were admitted preoperatively and re-admitted postoperatively after their stay on the intensive care unit. The thoracic drains and the urinary catheter were removed before the patient was transferred back to the

Table 1: The number of open-heart operations performed between February 1978 and July 1979.

Year	Month											
	J	F	M	A	M	J	J	A	S	O	N	D
1978	-	1	7	7	10	5	0*	12	0*	12	17	8
1979	14	14	18	8	18	16	14	end of study				

* Building alterations: no surgery

Table 2: Age and sex distribution of the patients.

Age group	Patients		
	Males	Females	Total
0 - 9 yrs.	0	1	1
10 - 19 yrs.	3	8	11
20 - 29 yrs.	5	0	5
30 - 39 yrs.	2	1	3
40 - 49 yrs.	45	7	52
50 - 59 yrs.	68	18	86
60 - 69 yrs.	15	8	23
Total	138	43	181

Table 3: The indication for surgery, type and number of operations and use of prosthetic material in 182 open-heart operations.

Indication for surgery	Type of operation	Number of operations	
		total	prosthetic material used
<u>Coronary sclerosis</u>	Aorto- coronary bypass graft (ACBG) only	127	0
-with left ventricular aneurysm	-with resection of left ventricular aneurysm	1	1
-with atrial septal defect (ASD)	-with closure of ASD	1	0
<u>Valvular heart disease</u>	Aortic valve replacement	17	17
	Mitral valve replacement	12	12
	Aortic and mitral valve replacement	4	4
-with coronary sclerosis	Mitral valve replacement with ACBG	2	2
<u>Other congenital and acquired anomalies</u>	Closure of ASD	7	5
	-with pulmonary valvulotomy	2	2
	Closure of ventricular septal defect	3	1
	Valvulotomy (mitral,pulmonary)	2	0
	-with annuloplasty	2	2
	Resection of left ventricular aneurysm only	2	2
Total		182	48

the general ward. On this ward there was a single room which could be used to isolate an infected patient when necessary.

2.2 OPERATING-SUITE

Two rooms in the operating-suite located on the second floor were used, though not exclusively, for cardio-thoracic operations. The ventilation system in the operating room had a multidirectional flow. Filtered air was introduced through perforated panels in the ceiling into each room and the air was exhausted through air-outlet opening in the walls one meter above the floor. The ventilation rate (air changes per hour) in the two rooms was 20.

2.3. INTENSIVE CARE UNIT

Intensive care was given in two separate wards. A two-bed room for intensive care was adjacent to the recovery room of the operating suite. To reach this intensive care room cardiac surgery patients had to be transferred from the operating room through the recovery room. This two-bed room was entered from outside the operating-suite through an air-lock. The ventilation system provided an air-flow from the unit to the corridor outside.

The second room for the intensive care of cardiac surgery patients was a four-bed room located on the seventh floor. This room, to which the patients were transferred after the first postoperative day, was part of the general intensive care unit of the hospital. Only cardio-thoracic and vascular surgery patients without evident infection were nursed in this four-bed room. The room was ventilated and the air-flow was directed from inside out. The room could only be entered through an air-lock. Cardiac surgery patients with an infection were transferred to an one-bed isolation room, or to a nine-bed room of the general intensive care unit, if the isolation room was occupied.

3. CLINICAL PROCEDURES

3.1. PREOPERATIVE PERIOD

3.1.1. PATIENTS

One hundred and sixty patients of the 182 patients were admitted to the department of cardiac surgery directly from home. The mean preoperative stay of these patients was eight days (range: 0-29 days). Twenty-two patients were already in the hospital before being transferred to the department of cardiac surgery. The mean preoperative stay of this second group of patients before operation was 40 days (range: 10-110 days).

3.1.2. BACTERIOLOGICAL SAMPLING AND INFECTIONS

On the day of admission to the department of cardiac surgery samples for bacteriological culture were taken from several sites on the skin (axillae, chest, wrists, groins, perineum) and from the nose and throat. If patients were able to expectorate sputum a specimen was cultured. Midstream urine specimens were also cultured. All patients were preoperatively seen by an oto-rhino-laryngologist, a dental surgeon, a pulmonologist and if indicated by a urologist. The presence of an infection was a reason to postpone the operation.

3.1.3. DISINFECTION OF THE SKIN

All patients admitted to the department of cardiac surgery washed themselves (whole body washing) twice daily with liquid soap and shampoo containing povidone-iodine 10% and 7.5% respectively (Betadine^R, Dagra, Diemen, The Netherlands).

3.1.4. SHAVING PROCEDURE

The evening before operation all patients, except emergency cases, were completely shaved, the hair of the scalp excluded. Shaving was done with a disposable razor blade. Skin disinfection was not performed afterwards.

3.1.5. ANTIMICROBIAL PROPHYLAXIS

The first 14 patients had amoxycillin administered prophylactically in an oral dose of 2 x 750 mg the day before surgery followed by ampicillin one hour prior to operation and three times daily for four days. To all other patients cephalothin was given prophylactically on the day of surgery, one gram intramuscularly one hour before operation and intravenously at

intervals of two hours during operation. After operation one gram was given at intervals of three hours. On the first day after operation cephalothin (one gram) was administered intravenously four times daily and then all prophylactic use of antibiotics was discontinued.

3.2. INTRA-OPERATIVE PERIOD

3.2.1. IMMEDIATE PREOPERATIVE PREPARATION

After induction of the anaesthesia and intubation, intravascular catheters used for haemodynamic monitoring and peripheral venous catheters were inserted by the anaesthesiologist who washed his hands with liquid soap containing povidone-iodine (Betadine^R). A central venous pressure catheter was inserted into the jugular vein. An arterial pressure monitoring catheter was introduced into the radial artery. If indicated a left atrial pressure catheter was inserted by the surgeon before closure of the chest. The various intravascular pressure monitoring catheters were connected to electronic transducer systems. An indwelling urinary catheter was inserted aseptically. Body temperature was recorded using two sterilized temperature probes. One was placed in the oesophagus and the other in the rectum. A nasogastric tube was inserted. The skin of the patient was disinfected with iodine (1% w/v) in ethanol (70% v/v). The operative field was draped with plastic adhesive skin drapes (3M, St. Paul, Minn., USA) and with linen sheets.

3.2.2. THE SURGICAL SCRUB AND ATTIRE

The members of the surgical team scrubbed their hands and forearms using autoclaved brushes and liquid soap containing povidone-iodine (Betadine^R) for five minutes. After drying hands and forearms with autoclaved linen towels they put on wraparound cotton, sterilized gowns. All males, including visitors, wore a clean trouser suit and all females wore a frock. The operating room staff wore clogs. The visitors used plastic shoe covers. The hair of the scalp of everyone present in the operating room was covered by a disposable cap. Disposable masks covered nose and mouth.

3.2.3. THE EXTRA CORPOREAL CIRCUIT

The equipment and procedures for the assembly, dismantling and bacterio-

logical monitoring of the extra corporeal circuit are described in Chapter V. The mean duration of extra corporeal circulation for the different types of surgery is shown in table 4.

3.2.4. WOUND CARE

The pericardium, the mediastinum and when necessary the pleura were drained with separate drains which were connected to disposable sterile, plastic drainage bottles (Mölnlycke Steritex A/S, Espergaerde, Denmark). In the intensive care unit these bottles were placed on suction. If present, the wound in the leg was drained with a closed drainage system connected to disposable sterile vacuum bottles (Mölnlycke Steritex A/S). The wounds in chest and leg were dressed in the operating room using sterilized dressings.

3.2.5. STERILIZATION AND CLEANING PROCEDURES

The instruments were wrapped in linen sheets and paper, sterilized by autoclaving and stored for at most one month. After operation the instruments were cleaned ultrasonically and washed in a washing machine. Sterile pack storage was separate from the room where used material was cleaned and wrapped. The respirator (Engström, Stockholm, Sweden) was sterilized once weekly in a formaldehyde steam sterilizer. Masks, tubing and other anaesthesia equipment were sterilized daily in formaline (4% v/v). The floor of the operating room was disinfected for 30 minutes with 1% v/v lyorthol (Lysoform^R, Berlin) after each operation.

3.2.6. MEAN DURATION OF OPERATIONS

The mean duration of the different types of operation are shown in table 4.

3.3. POSTOPERATIVE PERIOD

3.3.1. DURATION OF STAY IN THE INTENSIVE CARE UNIT

The mean duration of stay in the intensive care unit was four days (range: 1-14 days).

Table 4: The type of operation and the mean duration of operation and extra corporeal circulation (ECct) in 182 open-heart operations.

Type of operation	Number	Mean duration in minutes of	
		operation (range)	ECct
Aorto-coronary bypass graft	127	429(185-1020)	146(40-990)
Aorto-coronary bypass graft combined with other	4	420(405- 525)	135(120-185)
Aortic or mitral valve replacement	29	345(270- 510)	107(30-335)
Aortic and mitral valve replacement	4	390(380- 455)	135(100-150)
All other operations	18	350(190- 410)	89(15-185)

3.3.2. VENTILATORY ASSISTANCE AND DURATION OF INTUBATION

The patients were usually given ventilatory assistance using a respirator (Servo, Siemens, Elema, Sweden) until the morning of the first postoperative day. When the results of blood gas analysis while breathing spontaneously were satisfactory ventilatory assistance was terminated and the patients were extubated. Tubing of the respirator was sterilized by means of ethylene oxide. The humidifier and the nebulizer were filled with sterilized distilled water. The respirator was cleaned after extubation of the patients. During ventilatory assistance bronchial toilet and aspiration were performed as frequently as necessary. The bagging set was sterilized by means of ethylene oxide after extubation of the patient. The mean duration of the postoperative endotracheal intubation was one day (range:< 1-13 days). After extubation physiotherapy was used to improve patient's respiration.

3.3.3. INTRAVASCULAR CATHETERS AND MEAN DURATION OF THEIR USE

All the intravascular catheters used for pressure monitoring were removed as soon as the haemodynamic state permitted, usually on the first postoperative day. Intracardiac catheters were used in 110 patients. The mean duration of use of these catheters was one day (range:< 1-8 days). The intra-arterial catheters were in place for a mean period of two days (range:< 1-11 days). Peripheral venous catheters were removed when the patient could drink again and if parenteral administration of medicines was not longer necessary. The intravenous catheter removed last had been applied for a mean period of three days (range: 1-30 days).

3.3.4. URINARY TRACT CATHETERIZATION AND MEAN DURATION OF CATHETERIZATION

The urinary indwelling catheter, inserted in the operating room was connected to a new sterile drainage bag (Urimeter, S.R. Bard International, Sunderland, U.K.). The urinary catheter was removed from 141 patients on the first postoperative day. The mean duration of catheterization was one day (range:< 1-16 days).

3.3.5. WOUND CARE AND DURATION OF DRAINAGE OF THE WOUND

The dressings were removed from the wounds on the first postoperative day. The wounds were disinfected with a solution containing iodine (1% w/v) in ethanol (70% v/v) and then covered with wound spray (Nobecutane, Bofors, Nobel Pharma, Sweden). Closed drainage systems in the leg wounds were removed early. The duration of drainage of these wounds varied from one to seven days with a mean of two days. The tubes draining the pericardium, mediastinum and pleura were removed aseptically, when blood loss had become less than 20 ml per hour. The thoracic drains were removed after about two days (range: 1-16 days).

3.3.6. CLEANING PROGRAMME OF THE INTENSIVE CARE UNIT

Cleaning of the intensive care unit was done once a day. Floors were cleaned with a detergent, and monitors, furniture and accessories with a damp duster. The one-bed isolation room was disinfected with 1% v/v lyorthol (Lysoform^R) after the patient was transferred to the ward.

3.3.7. PERSONNEL

On the intensive care unit the staff wore caps, masks, plastic shoe covers and special clothing. When leaving this unit they covered their clothes with white coats. Visitors wore disposable gowns, caps, masks and plastic shoe covers. Before entering the intensive care unit in the air-lock, hands were washed with liquid soap containing povidone-iodine (Betadine^R).

4. REGISTRATION, DEFINITIONS AND OCCURRENCE OF POSTOPERATIVE INFECTIONS

The registration of infections was performed prospectively. Patients were visited and, if necessary, examined daily during hospitalization. The results of laboratory tests and microbiological cultures were reviewed daily. After discharge from the hospital patients were seen regularly at the out-patients' department up to 60 days postoperatively.

The criteria for postoperative infections were derived from the publication of Haley *et al.* (1) and were modified for the study.

Septicaemia was diagnosed when the patient had chills (except when occurring during a blood transfusion) and a positive blood culture, or

Table 5: The number and mean onset of postoperative infections in 178 patients after open-heart surgery.

Type of infection	Number of infections(%)	Mean time of onset in postoperative days (range)
Bacterial endocarditis (early-onset)	7 (3.9)	12 (7-24)
Septicaemia	7 (3.9)	5.1 (1-11)
Lower respiratory tract infection	48 (26.9)	1.5 (1- 4)
Bacteriuria	3 (1.7)	7.5 (6-15)
Incisional wound infection	8 (4.5)	8 (6-14)
Deep wound infection (mediastinitis, sternal osteomyelitis)	2 (1.1)	15.5 (12-19)

chills in conjunction with hypotension (systolic blood pressure ≤ 90 mm Hg) without a positive blood culture.

Lower respiratory tract infection was present if a purulent sputum, a positive culture and increased breath sounds were found.

Bacteriuria was present if a colony count showed the presence of 10^5 or more bacteria of the same species ml^{-1} of urine.

Wound infection was defined as by presence of purulent drainage from the skin wound (incisional wound infection). Stitch abscesses were not registered as a wound infection. Mediastinitis (deep wound infection) was diagnosed if pus was encountered in the mediastinum at re-operation, whereas the diagnosis of sternal osteomyelitis as a deep wound infection was established by the presence of necrosis of the bone found at operative exploration.

The clinical diagnosis of postoperative early-onset bacterial endocarditis (within 60 days after operation) was based on the persistence of unexplained fever, the finding of persisting leucocytosis, the occurrence of a new regurgitant cardiac murmur and the results of blood cultures (at least two cultures positive for the same microorganism).

Fever (temperature $\geq 38.5^{\circ}\text{C}$, measured rectally) and leucocytosis ($\geq 10,000$ white blood cells per cubic millimeter) occurring within the first three postoperative days were not used as indices for the occurrence of postoperative infections. Both may be present within this period after open-heart surgery in patients without infection (2-4).

Postoperative bacteriological sampling is described in detail in Chapter III.

Registration of postoperative infections was performed on 178 patients, since four patients died on the day of operation. Of these 178 patients, 63 (35%) had a postoperative infection (table 5). In 52 of these 63 patients a single infection occurred and in 11 patients more than one infection was diagnosed (ten patients with two infections, one patient with three infections). Early-onset bacterial endocarditis was diagnosed in seven (3.9%) of the 178 patients. The mean onset of this infection was 12 days after surgery. In seven (3.9%) other patients septicaemia complicated the postoperative course. Lower respiratory tract infections were the most frequently encountered infectious complication occurring in 48 (26.9%) patients, one to four days after the operation. Bacteriuria's occurred later but only in a small number of patients. Incisional wound infections were diagnosed in eight (4.5%) of the 178 patients. Of these eight patients one had a sternal osteomyelitis, and another one had a mediastinitis followed by a septicaemia.

REFERENCES

1. Haley, R.W., Quade, D., Freeman, H.E., Bennett, J.W. and the CDC Senic Planning Committee. Study on the efficacy of nosocomial infection control (SENIC Project). *Am.J.Epidemiol.* 111: 472,1980.
2. Goodman, J.S., Schaffner, W., Collins, H.A., Battersby, E.J. and Koenig, M.G. Infection after cardiovascular surgery. Clinical study including examination of antimicrobial prophylaxis. *New.Engl.J.Med.* 278:117,1968.
3. Bell, D.M., Goldmann, D.A., Hopkins, C.C., Karchmer, A.W. and Moellering, R.C. Unreliability of fever and leukocytosis in the diagnosis of infection after cardiac valve surgery. *J.Thorac.Cardiovasc.Surg.* 75: 87,1978.
4. Pien, F.D., Ho, P.W.L. and Fergusson, D.J.G. Fever and infection after cardiac operation. *Ann. Thorac.Surg.* 33: 382,1982.

CHAPTER III

POSTOPERATIVE INFECTIONS IN OPEN-HEART SURGERY PATIENTS:
RELATION BETWEEN THE CAUSATIVE MICROORGANISMS, THE
MICROORGANISMS ISOLATED ON ADMISSION AND THE MICROORGANISMS
ISOLATED FROM VARIOUS INDWELLING DEVICES

1. INTRODUCTION

Open-heart surgery is associated with a higher frequency of post-operative infections than closed-heart procedures (1). The sources of microorganisms causing these infections can be many and are often difficult to trace (2-5). The endogenous microflora, i.e. the resident microorganisms present on the surface of the skin and mucous membranes of the patient, is considered to be an important source especially since the skin and mucous membranes are penetrated during and after surgery. This creates a potential portal of entry to the tissues and the intravascular compartment. Preoperative microbiological culturing has been done in open-heart surgery patients (1,4,5) but its usefulness in pin-pointing the relation between the isolated microorganisms and those causing postoperative infections has not been thoroughly studied. Postoperative endocarditis occurring within 60 days after surgery is considered as early-onset infective endocarditis, which is most frequently caused by microorganisms present in the normal flora of the human skin (6). However, contamination with such microorganisms may also occur from various sources in the operating room (2,7-10). In addition postoperative infections of the respiratory tract (11-13,15), the urinary tract (11-13) and of wounds (11-15) are also potential sources of early-onset infective endocarditis. The microorganisms causing these extra-cardiac infections which by their occurrence create an extra postoperative risk for the patient, originate from a diversity of sources and reservoirs in and outside the operating room (16-19). Another source of infection identified after open-heart surgery are intravascular catheters (2,5,9,12,13). Other indwelling devices such as endotracheal tubes (2,5), urinary catheters (2,5,9,13) and thoracic drains (5) have been cultured postoperatively, but the relation between the microorganisms isolated and those causing postoperative infections has not been convincingly demonstrated.

In this chapter, we report the occurrence of postoperative early-onset endocarditis and septicaemia, postoperative respiratory tract infection, bacteriuria and postoperative wound infection in 178 open-heart surgery patients. The aim of the study was to find a relation between the microorganisms isolated from samples taken preoperatively on admission from patients and the microorganisms causing these postoperative infections. In addition, the tips of various indwelling devices were cultured after removal in order to study a possible relation between the presence of microorganisms on the devices and the microorganisms involved in subsequently occurring infections.

2. MATERIALS AND METHODS

2.1 CULTURES ON ADMISSION

One hundred and eighty two patients requiring open-heart surgery were sampled bacteriologically on the day of admission to the department of cardiac surgery. Samples were taken from several sites on the skin: axillae, chest, wrists, groins and perineum and also from the vestibules of the nose and from the throat using dry cotton-tipped swabs. The swabs were transported in Amies Charcoal Medium (Transwab^R, Medical Wire and Equipment Co. Ltd. Potley, Corsham, Wilts., England). Sputum was cultured if patients were able to produce a specimen. Sputum samples were collected in sterilized vials.

Culturing was performed in the Laboratory for Medical Microbiology at Eindhoven, the Netherlands (M.J.Haverkorn).

2.2 POSTOPERATIVE CULTURES

Postoperative cultures were taken from only 178 patients, as four patients died on the day of surgery.

Blood cultures were taken if the body temperature, measured rectally, was raised above 38.5°C. Blood (10 ml) was drawn from an antecubital vein after cleansing of the skin with iodine (1% w/v) in ethanol (70% v/v). Five ml of blood was injected into 15 ml Brain Heart Infusion (BHI) broth (Oxoid Ltd., Basingstoke, England) containing para-aminobenzoic acid (0.01% w/v), sodium citrate (0.14% w/v), white saponin (0.1% w/v, Merck, A.G. Darmstadt, Fed.Rep. Germany) and sufficient penicillinase (Mycofarm, Delft, The Netherlands) to counteract 10,000 units of penicillin. The other five ml of blood was injected into a bottle (LR-sample) containing two ml of sodium chloride solution (0.85% w/v) and liquoid (sodium polyanethole sulphate 0.11% w/v, Hoffmann-La Roche, Basel, Switzerland) and para-aminobenzoic acid (0.05% w/v). After inoculation, the cultures were submitted to the Laboratory for Medical Microbiology at Eindhoven.

Sputum samples were collected for bacteriological culture after removal of the endotracheal tube and when an infection of the respiratory tract was suspected.

Urinary samples were collected routinely from each patient on the morning of the first postoperative day and later if symptoms of an urinary tract

infection were present. Samples were collected from the chamber added to the drainage bag to measure the urine flow. When the catheter had been removed urine specimens from midstream samples were collected. Urine samples were transported in sterilized vials.

Wounds were sampled with dry cotton-tipped swabs if inflammation occurred or if exudate was produced. The swabs were inserted in Amies Charcoal Medium.

When the intravascular and urinary tract catheters, the endotracheal tubes and the wound and thoracic drains had been removed, the tips were cut, using sterilized scissors, and transferred in sterilized vials for culturing.

Culturing was performed in the Laboratory for Medical Microbiology at Eindhoven.

2.3. MICROBIOLOGICAL CULTURING, ANTIMICROBIAL SUSCEPTIBILITY TESTING AND TYPING OF STAPHYLOCOCCI

The cotton-tipped swabs were streaked routinely onto sheep blood (5% v/v) agar (Oxoid) plates which were incubated aerobically at 37°C for 24 to 48 hours. In addition, the nasal and skin swabs were streaked onto mannitol salt agar (Oxoid No 110) for selective isolation of staphylococci. The swabs used for sampling the groins and the perineum were also streaked onto MacConkey agar (Oxoid Ltd.) for isolation of *Enterobacteriaceae*. The throat samples were plated onto chocolate blood agar for isolation of *Haemophilus* species. The plates were incubated aerobically at 37°C for 24 to 48 hours, the chocolate blood agar plates were incubated in an atmosphere of 5% CO₂.

Aliquots of the sputum specimens were spread out in the inverted lid of a Petri dish and then inspected for the presence of purulent portions. From each aliquot a purulent portion was washed three times in sterilized saline (0.9% w/v). Two portions of each aliquot were Gram stained and microscopically examined. The presence of leucocytes was noted. If more than 25 squamous epithelial cells per 100 x field were seen, washings of purulent portions were repeated. If less than 25 squamous epithelial cells were seen, sheep blood, chocolate blood and MacConkey agar plates were inoculated qualitatively. The plates were incubated aerobically at 37°C for 24 hours, with the chocolate blood agar plates incubated in an atmosphere of 5% CO₂.

Blood cultures were processed as follows. From the first bottle containing BHI-saponin broth, three pour plates were prepared using

Blood Agar Base nr. 2 (Oxoid), containing glucose (1% w/v). The bottle designated as the LR-sample was subcultured into Brewer Thioglycollate broth (Difco, Detroit, U.S.A.) and into BHI broth. In addition, a pour plate using Blood Agar Base nr. 2 containing glucose (1% w/v) was prepared. The agar plates were incubated at 37⁰ C for three days and the broth media for seven days. Three pour plates (one from the LR-sample and two from the BHI-sample) were incubated in an atmosphere of 5% CO₂. These were inspected daily. Subcultures were made when growth was seen. After five days, blind subculturing of the media was done on Blood Agar Base nr.2 containing heated sheep blood (5%) and penicillin (0.1U), on a medium consisting of four parts Oxoid G.C. Agar Base and one part Veal infusion medium (Difco) containing 5% heated sheep blood agar and in a Brewer Thioglycollate broth. The latter medium was incubated for five days, the other media were incubated for two days. If growth was seen or if Gram stained smears indicated the presence of microorganisms, subcultures were performed on appropriate microbiological culture media.

Urine specimens were cultured semi-quantitatively. From each urine sample 0.1 ml undiluted and 0.1 ml 1:100 diluted urine were cultured onto sheep blood agar and MacConkey agar plates allowing after incubation at 37⁰C for 24 hours quantitation of the bacterial density in the sample. Microscopic examination of the Gram stained sediment was performed and the presence of uroepithelial cells, casts, leucocytes, erythrocytes and microorganisms was noted.

The tips of the different indwelling devices were rolled back and forth four times across the surface of sheep blood agar and MacConkey agar plates. Plates were incubated at 37⁰C for 24 hours.

Identification was performed by standard methods. The production of coagulase by staphylococci was tested by means of the tube test, using citrated rabbit plasma.

Antimicrobial susceptibility testing was performed using the disc diffusion method. The medium used was DST agar (Oxoid) and the discs used were Multodisks (Oxoid). Sensitivity was recorded using standard diameters for zones of inhibition.

Staphylococcus aureus isolates were phage typed at the National Institute of Public Health at Bilthoven, The Netherlands (J. van Leeuwen). *Staph. aureus* strains were considered to be identical if their phage type patterns were the same. All coagulase-negative staphylococci in this study were designated as *Staphylococcus epidermidis*. These isolates were sent to

the Department of Medical Microbiology of the State University of Limburg, The Netherlands (E.E.Stobberingh), for phage and biotyping. The methods used for typing and the phages used have been reported previously (20). Biotyping was performed using API-Staph gallery (API System S.A., Montalieu Vercieu, France). Strains were considered to be non-identical if they differed in one strong phage reaction or in one biotyping character.

With regard to the other microorganisms, the susceptibility patterns (antibiograms) were determined after identification. Isolates were considered epidemiologically to be the same strain if these patterns were the same.

2.4. DEFINITIONS AND REGISTRATION OF INFECTIONS

Infections were defined and registered as described in Chapter II.

2.5. STATISTICAL ANALYSIS

Statistical significance was tested using the two tailed Student t test and the chi square test.

3. RESULTS

3.1. CULTURES OF ADMISSION SAMPLES

Escherichia coli was cultured from the samples obtained on admission from 155 (85%) out of 182 patients (table 1). In a small number of patients this microorganism was present on the skin (groin,chest) and in the upper respiratory tract. *Klebsiella/Enterobacter* species, *Proteus* species and *Pseudomonas aeruginosa* were cultured from 20%, 16% and 2% of the 182 patients, respectively. Other Gram-negative species were isolated from samples of a few patients. Of the Gram-positive microorganisms, *Staph.aureus* was present in cultures taken from 65 (36%) patients. Other Gram-positive microorganisms except *Staph.epidermidis* and viridans streptococci were isolated from a low number of patients. Sputum specimens were obtained from 97 patients on admission. From 81 of these specimens no microorganisms were isolated. *Streptococcus pneumoniae* was the microorganism most frequently cultured from sputum specimens.

Table 1: The bacteriological culture results of samples collected from 182 open-heart surgery patients on admission and of 97 sputum specimens.

Microorganism	Sampling site/specimen					Number of patients with preoperative isolation of (%)
	skin	nose	throat	sputum	perineum	
<u>Gram-negative</u>						
<i>Escherichia coli</i>	12	3	4	3	150	155 (85)
<i>Klebsiella/Enterobacter</i> species	7	7	2	2	21	37 (20)
<i>Proteus vulgaris</i>	12	5	0	1	4	13 (7)
<i>Proteus mirabilis</i>	4	1	1	1	9	16 (9)
<i>Serratia</i> species	1	0	0	0	1	2 (1)
<i>Pseudomonas aeruginosa</i>	1	0	1	0	1	3 (2)
<i>Acinetobacter</i> species	1	1	0	0	1	3 (2)
<i>Haemophilus influenzae</i>	0	3	0	5	0	8 (4)
<i>Neisseria</i> species	0	2	7	0	0	9 (5)
<u>Gram-positive</u>						
<i>Staphylococcus aureus</i>	12	56	19	0	7	65 (36)
<i>Staphylococcus epidermidis</i>	180	133	5	0	158	182 (100)
<i>Sarcina</i> species	2	0	0	0	0	2 (1)
Haemolytic streptococcus group A	0	1	2	0	0	3 (2)
Haemolytic streptococcus non-group A	2	1	13	1	14	27 (15)
<i>Streptococcus viridans</i> group	2	3	157	0	11	163 (90)
<i>Streptococcus pneumoniae</i>	0	7	0	9	0	16 (9)
<i>Streptococcus faecalis</i>	1	0	0	1	11	11 (6)
Indifferent streptococci	0	0	0	0	3	3 (2)
Diphtheroids	2	1	0	0	6	9 (5)
<u>No isolate</u>	0	37	3	81	7	

3.2. INCIDENCE OF POSTOPERATIVE INFECTIONS AND THEIR CAUSATIVE MICROORGANISMS IN RELATION TO MICROORGANISMS ISOLATED ON ADMISSION AND TO MICRO-ORGANISMS ISOLATED FROM VARIOUS INDWELLING DEVICES

Postoperative infections occurred in 63 (35%) of 178 open-heart surgery patients. Single infections were diagnosed in 52 patients, whereas 11 patients had more than one postoperative infection (see Chapter II).

3.2.1. EARLY-ONSET BACTERIAL ENDOCARDITIS AND SEPTICAEMIA

Early-onset bacterial endocarditis occurred in six (18%) out of 34 patients who underwent valve replacement surgery (table 2). This infection did not occur in 11 other patients undergoing various operations entailing insertion of prosthetic material. Of the remaining 133 patients, early-onset bacterial endocarditis occurred in one patient who had undergone a direct closure of a ventricular septal defect.

Septicaemia occurred in seven patients. All of them underwent an aorto-coronary bypass graft operation (table 2). In table 3 the microorganisms causing these infections are given. Bacterial endocarditis was due to Gram-positive microorganisms (mainly *Staph.epidermidis*), sensitive for cephalothin, the antibiotic used for prophylaxis. Septicaemia was caused by Gram-positive or Gram-negative microorganisms. One patient had a polymicrobial septicaemia due to *Staph.epidermidis* and *Ps.aeruginosa*. Results of susceptibility testing showed that the Gram-positive isolates were sensitive for cephalothin and that the Gram-negative isolates were resistant.

Besides susceptibility testing, *Staph.epidermidis* causing early-onset bacterial endocarditis were phage and biotyped. The results of the typing of these strains were compared to those of the *Staph.epidermidis* strains isolated from the specimens obtained on admission. Phage typing revealed that the four strains causing this infection were non-typable. The other two methods showed that in three of the five patients the *Staph.epidermidis* strain causing the infection was similar to a strain present in the skin flora on admission, and in one of the five patients similar to a strain present in the nasal flora.

The causative microorganisms in most of the patients with septicaemia could not be isolated from the specimens taken on admission, or differed in their susceptibility patterns and/or biotypes from strains

Table 2: The number of patients with early-onset bacterial endocarditis or septicaemia after open-heart surgery (total: 178 patients).

Type of operation	total	bacterial endocarditis	septicaemia
Aorto-coronary bypass graft (ACBG)	124	0	7
ACBG with closure of atrial septal defect, or resection of left ventricular aneurysm	2	0	0
Aortic valve replacement	17	3	0
Mitral valve replacement	11	0	0
Aortic and mitral valve replacement	4	2	0
Mitral valve replacement with ACBG	2	1	0
Closure of ventricular septal defect	3	1*	0
Other operations			
-with use of prosthetic material	11	0	0
-without use of prosthetic material	4	0	0
Total	178	7	7

* Direct closure.

Tabel 3: The microorganisms isolated from blood cultures obtained from seven patients with early-onset bacterial endocarditis and seven patients with septicaemia after open-heart surgery in relation to the microorganisms isolated from admission samples in these 14 patients.

Microorganism	Number of patients with			
	bacterial endocarditis		septicaemia	
	total	similar microorganisms isolated on admission	total	similar microorganisms isolated from admission samples
<i>Klebsiella/Enterobacter</i> species	0	0	1	0
<i>Pseudomonas aeruginosa</i>	0	0	2*	0
<i>Staphylococcus aureus</i>	1	0	1	0
<i>Staphylococcus epidermidis</i>	5	4	3*	0
<i>Sareina</i> species	1	0	0	0
<i>Streptococcus viridans</i> group	0	0	1	0

*One patient had a polymicrobial septicaemia.

isolated from these patients at the time of admission.

In the study of the intravascular catheters the majority of the catheter tips was cultured: from a total of 451 intravascular catheter tips the results were available. From 24 (5.3%) tips derived from 23 patients, various microorganisms were isolated (table 4). None of the intracardiac catheter tip cultures showed growth, whereas five (3%) cultures of the intra-arterial catheter tips and 19 (11%) of the intravenous catheter tips were positive. The microorganism most often cultured was *Staph.epidermidis*.

The mean duration of the catheter in place was not statistically significantly different in patients with positive intra-arterial catheter tips and patients with negative intra-arterial catheter tip cultures (Student t test, $p=0.4$). Also no significant difference was found between the duration of intravenous catheters in place in patients with a positive tip culture compared to the duration of the intravenous catheter in place of patients with negative tip cultures (Student t test, $p=0.15$).

A relation between the microorganisms cultured from the intravascular catheter tips and from the samples taken on admission could be demonstrated in only a small number of the 17 patients with *Staph.epidermidis* positive tip cultures (table 5). Antibiograms of six *Staph.epidermidis* strains isolated from the tip cultures and from the skin flora were identical but biotyping revealed a similarity in only two of them. All six *Staph.epidermidis* were non-typable using phage typing.

Blood cultures taken shortly (0-2 days) after removal of the intravascular catheters were negative except in one case (table 5). In this patient *Klebsiella/Enterobacter* species was cultured from the intra-arterial as well as from the intravenous catheter tips and the blood sample. Later on a fatal septicaemia due to the same species occurred.

3.2.2. LOWER RESPIRATORY TRACT INFECTION

Lower respiratory tract infections occurred in 48 (26.9%) open-heart surgery patients (table 6). The incidence of this infection was not significantly different in patients undergoing an aorto-coronary bypass graft operation or in patients undergoing valve replacement surgery (chi Square test $p=0.4$). Most of the positive sputum cultures were found on the first postoperative day: 28 out of the 48 specimens with growth. Of the remaining 20 specimens, 14 were positive on the second, five on the third, and one on the fourth postoperative day. Forty cultures yielded growth

Table 4: The results of intravascular catheters tip cultures in open-heart surgery patients.

Catheter type	Number of catheter tips			Microorganism cultured				
	total	with negative culture	with positive culture	<i>Klebsiella/Enterobacter</i> species	<i>Staphylococcus epidermidis</i>	<i>Streptococcus faecalis</i>	<i>Bacillus</i> species	Unidentified Gram-positive rods
Intracardiac	110	110	0	-	-	-	-	-
Intra-arterial	164	159	5	1	2	1	1	-
Intravenous	177	158	19	2	15	2	-	1

Table 5: The microorganisms cultured from 24 intravascular catheter tips obtained from 23 open-heart surgery patients. The relation between these isolates and the results of the admission samples, the microorganisms causing bacteraemia after removal of the catheter and the microorganisms causing early-onset bacterial endocarditis (BE) and septicaemia in these patients.

Microorganism	positive catheter cultures	Number of patients with			
		admission cultures	similar microorganisms from blood cultures after removal of catheters	blood cultures from patients with BE	blood cultures from patients with septicaemia
<i>Klebsiella/Enterobacter</i> species	1	0	1	0	1
<i>Staphylococcus epidermidis</i>	17	6*, 2**	0	0	0
<i>Streptococcus faecalis</i>	3	0	0	0	0
Unidentified Gram-positive rods	1	0	0	0	0
<i>Bacillus</i> species	1	0	0	0	0

* Based upon similarity of susceptibility pattern of the isolates.

** Based upon similarity of susceptibility pattern and biotype of the isolates.

Table 6: The number of patients with a lower respiratory tract infection after open-heart surgery (total: 178 patients).

Type of operation	total	lower respiratory tract infection
Aorto-coronary bypass graft (ACBG)	124	39
ACBG with closure of atrial septal defect, or resection of left ventricular aneurysm	2	0
Aortic valve replacement	17	5
Mitral valve replacement	11	2
Aortic and mitral valve replacement	4	1
Mitral valve replacement with ACBG	2	0
Other operations		
-with use of prosthetic material	12	0
- without use of prosthetic material	6	1
Total	178	48

of one isolate, whereas eight contained two different microorganisms.

Enterobacteriaceae (*E.coli*, *Klebsiella/Enterobacter*, *Pr.vulgaris*, *Serratia* species) were the most frequently encountered microorganisms (table 7). Streptococci were isolated from specimens obtained from seven patients and *Candida albicans* were isolated from specimens obtained from eight patients. Of all bacterial isolates only ten were resistant to cephalothin.

In 14 out of the 48 patients with a postoperative lower respiratory tract infection the isolated species were similar to those cultured from the admission flora (table 7). In six of these 14 patients the microorganisms isolated from the postoperative sputum specimens were similar to those isolated from samples taken from the upper respiratory tract on admission. Admission samples from the perineum yielded similar species in ten of the 14 patients.

The relation between the culture results of the endotracheal tube tips and the occurrence of subsequent lower respiratory tract infection was also studied. All 161 endotracheal tubes from which the results of the tip cultures were available were removed on the first postoperative day, and 97 (60.3%) tips revealed growth on culture. Mainly *Enterobacteriaceae* and streptococci were isolated. In 33 of the 48 patients with a lower respiratory tract infection a similar microorganism was cultured from the endotracheal tube tip prior to the isolation from the sputum specimen. In 12 patients with a lower respiratory tract infection, the endotracheal tube tip cultures showed no growth of relevant bacteria.

3.2.3. BACTERIURIA

Postoperative bacteriuria was demonstrated in three patients (table 8). The urinary catheter was removed from all three patients one week before the onset of the bacteriuria. In the patient with a bacteriuria due to *Pr.mirabilis* this microorganism was not isolated from the samples taken on admission. In one patient the bacteriuria was due to *Str.faecalis*, *E.coli* and *Pr.mirabilis*. The latter two microorganisms were also isolated from perineum samples taken on admission. In another patient the bacteriuria was caused by a cephalothin resistant *Citrobacter freundii* and *E.coli*. A similar *E.coli* was also present on the perineum on admission.

The tips of at least 166 urinary tract catheters were cultured after removal of the catheter. Bacteria were isolated from 79 (47.6%) of

Table 7: The microorganisms isolated from sputum specimens after extubation, obtained from 48 open-heart surgery patients with a lower respiratory tract infection and the relation with microorganisms isolated from admission samples in these patients.

Microorganism	Number of patients with	
	a culture positive for	similar microorganisms isolated from admission samples
<i>Escherichia coli</i>	12 (1)*	8**
<i>Klebsiella/Enterobacter</i> species	17 (5)	5 +
<i>Proteus vulgaris</i>	4 (2)	0
<i>Serratia</i> species	1 (0)	0
<i>Pseudomonas aeruginosa</i>	2 (1)	0
<i>Haemophilus influenzae</i>	4 (1)	0
Haemolytic streptococcus non-group A	5 (1)	1 ++
<i>Streptococcus faecalis</i>	2 (0)	0
<i>Candida albicans</i>	9 (3)	0

* In parenthesis: the number of patients with sputum specimens from which more than one isolate was cultured.

** Admission samples from the nose and perineum in 1 patient, from the throat, sputum and perineum in 2 patients, from the throat in 1 patient and from the perineum in 4 patients.

+ Admission samples from the skin in 1 patient, from the nose in 1 patient, from the sputum and throat in 1 patient and from the perineum in 2 patients.

++ Admission samples from the perineum in 1 patient.

Table 8: The number of patients with a bacteriuria after open-heart surgery (total: 178 patients) and the causative microorganisms.

Type of operation	total	bacteriuria	microorganism
Aorto-coronary bypass graft (ACBG)	124	0	
ACBG with closure of atrial septal defect, or resection of left ventricular aneurysm	2	0	
Aortic valve replacement	17	1	<i>Pr. mirabilis</i>
Mitral valve replacement	11	0	
Aortic and mitral valve replacement	4	0	
Mitral valve replacement with ACBG	2	0	
Other operations			
- with use of prosthetic material	12	0	
-without use of prosthetic material	6	2	<i>E. coli, Str. faecalis</i> <i>Pr. mirabilis</i> <i>E. coli, Citr. freundii</i>
Total	178	3	

Table 9: The number of patients with a wound infection after open-heart surgery (total: 178 patients)

Type of operation	total	with an incisional wound infection on				with osteo- myelitis	with medias- tinitis
		sternum	groin	leg			
Aorto-coronary bypass graft (ACBG)	124	3	1	2	1*		1*
ACBG with closure of atrial septal defect, or resection of left ventricular aneurysm	2	0	0	0	0		0
Aortic valve replacement	17	0	1	0	0		0
Mitral valve replacement	11	0	0	0	0		0
Aortic and mitral valve replacement	4	1	0	0	0		0
Mitral valve replacement with ACBG	2	0	0	0	0		0
Other operations							
- with use of prosthetic material	12	0	0	0	0		0
- without use of prosthetic material	6	0	0	0	0		0
Total	178	4	2	2	1		1

* Both patients had also a postoperative incisional sternal wound infection.

Table 10: The microorganisms isolated from infected wounds in eight open-heart surgery patients and the relation with microorganisms isolated from admission samples in these patients.

Microorganism	Number of patients with				similar microorganisms isolated from admission samples	
	incisional wound infection on			sternal osteomyelitis		
	chest	groin	leg			
<i>Escherichia coli</i> , indifferent streptococcus, <i>Str. faecalis</i> , <i>Staphylococcus epidermidis</i>	0	1	1	0	0	2*
<i>Pseudomonas aeruginosa</i>	1	0	0	1	0	1**
<i>Staphylococcus epidermidis</i>	1	1	0	0	0	0
<i>Staphylococcus aureus</i>	1	0	1	0	0	0
<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i>	1	0	0	0	1	0

* In one patient *E. coli*, indifferent streptococci and *Staph. epidermidis* were isolated from the wound of the leg.

In the second patient *E. coli*, *Str. faecalis* and *Staph. epidermidis* were isolated from the wound of the groin.

In both patients a similar *E. coli* strain was preoperatively isolated from the perineum.

** Admission sample from the throat in this patient.

166 tips. The culture results of the remaining 12 tips were not available. In two cases microorganisms cultured from the tip were similar to those causing a subsequent bacteriuria.

3.2.4. WOUND INFECTION

Postoperative incisional wound infections occurred in eight (4.5%) patients of whom four had an incisional sternal wound infection (table 9). Subsequently one of these four patients had a sternal osteomyelitis and another patient had a sternal dehiscence together with a mediastinitis. Four patients had infections of the wound of the groin or the leg. Staphylococci, causing most of the wound infections (table 10) were sensitive for cephalothin, except in two cases. In two patients more than one microorganism was cultured from the infected wounds. *Ps.aeruginosa* was the cause of an incisional sternal wound infection and of the subsequently occurring sternal osteomyelitis. *Staph.aureus* and *Staph.epidermidis* were cultured from the pus obtained from the patient with a mediastinitis.

In three patients with a postoperative wound infection, the same microorganisms had been isolated from wound samples and from samples from the perineum, skin or the throat on admission (table 10).

To see whether a positive wound drain tip could predict the occurrence of a postoperative wound infection, the tips of wound drains and the tips of thoracic drains were cultured. The culture results of wound and thoracic drain tips of 142 and 177 patients respectively, were available. Microorganisms were cultured from seven (4.9%) wound drain tips, mainly *Staph.epidermidis*. *Ps.aeruginosa* was cultured from one wound drain tip. In this patient a postoperative incisional sternal wound infection occurred, due to a similar strain. Deep wound infections could not be related to the presence of a positive thoracic drain tip culture. Thirteen (7.4%) of the 177 thoracic drain tip cultures showed growth. Mainly *Staph.epidermidis* were cultured but subsequent infections due to the microorganism did not occur.

4. DISCUSSION

The incidence of postoperative infections in 178 open- heart surgery

patients was rather high. In total 75 postoperative infections occurred in 63 (35%) patients of whom 48 had a lower respiratory tract infection. Cephalothin, a first generation cephalosporin, was mainly used as antimicrobial prophylaxis. Susceptibility testing of the microorganisms causing postoperative infections showed that about 70% of the isolates were sensitive for this antibiotic. Antimicrobial prophylaxis using cephalothin as the single antibiotic has been previously used in open-heart surgery patients. The incidence of postoperative infections in patients who prophylactically received cephalothin has been reported (21-24). In these four reports, a total of 442 patients was involved. Analysis of the postoperative infections in these 442 patients showed that bacterial endocarditis occurred in one (0.2%) patient, bacteraemia in ten (2.3%) patients, lower respiratory tract infections in 30 (6.8%) patients, wound infections in 21 (4.8%) patients and bacteriuria in 43 (9.7%) patients. Comparing these incidences of infection with those found in our study, similar percentages for bacteraemia and wound infection were found. The incidences of the other infections differed markedly. Early-onset bacterial endocarditis was present in 3.9% of the patients in our study. The incidence of lower respiratory tract infections in our patients was almost four times higher. Bacteriuria occurred less frequently in our patients (1.7%).

The question can be raised if this comparison is a valid one since the incidences of each infection in the patients from the four different reports varied markedly and the patients involved belonged to different risk categories. Moreover, appropriate definitions of the infections were given in only two of the reports (22,24).

The relatively high incidence of lower respiratory tract infections in our patients might be partly due to the diagnostic criteria of a lower respiratory tract infection used in this study.

An incidence of 3.9% of early-onset bacterial endocarditis among the patients in our study is high, especially if the number of patients most at risk for prosthetic endocarditis, namely 47 patients with surgical prostheses, are taken into account.

Six of the seven cases with bacterial endocarditis were caused by *Staph.epidermidis* and *Staph.aureus* strains, all subjected to typing procedures. In four cases *Staph.epidermidis* was probably derived from patients' own admission flora. The onset of the infection (mean onset: 12 days after operation) suggests that these strains gained access into the blood stream during or after operation.

We have not performed assays to determine the cephalothin serum level. However, it is known that the serum cephalothin level during extra corporeal circulation is rather high when two gram of this antibiotic is administered just prior to cardiopulmonary bypass (25). Therefore the incidence of early-onset bacterial endocarditis is remarkably high since the microorganisms causing early-onset bacterial endocarditis were sensitive for this antibiotic. This means that contamination of the blood stream after surgery has to be taken into account, although no evidence is available.

Postoperative septicaemia's only occurred after aorto-coronary bypass graft operations and were caused by various microorganisms. The microorganisms involved were probably derived from exogenous sources since none of the microorganisms were cultured from samples taken from the patients on admission.

Postoperative wound infections were mainly caused by Gram-positive microorganisms whereas lower respiratory tract infections and bacteriuria's were mainly caused by Gram-negative microorganisms.

A possible relation between the microorganisms cultured preoperatively from the patients on the day of admission, and those causing postoperative infections was demonstrated in only about one third of the infections. Routinely performed culture procedures (1,4,5,21,23,26) are seldom thoroughly tested on their merits. Although Cooper *et al.* (26) also concluded from their data that the results of a preoperative bacteriological screening did not predict the occurrence of a postoperative infection, they have not defined the similarity of isolates. Comparing the microorganisms causing postoperative infections with those isolated from preoperative cultures, Frater and Santos (5) found a relation in only 21% of their infected patients. In another study (4) preoperative culture results were used to obtain insight into the frequency of postoperative acquisition of Gram-negative microorganisms. Typing of the microorganisms was not performed in any of these studies.

In our study *Staph.epidermidis* isolates were biotyped and phage typed and *Staph.aureus* isolates were phage typed. All isolates were tested for antimicrobial susceptibility. The susceptibility pattern, commonly referred to as antibiogram, was used, besides for clinical purposes, to determine a relation between the isolates. The antibiogram can be used as an epidemiological tool (27). However, the method has its limitations (28). Susceptibility to antibiotics is not a stable genetic property. It may be influenced by environmental conditions and by plasmids (27). The results of the phage

typing of *Staph.epidermidis* were disappointing and confirmed the inadequacy of the phage typing method, as reported previously (20).Therefore a relation between *Staph.epidermidis* isolates from the admission flora and the occurrence of infections caused by this microorganism and the presence of *Staph.epidermidis* on intravascular devices was based on the results obtained by comparison of their biotypes and of their antibiograms. Four out of five cases of postoperative early-onset bacterial endocarditis were caused by *Staph.epidermidis* strains identical to those present in the admission flora. In contrast septicaemia due to *Staph.epidermidis* was probably caused in all three cases by strains from exogenous sources. Only a small number of the *Staph.epidermidis* isolates cultured from intravascular catheter tips appeared to be identical to *Staph.epidermidis* isolated from the admission flora. Infections due to *Staph.aureus* occurred in four patients who all had *Staph.aureus* negative samples on admission, suggesting that these infections were due to strains acquired in the hospital. In the case of the other isolates causing postoperative infections the results of pre- and postoperative culturing were compared and if the same species were isolated pre- and postoperatively, the antibiograms of the isolates were compared. Similar isolates were found in about one third of the infections.

Culturing indwelling devices, such as intravascular catheters, urinary catheters and wound and thoracic drains was also unable to predict the occurrence of septicaemia, bacteriuria or wound infections. However, 69% of lower respiratory tract infections were caused by microorganisms similar to those cultured from the endotracheal tube tips prior to the onset of this infection.

Our results indicate that the preoperative bacteriological surveillance of open-heart surgery patients performed routinely on the day of admission, had only a small predictive value towards the occurrence of postoperative infections. Such surveillance can be useful for epidemiological studies to gain insight into the various sources of contamination. Another reason for taking preoperative samples from open-heart surgery patients is the need to be informed about the susceptibility or the resistance of microorganisms cultured from the endogenous flora. The results of preoperative sampling will provide data on which the prophylactic antimicrobial regimen can be adjusted (29).

REFERENCES

1. Goodman, J.S., Schaffner, W., Collins, H.A., Battersby, E.J. and Koenig, M.G. Infection after cardiovascular surgery. Clinical study including examination of antimicrobial prophylaxis. *New.Engl.J.Med.* 278:117,1968.
2. Watanakunakorn, C. Prosthetic valve infective endocarditis. *Prog. Cardiovasc. Dis.* 22:181,1979.
3. Hornick, R.B. Source of contamination in open-heart surgery. In: R.J.Duma, ed. *Infections of prosthetic heart valves and vascular grafts*. Baltimore: University Park Press, 1977; 81.
4. Rosendorf, L.L., Daicoff, G. and Baer, H. Sources of Gram-negative infection after open-heart surgery. *J.Thorac.Cardiovasc.Surg.* 67: 195,1974.
5. Frater, R.W.M. and Santos, G.H. Sources of infection in open-heart surgery. *N.Y. State J.Med.* 74:2386,1974.
6. Norenberg, R.G., Sethi, G.K., Scott, S.M. and Takaro, T. Opportunistic endocarditis following open-heart surgery. *Ann.Thorac. Surg.* 19: 592, 1975.
7. Carey, J.S. and Hughes, R.K. Control of infection after thoracic and cardiovascular surgery. *Ann. Surg.* 172: 916,1970.
8. Blakemore, W.S., Mc. Garrity, G.J., Thurer, R.J., Wallace, H.W., Mac Vaugh, H. III and Coriell, L.L. Infection by air-borne bacteria with cardiopulmonary bypass. *Surgery* 70: 830,1971.
9. Kluge, R.M., Calia, F.M., McLaughlin, J.S. and Hornick, R.B. Sources of contamination in open-heart surgery. *JAMA* 230:1415,1974.
10. Clark, R.E., Amos, W.C., Higgins, V., Bemberg, K.F. and Weldon, C.S. Infection control in cardiac surgery. *Surgery* 79:89,1976.

11. Stein, P.D., Harken, D.E. and Dexter, L. The nature and prevention of prosthetic valve endocarditis. *Am.Heart J.* 71: 393,1966.
12. Dismukes, W.E., Karchmer, A.W., Buckley, M.J., Austen, W.G. and Swartz, M.N. Prosthetic valve endocarditis. Analysis of 38 cases. *Circulation.* 48: 365,1973.
13. Dismukes, W.E. and Karchmer, A.W. The diagnosis of infected prosthetic heart valves: bacteremia versus endocarditis. In: R.J.Duma, ed. *Infections of prosthetic heart valves and vascular grafts.* Baltimore: University Park Press, 1977; 61.
14. Wilson, W.R. Prosthetic valve endocarditis: incidence, anatomic location, cause, morbidity and mortality. In: R.J. Duma, ed. *Infections of prosthetic heart valves and vascular grafts.* Baltimore: University Park Press, 1977; 3.
15. Block, P.C., DeSanctis, R.W., Weinberg, A.N. and Austen, W.G. Prosthetic valve endocarditis. *J.thorac.Cardiovasc.Surg.* 60: 540,1970.
16. Bagshawe, K.D., Blowers, R. and Lidwell, O.M. Isolating patients in hospital to control infection. Part I. Sources and routes of infection. *Br. Med. J.* 2: 609,1978.
17. Maki, D.G. Control of colonization and transmission of pathogenic bacteria in the hospital. *Ann. Int. Med.* 89 (part II): 777, 1978.
18. Baffes, T.G., Blazek, W.V., Fridman, J.L., Agustsson, M.H. and van Elk, J. Postoperative infections in 1,136 consecutive cardiac operations. *Surgery* 68: 791,1970.
19. Levenson, S.M. and Laufman, H. Infection hazard of surgical intensive care: isolation procedures in the surgical intensive care unit. In: J.M.Kinney, H.H. Bendixen and S.R. Powers, eds. *Manual of surgical intensive care.* Philadelphia: W.B. Saunders Comp. 1977; 151.

20. Staal, M.J., Stobberingh, E.E., Haverkorn, M.J. and van Boven, C.P.A. Application of phage-typing and biotyping to the epidemiology of coagulase-negative Staphylococci in cardiovascular surgery. In: J.Jeljaszewicz, ed. Staphylococci and Staphylococcal infections. Proceedings of IV international symposium on Staphylococci and Staphylococcal infections. Zbl. Bakt. Suppl. 10. Stuttgart-New York: Gustav Fischer Verlag, 1981; 189.
21. Conte, J.E. Jr., Cohen, S.N., Roe, B.B. and Elashoff, R.M. Anti-biotic prophylaxis and cardiac surgery. A prospective double-blind comparison of single-dose versus multiple-dose regimens. *Ann.Int.Med.* 76: 943,1972.
22. Goldmann, D.A., Hopkins, C.C., Karchmer, A.W., Abel, R.M., McEnany, M.T., Akins, C., Buckley, M.J. and Moellering, R.C., Jr. Cephalothin prophylaxis in cardiac valve surgery. A prospective double-blind comparison of two-day and six-day regimens. *J.Thorac.Cardiovasc.Surg.* 73: 470,1977.
23. Kini, P.M., Fernandez, M.D., Causay, R.S. and Lemole, G.M. Double-blind comparison of cefazolin and cephalothin in open-heart surgery. *J.Thorac.Cardiovasc.Surg.* 76: 506,1978.
24. Pien, F.D., Michael, N.L., Mamiya, R., Pakaki, H., Slavish, S., Bruce, A. and Moreno-Cabral, R.J. Comparative study of prophylactic antibiotics in cardiac surgery. Clindamycin versus cephalothin. *J.Thorac.Cardiovasc. Surg.* 77:908,1979.
25. Miller K.W., Chan, K.K.H., McCoy, H.G., Fisher, R.P., Lindsay, W.G., and Zaske, D.E. Cephalothin kinetics: Before, during, and after cardio-pulmonary bypass surgery. *Clin. Pharmacol. Ther.* 26: 54,1979.
26. Cooper, D.K.C., Norton, R., Mobin, M.A., Cleland, W.P., Bentall, H.H. and Darrell, J.H. A comparison of two prophylactic antibiotic regimes for open-heart surgery. *J.Cardiovasc.Surg.* 21: 279,1980.
27. Aber, R.C. and Mackel, D.C. Epidemiologic typing of nosocomial micro-organisms. *Am.J.Med.* 70:899,1981.

28. Goldmann, D. Laboratory procedures for infection control. In: E.H.Lennette, A.Balows, W.J. Hausler, Jr., and Truant, J.D., eds. Manual of clinical microbiology. 3^d ed. Washington, D.C.: American Society for Microbiology, 1980; 939.
29. Newson, S.W.B. Antibiotic prophylaxis for open-heart surgery. J.Antimicrob.Chemother. 4: 389,1978.

CHAPTER IV

DETECTION AND TREATMENT OF STAPHYLOCOCCUS AUREUS CARRIAGE IN RELATION TO THE OCCURRENCE OF POSTOPERATIVE STAPHYLOCOCCUS AUREUS INFECTIONS

1. INTRODUCTION

A relation between the preoperative carriage of *Staphylococcus aureus* in the nose of patients and the occurrence of postoperative wound infections has been reported (1-6). In patients who underwent thoracic surgery (7-9) or (open-) heart surgery (8,9), attention has also been drawn to the greater frequency of postoperative *Staph.aureus* infections among *Staph.aureus* carriers. It was suggested therefore that preoperative treatment of *Staph.aureus* nasal carriers would reduce the incidence of postoperative wound infection caused by *Staph.aureus* (2). Although the *Staph.aureus* carriers had a higher sepsis rate than non-carriers and the nasal carriage was reduced to a large extent after treatment, Henderson and Williams (2) could not demonstrate a reduction in the postoperative wound infection rates among the *Staph.aureus* nasal carriers who were treated preoperatively with nasal antimicrobial ointment when compared to a control group of un-treated *Staph.aureus* carriers. They suggested that this could be due to an inefficient swabbing technique or due to a variability of the presence of *Staph.aureus* in the nasal flora.

In this study, the reliability of the sampling method for detection of nasal and pharyngeal carriage of *Staph.aureus* and the persistence of this carriage in patients and hospital personnel was investigated. In addition the effect of the preoperative treatment of nasal carriers among patients on the occurrence of postoperative infections due to *Staph.aureus* was studied.

2. SUBJECTS AND METHODS

2.1. PREOPERATIVE SAMPLING OF PATIENTS, TREATMENT OF NASAL CARRIERS AND POSTOPERATIVE INFECTIONS

Samples from the nose, throat, several sites of the skin and the perineum were taken on the day of admission from 182 patients admitted for open-heart surgery, using dry cotton-tipped swabs. Both vestibules of the nose were sampled using one swab. The swab was rotated during sampling. The throat was sampled by rubbing the pharyngeal mucosa of the left and right pharyngeal wall between the two pharyngeal arches with one swab. The sites of the skin and the perineum were sampled by streaking twice a surface of approximately 4 cm², using one swab for each place.

Chlorhexidin digluconate (0.5% w/w) ointment was applied to the nasal

mucosa of 34 randomly selected patients with *Staph.aureus* positive nasal swabs.

Postoperative infections due to *Staph.aureus* were recorded prospectively according to the definitions given in Chapter II.

2.2. ACCURACY OF THE SAMPLING METHOD AND THE PERSISTENCE OF PREOPERATIVE *STAPH.AUREUS* CARRIAGE IN PATIENTS AND HOSPITAL EMPLOYEES.

In order to determine the accuracy of the swabbing technique employed to detect nasal and pharyngeal carriage of *Staph.aureus*, samples from these two sites were taken twice from 89 patients and from a group of 183 hospital employees (initial examination). This group consisted of 31 ward nurses and doctors, 48 laboratory technicians, 47 members of the operating room staff, 15 physiotherapists and 42 student nurses.

The persistence of the carriage of *Staph.aureus* on the nasal and pharyngeal mucosa was studied in the same 89 patients and 183 hospital employees by re-sampling once the nose and pharynx (follow up examination). The results of these samples were compared to the results of the first samples of the initial examination. The mean interval between the initial examination and the follow up examination was two days (range: 1-3 days) for the patients and seven days (range: 5-9 days) for the hospital employees. Those who used antimicrobial agents in the three weeks preceeding the initial examination or during the follow up period and those with an infection of the upper respiratory tract, were excluded from the study.

2.3. CULTURE METHODS, SUSCEPTIBILITY TESTING, PHAGETYPING AND STATISTICS.

Culture methods, susceptibility testing and phagetyping are described in Chapter III. All *Staph.aureus* strains were phage typed. The results were subjected to statistical analysis, using the chi square test on two observed grouped distributions.

3. RESULTS

3.1. THE PREOPERATIVE PRESENCE OF *STAPH.AUREUS* AND THE OCCURRENCE OF POSTOPERATIVE INFECTIONS.

Of 182 patients admitted for open-heart surgery, *Staph.aureus* was cultured from 65 (36%) patients of whom 56 had a *Staph.aureus* positive nasal swab (table 1). In 21 patients, this microorganism was also isolated from one of the other sites sampled. In nine patients, nasal swabs were negative but *Staph.aureus* was present in the throat of eight patients and on the skin of one patient. In seven patients, *Staph.aureus* was isolated from the perineum, but samples taken from other sample sites including the nose were also *Staph.aureus* positive.

Thirty four out of 56 patients with a *Staph.aureus* positive nasal swab were treated with the chlorhexidin containing ointment. *Staph.aureus* infections did not occur in treated or in un-treated *Staph.aureus* positive patients (table 2).

Six postoperative infections due to *Staph.aureus* occurred in four patients who were *Staph.aureus* negative on admission (table 2). Two patients had a wound infection and one had an early-onset bacterial endocarditis. A fourth patient had an incisional wound infection, a mediastinitis and a septicaemia. A common source of these infections was not likely as the phage types of the isolated strains differed per patient.

3.2. ACCURACY OF THE SAMPLING METHOD AND THE PERSISTENCE OF PREOPERATIVE *STAPH.AUREUS* CARRIAGE IN PATIENTS.

The results of the first nasal cultures showed that *Staph.aureus* was isolated from 33 (37%) of the 89 patients (table 3). The second sample, taken immediately after the first one, yielded *Staph.aureus* in three additional patients. This means that a total of 36 (40%) patients had *Staph.aureus* in their nose at the time of admission. Two consecutive samples taken from the throat revealed the presence of *Staph.aureus* in 18 (20%) patients whilst sampling once showed *Staph.aureus* to be present in 15 (17%) patients (table 3).

The results of the first sample obtained at the initial examination, were used to determine the persistence of *Staph.aureus* in the nasal and throat flora. The results of the follow up examination of the nasal flora

Table 1: The preoperative isolation of *Staph. aureus* from 182 patients.

Site	Number of patients (%)
Nose	35 (19.3)
Throat	8 (4.4)
Skin	1 (0.6)
Perineum	0
Nose + throat	7 (3.9)
Nose + skin	4 (2.2)
Nose + perineum	2 (1.1)
Nose + throat + skin	3 (1.7)
Nose + throat + perineum	1 (0.6)
Nose + skin + perineum	4 (2.2)
None	117 (64.3)
Total	182(100.0)

Table 2: The relation between the preoperative presence of *Staph. aureus* and the occurrence of postoperative infections due to *Staph. aureus* in 178 patients.

<i>Staph. aureus</i>	Number of patients		
	total	treated with nasal ointment	with postoperative <i>Staph. aureus</i> infections
isolated from			
	nose	34, treated	0
		22, not treated	0
	other site(s)	0	0
not isolated	113	0	4

Table 3: The detection of *Staph. aureus* in the nose and the throat of 89 patients by consecutive sampling.

Sampling site	Number of patients	first sample		second sample		cumulative results	
		positive (%)	negative (%)	positive (%)	negative (%)	positive (%)	negative (%)
Nose	89	33 (37)	56 (63)	34 (38)	55 (62)	36 (40)	53 (60)
Throat	89	15 (17)	74 (83)	16 (18)	73 (82)	18 (20)	71 (80)

performed two days later, showed that seven (21%) out of 33 patients with *Staph.aureus* in their nose at the initial examination became negative (table 4). Persistence was found in 26 (79%) of the initially *Staph.aureus* positive patients. However the phagetype of *Staph.aureus* from at least three patients differed from the phagetype of the *Staph.aureus* isolated at the initial examination. Three (5%) out of 56 patients initially negative, were positive at the follow up examination. The results of the follow up examination of the throat flora, two days after the initial examination, showed that seven (47%) out of 15 patients positive at the initial examination, became negative (table 4). Phage typing revealed that at least two out of eight patients had another strain than at the initial examination. Of the 74 initially *Staph.aureus* negative patients, 14 (19%) became *Staph.aureus* positive at the follow up examination.

3.3. ACCURACY OF THE SAMPLING METHOD AND THE PERSISTENCE OF *STAPH.AUREUS* CARRIAGE IN HOSPITAL EMPLOYEES.

The results of the first nasal cultures of the initial examination showed that *Staph.aureus* was isolated in 64 (35%) of 183 employees (table 5). The highest percentage was among the ward nurses (48%). The lowest percentage was among the physio-therapists (20%). The differences between the various categories were not significant ($p=0.4$). *Staph.aureus* was present in the throat flora of 20% of the employees (table 5). Laboratory technicians showed the highest percentage (27%) whereas the lowest percentage was found among the ward nurses. No statistically significant difference was seen among the various categories ($p=0.4$). The consecutive second nasal culture yielded *Staph.aureus* in 67 (37%) employees (table 6). Accumulation of the results of the samples showed that *Staph.aureus* was isolated from the nasal flora of 71 (39%) hospital employees. The results of both cultures taken from the throat showed that 45 (25%) employees were *Staph.aureus* positive (table 6). At the initial examination this microorganism was detected in 36 (20%) of them.

The follow up examination of the nasal flora of 174 hospital employees, performed seven days after the initial examination showed that 56 (32%) were *Staph.aureus* positive (table 7). Comparison between the results obtained at the follow up examination and the initial examination showed that 11 (19%) out of 59 employees who were initially positive, became negative.

Staph.aureus isolated from at least eight of the 48 employees who were

Table 4: The persistence of *Staph. aureus* in the nasal and throat flora of 89 patients.

Sampling site	Initial examination (1 st sample) number of patients (%)	Follow up examination number of patients (%)	Comparison of phage types
Nose	<i>Staph. aureus</i> positive 33(37)	<i>Staph. aureus</i> positive 26(79)	identical 20
		<i>Staph. aureus</i> negative 7(21)	different 3
			not determined 3
	<i>Staph. aureus</i> negative 56(63)	<i>Staph. aureus</i> positive 3(5)	
Throat		<i>Staph. aureus</i> negative 53(95)	
	<i>Staph. aureus</i> positive 15(17)	<i>Staph. aureus</i> positive 8(53)	identical 4
		<i>Staph. aureus</i> negative 7(47)	different 2
	<i>Staph. aureus</i> negative 74(83)	<i>Staph. aureus</i> positive 14(19)	not determined 2
		<i>Staph. aureus</i> negative 60(81)	

Table 5: The presence of *Staph.aureus* in the nasal and throat flora of 183 employees as shown by the first sample of the initial examination.

Category	Number of employees		
	total	<i>Staph.aureus</i> positive	
		nose (%)	throat (%)
Ward nurses	31	15 (48)	3 (10)
Laboratory technicians	48	14 (29)	13 (27)
Operating room personnel	47	18 (38)	9 (19)
Physiotherapists	15	3 (20)	2 (13)
Student nurses	42	14 (33)	9 (21)
Total	183	64 (35)	36 (20)

Table 6: The detection of *Staph. aureus* in the nose and the throat of 183 hospital employees by consecutive sampling.

Sampling site	Number of hospital employees	first sample		second sample		cumulative results	
		positive (%)	negative (%)	positive (%)	negative (%)	positive (%)	negative (%)
Nose	183	64 (35)	119 (65)	67 (37)	116 (63)	71 (39)	112 (61)
Throat	183	36 (20)	147 (80)	39 (21)	144 (79)	45 (25)	138 (75)

Table 7: The persistence of *Staph. aureus* in the nasal and throat flora of hospital employees.

Sampling site	Initial examination (1 st sample) number of subjects (%)	Follow up examination number of subjects (%)	Comparison of phage types
Nose	<i>Staph. aureus</i> positive 64 (35)	<i>Staph. aureus</i> positive 48 (81)	identical 35
		<i>Staph. aureus</i> negative 11 (19) not studied 5	different 8 not determined 5
	<i>Staph. aureus</i> negative 119 (65)	<i>Staph. aureus</i> positive 8 (7)	
		<i>Staph. aureus</i> negative 107 (93) not studied 4	
Throat	<i>Staph. aureus</i> positive 36 (20)	<i>Staph. aureus</i> positive 15 (48)	identical 12
		<i>Staph. aureus</i> negative 16 (52) not studied 5	different 1 not determined 2
	<i>Staph. aureus</i> negative 147 (80)	<i>Staph. aureus</i> positive 21 (15)	
		<i>Staph. aureus</i> negative 122 (85) not studied 4	

Table 8: The antimicrobial susceptibility of *Staph. aureus* isolated from the nose and throat flora of patients preoperatively and from the nose and throat flora of hospital employees.

Antimicrobial agent	Initial examination				Follow up examination			
	patients		hospital employees		patients		hospital employees	
	nose	throat	nose	throat	nose	throat	nose	throat
Penicillin	23*	30	25	49	7	29	27	50
Tetracyclin	96	100	94	94	93	100	100	94
Cloxacillin	100	100	100	100	100	100	100	100
Streptomycin	100	100	100	98	100	86	100	100
Clindamycin	100	100	100	100	100	100	100	100
Gentamicin	100	100	99	100	100	100	100	100
Cephalothin	100	100	100	100	100	100	100	100

* percentage susceptible *Staph. aureus* isolates.

Staph.aureus positive in both examinations, had another phage type in the follow up examination than the strain isolated at the initial examination.

The throat flora was also re-sampled seven days after the initial examination. Only 15 (48%) out of the 31 employees who were re-sampled and who were initially *Staph.aureus* positive remained *Staph.aureus* positive (table 7). At least one of the 15 subjects had another strain than at the initial examination. At the initial examination, no *Staph.aureus* was cultured from the throat of 147 employees. One week later, 21 (15%) of the 143 recultured employees had acquired this microorganism and at least 16 (52%) of the recultured employees had lost this microorganism.

3.4. SUSCEPTIBILITY OF *STAPH.AUREUS* TO ANTIMICROBIAL AGENTS

In total, 225 *Staph.aureus* strains were tested. Resistance to penicillin was found in more than half of the strains isolated from patients and hospital employees (table 8). All strains were susceptible to cephalothin, the antimicrobial agent used as prophylaxis for patients undergoing open-heart surgery.

4. DISCUSSION

The rate of *Staph.aureus* carriage is dependent on the accuracy of the method used to investigate this carriage. We used the most frequently employed sampling method, namely the swabbing method. After sampling the site being examined, the swab was smeared over the surface of a solid medium.

In order to determine the accuracy of this swabbing technique using direct plating the nose and throat were sampled twice by taking two consecutive samples. The results of these two consecutive samples revealed that *Staph.aureus* was not present in the first sample from 8.3% of the patients harbouring this microorganism in their nose and from 16.6% of the patients with *Staph.aureus* in their throat flora if only one sample was taken. Similar results of the first and second consecutive sampling of the nose and throat flora in hospital employees were found. Of the *Staph.aureus* positive employees, 9.9% of them would have been considered as negative if only one sample was taken from the nose. In case of the throat flora, 20% of the *Staph.aureus* positive employees would not have been detected if this sampling site was swabbed only once.

Differences in the number of *Staph.aureus* positive subjects can be due to differences in the sampling technique (10). A higher number of *Staph.aureus* positive subjects was found if moistened cotton-tipped swabs instead of dry cotton-tipped swabs were used (11). However, dry cotton-tipped swabs are most frequently used and results of comparative studies are not available. It has been suggested that the site of sampling in the nose influences the number of *Staph.aureus* positive samples. Samples obtained from the higher reaches of the nose yielded *Staph.aureus* more often than samples from the vestibule of the nose (12). However, according to others, swabbing beyond the vestibule might produce artificially low carrier rates (13,14). The culture method for the swabs used to detect *Staph.aureus* carriage affected the yield of positive samples. Polakoff *et al.* (15) incubated the swabs in the broth after direct plating. They found that only 88% of nasal carriers were detected by direct plating. The frequency of sampling seems to affect the number of positive samples as well. This was studied by Solberg (16) who determined the numbers of *Staph.aureus* colony forming units in five consecutive samples obtained from persistent *Staph.aureus* carriers. The first two samples yielded higher numbers of organisms than the last two. Therefore, more than two consecutive samples to detect the presence of *Staph.aureus* will have only a limited increasing effect on the detection rate of *Staph.aureus* positive subjects (16).

Comparing the results of the two consecutive samples obtained from the nose and the throat of the subjects of our study, it appeared that the increase of *Staph.aureus* positive throat samples was markedly higher than the increase of *Staph.aureus* positive nose samples. This suggests that the failure of a single swabbing to isolate *Staph.aureus* from the pharyngeal area is greater than in case of nasal swabbing, probably due to the lower number of *Staph.aureus* in the throat flora compared to the number in the nasal flora (16).

The transiency of the presence of *Staph.aureus* in the throat flora was significantly greater than in the nasal flora ($p < 0,03$). Among patients, 21.2% of the initially positive patients lost *Staph.aureus* from their nares and 5.4% of the initially negative patients acquired this microorganism at this site. Within two days, however, *Staph.aureus* was lost from the throat flora in 46.7% of the initially positive patients and was acquired in 18.9% of the initially negative patients. Hospital employees were re-investigated one week after the initial examination *Staph.aureus* was no longer present in the nose flora of 18.6% and in the throat flora of 51.3% of the initially

Staph.aureus positive employees. Acquisition of *Staph.aureus* in the nasal and throat flora of hospital employees occurred in 6.9% and in 14.6%, respectively. These findings in conjunction with those obtained from the patients showed that the presence of *Staph.aureus* in the nasal and throat flora was rather transient within well defined but short periods. Surprisingly, this transiency was not caused by an increased acquisition but was due to a significant loss of *Staph.aureus* from the flora in both patients and employees within the rather short intervals ($p \leq 0,02$).

It is reported that among patients during hospitalization the number of *Staph.aureus* positive patients is increased (1,10,13) and that among hospital employees the rate of carriers is higher than that of a general population and even exceeds that of patients (10,13). However, Burke and Corrigan (17) and Williams *et al.* (13) indicated that among patients the increase is variable and that a fall in the number of *Staph.aureus* positive patients can be noticed inside the hospital. Because a decrease in the nasal carriage was observed in patients nursed in artificially ventilated wards and in patients nursed in separate rooms, this fall was apparently not directly related to environmental differences (13). A factor accounting for a decrease of *Staph.aureus* positive patients during hospitalization has been reported to be the use of antibiotics (18). However, in other studies the use of antibiotics was shown to result in acquisition of *Staph.aureus* (19).

Our patients, not treated with antimicrobial agents, had a significant loss of *Staph.aureus* within two days after admission. It might be that this loss was due to the presence of antibiotics in the environment which can eliminate antibiotic sensitive strains (20), creating a void for the resistant strains (21). However, the *Staph.aureus* strains isolated from nasal and throat flora were mostly sensitive for the antibiotics tested, except penicillin. Therefore, the loss of *Staph.aureus* must be attributed to as yet unknown factors. It is tempting to speculate that such factors are related to the ability of the epithelial cells in the nose and the throat to adhere this microorganism.

A higher postoperative infection rate has been reported to occur in patients with *Staph.aureus* positive nose cultures compared to patients without *Staph.aureus* in their nasal flora (1-6). In other studies no relation was found between the presence of *Staph.aureus* in the nasal flora of patients on admission and the occurrence of postoperative infections (22,23). We found, in our patients, no relation between the

results obtained from the preoperative surveillance cultures and the occurrence of postoperative infections due to *Staph.aureus*, regardless of preoperative topical antimicrobial treatment. However, the number of patients in our study was small. The four patients with a postoperative infection due to *Staph.aureus* were negative on admission for this microorganism. These four patients might have been so-called light *Staph.aureus* carriers (24) who are unlikely to be detected by a single nasal sampling. Because we found that five percent of the patients without *Staph.aureus* in their nasal flora on admission acquired this microorganism within two days, another explanation might be that these four patients became positive. A third possibility which was not investigated, is that contamination of the patient occurred in the operating room during surgery from various sources.

REFERENCES

1. Williams, R.E.O., Jevons, M.P., Shooter, R.A., Hunter, C.J.W., Girling, J.A., Griffiths, J.D. and Taylor, G.W. Nasal staphylococci and sepsis in hospital patients. *Br.Med.J.* 2: 658,1959.
2. Henderson, R.J. and Williams, R.E.O. Nasal disinfection in prevention of post-operative staphylococcal infection of wounds. *Br.Med.J.* 2: 330,1961.
3. Calia, F.M., Wolinsky, E., Mortimer, E.A. Jr., Abrams, J.S. and Rammelkamp, C.H. Jr. Importance of the carrier state as a source of *Staphylococcus aureus* in wound sepsis. *J.Hyg. (Camb)*. 67: 49,1969.
4. Siebbeles, H.W.R. Onderzoek naar de bronnen van de postoperatieve wond-infecties met *Staphylococcus aureus*. Amsterdam, 1968. Dissertation.
5. Bengtson, S., Hambræus, H. and Laurell, G. Wound infection after surgery in a modern operating suite. *J.Hyg.(Camb.)* 83: 41,1979.
6. Dyas, A.C., Eden, P.J., Eastwood, D., Bentley S., Burdon, D.W., Alexander-Williams, J. and Keighly, M.R.B. Sources of staphylococcal wound sepsis in surgical patients. *J.Hosp.Inf.* 3: 345,1982.
7. Weinstein, H.J. The relation between the nasal-staphylococcal-carrier state and the incidence of postoperative complications. *New.Surg.J.Med.* 260: 1303,1959.
8. Lindbom, G. Studies of the epidemiology of staphylococcal infections. 2. Staphylococcal infections in a thoracic surgery unit. *Acta Chir. Scand.* 128: 421,1964.
9. Lindbom, G., Laurell, G. and Grenvik, A. Studies on the epidemiology of staphylococcal infections. 3. Influence of factors inherent in the patient and his operation. *Acta Pathol. Microbiol.Scand.(B)*. 69: 219,1967.

10. Williams, R.E.O. Healthy carriage of *Staphylococcus aureus*: its prevalence and importance. Bact.Rev. 27: 56,1963.
11. Borst, J. Staphylococcen in een kraamkliniek. Een epidemiologisch onderzoek met behulp van bacteriofaagtypering naar de besmetting van moeders, zuigelingen en personeel. Amsterdam,1960. Dissertation.
12. Stratford, B., Rubbo, S.D., Christie, R. and Dixon,S. Treatment of the nasal carrier of *Staphylococcus aureus* with framycetin and other anti-bacterials. Lancet 2: 1225,1960.
13. Williams, R.E.O., Blowers, R., Garrod, L.P. and Shooter, R.A. In: Hospital infection. Causes and prevention. 2nd ed. London: Lloyd-Luke Ltd., 1966;22.
14. Moss, B., Squire, J.R., Topley, E. and Johnston, C.M. Nose and skin carriage of *Staphylococcus aureus* in patients receiving penicillin. Lancet 1: 320,1948.
15. Polakoff, S., Richards, L.D.G., Parker, M.T. and Lidwell, O.M. Nasal and skin carriage of *Staphylococcus aureus* by patients undergoing surgical operations. J.Hyg. (Camb.) 65: 559, 1967.
16. Solberg, C.O. A study of carriers of *Staphylococcus aureus* with special regard to quantitative bacterial estimations. Acta Med. Scand. 178: suppl. 436,1965.
17. Burke, J.F. and Corrigan, E.A. Staphylococcal epidemiology on a surgical ward. Fluctuations in ward staphylococcal contents, its effect on hospitalized patients and the extent of endemic hospital strains. New.Eng.J.Med. 264: 321,1961.
18. Lidwell, O.M., Polakoff, S., Jevons, M.P., Parker, M.T., Shooter, R.A., French, V.I. and Dunkerley, D.R. Staphylococcal infection in thoracic surgery: experience in a subdivided ward. J.Hyg.(Camb.) 64: 321,1966.

19. Knight, V. and Holzer, A.R. Studies on staphylococci from hospital patients. I. Predominance of strains of group III phage patterns which are resistant to multiple antibiotics. J.Clin. Invest. 33: 1190,1954.
20. Gould, J.C. Environmental penicillin and penicillin resistant *Staphylococcus aureus*. Lancet 1: 489,1958.
21. Williams, R.E.O., Blowers, R., Garrod, L.P. and Shooter, R.A. In: Hospital infection. Causes and prevention. 2nd ed. London: Lloyd-Luke Ltd., 1966; 272.
22. Public Health Laboratory Service. Incidence of surgical wound infection in England and Wales. Lancet 2: 659,1960.
23. Bassett, H.F.M., Ferguson, W.G., Hoffman, E., Walton, M., Blowers, R. and Conn, C.A. Source of staphylococcal infection in surgical wound sepsis. J.Hyg.(Camb.).61: 83,1963.
24. Shooter, R.A., Thorn, B.T., Dunkerly, D.R., Taylor, G.W., Parker, M.T. John, M. and Richards, J.D.G. Postoperative segregation of patients in a surgical ward. Brit.Med.J.2: 1567, 1963.

CHAPTER V

BACTERIOLOGICAL SURVEILLANCE OF THE EXTRA CORPOREAL CIRCUIT;
RELATION BETWEEN THE MICROORGANISMS ISOLATED AND THOSE INVOLVED
IN THE OCCURRENCE OF POSTOPERATIVE BACTERAEemia, SEPTICAEemia,
AND/OR EARLY-ONSET BACTERIAL ENDOCARDITIS

1. INTRODUCTION

The incidence and seriousness of postoperative infections in open-heart surgery is higher than in closed-heart surgery (1-4). This suggests that the use of the extra corporeal circuit (ECct) may be one of the risk factors for acquiring infections after open-heart surgery. The finding of a high level of contamination of the oxygenator at the end of the extra corporeal circulation (ECCu) supports this suggestion (5,6). However, not always could a contribution of the ECct to the probability of postoperative infections be demonstrated (7,8).

Contamination of the ECct can occur at different moments. Before the open-heart operation, the system can be contaminated during assembly of the circuit and during the priming of the circuit with a priming solution and donor blood. During the operation the operative field is usually contaminated with microorganisms from several sources (9). Blood from the operative field is aspirated by suckers into the cardiotomy reservoir and returned to the oxygenator of the ECct. From there, contamination of the intravascular compartment of the patient can occur. The relevance of such contamination in relation to the occurrence of postoperative bacteraemia, septicaemia and infective endocarditis is not clear (10).

As part of our infection surveillance programme, we studied the contamination rate of the ECct regardless of the source. Samples from the circuit were taken prior to and at the end of the ECCu. In this chapter, the results of the bacteriological monitoring in relation to the occurrence of postoperative bacteraemia, septicaemia and/or early-onset bacterial endocarditis (BE) are reported.

In addition, the contamination of the ECct was studied in more detail in a number of operations in order to determine more accurately the contamination rate and the relation to postoperatively occurring bacteraemia, septicaemia and/or BE.

2. MATERIALS AND METHODS

2.1. THE EXTRA CORPOREAL CIRCUIT AND ITS ASSEMBLY.

The ECct connected to the heart lung machine (Sarns 5000 Console, Sarns, Ann Arbor, Michigan, U.S.A.) used during this study was composed of the

following elements:

1. the oxygenator (Galen Optiflo 1, Cobe, Denver, U.S.A.)
2. the cardiotomy reservoir (Cobe, Denver, U.S.A.)
3. the arterial line filter (Swank HF 6000, Cobe, Denver, U.S.A.)
4. the arterial cannula (Sherwood, Petit Rechain, Belgium) and the tubes of the arterial line (Tygon S 50 HL, Norton Company, Akron, U.S.A.)
5. the venous cannula (Porges Couvelair, Porges, Paris, France) and the tubes of the venous lines (Tygon S 50 HL)
6. the left ventricle cannula (Porges Couvelair) and the tubes of the cardiotomy suction set
7. the suckers and the tubes of the cardiotomy suction set (Tygon S 50 HL)

A diagram of the ECct is shown in figure 1.

The ECct was assembled the day before operation in a separate room in which the sterilized elements were stored. This room was situated in the sterile zone of the operating suite. After washing and cleaning the hands using povidone-iodine soap (Betadine^R, Dagra, Diemen, The Netherlands), the perfusionist assembled the circuit. During the assembly, he wore a face-mask and a cap. No other persons were allowed to enter this room. All elements of the circuit were disposable and pre-sterilized and used within the indicated period of sterility guarantee. The tubes connecting the different elements (arterial and venous lines, cardiotomy suction set) were sterilized in the hospital using ethylene-oxide and also stored in the assembly room. On the day of operation, the heart lung machine was rolled into the operating room. After the operation, the heart lung machine was dismantled and cleaned in a room outside the sterile zone of the operating suite.

Just prior to operation, the extra corporeal circuit was filled with the priming solution. This solution contained haemaccel (Behring Institute AG, Marburg, Fed.Rep.Germany) 2500 ml; human albumen (20% w/v; Institut Merieux, Lyon, France) 125 ml; mannitol (10 % w/v) 100 ml; heparin 125 mg in 2.5 ml; potassium chloride and sodium bicarbonate in concentrations depending on the results of blood analysis. Depending on the preoperative hematocrit of the patient donor blood was added to this priming solution.

2.2. BACTERIOLOGICAL SAMPLING AND METHODS

The ECct was studied during the last 121 operations because the assembly of the ECct during the first ten months of the survey period was not performed according the procedures as described above.

A sample was collected from the priming solution in the ECCT before starting the ECCu. The 121 samples were drawn from the venous inlet of the oxygenator (figure 1, no 8). During the open-heart operation a blood sample was drawn from the sampling port of the oxygenator (figure 1, no. 9) five minutes before terminating the ECCu. During 45 ECCu's randomly selected from the 121 open-heart operations studied, blood samples were taken at regular intervals of 30 minutes from the venous inlet of the oxygenator (figure 1, no. 8) and from the outflow side of the cardiotomy reservoir (figure 1, no. 10) concurrently. All samples were taken by the perfusionist. Ten ml of the priming solution or of blood from the ECCT was inoculated into two blood culture media after the caps of the bottles had been disinfected with iodine (1% w/v) in ethanol (70% v/v). Bacteriological studies done at the Laboratory for Medical Microbiology, Eindhoven, The Netherlands, were identical to those described for processing blood cultures in Chapter III.

The methods for isolation, identification, susceptibility testing, phage and biotyping (11) and the criteria for comparison of the strains were as described previously (Chapter III).

2.3. DEFINITIONS.

Postoperative bacteraemia was defined as the isolation of identical microorganisms from two or more blood cultures obtained on separate occasions (12).

Postoperative septicaemia was diagnosed when the patient had chills and a positive blood culture, or chills in conjunction with hypotension (systolic blood pressure $\leq$ 90 mm Hg) without a positive blood culture.

The diagnosis of BE was based on the persistence of unexplained fever, the finding of persisting leucocytosis, the occurrence of a new regurgitant cardiac murmur and the isolation of identical microorganisms from at least two blood cultures.

Figure 1: The extra corporeal circuit.

Legend:

- 1 = oxygenator
- 2 = cardiectomy reservoir
- 3 = arterial filter
- 4 = arterial line
- 5 = venous line
- 6 = left ventricle drain
- 7 = cardiectomy suction lines
- 8,9,10 = sampling sites for bacteriological cultures

3. RESULTS

3.1. SINGLE CULTURES FROM THE PRIMING SOLUTION BEFORE STARTING AND FROM THE BLOOD OF THE OXYGENATOR AT THE END OF 121 EXTRA CORPOREAL CIRCULATIONS

Microorganisms were isolated from 31 (25.6%) of the 121 samples from the priming solution before the ECCu was initiated (table 1). At the end of the ECCu, bacteria were isolated from six (5.0%) out of 121 samples from the oxygenator blood (table 1). In three open-heart operations samples from both the priming solution and the oxygenator blood were positive but in only one case the same microorganism (*Bacillus* species) was cultured from the priming solution and from the blood of the oxygenator. Mainly *Staph. epidermidis* and *Bacillus* species were cultured from the priming solution (table 2). *Staph. epidermidis* were tested for susceptibility to cephalothin. Two strains were resistant. Two out of three *Sarcina* species isolated were also resistant to this antibiotic. An unidentified Gram-negative rod and an unidentified fungus species were cultured once. Mainly *Bacillus* species were cultured from the oxygenator samples (table 2). *Escherichia coli*, *Citrobacter freundii* and *Aspergillus* species were isolated once. *E. coli* was sensitive for cephalothin and the other two microorganisms were resistant to this antibiotic.

Of the samples of the priming solution from which bacteria were isolated, six yielded growth of more than one microorganism. One of these six samples contained four different microorganisms whereas five samples yielded growth of two different isolates. In one of the six positive blood cultures from the oxygenator two different microorganisms (*E. coli* and viridans streptococci) were isolated. Another sample of the blood from the oxygenator yielded growth of four different microorganisms (*E. coli*, viridans streptococci, *Bacillus* species and *Aspergillus* species).

No relation was found between the microorganisms cultured from the samples taken before and at the end of the ECCu and the occurrence of postoperative bacteraemia, septicaemia and BE (table 3).

The bacteriological findings from the oxygenator samples initiated postoperative antimicrobial treatment in two patients. One patient with a positive blood culture due to *E. coli* and viridans streptococci was postoperatively treated with penicillin and gentamicin. He later developed BE due to *Staph. epidermidis*. A second patient with a blood culture from the oxygenator yielding *Citr. freundii* resistant to cephalothin was

Table 1: The number of open-heart operations with positive samples from the priming solution obtained before initiating the extra corporeal circulation (ECCu) and from the oxygenator obtained at the end of the extra corporeal circulation during 121 operations.

Type of operation and total number	Number of operations with positive samples obtained	
	before ECCu (priming solution)	at the end of ECCu (oxygenator blood)
Aorto-coronary bypass graft	84	25
Aortic valve replacement	13	4
Mitral valve replacement	10	0
Aortic and mitral valve replacement	4	0
Closure of atrial or ventricular septal defect	9	2
Valvulotomy	1	0
Total	121	31
		6

Table 2: The microorganisms isolated from the priming solution before initiating the extra corporeal circulation (ECCu) and from the blood from the oxygenator at the end of the extra corporeal circulation.

Microorganism	Sampling time	
	before ECCu (priming solution)	at the end of ECCu (oxygenator blood)
<i>Staphylococcus epidermidis</i>	15 (2)*	0
<i>Staphylococcus aureus</i>	3	0
<i>Bacillus</i> species	12	5
<i>Sarcina</i> species	3 (2)	0
<i>Streptococcus viridans</i> group	0	1
Gram-positive rods (unidentified)	2	0
Diphtheroids	2	1
Gram-negative rods (unidentified)	1	0
<i>Citrobacter freundii</i>	0	1 (1)
<i>Escherichia coli</i>	0	1
<i>Aspergillus</i> species	0	1 (1)
Other fungi (unidentified)	1	0
Total	39	10

* In parenthesis: number of strains resistant to cephalothin.

Table 3: The relation between the presence of microorganisms in samples obtained before and at the end of the extra corporeal circulation (ECCu) and the occurrence of postoperative bacteraemia, septicaemia and early-onset bacterial endocarditis.

Number of patients	Number of patients with a postoperative		
	bacteraemia	septicaemia	bacterial endocarditis
with positive samples before and/or at the end of ECCu	40	3 (0)*	0
with negative samples before and/or at the end of ECCu	81	9	5
Total	121	12	5
			7

*In parenthesis: number of cases with identical strains cultured during operation and postoperatively.

postoperatively treated with cefuroxim. The postoperative course was uneventful.

3.2. MULTIPLE CULTURES FROM THE CARDIOTOMY RESERVOIR AND FROM THE VENOUS INLET OF THE OXYGENATOR DURING THE EXTRA CORPOREAL CIRCULATION OF 45 OPEN-HEART OPERATIONS

In 45 out of the 121 open-heart operations, samples were taken at regular intervals from the cardiotomy reservoir and the venous inlet of the oxygenator. In total, 158 samples from the cardiotomy reservoir and 158 samples from the oxygenator were taken. Cultures taken during 23 (51%) out of the 45 ECCu's showed the presence of microorganisms (table 4). Eighteen samples taken from the cardiotomy reservoir used during 16 ECCu's were positive. The results of the samples concurrently taken from the venous inlet of the oxygenator showed that nine samples were positive during eight open-heart operations. During only one ECCu were samples from both the cardiotomy reservoir and from the oxygenator positive. Two different microorganisms were isolated. Single sampling performed before and at the end of these 45 ECCu's showed that the priming solution was positive in nine cases, whereas only one sample taken at the end of the ECCu was positive (table 4).

A variety of microorganisms was isolated from the cardiotomy reservoir and from the blood of the oxygenator (table 5). From the venous inlet of the oxygenator only Gram-positive bacteria and one fungus species were cultured whereas from the cardiotomy reservoir Gram-positive microorganisms, an *Aspergillus* species, Gram-negative rods (*Acinetobacter*, *Serratia*) and *Neisseria* species were cultured. All isolates were sensitive for cephalothin except the isolated *Serratia* species. The patient operated with use of an ECCt contaminated by this *Serratia* species was treated postoperatively with gentamicin.

The occurrence of postoperative bacteraemia, septicaemia and/or BE could not be related to the occurrence of contamination of the ECCt as demonstrated by single sampling before and at the end of the ECCu or by multiple sampling during ECCu (table 6). Cumulation of the results of the single and multiple sampling programmes resulted in 30 (67%) positive ECCt's. A relation between the use of positive ECCt's and the occurrence of postoperative bacteraemia, septicaemia and/or BE could also not be demonstrated.

Table 4: The number of contaminated extra corporeal circulations (ECCu) as shown by single samples taken before and at the end of the ECCu and by multiple samples taken during 45 ECCu's.

Type of operation and number	Single sampling			Multiple sampling				cumulative results
	before ECCu		total number of contaminated ECCu's	during ECCu		total number of contaminated ECCu's		
	(priming solution)	(oxygenator blood)		(venous inlet oxygenator)	(cardiotomy reservoir)			
Aorto-coronary bypass graft 31	8	0	8	5	12	17	23	
Aortic valve replacement 4	1	0	1	0	2	2	2	
Mitral valve replacement 6	0	0	0	1	0	1	1	
Aortic and mitral valve replacement 2	0	1	1	2	2	3*	4	
Closure of atrial or ven-tricular septal defect 2	0	0	0	0	0	0	0	
Total 45	9	1	10	8	16	23	30	

* Samples both from the venous inlet of the oxygenator and from the cardiotomy reservoir were positive in one patient.

Table 5: The microorganisms isolated from the cultures from the oxygenator before, during and at the end, and from the cardiomy reservoir during the extra corporeal circulation (ECCu) of 45 operations.

Microorganism	Single sampling		Multiple sampling	
	before ECCu (priming solution)	at the end of ECCu (oxygenator blood)	(venous inlet oxygenator)	during ECCu (cardiomy reservoir)
<i>Staphylococcus epidermidis</i>	3	0	2	1
<i>Staphylococcus aureus</i>	1	0	0	0
<i>Bacillus</i> species	4	0	3	2
<i>Sarcina</i> species	0	0	2	2
<i>Streptococcus viridans</i> group	0	0	1	0
<i>Streptococcus faecalis</i>	0	0	0	1
Gram-positive rods (unidentified)	1	0	1	3
Diptheroids	0	1	0	4
<i>Propionibacterium</i>	0	0	0	1
<i>Acinetobacter</i> species	0	0	0	1
<i>Serratia</i> species	0	0	0	1 (1)*
<i>Neisseria</i> species	0	0	0	1
Gram-negative rods (unidentified)	0	0	0	1
<i>Aspergillus</i> species	0	0	0	1
Other fungi (unidentified)	0	0	1	0
Total	9	1	10	19

Table 6: The relation between the presence of microorganisms in samples obtained by single sampling before and at the end, or by multiple sampling during extra corporeal circulation (ECCu) and the occurrence of postoperative bacteraemia, septicaemia and/or early-onset bacterial endocarditis.

Sampling frequency	Number of ECCu's	Number of patients with a postoperative		
		bacteraemia	septicaemia	bacterial endocarditis
Single samples before and at the end of ECCu	positive	2 (0)*	0	0
	negative	3	1	2
Multiple samples during ECCu	positive	2 (0)*	0	1 (0)*
	negative	3	1	1
Cumulation of single and multiple samples	positive	4 (0)*	0	1 (0)*
	negative	1	1	1

* In parenthesis: Number of cases with identical strains cultured during operation and postoperatively.

4. DISCUSSION

An attempt to determine the clinical relevance of isolating micro-organisms from the priming fluid and blood samples during ECCu was made by evaluating the results of these cultures and those of the postoperative blood cultures. Based upon the results obtained from single samples taken before and at the end of the ECCu we found no relation between the use of a contaminated ECct and the occurrence of postoperative bacteraemia, septicaemia and/or BE. In the cases of postoperative BE more infections occurred in patients being operated with culture negative ECct's than in patients with culture positive ECct's. This suggests that intraoperative contamination of the ECct is less significant than intravascular contamination from other sources. However, three patients were treated postoperatively with appropriate antibiotics to treat a possible intravascular infection as soon as the culture results became available. The absence of a correlation between positive cultures obtained during operation and postoperative clinical findings might be due to an inefficient sampling procedure. Blakemore *et al.* (5), applying an extensive sampling programme claimed that clinical post-operative infections were caused by microorganisms of the same species as those recovered from the blood in the ECct. We sampled the ECct intensively in 45 operations and we again found no relation between the use of culture positive ECct's and the occurrence of postoperative bacteraemia, septicaemia and/or BE. In other studies the clinical significance of positive ECct cultures has not been established either (10,13).

The results obtained from single cultures taken from the ECct before and at the end of the ECCu, showed a rather high contamination rate. Microorganisms were recovered from 31 (25.6%) out of 121 samples from the priming solution before the ECCu was initiated. Taking into account the relatively small volume cultured (10 ml) from about 3000 ml of priming solution the number of micro-organisms in this solution was rather high. This indicates that the heart lung machine was contaminated during the assembly procedure or during filling of the ECct with the priming solution. In this study the various sources from which the isolated microorganisms could have derived were not studied. However, published data (5,14) do suggest that a lower number of positive priming solution samples can be obtained.

The number of positive cultures obtained from the oxygenator at the end of the ECCu was relatively low. This low number of positive samples may be due to an inadequate sample volume or to an effect of the prophylactically

administered antibiotics or to the antibacterial properties of human blood.

Other investigators, also studying small volumes (5-10 ml) collected from the ECCT, found contamination rates similar to ours (4,10,13,14). Blakemore *et al.* (5) increased the sample volume from 5 ml to 25 ml and the frequency of sampling by obtaining additional samples on several occasions, and found that the contamination rate of the ECCT increased to 75%. We increased the sampling frequency during 45 ECCu's and isolated microorganisms from 30 (67%) ECCT's. If in these 45 ECCu's only single sampling was performed, microorganisms would have been isolated from ten (22%) instead of 30 ECCT's.

Apart from the increase of the sampling frequency, the volume cultured was relatively small. Culturing the disposable oxygenator after filling postoperatively with broth, Dankert (6) reported that the inside of the oxygenators was contaminated in about 80%.

Another factor to consider is the effect of prophylactically administered antibiotics on the culture results. The isolation rate of microorganisms from samples taken during ECCu was increased from 8.3% to 17.7% when the prophylactically administered antibiotics were specifically neutralized in the blood culture medium used (10). This is further supported by the results obtained by Kluge *et al.* (9). In this study cephalothin (1 gm intramuscularly every six hours) and kanamycin (0.5 gm intramuscularly every 12 hours) were used as prophylaxis for open-heart surgery patients. Serum levels were assayed and were found to be inadequate to kill most bacteria, but the results of the cultures from the oxygenator, using media without an inactivator, revealed that only two out of the 66 samples contained bacteria. One of our media contained sufficient penicillinase to counteract 10,000 units of penicillin. Although the serum level of cephalothin, the antibiotic prophylactically administered in our patients, was not assayed it is very likely that cephalothin levels were rather high during ECCu (15). Therefore, our finding that all isolates from the oxygenator, except one, were sensitive to cephalothin indicates that the amount of penicillinase in the media used was high enough to counteract cephalothin present in the blood samples, although it is known that penicillinase in lower concentrations is not the most appropriate inactivator of cephalothin (16,17).

The presence of microorganisms in the priming solution before ECCu did not predict the presence of microorganisms in oxygenator blood at the end of ECCu. This reduction might be caused by antibacterial activity of the blood. However, further studies are necessary to determine the effect of blood alone or in combination with antibiotics on the viability of microorganisms

contaminating the heart lung machine. From animal studies it is known that only serum resistant *E.coli* (18) and *Pseudomonas aeruginosa* (19) were able to induce endocarditis.

Another relevant question is how during ECCu contamination of the heart lung machine occurred. Partly the microorganisms might have been derived from the preoperatively contaminated heart lung machine itself but also from the patient's own flora and from the environment of the operating room, especially from the air. The ECCT can be directly and indirectly contaminated from the air. Direct contamination can occur due to suction of air into the cardiectomy reservoir. The ECCT can be indirectly contaminated from the air by microorganisms first sedimented into the wound and then sucked with blood into the cardiectomy reservoir.

Cultures taken from the cardiectomy reservoir during 45 operations revealed that 16 (36%) reservoirs were contaminated. The reservoirs were contaminated twice as often as the blood from the venous inlet of the oxygenator suggesting a possible role of the reservoir as a site of entry of microorganisms into the circuit. Another feature indicating the difference between these two sample sites was the finding of a much wider variety of bacterial species in samples obtained from the reservoir. Contamination of the cardiectomy reservoir was found to be reduced when airborne contamination of the wound area was prevented (6,14).

From the results we conclude that microorganisms which often cause postoperative infective endocarditis were isolated from the ECCT. Furthermore, the yield of positive cultures from the ECCT can be increased if appropriate culturing procedures and intensive sampling are performed. Microorganisms cultured from samples taken from the ECCT were not involved in postoperative bacteraemia, septicaemia and/or BE. In agreement with others (10) our results also showed that there was no relation between the use of a contaminated ECCT and the occurrence of postoperative bacteraemia, septicaemia and/or BE. This indicates that other sources than the ECCT might be more important in inducing postoperative bacteraemia, septicaemia and/or BE.

REFERENCES

1. Kittle, C.F., and Reed, W.A. Antibiotics and extra corporeal circulation. *J.Thorac.Surg.* 41: 34,1961.
2. Stein, P.D., Harken, D.E., and Dexter L. The nature and prevention of prosthetic valve endocarditis. *Am.Heart J.* 71: 393,1966.
3. Goodman, J.S., Schaffner, W., Collins, H.A., Battersby, E.J., and Koenig, M.G. Infection after cardiovascular surgery. Clinical study including examination of antimicrobial prophylaxis. *New. Engl.J.Med.* 278: 117,1968.
4. Carey, J.S. and Hughes, R.K. Control of infection after thoracic and cardiovascular surgery. *Ann.Surg.* 172: 916,1970.
5. Blakemore, W.S., McGarrity, G.J., Thurer, R.J., Wallace, H.W., MacVaugh, H. III and Coriell, L.L. Infection by air-borne bacteria with cardiopulmonary bypass. *Surgery* 70: 830,1971.
6. Dankert, J. The use of a mobile cross-flow unit in open-heart surgery: a bacteriological evaluation. *Ant.v.Leeuwenh.* 44: 247, 1978.
7. Baffes, T.G., Blazek, W.V., Fridman, J.L., Agustsson, M.H., and van Elk, J. Postoperative infections in 1,136 consecutive cardiac operations. *Surgery* 68: 791,1970.
8. Frater, R.W.M., and Santos, G.H. Sources of Infection in open-heart surgery. *N.Y. State J.Med.* 74: 2386,1974.
9. Kluge, R.M., Calia, F.M., McLaughlin, J.S. and Hornick, R.B. Sources of contamination in open-heart surgery. *JAMA* 230: 1415, 1974.
10. Freeman, R. and Hjersing, N. Bacterial culture of perfusion blood after open-heart surgery. *Thorax* 35: 754,1980.

11. Staal, M.J., Stobberingh, E.E., Haverkorn, M.J. and van Boven, C.P.A. Application of phage-typing and biotyping to the epidemiology of coagulase-negative Staphylococci in cardiovascular surgery. In: J.Jeljaszewicz, ed. Staphylococci and Staphylococcal infections. Proceedings of IV international symposium on Staphylococci and Staphylococcal infections. Zbl.Bakt.Suppl.10 Stuttgart-New York: Gustav Fischer Verlag, 1981;189.
12. Burke, J.P. Infections of cardiac and vascular prosthesis. In: J.V. Bennett and P.S. Brachman, eds. Hospital Infections. Boston: Little, Brown and Company, 1979; 307.
13. Yeh, T.J., Anabtawi, I.N., Cornett, V.E., White A., Stern, W.H., and Ellison, R.G. Bacterial endocarditis following open-heart surgery. Ann.Thorac.Surg. 3: 29,1967.
14. Lathrop, G.D., Brockett, R.M., and Blouse, L.E. Epidemiologic surveillance for *Staphylococcus epidermidis* infections, related to cardiopulmonary bypass. Zbl. Bakt. Hyg., I.Abt. Orig. A 241: 108,1978.
15. Miller K.W., Chan, K.K.H., Mc Coy, H.G., Fisher, r.P., Lindsay and Zaske, D.E. Cephalothin kinetics: Before, during and after cardiopulmonary bypass surgery. Clin.Pharmacol. Ther. 26: 54, 1979.
16. Newsom, S.W.A. and Walsingham, N.M. The use of B-lactamases in the clinical laboratory. J.Med.Microbiol. 6: 59,1973.
17. Russell, A.D., Ahonkhai, I., and Rogers, D.T. Microbiological applications of the inactivation of antibiotics and other antimicrobial agents. J.Appl. Bact. 46: 207, 1979.
18. Durack, D.T., Beeson, P.B. Protective role of complement in experimental ~~Escherichia~~ *Escherichia coli* endocarditis. Infect.Immun. 16(1): 213, 1977.
19. Archer, G., Fekety, F.R., Jr.: Experimental endocarditis due to *Pseudomonas aeruginosa*. I. Description of a model. J.Infect.Dis. 134: 1,1976.

CHAPTER VI

THE SIGNIFICANCE OF ISOLATION OF STAPHYLOCOCCUS EPIDERMIDIS FROM
BLOOD CULTURES OBTAINED FROM PATIENTS AFTER OPEN-HEART SURGERY

1. INTRODUCTION

Coagulase-negative staphylococci, which are called in this study *Staphylococcus epidermidis* are often regarded as contaminants of blood cultures (1) due to their presence in the microbial flora of the human skin and mucous membranes, their presence in the air and at various other sites. If *Staph.epidermidis* is isolated from a blood culture from a patient after open-heart surgery, especially after a valve replacement operation, this microorganism merits attention because of its possible role in inducing septicaemia or intravascular infections. One of these intravascular infections is so-called prosthetic valve endocarditis (PVE) occurring after prosthetic valve replacement surgery. PVE can be classified according to the time period in which the disease occurs. Early-onset PVE is defined as an endocarditis occurring within 60 days of valve implantation (2,3). Late-onset PVE occurs more than 60 days after valve implantation (2,3). The mortality of PVE is high. In early-onset PVE the mortality (71.4%) is significantly higher than in late-onset PVE: 45.6% (4). This indicates that PVE is a serious infectious complication of open-heart surgery. Unfortunately, an early diagnosis of PVE is difficult because of the lack of specific symptoms (5-7). Therefore, PVE often creates a clinically important, difficult, diagnostic dilemma (8). *Staph.epidermidis* is the most frequently isolated species causing early-onset PVE (3,4). In late-onset PVE *Staph.epidermidis* is also frequently isolated (3,4). If *Staph.epidermidis* is isolated from blood cultures obtained from patients after open-heart surgery with prosthesis implantation the differentiation of contaminated blood cultures from valid positive cultures due to a bacteraemia or an intravascular infection is necessary (9). The isolation of an identical microbial species from at least two blood cultures has been regarded as a major clue to the diagnosis of PVE (2,3,6,10,11).

In the first seven months after starting cardiac surgery in February 1978, 18 patients out of 37 from whom postoperative blood cultures were collected, had positive blood cultures mainly due to *Staph.epidermidis*. However, symptoms of septicaemia or early-onset PVE were absent.

Usually multiple blood samples are drawn within a certain period of time to differentiate contamination from bacteraemia. In the literature data about the frequency of contamination of blood cultures drawn from different sites concurrently are lacking (12).

In this study we evaluated the results of paired blood samples

concomitantly taken from patients after open-heart surgery.

2. MATERIALS AND METHODS

The total number of patients from whom paired blood samples were drawn was 273. The number of patients initially involved was enlarged because the number of patients involved in the other parts of the study was too small to achieve the probability of significant results. Therefore, we extended our study beyond the indicated period (Chapter II) and included an additional number of 137 open-heart surgery patients.

Blood cultures were taken postoperatively if the body temperature, measured rectally, was raised above 38.5°C , or if signs and symptoms consistent with septicaemia and/or an intravascular infection existed. Furthermore, during the course of an antimicrobial therapy of PVE additional bloodcultures were taken frequently. Paired blood culture samples were obtained by concurrent venipuncture from the antecubital vein of the left and the right arm of the patient after cleansing of the skin with iodine (1% w/v) in ethanol (70% v/v). The screw caps of the culture bottles were also cleansed with iodine in ethanol. After collection of the blood (10 ml), the needle of the syringe was replaced by a new disposable sterilized needle, and the blood was injected into two bottles containing culture media (see Chapter III). The culturing procedures, the susceptibility testing and the biotyping of the *Staph. epidermidis* isolates have been previously described in detail (see Chapter III).

3. RESULTS

A total of 537 paired blood samples was obtained from 273 patients after open-heart surgery (table 1). Samples were taken from 229 patients, in whom no prosthetic material was inserted. Most of them (216) had an aorto-coronary bypass graft operation. The remaining 44 patients had a Björk-Shiley prosthetic valve implanted. Paired blood samples were taken from the patients with a prosthetic valve almost three times as often as from the other patients.

Staph.epidermidis was not cultured from 442 (82.3%) of the 537 paired samples (table 2). From 88 (16.4%) out of the 537 blood culture pairs, *Staph.epidermidis* was isolated from one of the two cultures whereas in seven

Table 1: The number of blood cultures obtained by paired sampling from open-heart surgery patients.

Type of operation	Patients (%)	Paired blood culture samples (%)
Aorto-coronary bypass graft and other operations without use of prosthetic material	229 (84)	354 (66)
Prosthetic valve replacement	44 (16)	183 (34)
Total	273 (100)	537 (100)

Table 2: The isolation of *Staphylococcus epidermidis* from paired blood cultures obtained from patients after open-heart surgery.

<i>Staphylococcus epidermidis</i> isolated from	Number of paired samples (%)
both samples	7 (1.3)
one sample	88 (16.4)
none of the two samples	442 (82.3)
Total	537 (100.0)

(1.3%) blood sample pairs both cultures yielded growth of *Staph.epidermidis*. These seven positive pairs were obtained from seven different patients. Three of them had undergone a prosthetic valve implantation and one was treated afterwards for an early-onset PVE due to *Staph.epidermidis*. In this latter patient both *Staph.epidermidis* isolates from the paired samples had an identical biotype and susceptibility pattern. The other six patients showed during and after their febrile period no signs and symptoms of an intravascular infection and therefore antimicrobial treatment was not given. The strains of *Staph.epidermidis* isolated from the paired samples of these six patients showed a different biotype and susceptibility pattern, and were therefore considered to be non-identical.

4. DISCUSSION

Staph.epidermidis is generally regarded as a non-pathogenic microorganism present in the microflora of the skin and mucous membranes of men. In hospitals this microorganism can be easily isolated from the air and from several environmental sites. Therefore, the isolation of *Staph.epidermidis* from clinical specimens including blood samples, has been regarded for many years as contamination (13). However, in the last decade *Staph.epidermidis* has been recognized as the cause of serious infections, occurring after insertion of surgical prostheses in neurosurgery (14,15), orthopaedic surgery (14,16), vascular surgery (17) and open-heart surgery (2-7,14,18-25) patients. In addition, this microorganism has caused postoperative infections after general (26-29) and closed-heart surgery (18,20), urinary tract infections (27,30) and indwelling vascular catheter-associated infections (31,32). In neutropenic patients serious infections due to *Staph.epidermidis* have also been reported (33).

Since early-onset PVE is often caused by *Staph.epidermidis* (3,4), *Staph.epidermidis* isolated from blood cultures obtained from patients after open-heart surgery cannot be dismissed as representing a contaminant. Multiple isolations of *Staph.epidermidis* from repeated blood cultures are used to distinguish between contaminated and valid positive blood cultures due to bacteraemia or septicaemia (9). The time intervals between the multiple blood collections are seldom indicated (9,12,33,34).

We collected paired blood samples concurrently from patients after open-heart surgery to distinguish between contamination and bacteraemia

due to *Staph.epidermidis*. Eighty-eight out of 537 paired blood samples yielded growth of *Staph.epidermidis* in one of the two samples, suggesting contamination. Both samples were positive for *Staph.epidermidis* in seven out of the 537 paired blood samples, suggesting bacteraemia. In order to assess if a number of these seven positive paired samples contained *Staph.epidermidis* due to contamination we evaluated the results as follows. If single sampling had been performed instead of paired sampling, 51 (seven plus half of the 88 samples) out of 537 single samples would have been positive for *Staph.epidermidis*, corresponding to a probability of 9.5% positive samples. Assuming that these 51 samples were positive due to contamination, the probability of obtaining two *Staph.epidermidis* positive cultures after a repeated sampling would have been $(9.5\%)^2$ of 537. This would have meant that on five occasions two samples could be expected to contain *Staph.epidermidis* as a result of contamination. We isolated *Staph.epidermidis* in seven cases from both samples. Applying the chi square test for testing statistical significance no statistical difference was found between the five sample pairs to be expected to contain *Staph.epidermidis* and the seven pairs from which this microorganism was actually isolated ($p=0.8$). This indicates that a significant contribution of bacteraemia to the probability of blood cultures positive for *Staph.epidermidis* was not found. This conclusion is further supported by results obtained from biotyping and susceptibility testing, because non-identical *Staph.epidermidis* strains were isolated from each of six of the seven positive paired samples. In one of the seven cases biotyping and susceptibility testing revealed the presence of identical *Staph.epidermidis* strains in both samples. In contrast to the other six patients, this patient had additional signs and symptoms of an early-onset PVE and was treated with appropriate antimicrobial agents. This finding illustrates that biotyping and susceptibility testing of multiple isolated *Staph.epidermidis* can add essential information for differentiating contamination and bacteraemia if paired blood samples are taken. If multiple blood samples are drawn repeatedly these test procedures can also be helpful to distinguish between contamination and bacteraemia.

REFERENCES

1. MacGregor, R.R. and Beaty, H.N. Evaluation of positive blood cultures. Guidelines for early differentiation of contaminated from valid positive cultures. Arch. Int. Med. 130: 84,1972.
2. Dismukes, W.E. and Karchmer, A.W. The diagnosis of infected prosthetic heart valves: bacteremia versus endocarditis. In: R.J.Duma, ed. Infections of prosthetic heart valves and vascular grafts. Baltimore: University Park Press, 1977; 61.
3. Watanakunakorn, C. Prosthetic valve infective endocarditis. Prog. Cardiovasc. Dis. 22: 181,1979.
4. Mayer, K.H. and Schoenbaum, S.C. Evaluation and management of prosthetic valve endocarditis. Prog. Cardiovasc. Dis. 25: 43,1982.
5. Amoury, R.A., Bauman, F.O.Jr. and Malm, J.R. Endocarditis associated with intracardiac prostheses. J.Thorac.Cardiovasc.Surg., 51:36,1966.
6. Dismukes, W.E., Karchmer, A.W., Buckley, M.J., Austen, W.G. and Swartz, M.N. Prosthetic valve endocarditis. Analysis of 38 cases. Circulation 48: 365,1973.
7. Wilson, W.R., Jaumin, P.M., Danielson, G.K., Giuliani, E.R. Washington II, J.A. and Geraci, J.E. Prosthetic valve endocarditis. Ann. Intern. Med. 82: 751,1975.
8. Weinstein, L. Infected prosthetic valves: A diagnostic and therapeutic dilemma. New Eng.J.Med. 286: 1108, 1972.
9. Burke, J.P. Infections of cardiac and vascular prosthesis. In: J.V.Bennett and P.S. Brachman, eds. Hospital Infections. Boston: Little, Brown and Company, 1979; 307.
10. Block, P.C., DeSanctis, R.W., Weinberg, A.N. and Austen, W.G. Prosthetic valve endocarditis. J.Thorac. Cardiovasc. Surg. 60: 540,1970.

11. Rossiter, S.J., Stinson, E.B., Oyer, P.E., Craig Miller, D., Schapira, J.N. Martin, R.P. and Sumway, N.E. Prosthetic valve endocarditis. Comparison of heterograft tissue valves and mechanical valves. J.Thorac.Cardiovasc.Surg. 76: 795,1978.
12. Lewis, J.F. and Alexander, J.J. Blood cultures in bacteremia. South.Med.J. 75: 147,1982.
13. Kloos, W.E. and Smith, P.B. Staphylococci. In: E.H.Lennette, A.Balows, W.J.Hansler, Jr., and J.P. Truaut, eds. Manual of clinical microbiology. 3^d ed. Washington, D.C.: American Society for Microbiology, 1980; 83.
14. Garvey, G. Endovascular and prosthetic implant infections. In: M.H.Grieco, ed. Infections in the abnormal host. New York: Yorke Medical Books, 1980; 693.
15. Verhoef, J., Peterson, P.K., Williams, D.N., Laverdiere, M. and L.D.Sabath. Atrio-ventricular shunt infections and endocarditis due to *Staphylococcus epidermidis*. Zbl. Bakt. Hyg. I. Abt. orig. A 241: 95,1978.
16. Clarke, A.M. Prophylactic antibiotics for total hip arthroplasty- the significance of *Staphylococcus epidermidis*. J. Antimicrob. Chemother. 5: 493, 1979.
17. Liekweg, W.G., Levinson, S.A. and Greenfield, L.J. Infections of vascular grafts: incidence, anatomic location, etiologic agents, morbidity and mortality. In: R.J.Duma, ed. Infections of prosthetic heart valves and vascular grafts. Baltimore: University Park Press, 1977; 239.
18. Quinn, E.L. and Cox, F. Jr. *Staphylococcus albus (epidermidis)* endocarditis: report of 16 cases seen between 1953 and 1962. Antimicrob. Agents Chemother. 3: 635, 1964.
19. Geraci, J.E., Hanson, K.C., and Giuliani, E.R. Endocarditis caused by coagulase-negative staphylococci. Mayo Clin. Proc. 43: 420,1968.

20. Keys, T.F. and Hewitt, W.L. Endocarditis due to Micrococci and *Staphylococcus epidermidis*. Arch. Intern. Med. 132: 216,1973.
21. Slaughter, L., Morris, J.E. and Starr, A. Prosthetic valvular endocarditis. A 12-year review. Circulation 47: 1319,1973.
22. Speller, D.C.E. and Mitchell, R.G. Coagulase-negative staphylococci causing endocarditis after cardiac surgery. J.Clin.Path. 26: 517,1973.
23. Hornick, R.B. Source of contamination in open-heart surgery. In: R.J. Duma, ed. Infections of prosthetic heart valves and vascular grafts. Baltimore: University Park Press, 1977; 81.
24. Marples, R.R., Hone, R., Notley, C.M., Richardson, J.F. and Crees-Morris, J.A. Investigation of coagulase-negative staphylococci from infections in surgical patients. Zbl. Bakt. Hyg. I. Abt. Orig. A. 241: 140, 1978.
25. Lathrop, G.D., Brockett, R.M. and Blouse, L.E. Epidemiologic surveillance for *Staphylococcus epidermidis* infections related to cardiopulmonary bypass. Zbl. Bakt. Hyg. I. Abt. Orig. A. 241:108,1978.
26. Wilson, T.S. and Stuart, R.D. *Staphylococcus albus* in wound infection and in septicemia. Can. Med. Assoc. J. 93: 8,1965.
27. Blouse, L.E., Lathrop, G.D., Kolonel, L.N. and Brockett, R.M. Epidemiologic features and phage types associated with nosocomial infections caused by *Staphylococcus epidermidis*. Zbl. Bakt. Hyg. I.Abt. Orig. A., 241: 119, 1978.
28. Jara, F.M., Toledo-Pereyra, L., Lewis, J.W. and Magilligan, D.J. The infected pacemaker pocket. J.Thorac. Cardiovasc. Surg. 78: 298,1979.
29. Sewell, C.M., Clarridge, J.E., Young, E.J. and Guthrie, R.K. Clinical significance of coagulase-negative staphylococci.J.Clin.Microbiol. 16: 236,1982.

30. Marsik, F.J. and Brake, S. Species identification and susceptibility to 17 antibiotics of coagulase- negative staphylococci isolated from clinical specimens. J.Clin. Microbiol. 15: 640,1982.
31. Forse, R.A., Dixon, C., Bernard, K., Martinez, L., McLean, A.P.H. and Meakins, J.L. *Staphylococcus epidermidis*: an important pathogen. Surgery 86: 507:1978.
32. Sitges-Serra, A., Puig, P., Jaurietta, E., Garau, J., Alastrue, A. and Sitges-Creus, A. Catheter sepsis due to *Staphylococcus epidermidis* during parenteral nutrition. Surg. Gynecol. Obstet. 151: 481,1980.
33. Wade, J.C., Schimpff, S.C., Newman, K.A. and Wiernik, P.H. *Staphylococcus epidermidis*: an increasing cause of infection in patients with granulocytopenia. Ann. Int. Med. 97: 503,1982.
34. Barry, A.L. Clinical specimens for microbiologic examination. In: P.D. Hoeprich, ed. Infectious Disease, 2nd ed. Hagerstown: Harper and Row, 1977; 91.

CHAPTER VII

GENERAL DISCUSSION AND CONCLUSIONS

The risk of acquiring an infection after open-heart surgery is determined by several factors: the presence of many potential sources of contamination, the implantation of prosthetic material and the impairment of resistance of the patient.

Many occasions occur, either during or after operation, on which the patient can be contaminated or infected by potential pathogenic microorganisms (1-6). During operation the operative field is contaminated by microorganisms derived from the air in the operating room (2) and from the hands of the members of the surgical team since their gloves are quite often pierced during surgery (7). By continuous suction on the cardiotomy suckers connected to the extra corporeal circuit, microorganisms from the operative field can be introduced into the intravascular compartment. Entry to the intravascular compartment can also occur from the inserted intravascular catheters(8-14), and from the pressure transducer systems (14-18).

Another risk factor is the implantation of foreign material which increases the susceptibility of the patient to infections by microorganisms normally considered of low virulence, e.g. coagulase-negative staphylococci, further indicated as *Staphylococcus epidermidis* (19). The adherence of this particular microorganism onto prosthetic valve material is not well understood. The finding of Christensen *et al.* (20) suggesting that slime producing *Staph.epidermidis* are more often associated with intravascular catheter-associated infections than non-slime producing strains, might imply that this extra cellular product plays a role. Also the type of prosthetic material seems to be of importance since Sugarman *et al.* (21,22) showed that certain materials were more easily colonized by *Staph.epidermidis* than other types of synthetic material or suture material.

The impairment of resistance of patients undergoing open-heart surgery, associated with the use of the extra corporeal circuit, is another risk factor which has to be considered. Although not all studies on this aspect showed the same results (23), impairment of the functions of leukocytes during and after extra corporeal circulation has been described (24-26). Furthermore, it has been shown that the clearance by the reticuloendothelial system is decreased during extra corporeal circulation (27).

After the open-heart operation the patient is cared for in an intensive care department. Sources and routes of contamination here are numerous. They are inherently associated with the intensive treatment (14,28-30).

At the start of cardiac surgery in the Catharina Hospital at Eindhoven an infection surveillance programme was introduced and carried out. Procedures

and measures for prevention of infection were described and made available to everyone concerned. The personnel of the department was regularly informed about the necessity of performing the recommended precautions and instructed to maintain a high quality of aseptic handling. In addition an explanation was given as to why cultures had to be taken. The incidence and type of infections were registered prospectively. A prospective registration and documentation of the infections occurring in the patients treated in the department of cardiac surgery from the very start and using strictly defined criteria, seemed important to monitor the quality of the precautions and to increase the awareness of the susceptibility to infection of patients undergoing open-heart surgery. The particular purpose of this study was, in addition to the registration, the assessment of the efficacy of some of the procedures and measures of the infection surveillance programme.

One of the procedures in the infection surveillance programme was, as mentioned in the literature (4,5,31-34), the preoperative bacteriological sampling of various body sites of open-heart surgery patients on admission with the purpose to inventory the patient's microflora. Evaluation of the results of these cultures in relation to the microorganisms causing postoperative infections revealed that the microorganisms present in the admission flora of four patients with a postoperative early-onset bacterial endocarditis (BE), of 14 patients with a lower respiratory tract infection, of two patients with a bacteriuria and of four patients with a postoperative wound infection out of the total of 178 patients under study, were identical to those causing the postoperative infections. The majority of the postoperative infections was therefore caused by microorganisms not found in the preoperative cultures. This suggests that either the microorganisms were present but not detected by the method used, or the microorganisms were acquired during the patient's stay in the hospital. A similar finding is that only 12% of the *Staph.epidermidis* strains isolated from intravascular catheter tip cultures were identical to strains present in the admission flora.

The tips of these and other indwelling devices such as endotracheal tubes, wound drains and urinary catheters were as well cultured to test the assumption that a positive tip culture would predict the occurrence of a postoperative infection caused by the same microorganism. This study indicated that in general no relation was found between the microorganisms present on the tips of the intravascular catheters and of the wound and thoracic drains cultured after removal and the microorganisms causing postoperative

infections. The results of the cultures of the tips of the endotracheal tubes showed in 69% of the lower respiratory tract infections a similar microorganism as those causing the infection in the same patient. In two cases of postoperative bacteriuria the microorganisms cultured from the urinary catheter tip were identical to those causing a subsequent bacteriuria.

Since the occurrence of postoperative infections due to *Staphylococcus aureus* has been related to the preoperative presence of this microorganism in the endogenous nasal flora of patients, one of the elements in the infection surveillance programme was the screening of *Staph. aureus* carriage. Sixty percent of the patients with *Staph. aureus* positive nose samples were preoperatively treated with a nasal antimicrobial ointment. Assessment of the efficacy of this measure was, however, not possible due to the small number of postoperative infections caused by *Staph. aureus*. These occurred only in patients with *Staph. aureus* negative samples. In the group of un-treated nasal carriers infections did not occur. In most surveillance programmes the sampling method is not evaluated. The present study, however, indicated that the sampling technique to detect *Staph. aureus* nose and throat carriers by single swabbing has a limited accuracy. The inconstancy of the presence of this microorganism in the nose and throat flora was demonstrated by the results of a repeated sampling of a rather large number of subjects.

Postoperative infections in open-heart surgery patients have also been suggested to originate from the use of a contaminated extra corporeal circuit (2,35). To assess the possible role of a source of infection the extra corporeal circuit was sampled twice. The results were related to the occurrence of postoperative bacteraemia, septicaemia and/or BE. Even after an increase of the sampling frequency no relation could be shown between the microorganisms isolated from the samples and the occurrence of postoperative bacteraemia, septicaemia and/or BE.

Contamination of blood cultures occurs occasionally but at a definite rate depending on the precautions taken. The most frequent cause of contamination is *Staph. epidermidis*, due to its ubiquitous presence on the skin and in the hospital and laboratory environment. *Staph. epidermidis* is also the most frequent cause of prosthetic valve endocarditis, a complication with a high - 46-71% - mortality rate (36). It is therefore important in case of isolation of *Staph. epidermidis* from a blood culture obtained from an open-heart surgery patient to differentiate between contamination and infection. The approach taken in this study to evaluate the significance of *Staph. epidermidis* positive blood cultures was to take paired blood samples. This

was based on the assumption that the isolation of *Staph.epidermidis* from one of the two blood samples indicates contamination, whereas the isolation of this microorganism from both samples suggests bacteraemia or an intravascular infection. The results showed that 1.3% of the paired samples were both positive for *Staph.epidermidis*. Statistically this percentage of positive paired blood cultures could be explained as the result of contamination. This conclusion was confirmed by additional typing of the strains isolated from these positive paired samples. This indicated that the strains were different in six out of the seven cases. It is clear that to support the clinical diagnosis of an intravascular infection due to *Staph.epidermidis*, multiple blood cultures should be taken to exclude false positive results. This can be done by taking twice paired blood samples within one hour. Furthermore, the isolated strains should be typed as detailed as possible to establish (non-)identity. Rigorous aseptic precautions should be taken to reduce the chance of contamination.

The registration of postoperative infections in this study encompassed a period that should be considered as the initial phase in the history of the department of cardiac surgery of the Catharina Hospital at Eindhoven. In this period 182 open-heart operations were performed. The overall infection rate based on the data of 178 open-heart operations was 35%, whereas the incidence of prosthetic valve endocarditis was 18% in 34 valve replacement operations. Comparison of these data with those reported in the literature is difficult and of limited value. Most studies are retrospective and the data are derived from patient populations heterogeneous with regard to sex, age and type of surgery, as well as to the antimicrobial regimen used for prophylaxis. The variation in definitions to delineate postoperative infections -as illustrated by one report (33) that does not mention the definitions- is another factor that seriously hampers comparison. Since also the available facilities and local conditions do affect the infection rate, it is necessary that a department of cardiac surgery introduces its own system for registration of postoperative infections.

Comparison of the observed infection rates with those reported in the literature, taking the above mentioned limitations into account, shows that both the overall rate of postoperative infections and the incidence of prosthetic valve endocarditis is higher than generally reported by others. It is not possible to indicate one obvious reason or cause for this difference. Lack of routine in keeping high standards of aseptic precautions, the relatively long period between admission and operation, the relatively

long operation and perfusion times are factors which to all likelihood contributed to the relative high incidence of infections observed during the period of study.

Two other studies (37,38) reported the results of infection surveillance in open-heart surgery. Both reports describe a decrease of the infection rates as a result of amelioration of the infection surveillance programme. In the period of the present study an infection surveillance programme was introduced in the department of cardiac surgery. By emphasizing regularly the importance of aseptic handling and by providing relevant information, the awareness of the necessity to prevent infections increased, and the members of the team of the department of cardiac surgery became familiar with the surveillance programme. Strict and meticulous aseptic handling can only be achieved if the rationale for this is understood. This, however, is a process that needs time. Therefore, it could not be expected that a decrease in the infection rate as a result of surveillance would become apparent in the period of study. However, the results obtained after the present study was concluded, indicate that the continued infection surveillance has significantly ameliorated the contamination and infection rates (39). This is illustrated by the results of bacteriological sampling of the extra corporeal circuit and by the incidence of postoperative early-onset bacterial endocarditis. In the period from January to June 1980, 262 extra corporeal circuits were bacteriologically monitored. In 20 (7.6%) and 5 (1.9%) of the samples taken from the priming solution and the blood of the oxygenator respectively, bacteria were detected. This is a significant decrease in comparison with the 25.6% ($p < 0.001$) and 5% ($p = 0.015$) positive samples of priming solution and of oxygenator blood respectively, as reported in this study (Chapter V). Similarly, the incidence of bacterial endocarditis recorded after 100 valve replacement operations performed between May 1981 and March 1983 was 1%. Again a highly significant ($p < 0.001$) decrease in comparison with the in this study (Chapter III) reported incidence of 18% in 34 valve replacement operations.

The results of the study permit the following conclusions or recommendations:

1. The management of a department of cardiac surgery should include an infection surveillance programme. It is essential that such a programme is introduced from the very start of the department. The present study demonstrated the usefulness of an early introduction of an infection surveillance programme. Although it did not prevent a rather high incidence of postoperative infections in the period of this study, it brought to the attention the shortcoming of the infection surveillance. It is only after a certain time period that the full benefit of an infection surveillance programme can be expected to become apparent, and as is shown by later results, indeed became apparent.
2. The criteria used for the diagnosis of postoperative infections in open-heart surgery should be clear, unambiguous and preferably generally agreed upon. The data obtained by prospective registration of infections should be interpreted in relation to these criteria as well as to the phase of development of the department of cardiac surgery.
3. Routine preoperative bacteriological sampling of different sites on the skin and of mucous membranes of a cardiac surgery patient on the day of admission has a very limited value in predicting the microorganisms causing postoperative infections.
4. Culturing routinely the tips of indwelling devices removed postoperatively from open-heart surgery patients has no predictive value towards subsequently occurring infections and their causative microorganisms. An exception can be made for the tips of the endotracheal tubes.
5. Bacteriological sampling of the extra corporeal circuit before, during and at the end of extra corporeal circulation has no predictive value towards the occurrence of postoperative bacteraemia, septicaemia and/or early-onset bacterial endocarditis.
6. In this study preoperative carriage of *Staph.aureus* in open-heart surgery patients could not be associated with a higher rate of postoperative infections among these carriers.

7. The method of swabbing once the nose and throat of patients and hospital personnel to detect carriage of *Staph.aureus* has a limited accuracy.

8. Carriage of *Staph.aureus* in the nose and throat of patients and hospital personnel is variable even within a short period. This variability of carriage is greater in throat than in nose carriers.

9. The isolation of *Staph.epidermidis* from both cultures of a pair of blood samples concurrently obtained from patients after open-heart surgery does not necessarily indicate the occurrence of bacteraemia or an intravascular infection due to this microorganism.

To support the clinical suspicion or diagnosis of an intravascular infection caused by *Staph.epidermidis* paired blood samples should be taken twice within one hour. This procedure permits, in addition to characterization of the isolated strains using various typing techniques, an estimation of the chance of contamination.

REFERENCES

1. Carey, J.A. and Hughes, R.K. Control of infection after thoracic and cardiovascular surgery. *Ann. Surg.* 172: 916,1970.
2. Blakemore, W.S., Mc.Garrity, G.J., Thurer, R.J., Wallace, H.W., Mac Vaugh, H. III and Coriell, L.L. Infection by air-borne bacteria with cardiopulmonary bypass. *Surgery* 70: 830,1971.
3. Kluge, R.M., Calia, F.M., McLaughlin, J.S. and Hornick, R.B. Sources of contamination in open-heart surgery. *JAMA* 230: 1415,1974.
4. Rosendorf, L.L., Daicoff, G. and Baer, H. Sources of Gram-negative infection after open-heart surgery. *J.Thorac.Cardiovasc.Surg.* 67: 195, 1974.
5. Frater, R.W.M. and Santos, G.H. Sources of infection in open-heart surgery. *N.Y. State J.Med.* 74:2386, 1974.
6. Hornick, R.B. Source of contamination in open-heart surgery.
In: R.J.Duma, ed. *Infections of prosthetic heart-valves and vascular grafts*. Baltimore: University Park Press 1977; 31.
7. Cruse, P.J.E. and Foord, R. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. *Surg.Clin.North Am.* 60:27,1980.
8. Goldmann, D.A., Maki, D.G., Rhame, F.S., Kaiser, A.B., Tenney, J.H. and Bennett, J.V. Guidelines for infection control intravenous therapy. *Ann.Intern.Med.* 79: 848,1973.
9. Maki, D.G., Goldmann, D.A. and Rhame, F.S. Infection control in intravenous therapy. *Ann.Intern.Med.* 79: 867, 1973.
10. Konold, P., Ullman, U., Schrader, C.P. and Kieninger, G. Klinische und bakteriologische Beobachtungen bei intravenös eingeführten Kathetern. *Dtsch. Med. Wochenschr.* 99: 1009, 1974.

11. Maki, D.G., Weise, C.E. and Sarafin, H.W. A semiquantitative culture method for identifying intravenous, catheter-related infection. New. Engl. J.Med. 296: 1305,1977.
12. Band, J.D. and Maki, D.G. Infections caused by arterial catheters used for hemodynamic monitoring. Am.J.Med. 67:735,1979.
13. Anonymous. Monitoring devices and septicaemia (Editorial). Br.Med.J. 2: 1747,1979.
14. Meakins, J.L., Wicklund, B., Forse, R.A. and McLean, A.P.H. The surgical intensive care unit: current concepts in infection. Surg.Clin.North Am. 60:117,1980.
15. Weinstein, R.A., Emori, T.G., Anderson, R.L. and Stamm, W.E. Pressure transducers as a source of bacteremia after open-heart surgery. Report of an outbreak and guidelines for prevention. Chest 69: 338,1976.
16. Buxton, A.E., Anderson, R.L., Klimek, J. and Quintiliani, R. Failure of disposable domes to prevent septicaemia acquired from contaminated pressure transducers. Chest 74: 508, 1978.
17. Dreyden, G.E. and Brickler, J. Stopcock contamination. Anesth. Analg. 58: 141,1979.
18. Donowitz, L.G., Marsik, F.J., Hogt, J.W. and Wenzel, R.P. *Serratia marcescens* bacteremia from contaminated pressure transducers. JAMA 242: 1949, 1979.
19. Garvey, G. Endovascular and prosthetic implant infections. In: M.H. Grieco, ed. Infections in the abnormal host. New York: Yorke Medical Books, 1980; 693.
20. Christensen, G.D., Simpson, W.A., Bisno, A.L. and Beachey, E.H. Adherence of slime-producing strains of *Staphylococcus epidermidis* to smooth surfaces. Infect.Immun. 37: 318,1982.

21. Sugarman, B. and Musher, D. Adherence of bacteria to suture materials. *Proc. Exp. Biol. Med.* 167: 156, 1981.
22. Sugarman, B. In vitro adherence of bacteria to prosthetic vascular grafts. *Infection* 10: 9, 1982.
23. Kaplan, E.L., Castaneda, A.R., Ayoub, E.M. and Quie, P.G. Effects of cardiopulmonary bypass on the phagocytic and bactericidal capacities of polymorphonuclear leukocytes. *Circulation* 37 (supp. II): 158, 1968.
24. Kusserow, B.K. and Larrow, R. Studies of leukocyte response to prolonged blood pumping - effects upon phagocytic capability and total white cell count. *Trans. Amer. Soc. Artif. Intern. Organs*, 14: 261, 1968.
25. Kusserow, B., Larrow, R. and Nichols, J. Perfusion- and surface-induced injury in leukocytes. *Fed. Proc.* 30: 1516, 1971.
26. Silva, J. Jr., Hoeksema, H. and Fekety, F.R. Transient defects in phagocytic functions during cardiopulmonary bypass. *J. Thorac. Cardiovasc. Surg.* 67: 175, 1973.
27. Subramanian, V., Lande, A.L., Gans, H., Lowman, J.T. and Lillehei, C.W. Depression of host-defense mechanism following extracorporeal circulation. *Trans. Amer. Soc. Artif. Intern. Organs*, 15: 165, 1969.
28. Northey, D., Adess, M.L., Hartsuck, J.M. and Rhoades, E.R. Microbial surveillance in a surgical intensive care unit. *Surg. Gynecol. Obstet.* 139: 321, 1974.
29. Levenson, S.M. and Laufman, H. Infection hazard of surgical intensive care: isolation procedures in the surgical intensive care unit. In: J.M. Kinney, H.H. Bendixen and S.R. Powers, eds. *Manual of surgical intensive care*. Philadelphia: W.B. Saunders Comp., 1977; 151.
30. Bernard, H.R. The control of infection. In: J.M. Kinney, H.H. Bendixen and S.R. Powers, eds. *Manual of surgical intensive care*. Philadelphia: W.B. Saunders Comp., 1977; 203.

31. Goodman, J.S., Schaffner, W., Collins, H.A., Battersby, E.J. and Koenig, M.G. Infection after cardiovascular surgery. Clinical study including examination of antimicrobial prophylaxis. *New.Engl.J.Med.* 278: 117,1968.
32. Conte, J.E. Jr., Cohen, S.N., Roe, B.B. and Elashoff, R.M. Antibiotic prophylaxis and cardiac surgery. A prospective double-blind comparison of single-dose versus multiple-dose regimens. *Ann.Int.Med.* 76, 943,1972.
33. Kini, P.M., Fernandez, M.D., Causay, R.S. and Lemole, G.M. Double-blind comparison of cefazolin and cephalothin in open-heart surgery. *J.Thorac. Cardiovasc.Surg.* 76: 506,1978.
34. Cooper, D.K.C., Norton, R., Mobin, M.A., Cleland, W.P., Bentall, H.H. and Darrell, J.H. A comparison of two prophylactic antibiotic regimes for open-heart surgery. *J.Cardiovasc. Surg.* 21: 279,1980.
35. Lathrop, G.D., Brockett, R.M. and Blouse, L.E. Epidemiologic surveillance for *Staphylococcus epidermidis* infections, related to cardiopulmonary bypass. *Zbl. Bakt. Hyg., I.Abt.Orig.A* 241: 108,1978.
36. Mayer, K.H. and Schoenbaum, S.C. Evaluation and management of prosthetic valve endocarditis. *Prog.Cardiovasc. Dis.* 25: 43,1982.
37. Hughes, R.K. A method of improved anti-sepsis for open-heart surgery. *Ann.Thorac.Surg.* 2: 230, 1966.
38. Clark, R.E., Amos, W.C., Higgins, V., Bemberg, K.F. and Weldon, C.S. Infection control in cardiac surgery. *Surgery* 79: 89,1976.
39. Bredée, J.J. Personal communication.

CHAPTER VIII

SUMMARY

Increasing attention has been given to the occurrence of infections following cardiac surgery (Chapter I). There are numerous risk factors for acquiring infections associated with the treatment of open-heart surgery patients. Postoperative infective endocarditis has been thoroughly studied, in contrast to extra-cardiac infections after open-heart surgery. Surveillance has been advocated for the control of the incidence of hospital associated infections. The purpose of this study was to assess prospectively the efficacy of certain parts of an infection surveillance programme, as used during the first 18 months after commencing cardiac surgery in the Catharina Hospital at Eindhoven, The Netherlands.

In total 182 open-heart operations were performed in this period. Registration of postoperative infections was performed for 178 patients, as four patients died on the day of surgery. Infections were registered prospectively according to definitions described in Chapter II. In this chapter, the architectural design, the facilities of the department and the clinical procedures as applied before, during, and after open-heart operations are described in detail. In addition the incidences of infections are given. Postoperative infections occurred in 63 (35%) patients of whom 11 had more than one infection. Early-onset bacterial endocarditis (BE) and septicaemia were each diagnosed in seven (3.9%) patients. Lower respiratory tract infections occurred in 48 (26.9%), bacteriuria in three (1.7%), and wound infections in eight (4.5%) patients.

Microorganisms causing postoperative infections can derive from numerous sources. The microbial flora of the patient present on admission to the department of cardiac surgery, can be such a source. Therefore preoperative microbiological culturing has been done in open-heart surgery patients, but its usefulness in pin-pointing the relation between the isolated microorganisms and those causing postoperative infections has not thoroughly been studied. In Chapter III an attempt was made to find such a relation. The results showed that microorganisms present in the admission flora were involved in about one third of the postoperative infections. This suggests that most infections were due to microorganisms acquired during hospitalization. The majority of the septicaemia's and BE's was caused by staphylococci, whereas lower respiratory tract and urinary tract infections were mainly caused by various Gram-negative species. From the infected wounds both staphylococci and Gram-negative microorganisms were isolated. Susceptibility testing of the isolates causing postoperative infections showed that about 70% of them were sensitive to cephalothin, the prophylactic antibiotic used.

In addition, the results of culturing the tips of various indwelling devices after removal showed that the presence of microorganisms on these devices generally did not predict a subsequently occurring post-operative infection. Only cultures of the tip of the endotracheal tubes yielded similar microorganisms as those causing the lower respiratory tract infections in 69% of these infections.

The reliability of the sampling method for the detection of nasal and pharyngeal carriage of *Staphylococcus aureus* and the persistence of this carriage among patients and hospital personnel was investigated (Chapter IV). The accuracy of the swabbing technique was determined by sampling twice consecutively the nose and the throat of patients and hospital employees (initial examination). It was found that *Staph. aureus* was not present in the first sample from 8.3% of the patients harbouring this microorganism in their nose as revealed by the results of the second consecutive sample, and from 16.6% of the patients with *Staph. aureus* in the throat flora. Similar results after consecutive sampling were found among hospital employees. Re-sampling the nasal and pharyngeal mucosa of patients after two days and of hospital employees after seven days (follow up examination) revealed that the presence of *Staph. aureus* at these sites was rather transient, mainly due to a significant loss of this microorganism. This loss must be attributed to as yet unknown factors. Both the inaccuracy of the sampling method and the transiency of the presence of *Staph. aureus* in the nose and throat flora of patients may explain why no relation was found between preoperative carriage of *Staph. aureus* and the occurrence of postoperative infections due to this microorganism.

As part of the infection surveillance programme the contamination rate of the extra corporeal circuit was studied in Chapter V. Microorganisms were cultured from 31 (25.6%) of the 121 samples from the priming solution before the extra corporeal circulation was initiated, and from six (5.0%) out of 121 samples from the oxygenator blood at the end of the extra corporeal circulation. From the priming solution samples mainly *Staphylococcus epidermidis* and *Bacillus* species were cultured. From the oxygenator samples, *Bacillus* species, Gram-positive and Gram-negative microorganisms as well as *Aspergillus* species were isolated. No relation was found between the results of the bacteriological monitoring before and at the end of the extra corporeal circulation and the occurrence of postoperative bacteraemia, septicaemia and/or BE. Because an increased sampling frequency might enhance the number of positive samples the extra corporeal circuit was

studied in more detail in 45 operations. Although cumulation of the results of single and multiple sampling yielded 30 positive out of 45 examined extra corporeal circuits, again no relation could be demonstrated between the use of a contaminated circuit and the occurrence of postoperative bacteraemia, septicaemia and/or BE.

Although *Staph.epidermidis* is generally considered to be a non-pathogenic microorganism, known as a frequent contaminant of blood cultures, it can cause serious postoperative infections especially after insertion of surgical prostheses. The diagnosis of a postoperative intravascular infection caused by *Staph.epidermidis* is based on its isolation from several blood cultures, to differentiate contaminated from valid positive blood cultures. In Chapter VI this problem was assessed by examining the results of concurrently taken paired blood samples from 273 patients after open-heart surgery. Seven (1.3%) out of 537 paired samples contained *Staph.epidermidis* in both cultures. Although the isolation of *Staph.epidermidis* from both blood cultures of a sample pair suggests a bacteraemia due to *Staph.epidermidis*, statistical analysis showed that the seven paired blood samples could be explained to be positive for *Staph.epidermidis* as a result of contamination. This was supported by the clinical course and by the results obtained from additional susceptibility testing and biotyping, which indicated non-identity of the isolated strains.

CHAPTER IX

SAMENVATTING

In de afgelopen decennia is in toenemende mate aandacht geschonken aan het probleem van het optreden van infecties na hartchirurgie (hoofdstuk I). Patienten die een open-hartoperatie ondergaan zijn blootgesteld aan talrijke risicofactoren voor het krijgen van deze postoperatieve infecties. Over postoperatieve endocarditis is veel meer geschreven dan over extracardiale infecties na open-hartchirurgie.

Infectiebewaking is een middel ter preventie van ziekenhuisinfecties. In dit proefschrift wordt een prospectief onderzoek beschreven naar enkele methoden ter bewaking van infecties. Deze methoden waren onderdeel van een infectiebewakingsprogramma toegepast tijdens de eerste 18 maanden na het beginnen van hartchirurgie in het Catharina Ziekenhuis te Eindhoven. In deze periode, van februari 1978 tot juni 1979, werden 182 open-hartoperaties verricht. Er werd een registratie gedaan van infecties die optraden na 178 van deze 182 open-hartoperaties, aangezien vier patienten stierven op de dag van de operatie. Deze registratie droeg een prospectief karakter en was gebaseerd op de in hoofdstuk II beschreven diagnostische criteria. In hoofdstuk II wordt tevens een voor deze studie relevante beschrijving gegeven van ruimtelijke en materiële voorzieningen van de cardio-chirurgische afdeling van het Catharina Ziekenhuis te Eindhoven, alsmede van de klinische procedures die onderdeel vormden van de behandeling van de patient voor, tijdens en na een open-hartoperatie. Tenslotte worden in dit hoofdstuk de incidenties van infecties optredend na deze 178 open-hartoperaties weergegeven. Vijfenzestig (35%) patienten maakten een postoperatieve infectie door waarvan 11 meer dan één infectie. Vroeg optredende (binnen 60 dagen) postoperatieve endocarditis en postoperatieve sepsis traden elk op bij zeven (3.9%) patienten. Postoperatieve lage luchtweginfecties werden gezien bij 48 (26.9%), bacteriurie bij drie (1.7%) en postoperatieve wondinfecties bij acht (4.5%) van de 178 patienten.

De micro-organismen die postoperatieve infecties veroorzaken kunnen uit diverse bronnen afkomstig zijn. De microbiële flora van de open-hartpatienten zelf, zoals aanwezig op de eerste dag van de opname, kan een dergelijk bron zijn. Daarom worden in sommige cardio-chirurgische klinieken pre-operatief bacteriologische kweekuitstrijkjes genomen van diverse plaatsen van de huid en slijmvliezen van open-hartoperatiepatienten. Er is echter nooit een grondige studie verricht naar de waarde van een dergelijk bacteriologisch onderzoek, met als doel het bestuderen van de relatie tussen de micro-organismen die eenmalig pre-operatief van de patient gekweekt worden en de micro-organismen die postoperatief infecties veroorzaken. In hoofdstuk

III worden de resultaten van een dergelijk onderzoek weergegeven. Deze toonden aan dat bij ongeveer één derde van de postoperatieve infecties een gelijksoortig microörganisme geïsoleerd werd als uit de pre-operatieve kweken van de patient. Dit suggereert dat het merendeel van de infecties veroorzaakt werd door microörganismen waarmee de patient tijdens het verblijf in het ziekenhuis gekoloniseerd werd. Postoperatieve endocarditis en sepsis werden voor het grootste gedeelte veroorzaakt door staphylococcen terwijl bij lage luchtweg- en urineweginfecties vooral Gram negatieve microörganismen werden geïsoleerd. Wondinfecties werden zowel door Gram negatieve als Gram positieve microörganismen veroorzaakt. In zeventig procent van de infecties waren de microörganismen gevoelig voor het als profylactisch antibioticum toegediende cephalotine, zoals bleek uit de resistentiebepaling van de isolaten. In dit hoofdstuk werd aan de hand van de resultaten van de kweken van de tip van de bij de patient verwijderde intravasculaire lijnen, wonddrains en urine-catheters aangetoond dat de aanwezigheid van microörganismen op de tip van deze lijnen en drains een postoperatieve infectie veroorzaakt door dezelfde microörganismen, over het algemeen niet kon voorspellen. Alleen bij 69% van de patienten met een lage luchtweginfectie werd een gelijksoortig microörganisme gekweekt van de tip van de endotracheale tube.

De betrouwbaarheid van de uitstrijkmethode ter opsporing van neus- en keel dragers van *Staphylococcus aureus* onder patienten en ziekenhuispersoneel en de continuïteit van dit dragerschap in de tijd was doel van onderzoek in hoofdstuk IV. De nauwkeurigheid van de uitstrijktechniek werd onderzocht door middel van twee direct na elkaar uitgevoerde kweekuitstrijken uit de neus en keel van patienten en ziekenhuispersoneel (eerste onderzoek). Van de patienten zou 8,3% niet als *Staph. aureus* neus dragers en 16,6% niet als *Staph. aureus* keel dragers herkend zijn als slechts éénmaal uitgestreken was. Tweemaal uitstrijken van de neus en keel van het ziekenhuispersoneel leverde gelijkwaardige percentages op. De continuïteit van het *Staph. aureus* neus- en keel dragerschap werd onderzocht door de keel- en neus flora opnieuw te onderzoeken (tweede onderzoek) met behulp van één uitstrijkje op de tweede dag na het eerste onderzoek bij de patienten en op de zevende dag bij het ziekenhuispersoneel. De aanwezigheid van *Staph. aureus* in de neus- en keel flora bleek uit dit tweede onderzoek in beide groepen niet constant, voornamelijk als gevolg van het verdwijnen van dit microörganisme uit de neus- en keel flora. Wij konden dit verlies niet verklaren. De beperking van de uitstrijktechniek en de in tijd variabele aanwezigheid van *Staph. aureus* in de neus- en keel flora van patienten zouden een verklaring kunnen zijn voor het door

ons niet kunnen vaststellen van de relatie tussen het preoperatief dragerschap van *Staph.aureus* bij patienten en het optreden van postoperatieve infecties door dit microörganisme. Deze relatie werd door anderen wel aangetoond.

Een ander onderdeel van het infectiebewakingsprogramma, het bacteriologisch bewaken van het extracorporele circuit voor en tijdens de extracorporele circulatie, is onderwerp van de studie beschreven in hoofdstuk V. Voor het begin en tegen het einde van de extracorporele circulatie werd een kweekmonster afgenomen uit de inhoud van het circuit. Uit 31 (25.6%) van de 121 kweekmonsters van de vloeistof waarmee het circuit voor de extracorporele circulatie werd gevuld, werden microörganismen gekweekt. Zes (5.0%) van de 121 kweekmonsters van het bloed van de oxygenator, afgenomen op het einde van de extracorporele circulatie, waren positief. Uit de circuitvloeistof voor aanvang van extracorporele circulatie werden vooral *Staphylococcus epidermidis* en *Bacillus* gekweekt, terwijl uit de oxygenatormonsters *Bacillus*, *Aspergillus*, Gram positieve en Gram negatieve microörganismen werden geïsoleerd. Er werd geen verband gevonden tussen de resultaten van het bacteriologisch onderzoek van de inhoud van het extracorporele circuit voor begin en einde van de extracorporele circulatie en het optreden van postoperatieve bacteriëmie, sepsis en/of endocarditis. Het onderzoek naar de waarde van het bacteriologisch bewaken van het extracorporele circuit werd uitgebreid tijdens 45 operaties, veronderstellend dat een groter aantal kweekmonsters een toename van het aantal positieve monsters zou laten zien. Hoewel onder deze 45 operaties, waarbij frequenter bloedkweken werden afgenomen, 30 gecontamineerde circuits werden gevonden, werd wederom geen relatie vastgesteld met het optreden van post-operatieve bacteriëmie, sepsis en/of endocarditis na deze 45 operaties.

Staph.epidermidis wordt over het algemeen beschouwd als een niet pathogeen microörganisme. Het wordt regelmatig als contaminant uit bloedkweken geïsoleerd. *Staph.epidermidis* kan echter postoperatieve infecties veroorzaken vooral na implantatie van een chirurgische prothese. Voor de diagnostiek van postoperatieve intravasculaire infecties veroorzaakt door *Staph.epidermidis* is het belangrijk een onderscheid te maken tussen een *Staph.epidermidis* positieve bloedkweek ten gevolge van contaminatie dan wel ten gevolge van bacteriëmie. Dit kan door middel van herhaaldelijk isoleren van dit microörganisme uit een serie bloedkweken. In hoofdstuk VI worden de resultaten besproken van 537 paarsgewijze afgenomen bloedkweken afkomstig van 273 patienten na open-hartchirurgie. Beide bloedkweken van zeven (1.3%) gepaarde

monsters bevatten *Staph.epidermidis*. Hoewel de isolatie van *Staph.epidermidis* uit beide kweekmonsters van paarsgewijs afgenomen bloedkweken suggestief is voor een bacteriamie door *Staph.epidermidis*, kon de isolatie van *Staph.epidermidis* uit deze zeven gepaarde bloedkweken op statistische gronden verklaard worden door contaminatie. Deze bevinding werd ondersteund door het postoperatieve klinisch beloop bij deze patienten en door aanvullend onderzoek van het resistentiepatroon en het biotype van deze stammen, die de ongelijkheid van deze isolaten aantoonde.

Dankbetuiging

Het materiaal voor het onderzoek beschreven in dit proefschrift werd verzameld in het Catharina Ziekenhuis te Eindhoven.

Velen hebben op één of andere wijze hun bijdrage geleverd aan de verwezenlijking van dit proefschrift. Het lijkt haast ondoenlijk een ieder hiervoor persoonlijk te vermelden, gezien het grote aantal betrokkenen. Allen die, in welke mate dan ook, ergens op de lange weg naar de voltooiing hun medewerking hebben verleend, dank ik oprecht voor hun inzet.

Enkele personen wil ik apart vermelden, in chronologische volgorde van betrokkenheid, in de hoop dat mijn erkentelijkheid jegens hen die onbesproken blijven hierdoor niet in kracht inboet.

Dr.J.Bredée en drs.Y.Mashour, cardiochirurgen van het Catharine Ziekenhuis te Eindhoven, en Dr. M.Haverkorn, Hoofd van het Laboratorium voor Medische Microbiologie te Eindhoven, hebben mijn belangstelling gewekt voor het probleem en de noodzaak doen inzien van infectiebewaking in open-hart-chirurgie. Mijn eerste activiteiten op het terrein van het wetenschappelijk onderzoek in het algemeen en met betrekking tot dit onderwerp in het bijzonder vonden plaats door hun stimulans en enthousiasme. Administratief en moreel waren vooral Mw. D.Weenink maar ook de andere dames van het secretariaat cardiochirurgie hierin een grote steun.

De medewerkers van de afdeling extra corporele circulatie, de verpleegkundigen van de operatiekamer, van de intensive care, en van de afdeling 7 West, alsmede de collegae intensivisten, de medewerkers van het klinisch-chemisch laboratorium, van de röntgenafdeling en van de afdeling fysiotherapie van het Catharina Ziekenhuis te Eindhoven hebben hun medewerking verleend aan het verzamelen van gegevens, waarvoor mijn dank.

Mw. Willekens, bibliothecaresse van het Catharina Ziekenhuis heeft mij op deskundige wijze bijgestaan in het verzamelen van de literatuur.

De directie van het Catharine Ziekenhuis heeft van meet af aan steun verleend aan het onderzoek, waarvoor ik haar zeer erkentelijk ben.

Het omvangrijk bacteriologisch onderzoek werd verricht op het Laboratorium voor Medische Microbiologie te Eindhoven (Hoofd: Dr.M.Haverkorn) en op het Laboratorium van de Capaciteitsgroep Medische Microbiologie van de Rijksuniversiteit Limburg (Hoofd: Prof.Dr.C.van Boven). De enthousiaste medewerking van onder andere Mw.H. de Wilde, de Heer A.Dorst, Dr. M.Haverkorn, respectievelijk Dr. E.Stobberingh en Prof.Dr. C.van Boven heeft mij enorm gestimuleerd.

Toen het onderzoek promovabele vormen begon aan te nemen hebben Prof.Dr.J.Homan van der Heide en drs. J.Dankert zich bereid verklaard mij verder te begeleiden op de weg naar voltooiing van het proefschrift, respectievelijk als promotor en co-promotor. In een later stadium heeft Prof.Dr.C.van Boven de gelegenheid geboden de promotie in Maastricht te laten plaatsvinden en heeft hij als promotor zijn enthousiaste begeleiding gegeven.

Bij de verwerking van de gegevens ondervond ik alle steun en deskundige medewerking van Dr.Ir.N.Linssen (Technische Hogeschool Eindhoven), Ir.L.van der Stee en Dr. Ir.H.Journée (Afdeling Neurochirurgie, Academisch Ziekenhuis Groningen), en dra. A.Staal.

Mw.D.Weenink, Mw.M.Wiersma, Mw.G.Bathoorn en Mw.B.Hüttenberger dank ik hartelijk voor het vele en goede typewerk.

Prof.Dr.D.Klein, Prof.Dr.H.Sluite, Dr.J.Bredée, drs.Y.Mashour, Mw. H.Mashour, drs.P.Hendel, drs. A.Buchthal en drs.S.Terpstra dank ik voor hun kritische opmerkingen over inhoud en taal, en de Heer D.Buiter en Mevr. N.Putman voor de grafische verzorging van het proefschrift.

Mijn promotores, Prof.Dr.J.Homan van der Heide en Prof.Dr.C.van Boven, en bovenal mijn co-promotor drs.J.Dankert dank ik zeer voor hun enorme toewijding en inzet die, nadat de basis van het werk in Eindhoven dankzij de medewerking van Dr.M.Haverkorn, Dr.J.Bredée en drs.Y.Mashour was gelegd, de totstandkoming van dit proefschrift mede hebben doen verwezenlijken.

Prof.Dr.G.Kootstra, Prof.Dr.G.Flendrig en Dr.M.Haverkorn ben ik zeer erkentelijk voor hun bereidheid als referent te willen hebben optreden en als zodanig hun kritisch en waardevol commentaar op het manuscript gegeven te hebben.

Zonder de jarenlange actieve en passieve steun van mijn dierbare vrouw was dit proefschrift nooit tot stand gekomen.

Tenslotte betuig ik mijn dank aan de Nederlandse Hartstichting die de publicatie van dit proefschrift financieel heeft ondersteund.

CURRICULUM VITAE

The author of this thesis was born in Amsterdam on the 17th of August, 1949. He attended the European School of Brussels, where in June 1967 he obtained his European Baccalaureat. In November 1974 he graduated from the Medical Faculty of the University of Utrecht. The following year he fulfilled a supplementary medical training in order to work at a missionary hospital in Uganda as a general physician where he worked from 1975 to 1977. After his return to The Netherlands he was a junior resident in the department of cardiac surgery of the Catharina Hospital at Eindhoven. During this time he became interested in surveillance of infections in open-heart surgery. The fruit of this interest is this thesis. In January 1980 he started training general surgery at the same hospital (Head of the Department: Dr. J.G.Prins). This enabled him to continue his training in neurosurgery which he started in July 1981 at the Neurosurgical Department of the University Hospital of Groningen (Head: Prof. Dr. J.W.F.Beks).