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Extended follow-up of patients suspected of having joint sepsis after total joint replacement

By O. M. LIDWELL

Formerly of the Cross Infection Reference Laboratory, Colindale, London

E. J. L. LOWBURY

Formerly of the Medical Research Council Burns Unit, Accident Hospital, Birmingham

W. WHYTE

Building Services Research Unit, University of Glasgow

R. BLOWERS

Formerly of the Medical Research Council Clinical Research Centre, Northwick Park Hospital, Harrow

AND D. LOWE

Formerly of the Medical Research Council Biostatistics Unit, Cambridge

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SUMMARY

During an average follow-up time of about $2\frac{1}{2}$ years after total hip or knee-joint replacement in 8052 patients, suspected joint infection was recorded in 85 patients whose joints had not been re-operated during that period. The hospital records of 72 of these patients were examined after a further period, averaging about 5 years. Thirty-five of these had suffered continuing major problems with the joint, 18 of which had been revised, and a further 9 joints needed such treatment. Infection was confirmed in 17 of the 35. These numbers are proportionately about three times greater than those observed among a set of matched controls followed-up for a similar period. The evidence from the extended follow-up suggests that the failure rate, unassociated with infection, reached about 5% by 7 years after operation and that late infections, manifested between about $2\frac{1}{2}$ and 7 years after operation, were about as frequent as those confirmed during the first $2\frac{1}{2}$ years.

INTRODUCTION

In the course of an investigation into the influence of ultraclean air systems in the operating room on the incidence of joint sepsis after operations for total hip or knee-joint replacement the patients's progress was followed for periods up to

Requests for reprints to O. M. Lidwell, MRC Common Cold Unit, Harvard Hospital, Coombe Road, Salisbury, Wilts. SP2 8BW

4 years (Lidwell *et al.* 1982; 1983*a*, *b*; 1984). In addition to cases of joint sepsis observed at re-operation after a failure of the prosthesis, there were approximately equal numbers of instances when the surgeon suspected sepsis in the joint but this diagnosis was not confirmed because no further operation on the joint had been done by the time the study was terminated. The incidence of this 'suspected sepsis' was less when prophylactic antibiotics had been given and also when the operations had been done in rooms with an ultraclean air system (Lidwell *et al.* 1984). Comparison of the magnitude of the effect of these operating conditions on the incidence of 'suspected joint sepsis' with that of the same conditions on the incidence of confirmed joint sepsis is consistent with the hypothesis that about 80 % of the cases of 'suspected sepsis' were in fact associated with bacterial infection in the joint. It was of interest, therefore, to follow the experience of this group of patients over an extended follow-up period; this paper reports the results of such an investigation.

METHODS

Suspected sepsis in the joint had been reported but, in the absence of re-operation on the joint, not confirmed, in 85 patients (Lidwell *et al.* 1984). Three of these patients had died by the end of the original study and for six patients, at two hospitals, further follow-up was not convenient. Questionnaires were sent out, $4\frac{1}{2}$ years after the end of the first study, to the 11 hospitals at which the original operations on the remaining 76 patients had been carried out. No cases of suspected joint sepsis had been reported from the other 6 hospitals included in the study; at 4 of these the incidence of joint sepsis was very low, only 2 cases having been recorded during the study, but there had been no fewer than 14 at the other 2 hospitals together. The same senior surgeon was responsible for the orthopaedic departments at both of these and it seems likely that he did not record suspected sepsis considering this to be too subjective a diagnosis.

The follow-up was confined to information already recorded for the patients at the hospital or by the surgeon responsible. In general, no further search was made but this was done in some instances. The information sought included any further operation on the joint, bacteriological or other evidence of infection and whether re-operation was anticipated or would have been done in the absence of contra-indications.

Questionnaires were also sent out, to be similarly completed, for a set of matched controls in the same hospitals. When the number of cases of 'suspected joint sepsis' at a hospital was fewer than 10, 2 matched controls were selected for each index case to reduce the risk of failure to trace a control at that hospital. In all, 103 controls were selected. These were matched, as closely as possible, with the individual cases of 'suspected sepsis' for the following factors in the order given: (1) postoperative wound infection; (2) treatment with prophylactic antibiotics; (3) operation in ultraclean air (a) staff wearing conventional clothing (b) body-exhaust suits or a plastic patient isolator used; (4) rheumatoid arthritis; and finally, if there were several cases with a similar degree of matching, (5) operation date closest in time to the index case.

All these factors had earlier been shown to affect the risk of joint sepsis. It was

Table 1. *Distribution of operation conditions and wound infection: % in specified category*

	Suspected joint sepsis	Matched controls	Complete study
Operation on knee	25	22	16
With rheumatoid arthritis	18	19	17
Operated in conventionally ventilated operating room	68	68	51
Operated in ultraclean-air system with conventional clothing	18	21	22
Operated in ultraclean-air system with body-exhaust suits or plastic isolator	14	11	26
Prophylactic antibiotics given	57	57	72
Postoperative wound condition:			
No evidence of sepsis	71	76	92
Possible sepsis	7	5	3
Minor sepsis	12	14	4
Major sepsis	10	5	1
Number of patients	72	97	8052

not possible to find controls with an exact match for all the factors for every index case. When this occurred the closest match available was selected.

RESULTS

No hospital records were traced for 4 of the instances of 'suspected joint sepsis' nor for 6 of the matched controls. This represents a loss of just over 5 %. The degree of comparability between the traced cases of 'suspected joint sepsis' and their matched controls is given in Table 1. There are no significant differences, although there is an appreciably larger incidence of major wound sepsis in the 'suspected sepsis' group. Also given in the table is the distribution of the same factors in the whole study population. The differences between this distribution and those for the 'suspected sepsis' and matched controls series reflect the influence of the factors concerned on the incidence of 'suspected sepsis'.

Follow-up duration

Fig. 1 shows the distribution of recorded follow-up times. Within the original study period this did not differ between the cases of 'suspected sepsis' and the matched controls and both were similar to that for the whole study population. It has been pointed out (Lidwell *et al.* 1982) that, although the recorded follow-up times during the study were substantially shorter than those possible according to the protocol, the time distribution of re-operation and confirmed joint sepsis indicated that a large majority, if not all, of failures of the prosthesis were recorded throughout the full extent of the possible follow-up time.

Follow-up during the extended period reported in this paper could have reached to more than 9 years after initial operation, with a median of nearly 7 years. Extended follow-up recorded for the cases of 'suspected sepsis', median 5·0 years,

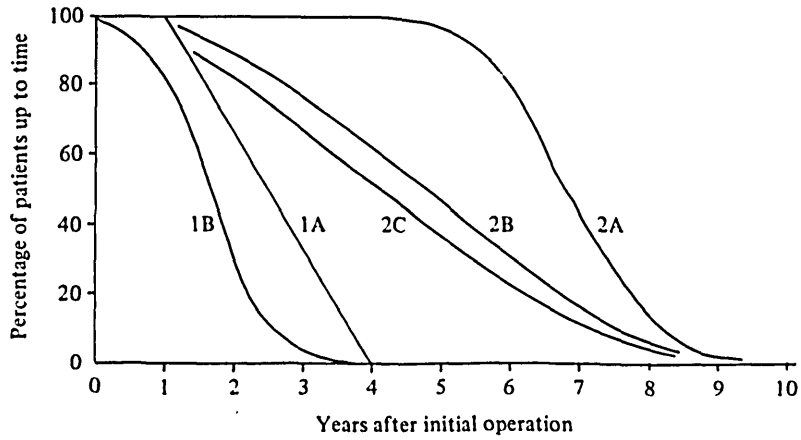

Fig. 1. Time distribution of extended follow-up. 1A, Maximum possible follow-up in the original study according to the protocol. 1B, Recorded follow-up in the original study for cases of 'suspected joint sepsis' and for matched controls (indistinguishable). 2A, Maximum possible extended follow-up calculated from the start and finish dates at the several hospitals. 2B, Duration of extended follow-up in the hospital records for cases of 'suspected joint sepsis'. 2C, Duration of extended follow-up in the hospital records for the matched controls.

was somewhat longer than that for the 'matched controls', median 4·1 years. The longest interval recorded was 9 years 1 month among the cases of suspected sepsis and 8 years 10 months among the matched controls.

However, as will appear later from the time distribution of re-operations it seems that, for the extended follow-up also, most of the instances of failure of the prosthesis that occurred within the full duration of the maximum possible follow-up time, determined by the termination of the investigation, were reported. Ten deaths were reported among those with 'suspected sepsis' and the same number among the matched controls.

Incidence of failure of the prosthesis and of joint sepsis

The clinical problems experienced during the extended follow-up period by the patients with 'suspected sepsis' and by the matched controls are summarized in Table 2. No further information beyond the original study period had been recorded for 10% of those patients in whom joint sepsis had been suspected, nor for 15% of the matched controls. In addition, the reports indicated satisfactory progress or only minor problems for over 40% of those with 'suspected joint sepsis' and for two-thirds of the matched controls. However, nearly half of those with 'suspected' joint sepsis had major problems, with the prosthesis removed from one-quarter. Approximately half of the major problems were associated with infection in the joint, either bacteriologically confirmed (in more than three-quarters) or clinically apparent. In contrast, major problems during this period were only encountered in 18% of the matched controls, and the prosthesis was removed from no more than 7%; infection in the joint was confirmed in only 4%, all among those from whom the prosthesis was removed. Re-operation without

Table 2. *Experience during extended follow-up*

	Patients with 'suspected' joint sepsis			Matched controls		
	Hips	Knees	All joints	Hips	Knees	All joints
Number of patients. . .	54	18	72	76	21	97
No further information	9%	11%	10%	20%	0%	15%
Satisfactory or only minor problems	44	33	42	67	67	66
Serious problems*	11 (7)	11 (6)	11 (7)	5 (0)	19 (0)	8 (0)
Prosthesis removed	24 (17)	28 (11)	25 (15)	7 (4)	10 (5)	7 (4)
Re-operation desirable†	11 (2)	17 (0)	12 (1)	1 (0)	10 (0)	3 (0)
All major problems	46 (26)	56 (17)	49 (24)‡	13 (4)	38 (5)	18 (4)§

Apart from the first row all the figures are percentages, with those for infections given in parentheses.

* Re-operation without removal of the prosthesis, prolonged infection with discharging sinus or abscess or, in the absence of infection, prolonged pain, sometimes with radiological loosening. Four of these 16 patients died during the extended follow-up period.

† Re-operation awaited, refused, or not advisable due to poor health of patient.

‡ Corresponds to 17 actual infections; 5 with *Staphylococcus aureus*, 1 with an intestinal species, and 6 with other identified species (mostly coagulase-negative staphylococci), in 5 instances no organism was isolated.

§ Corresponds to 4 actual infections; one with *Staphylococcus aureus* and 3 with other identified species.

associated infection was more frequent after replacement of the knee joint than of the hip (22% as compared with 7%) after the diagnosis of 'suspected joint sepsis'.

The species of organisms associated with the infections and the proportion of cases from which presumptively causative organisms were isolated were very similar to those reported during the first years after initial operation (Lidwell *et al.* 1983*a*). Bacteria were isolated from 76% of the re-operations which were clinically assessed as septic during the extended follow-up period, very similar to the 79% in the initial study. *Staphylococcus aureus* was found in 29%, compared with 31% in the earlier period. The proportion of intestinal organisms isolated was 5%, compared with 15% during the earlier period, but this corresponded to only a single isolation. The proportion of 'other species', including skin commensals (mostly coagulase-negative staphylococci) was somewhat greater, more than 40% compared with just over 30%.

While the incidence of 'suspected joint sepsis' was less when the operation had been done in ultraclean air or when prophylactic antibiotics had been given at the time of the insertion of the prosthesis, and even less if both these conditions applied, the proportion of those diagnosed as 'suspected joint sepsis' who subsequently were re-operated or suffered major problems was rather similar whatever the original operating conditions, or whether postoperatively wound infection occurred (Table 3). The same was also true for the matched controls. Owing to the doubled number of matched controls from the hospital which had reported relatively few cases of 'suspected' joint sepsis, constituting about one third of the total number, the controls are not exactly balanced in respect of

Table 3. *Experience during extended follow-up in relation to conditions at the initial operation*

	Joint sepsis 'suspected'			Matched controls		
	Number	Major problems (%)	Infected (%)	Number	Major problems (%)	Infected (%)
Conventional ventilation no antibiotics	26	50	27	34	18	6
Either ultraclean air *or* antibiotics given	28	50	25	40	18	2
Both ultraclean air *and* antibiotics	18	44	17	23	22	4
Possible wound infection, or sepsis	21	43	14	23	17	9
All patients	72	49	24	97	18	4

hospital differences. It was not practicable to obtain a larger number of extended follow-up records from the hospitals reporting the larger number of cases of 'suspected' joint sepsis. However, although this group of hospitals differed from the first in that a larger proportion of cases of joint sepsis was preceded by wound infection and that a smaller proportion of these patients had received prophylactic antibiotics, the subsequent experience of the two groups did not differ significantly. Among the 48 controls from the 3 hospitals with the larger number of cases of 'suspected' joint sepsis, 5 were re-operated and 4 had continuing serious problems, 3 of these 9 were associated with infection. Among the 49 controls from the other group of hospitals, 4 were re-operated and 5 had continuing serious problems; also 9, of which 1 was associated with infection. In both groups the frequency of re-operation on the joint and of 'all major problems' was between 2·4 and 3 times greater among those with 'suspected sepsis' than among the controls. The proportion of 'major problems' associated with infection among those with 'suspected sepsis' was almost exactly 50 % in both groups. In view of the similarity of these figures no allowance has been made for the lack of balance referred to above in computing the Tables and Figures.

The data from the extended follow-up can also be used to derive an estimate of the incidence of failure of the prosthesis, unassociated with infection, during the years following the end of the main study; although the number of patients included in the control set was rather few for this purpose. Among the 97 controls the prosthesis was removed during the extended follow-up period from three patients (3·1 %) in whom there was no evidence of joint infection (see Table 2, last column, 7–4 %). This was also the experience of seven patients in the 'suspected' sepsis group (see Table 2 All joints, column 3, 25–15 % of 72 patients) but this corresponds to only about 0·1 % of the approximately 7000 patients at those hospitals at which the cases of 'suspected sepsis' included in the extended follow-up were diagnosed. In addition a further 3 % of the control group were reported as needing re-operation by the end of the extended follow-up period of which, perhaps, one half might be found to be without evidence of infection.

During the average $2\frac{1}{2}$ post-operative years of the main study the prosthesis was

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removed without any evidence of infection in 127 of the 8052 patients or 1·6%. Thus the total proportion of failed prostheses over an average of 7 years postoperative observation would seem to have been about 5%, i.e.

Failure during the first $2\frac{1}{2}$ years	127/8052 = 1·6%
Failure during extended follow-up:	
among 'suspected sepsis' group	7/7000 = 0·1%
among matched controls	3/97 = 3·1%
Total	= 4·8%

The failure rate after operations on the knee (49/1270 = 3·9%) was about three times greater during the main study than that after hip-joint replacement (78/6782 = 1·2%). This difference continued during the extended follow-up; among those patients with 'suspected sepsis' 39% of the knees suffered from 'major' problems as compared with 20% of the hips, while among the matched controls the corresponding figures were 33% for knees but only 9% for hips.

The likely incidence of late joint infection is less easily estimated because the matched controls differed, as has been stated, from the overall study population in those respects that have been shown to influence the incidence of joint sepsis in the years immediately after the insertion of a prosthesis and might, therefore, be supposed to do so over the extended follow-up period also. If the relative risk factors, deduced in the original study, for both the conditions at operation, ultraclean air and use of prophylatic antibiotics, and the development of post-operative wound sepsis (Lidwell *et al.* 1984, Tables 1 and 6) are applied to the distribution of these factors among the matched controls then the calculated risk of deep joint sepsis during the earlier period for this group was 4·2 times that for the whole original study population. If this proportion is then applied to the 4 cases of deep joint sepsis recorded among the 97 matched controls during the extended follow-up period then the estimated number of such cases, in the same hospitals, among those not re-operated for, or suspected of, joint sepsis, 6112, in the earlier period is $(4/4{\cdot}2) \times (6112/97) = 60$. To this must be added the 11 cases of confirmed deep joint sepsis observed during the follow-up period among those with previously suspected joint sepsis (see Table 2, column 3 – All Joints, 15% of 72), a total of 71. This is slightly greater than the 69 cases of deep joint sepsis recorded in the same population during the original study period, i.e. only about one half of such cases arising by the end of an average 7-year follow-up would seem to have been observed during the average of $2\frac{1}{2}$ years of follow-up in the original study.

Time interval to re-operation

The value of 7 years given above for the average effective follow-up time is based on the following assumption, suggested by the distribution of intervals between insertion of the prosthesis and reoperation, that any failure of the joint within the possible follow-up period (limited by the date the investigation ended) was usually recorded, even though the actual intervals up to the last recorded observations for patients not re-operated were substantially less (Fig. 1, curves 2B, 2C).

Figs 2 and 3 show the time intervals to re-operation, the first in relation to the time of insertion of the prosthesis, the second in relation to the additional period of observation after the termination of the original study. It is clear that the higher

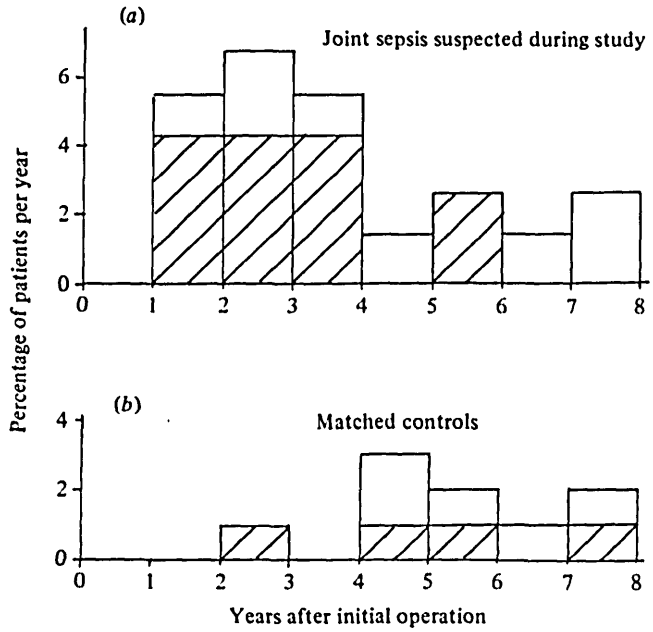

Fig. 2. Interval between initial operation and subsequent re-operation in the joint during the period of extended follow-up. (*a*) Cases of 'suspected joint sepsis'. (*b*) Matched controls. Re-operation showing confirmed sepsis is indicated by the hatched areas.

failure rate among the patients with 'suspected joint sepsis' compared with that for the matched controls occurred entirely within the first 2 years after the end of the main study period.

The relative constancy of the annual incidence, apart from this excess, right up to 7–8 years after the initial operation can most easily be accounted for by the assumption that prosthetic failure was effectively reported throughout this time. A similar pattern could possibly result if both the risk of joint sepsis and of breakdown increased rapidly beyond the fifth year so as to compensate for a reduction in the number of patients observed.

Variation between hospitals

There were no significant differences between the hospitals in respect of the proportionate incidence of 'major problems' or re-operation during the period of extended follow-up. The number of instances at each hospital was small so that only large differences would have been apparent.

DISCUSSION

The diagnosis of 'suspected joint sepsis' must, inevitably, involve clinical judgement rather than objective assessment; the only recorded symptom in most cases was pain. The correlations earlier established between the incidence of suspected joint sepsis and the operation conditions (Lidwell *et al.* 1984) together with the substantially less favourable prognosis for patients with 'suspected sepsis'

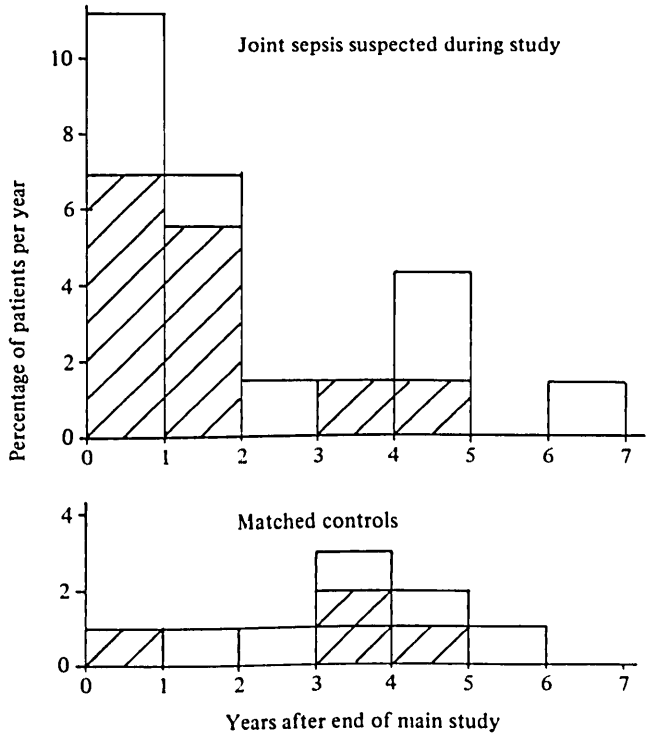

Fig. 3. Interval between the last recorded follow-up data for the individual patient in the study and subsequent re-operation on the joint. (*a*) Cases of 'suspected joint sepsis'. (*b*) Matched controls. Re-operation showing confirmed sepsis is indicated by the hatched areas.

demonstrated here show that the surgical opinion was generally well founded. Only about half of the patients so diagnosed experienced a satisfactory result of the arthroplasty when this was assessed over a further period of about 5 years beyond that of the original study. Although bacterial infection was substantiated in only about one-quarter of the patients this is not inconsistent with the opinion that the condition was in most cases associated with infection. Treatment and natural recovery may well have led to the elimination of bacteria from the joint. When the relatively unfavourable prognosis was substantiated this was usually within a period of 2 years from the beginning of the extended follow-up period. Beyond this time the rate of joint breakdown did not significantly differ from that among patients in whom joint sepsis had not been suspected.

An overall assessment of the data obtained from the extended follow-up suggests that joint sepsis continued to become evident during this period, at such a rate that the number observed was about the same as that confirmed during the main study, i.e. the incidence rates already reported for a mean follow-up of about $2\frac{1}{2}$ years are about one half of those to be found during a follow-up time of about 7 years. Some of these later infections might be due to haematogenous spread but this would not be influenced by conditions at the time of operation and the apparent incidence of 4 % if these are ignored is far higher than has been accepted for this route (Charnley, 1979). However, the estimated values are subject to a

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wide range of possible error in view of the small number of events from which they are derived.

The prosthesis failure rate of about 5%, without apparent infection, over the full period, an average of about 7 years, may be compared with the 16% reported by Mueller (1981) and the 10% reported by Salvati *et al.* (1981) over a period of about 10 years after insertion. Charnley (1979) records a substantially lower revision rate in a series extending up to 15 years but his figures are not exactly comparable with those given in the papers cited above or reported here. The problems of long-term survival of total hip replacement are discussed by Harris & White (1982).

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