INFECTION AFTER TOTAL HIP REPLACEMENT

WITH SPECIAL REFERENCE TO A DISCHARGE FROM THE WOUND

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The risk factors associated with 34 deep infections from a consecutive series of 803 total hip replacements have been analysed using standard actuarial methods. The follow-up ranged from 3 to 10 years.

Absence of prophylactic antibiotics, complications after operation, discharging wounds, previous operations and remote infection were related to the development of deep periprosthetic infection. An early discharge from the wound with growth of micro-organisms, though superficial in appearance, proved to be associated with a high risk of developing late deep infection.

The mechanisms associated with deep infection involved multiple interrelated risk factors. Multiple regression analysis of our data indicated that these risk factors, when acting together, potentiate their effect on the development of the deep infection.

In the controversy whether infection after total hip replacement is acquired in the operating room or arises in the ward as a result of cross-infection, some authors consider the discharging wound as an important source of the late periprosthetic infection (McLauchlan *et al.* 1976; Müller 1976; Franco, Baer and Enneking 1977; Andrews *et al.* 1981), whereas others did not observe any correlation between discharge from the wound and the late deep infection (Aglietti, Salvati and Wilson 1973; Aglietti *et al.* 1974; Freeman *et al.* 1977; Wilson 1977). In spite of this controversy, we were unable to find any report studying more extensively the association between the early superficial discharge from the wound and the late deep infection.

The purpose of this paper is to study the risk factors associated with the deep periprosthetic infection after total hip replacement with the interest focused on the complications in the healing of the operative wound.

PATIENTS AND METHODS

The first 803 total hip replacements performed on 695 patients in our clinic between March 1, 1970, and December 31, 1977, were chosen for this study. The mean age of the patients was 64 years (range 32 to 81 years).

Most patients were being followed up at regular intervals. A final review was made early in 1981 and

questionnaires were then answered by 609 patients with 706 total hip replacements. We also registered all revision procedures of the implanted joint for the 86 patients with 97 total hip replacements who had died in the course of the study period. The shortest follow-up for all patients living to the end of the study was three years.

The diagnoses for the hip operation were as follows: primary osteoarthritis in 587 hips, osteoarthritis secondary to congenital dislocation of the hip or epiphyseolysis in 82, rheumatoid arthritis in 55, post-traumatic changes in 71 and other diagnoses in eight. In the 145 hips previously operated on the indications for total joint replacement were 33 failed hemiarthroplasties and 112 failed extra-articular procedures.

The first 113 total hip replacements were done without antibiotic prophylaxis; routine antibiotic prophylaxis according to the method described by Carlsson, Lidgren and Lindberg (1977) was used in the 690 subsequent operations.

Deep infection after total hip replacement was defined as periprosthetic sepsis which led to reoperation (Lidwell *et al.* 1982). The most important criteria considered for the assessment of the presence of sepsis were isolation from the joint of potentially pathogenic micro-organisms (isolated in 28 cases), pus in the joint (observed in 23 cases), a sinus (17 cases), raised erythrocyte sedimentation rate when previously not raised (30 cases) and suggestive histological findings (in 21 out of the 24 cases with stained specimens available). **Data analysis.** To avoid statistical problems arising from the differences in the length of follow-up of individual total hip replacements we used standard actuarial methods for the statistical analysis (Breslow 1975; Dobbs 1980).

The *survival* was measured from the date of insertion to the date of the first revision procedure. Life tables

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Table I. Micro-organisms isolated from the wound related to the prophylactic regime (percentages)

Micro-organism	No prophylaxis		Flucloxacillin	
	Superficial discharge (n=31)	Deep infection (n=18)	Superficial discharge (n=84)	Deep infection (n=16)
<i>Staphylococcus aureus</i>	39	61	10	19
<i>Staphylococcus albus</i>	19	22	17	6
Gram-negative	16	11	31	25
Other	23	6	14	31
No growth	35	11	40	25

were computed for the whole prosthetic population divided into subgroups according to the *risk factors*.

The risk of having deep infection in a subgroup was estimated as a *relative risk rate* which was simply the ratio of observed (*O*) to expected (*E*) number of infections. The association between any risk factor and the deep infection was estimated by the *risk ratio*, defined as the ratio of the risk of having deep infection in the presence of the factor to that in the absence of the factor.

The significance of the risk ratio was tested by means of the log rank test (Peto *et al.* 1977). The computer program used for computations of regression analysis and survival data was the Proportional Hazard General Linear Procedure from the Statistical Analysis System, Inc., version 79.5.

RESULTS

Deep periprosthetic infection was diagnosed in 34 total hip replacements. In 10 cases the infection was diagnosed in the first three months (early deep infection). Nine early deep infections started as spontaneously discharging haematomata, in seven cases with initially sterile culture. By definition, all nine haematomata extended beneath the fascia, needed extensive surgical therapy and did not heal during the first three weeks.

In most of the 24 cases of late deep infection the symptoms developed insidiously and we were unable to find any certain date for the start of symptoms. The annual probability of reoperation for deep infection, calculated from the number of hips at risk, varied only slightly during the seven years studied. No reoperations for deep infection were carried out after the seventh year (Fig. 1).

Staphylococcus aureus was the most common micro-organism found in the deep infections as well as in the superficially discharging wounds with positive cultures. The frequency of the isolation of *Staphylococcus aureus* was influenced only by the use of prophylactic antibiotics (Table I); the time of manifestation of deep infection (early or late) was without influence.

Bacteriological samples (opening and closing swabs) were taken during the operations of 160 consecutive total hip replacements with antibiotic prophylaxis. Micro-

organisms were cultivated in samples from 18 wounds: *Staphylococcus albus* grew in samples from 11 wounds, *Staphylococcus aureus* was never recovered. None of these 160 total hip replacements developed periprosthetic infection.

Investigated factors without proven association with deep infection

The patient's age and sex, cortisone treatment, diabetes, operation time, blood loss, perioperative complications, urethral catheterisation for more than 24 hours, a temperature rise over 38 degrees Celsius on the seventh day, extreme obesity, the surgeon and the indication for operation did not show any statistically significant association with deep periprosthetic infection.

Factors associated with the development of deep periprosthetic infection

Early discharge from the operative wound. A superficial discharge was observed in 115 wounds. By definition, all these wounds were completely healed before the twenty-first day without active surgical therapy. Potentially pathogenic micro-organisms were cultivated from the draining material in 70 wounds (infected discharge). In 45 wounds the draining material was sterile. According to the surgeons' assessment only 32 wounds showed signs of superficial inflammation.

The hips which developed a superficial discharge

Fig. 1

The annual probability of reoperation for deep infection as a percentage versus time since operation. Bars represent standard error (the positive element only being shown).

Table II. Observed numbers of deep infections and risk ratios for six risk factors (life table estimates)

Risk factor	Factor present			Factor absent			Risk ratio
	Number of THR	Infections observed (O)	Relative risk rate (O/E)	Number of THR	Infections observed (O)	Relative risk rate (O/E)	
Prophylactic antibiotics	690	16	0.55	113	18	3.65	0.15†
Complication after operation	38	6	4.11	765	28	0.94	4.4†
Wound discharge	115	11	2.46	688	23	0.78	3.2†
Previous operations	145	14	2.37	658	20	0.71	3.3†
Remote infection	93	9	2.46	710	25	0.83	3.0*
Metal-on-plastic prosthesis	348	6	0.38	455‡	28	1.54	0.24†

Significance: * $P < 0.01$; † $P < 0.001$

‡These were metal-on-metal prostheses

Table III. Occurrence of deep infection related to the healing of the operative wound and the prophylactic regime

Healing of the operative wound	No prophylaxis			Prophylaxis		
	Number of THR	Number of infections observed (O)	Relative risk rate (O/E)	Number of THR	Number of infections observed (O)	Relative risk rate (O/E)
Undisturbed	76	7	1.95	603	7	0.27
Complicated:						
superficial discharge sterile	11	1	1.75	34	1	0.88
superficial discharge infected	20	4	6.15	50	5	2.14
deep discharge infected	6	6	—	3	3	—
TOTAL	113	18		690	16	

carried a 3.2 times higher risk of developing late deep infection than the hips which healed uneventfully (Table II). The risk of deep infection in the presence of a discharging wound was further influenced by the character of the exudate (sterile or presence of micro-organisms) and by the use of prophylactic antibiotics (Table III).

In five of the nine late deep infections preceded by an infected discharge, micro-organisms isolated from the draining material were later recovered at the time of reoperation on the infected hip. The periprosthetic sepsis led to reoperation earlier for total hip replacements with postoperative wound discharge than for those with an uneventful healing of the wound (Fig. 2).

Four of the 11 patients with the late deep infection preceded by the discharge from the operative wound have had good performance of their replaced hips and normal erythrocyte sedimentation values one year after operation; this was so also in five patients out of the group of 13 patients with the late deep infection which followed after an uneventful healing of the operative wound.

Prophylactic antibiotics. The total hip replacements done without any prophylactic antibiotic regime were at seven

times higher risk of having deep infection than those on prophylactic regime (Table II). The effect of prophylactic antibiotics on the development of the deep infection interacted with the effect of wound discharge in many ways. The frequency of the discharging wounds and of

Fig. 2

Overall rate of reoperations for deep infection related to the healing of the operative wound, as a percentage versus time since operation.

the early deep infections was significantly lower in hips on the prophylactic regime. The hips with infected discharge were at three times lower risk (risk ratio 0.35) of having deep infection if on a prophylactic regime. In addition, in those without wound discharge, the replacements done with a prophylactic regime were at seven times lower risk of having late deep infection compared with those without prophylaxis (Table III).

Complication after operation. Complications needing surgical reintervention (for example, evacuation of a closed haematoma, open reduction of a dislocated prosthesis, removal of broken cerclage wires) occurred after 38 total hip replacements. These cases carried a very high risk of having deep infection (risk ratio 4.4, Table II).

Previous operations. The risk of having deep infection was three times higher for the total hip replacements done on hips which had had previous operations (risk ratio 3.3) than for those in an untouched area (Table II). The risk of having deep infection increased seven times if such replacement was followed by a discharge from the operative wound (Table IV).

Remote infections. Ninety-three patients developed remote infection (in 72 cases in the urinary tract) after the total hip replacement. The risk of having deep infection for these patients was three times higher than for those without remote infection (Table II), but there was no

Table IV. The effect of postoperative discharge and previous operations on the risk of deep infection

Risk factor	Number of THR	Number of infections observed (O)	Relative risk rate (O/E)	Risk ratio
Wound discharge and previous operations	31	6	4.2	7.0
Wound discharge only	84	5	1.54	2.5
Previous operations only	114	8	1.77	2.9
Without risk factors	574	15	0.60	1.0*
TOTAL	803	34		

* Reference population

Table V. Standardised regression coefficients of the six variables, used for calculation of the risk score

Variable	Regression coefficient	Standard error	P value*
Prophylactic antibiotics	-0.612	0.123	<0.001
Superficial discharge	0.410	0.116	<0.01
Complication after operation	0.395	0.161	<0.01
Previous operations	0.324	0.123	<0.01
Remote infection	0.269	0.114	<0.05
Metal-on-plastic prosthesis	-0.516	0.276	NS

* Chi-square estimate

Fig. 3

Survival without deep infection for three groups of total hip replacement according to their prognostic scores (S), as a percentage versus time since operation.

correlation between the organisms isolated from the source of remote infection and those recovered at the time of debridement of the infected joint.

Type of prosthesis. The risk of having deep infection was four times higher for the 455 metal-on-metal prostheses (McKee-Farrar type) than for the 348 metal-on-plastic ones (Christiansen type), but the metal-on-metal type was being used without antibiotics in 112 cases. After adjustment for this factor (Table V) the statistical significance of the difference between both types disappeared.

Simultaneous effect of risk factors. We used a regression analysis of survival data for the study of the relative importance of each of the risk factors when they occurred simultaneously. The time interval in months from the moment of insertion to the moment of revision operation was chosen as the dependent variable.

The results of this analysis showed that under these conditions the use of prophylactic antibiotics, superficial discharge, complications after operation, previous operations and remote infection were all associated with the development of the deep infection.

As a means of providing a graphic display of the combined effects of the six risk factors on the development of the deep infection we computed the survivorship curves (for survival without deep infection) for groups of total hip replacements with various combinations of risk factors. For this purpose we first calculated a risk score (S) for every total hip replacement. The risk scores were derived from the standardised regression coefficients in Table V. These scores were then used to divide the whole population into three, arbitrarily chosen, prognostic groups with low, medium and high risk of having deep infection.

The low-risk group ($S < 0.5$) contained 564 total hip replacements with five deep infections; the medium-risk group ($0.5 < S < 2.0$) 166 hips with 10 deep infections; and the high-risk group ($S > 2.0$) 73 hips with 19 deep

infections. The probabilities of survival without a deep infection through the 10 years of follow-up were then calculated within each prognostic group.

The survivorship curves are displayed in Figure 3. From this figure it is obvious that the probability of surviving the 10 years without a deep infection decreased as the risk score increased—that is, as more risk factors were involved. It is also obvious, by the comparison of survival chances of the total hip replacements in the high-risk group with those in the medium and low-risk groups that the simultaneous effect of several adverse risk factors, when they were acting together, did not just add but compounded their effect.

DISCUSSION

The results of the present study showed that there was a large group of infected hip replacements in which the deep infection was associated with an early discharge even though the wound was completely healed by the time the patient left the hospital.

The validity of this conclusion is based on the acceptance that we have reliably registered the wound discharge after the replacement operations. We assessed our reliability in a prospective study during 1976 and 1977 on 2371 consecutive clean orthopaedic operations and 249 total hip replacements (Borgström, Bäckman and Surin 1980; Surin, Borgström and Bäckman 1982). We found that the recording of all complications of wound healing was very reliable for operations using bone cement. It also appeared that the diagnosis of the superficial wound infection, based on the assessment of the individual surgeon, was subject to serious personal variations and as such unreliable. Since the bacteriological samples and the nurses' reports reliably identified all discharging wounds, we chose this criterion for our classification.

Our classification of infected discharge, based on the bacteriological evidence, is in accordance with the definition of "superficial infection" as used by Fitzgerald *et al.* (1973), Wilson (1977) and Salvati *et al.* (1982), or with the definition of "minor infection" as used by McLauchlan *et al.* (1976). Although some may object to the classification of wound discharge from which organisms were isolated as infected discharge, we believe that this designation was justified because these cases were at significantly greater risk of having deep sepsis. This position was supported by further analysis of our data which showed that the risk of having late deep infection after the early wound discharge was closely related to the isolation of micro-organisms from the discharging material, irrespective of the presence of other clinical signs of inflammation. We believe that these colonised discharging wounds constitute a special form of infection with great risk of developing late periprosthetic sepsis.

The frequency of superficial infections after total hip replacement varies in different reports from 1.4 to 8.3 per cent (McLauchlan *et al.* 1976; Fitzgerald *et al.* 1977; Josefsson, Lindberg and Wiklander 1981), depending among other things on the surveillance of infection and the regime of prophylactic antibiotics.

The problem with early discharging wounds is to decide whether the discharging material is localised only to the superficial tissues or involves the deep tissues from the outset. Our observation that the late deep infections that followed an early discharge led to reoperation earlier than the deep infections in hips with undisturbed wound healing may indicate that the initial diagnosis of deep infection was missed in these cases. However, all discharging wounds with discharge classified as superficial healed completely and quickly after local wound care. None of these hips gave rise to any suspicion of deep infection at the last check-up before the patient left hospital. Thus, it is conceivable, as supposed by Charnley (1972), that in these cases the periprosthetic infection was present before the point when it manifested itself, even though the wound healed completely and there were no local or systemic signs of deep infection in the early postoperative period.

Several authors agree that the draining haematoma, initially sterile, may become cross-infected on the ward and then represent a very important route for the early deep infection (McLauchlan *et al.* 1976; Müller 1976; Fitzgerald *et al.* 1977; Schwan *et al.* 1977; Andrews *et al.* 1981). It is more difficult to find studies relating the early discharge to the development of the late sepsis. In a series of 2424 total hip replacements, Stadler and Henche (1976) observed that 29 superficial infections were followed by four late infections and 14 out of 30 late infections were preceded by early haematomata. Hill *et al.* (1981) observed that a positive culture from the tips of the vacuum drainage tubes at the time of their removal was a strong predictor of late periprosthetic sepsis. In the series of McLauchlan *et al.* (1976) the aetiology of deep infections was related to wound discharges that were secondarily infected in the ward. Charnley (1972, 1979) believed that superficial infections were probably the result of local elements in the wound combined with the cross-infection in the ward. He concluded that there was no way of knowing how often superficial infection might eventually infect an underlying implant. Failure to define and document the occurrence of superficial infections may be the major reason that some previous reports (Aglieiti *et al.* 1974; Freeman *et al.* 1977; Wilson 1977) have found a negligible impact of this complication on the development of late deep infection.

Patients who had undergone previous operations were at a very high risk of having deep sepsis if they had a discharge from the wound after the replacement operation. It is not clear whether the early discharge and the late infection in these cases were only related to the limited ability of the dense scar tissue to heal after

incision or whether the draining wound was an indication of low-grade sepsis in the scar tissues. In retrospect, only three out of the 14 deep infections in patients with previous operations seemed to have had low-grade sepsis at the time of total hip replacement.

The fact that early discharge was significantly associated with late deep sepsis does not, of course, prove a causal relation. The development of wound discharge may indicate the seriousness of other studied factors and not an independent factor for late deep infection. Since the multiple regression analysis was adjusted for the potential compounding by other studied factors, our observation that the wound drainage remained a significant predictor even in the multiple regression model cannot be attributed to such additional effects. It remains also possible that the wound discharge was a marker of an unmeasured factor, such as low serum protein levels (Müller 1976; Fitzgerald *et al.* 1977).

The evidence derived from our bacteriological results is inconclusive. There was only a poor match between the frequency of micro-organisms recovered from the discharging wounds and those recovered from the deep sepsis. Frequency figures for micro-organisms recovered from the wound during the replacement operations did not come close to a match with those for the deep sepsis. Thus our bacteriological evidence gave no support to the theory that the airborne contamination during the operative procedure was related to the development of deep sepsis. It is, however, apparent that other factors, such as remote infection or infected discharge, though significantly associated with the development of the deep sepsis in our study, would not be considered as related to the deep sepsis if the proof were based on the bacteriological evidence only.

The difficulty of correlating the bacteria of the deep sepsis with those of the environment has been recognised by several authors (Irvine, Johnson and Amstutz 1974; Franco, Baer and Enneking 1977; Freeman *et al.* 1977; Tietjen, Stinchfield and Michelsen 1977; Laufman 1979). Charnley (1979) believed that these difficulties were

related to our insufficient knowledge of the pathogenicity of some strains of *Staphylococcus albus*.

We believe that one should consider the effect of a massive antibiotic treatment, which many patients received before the debridement operation, on the micro-organisms recovered at a later revision. We observed this effect in three cases. The sterile aspiration of the hip done three to five months before revision operation, recovered *Staphylococcus aureus* in two cases and beta-haemolytic streptococci in one. Massive antibiotic treatment was given but continuing pain and high erythrocyte sedimentation rates made revision operation necessary. At revision operation one case grew only *Staphylococcus albus* and two cases *Propionibacterium* strains.

It may be argued that to judge the deep infection rates in our study only by the number of revisions actually performed could underestimate the situation as there might have been cases where the patient, although in considerable pain, was considered physically unfit for revision operation. To estimate the magnitude of this error, we assessed all patients with prostheses still *in situ* (577 total hip replacements) in terms of pain before the closing date of this study. There were 21 such painful hips. Extensive clinical, radiological and laboratory investigations as well as revision procedures in seven cases did not reveal any case of deep infection among them.

We believe that the most important result emerging from our study is the observation (in Tables III, IV and V and in Fig. 3) that the development of a deep infection is the result of many factors acting together, some of them more important than others, and that the combination of two or more factors is substantially more influential than simple addition of their effects. Charnley (1979) and McLauchlan *et al.* (1976) both pointed out that it is fallacious to compare infection rates for isolated variables only. Instead, future study and future protective measures should be directed against every conceivable factor and route of infection because this problem is multifactorial.

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