Intra-operative bacterial contamination
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SUMMARY
As described in Chapter 1 infection is one of the most common complications in surgery. In particular deep periprosthetic infections in orthopaedic surgery constitute a disaster for both patient and doctor. Conservative estimates of infection rates average 1-2% for hip implants and 2-4% for knee implants. The number of joint replacements is expected to double in the next twenty years and if the infection rate is not reduced, also the incidence of infection will double, yielding increased morbidity, hospital stay and costs to the healthcare system. Deep prosthetic infections can be subdivided in (i) early (within three months after surgery), (ii) delayed (within one-and-a-half to two years after surgery) or (iii) late infections. Both early and delayed infections can be caused during surgery by direct contact with the wound, airborne colonisation or by cross-infection on the ward. Late infection is considered mostly to be caused by blood-borne contamination, for example during insertion of a urinary catheter, infection of an intravenous canula, skin or dental sepsis. This thesis focuses on the early and delayed infections caused by intra-operative contamination.

Intra-operative bacterial contamination may be present in every operating room, and constitutes a possible risk for postoperative wound healing problems and periprosthetic infection, but to what extent remains unclear. In Chapter 2 the results of a study is presented in which we investigated whether bacterial contamination of the instruments and bone during primary prosthesis insertion was associated with prolonged wound discharge, and subsequent periprosthetic infection. During 100 total hip arthroplasties, four intra-operative cultures were taken from the instruments and two portions of removed bone. Postoperatively, the duration of wound discharge was monitored, taking day 5 as the cut-off point. All patients were followed for two years to find out whether periprosthetic infection occurred. Bacterial contamination was present during 36 operative procedures (36%). A significant association was found between intra-operative contamination and prolonged wound discharge, with a relative risk (RR) of 2.5. The culturing of removed bone had a positive predictive value of 81-90% for prolonged wound discharge. Other factors associated with prolonged wound discharge were rheumatoid arthritis (RR 6.4), use of cement (RR 1.6) and increased blood loss (RR 1.5). We conclude that there is a significant association between intra-operative contamination, prolonged wound discharge and periprosthetic infection.

In Chapter 3 the aim was to evaluate whether behavioural and systemic measures in the operating theatre will decrease intra-operative contamination during total hip or knee
replacements. The influence of these measures on subsequent prolonged wound discharge, superficial surgical site infection and deep periprosthetic infection during an 18 month follow-up is also investigated. During 207 procedures, four swabs were taken from instruments at the beginning and at the end of the procedure. Removed material from the bone (acetabulum and femur in case of the hip joint; femur and tibia in case of the knee joint) was tested for contamination as well. At first, 70 operations in an old situation were included (control group), after which the first behavioural measure was introduced: better use of the area directly beneath the plenum. During 67 operations in this new situation cultures were taken (group 1), followed by the introduction of a strict protocol based on the adherence to operating room-rules and the installation of a new laminar flow system. 70 operations (group 2) were monitored after this second intervention. The control group showed intra-operative contamination in 23/70 (32.9%) of the cases, group 1 showed contamination in 34.3% of the cases (23/67) and group 2 showed contamination in 6/70 cases, corresponding to 8.6%. The parameters prolonged wound discharge and superficial surgical site infection also decreased drastically in group 2 as did the incidence of deep periprosthetic infection, but this did not reach statistical significance. This study shows that the combination of systemic and behavioural changes in an operating room significantly decreases the incidence of intra-operative bacterial contamination, subsequent prolonged wound discharge and superficial surgical site infection. After 18 months of follow up there was also a decrease in deep periprosthetic infection.

Bacterial adhesion to and transfer between surfaces is a complicated process. With regard to the success of biomaterials implants, studies on bacterial adhesion and transfer should not be confined to biomaterials surfaces in the human body, but should also encompass surfaces in the operating room, where the origin of many biomaterials related infections is found. The purpose of Chapter 4 was to quantify the transfer of *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Propionibacterium acnes* from one operating room material to another, while accounting for surface hydrophobicity and roughness, moistness and application of friction during transfer. The tested operating room materials were glove, broach, theatre gown and light handle. As a possible clinical intervention method to prevent transfer, it was investigated whether dipping the gloves in a chlorhexidine splash-basin affected the viability of the transferred bacteria. Transfer (moist and without friction) was demonstrated to some extent with all bacterial strains and with every tested material, ranging from 17 to 71%, and was
influenced by the bacterial strain, moistness of the inoculum, the application of friction and the characteristics of both the donating and the receiving surface. Dipping the glove material in 4% or 0.4% chlorhexidine solutions killed all bacteria present, regardless of whether surfaces were dried or moist and thus prevented transfer.

The aim of the study as described in Chapter 5 was to evaluate our research laboratory tissue and biomaterial culturing (RLTC and BC, respectively) during revision surgery of hip and knee, initially clinically diagnosed either as septic or aseptic loosening. The results are compared with the new routine hospital culturing (NRHC) method. In total, intra-operative culturing was performed in 59 consecutive patients who underwent revision of their prosthesis. The indication for revision was suspected septic loosening in 14 cases (7 with conventional and 7 with laminar airflow) and suspected aseptic loosening in 45 cases (23 with conventional and 22 with laminar airflow). In order to investigate whether infectious complications occurred related to the revision surgery, all patients were followed for at least 18 months. In the group of 14 patients with septic loosening, NRHC showed microbial growth in 8 of the 14 (57.1%) cases, RLTC revealed bacteria in 9/14 (64.3%) cases and BC showed growth in all 14 cases. Alternatively, the group of 45 patients with suspected aseptic loosening showed microbial growth during NRHC in only 4/45 (8.9%) cases, while RLTC showed growth in 13/45 (28.9%) cases, and BC in 16/45 (35.6%) cases. After follow-up it seemed that BC had a positive predictive value of 75% and a negative predictive value of 100% for the (re-)occurrence of periprosthetic infection after revision arthroplasty for suspected aseptic loosening. In the operating theatre with conventional airflow RLTC and BC showed microbial growth in 15/23 cases (65%), compared to 3/22 (14%) with laminar airflow, suggesting that in many cases intra-operative contamination might have played a key role.

Chapter 6 encompasses an economic evaluation of prosthetic joint infections. Firstly, the scope of the social costs generated by patients who undergo a primary or revision-operation for a hip or knee implant was evaluated, as well as the cost increase upon development of a deep peri-prosthetic infection. Subsequently, it was investigated whether there are differences in these costs between patients with positive and negative intra-operative cultures in order to demonstrate that intra-operative culturing is a cost-effective means in clinical practice to prevent a possible peri-prosthetic infection due to intra-operative contamination. The mean total costs of placing a primary prosthesis was €16,846 (€5890 - €59,180). Within the follow
up of 18 months 2 patients with a hip prosthesis developed a deep periprosthetic infection, with a cost of €45.034 and €59.180. The mean total cost of patients without a deep periprosthetic infection (N=48) was €15.376 (€5890 - €53.247). Revision of an aseptic loosened prosthesis (N=25) had a mean total costs of €36.798, and revision of a septic loosened prosthesis €52.750 (N=10). Total costs of patients with positive culture outcomes were considerably higher than costs of patients with negative culture outcomes in both the primary and revision group. These patients could be identified early using the culture techniques applied in the current study. As used culture methods do not lengthen operating time and are not expensive the authors recommend that intra-operative cultures be routinely conducted during both primary and revision arthroplasty, both from an economic as well as a medical perspective.

As indicated in the General Discussion (Chapter 7), this thesis shows that to prevent and treat periprosthetic infection appropriately, it is necessary to take measures pre-, intra-, and post-operatively. Pre-operatively by screening the patients, intra-operatively by taking cultures and altering operating room discipline and airflow system, and potentially by decreasing bacterial transfer, and post-operatively by monitoring wound discharge and measuring also other infection parameters. As treating an infected prosthesis is proven to be very expensive, it seems cost-effective to take all these measures.