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SEPTIC ARTHRITIS IN MALES WITH HAEMOPHILIA

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Abstract

We used data collected as part of the Universal Data Collection (UDC) surveillance project in haemophilia treatment centers (HTC) to study the incidence, risk factors, and impact of septic arthritis among males with haemophilia. Patients participating in UDC on 2 or more occasions were included. Cases were defined as patients with documented joint infection. Characteristics of the cases were compared with those of haemophilia patients without infection. Among the 8026 eligible patients with 36,015 person-years of follow-up, 30 (0.37%) had a documented joint infection (incidence rate 83 per 100,000 person-years). In a logistic regression model, only increasing age (OR = 6.1 for age ≥30), race/ethnicity other than white (OR = 3.9), presence of inhibitor (OR = 3.9), invasive procedure in the past year (OR = 2.7) and presence of one or more target joints (OR = 3.2) remained statistically significant. CVAD use and HCV and HIV infection were not associated with septic arthritis risk after adjusting for potential confounders. Study limitations include possible underestimation of septic arthritis rate in this population and its retrospective design. We conclude that septic arthritis is an uncommon complication of haemophilia occurring primarily in joints most affected by bleeding and reparative surgical interventions.

Keywords

Hemophilia; Haemophilia; Joint disease; Arthropathy; Infectious arthritis; Epidemiology

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INTRODUCTION

The incidence of septic arthritis in the general population is approximately 2–6 cases per 100,000 population per year and most commonly affects young children and the elderly [1, 2]. Infection in a joint is usually seeded hematogenously, and the most frequent causative organisms are Staphylococcal and Streptococcal species. Predisposing factors include underlying joint and connective tissue disease (e.g., rheumatoid arthritis), the presence of a joint prosthesis, previous joint surgery, immunosuppression, and diabetes [2, 3].

Septic arthritis is more common in patients with haemophilia than the general population and is associated with considerable morbidity including loss of range of motion in the affected joint and, among patients with a prosthesis, removal of the artificial joint [4, 5]. Over the last 2 decades, a number of published case reports and series have implied that the incidence of septic arthritis among people with haemophilia may have increased with the appearance of human immunodeficiency virus (HIV) infection [4, 6–9] and increased use of central venous access devices (CVAD) for prophylaxis [10, 11]. Moreover, the overall rate of prosthetic joint infection after arthroplasty in haemophilia patients (especially if HIV positive) has been reported to be much higher than that reported in the non-haemophiliac population [5, 12, 13]. However, considerable uncertainty remains in the literature about the incidence of and risk factors for septic arthritis in haemophilia because of differences in study design and variations in the populations studied.

The Universal Data Collection (UDC) project, a voluntary surveillance program involving 136 federally funded haemophilia treatment centers (HTCs) in the United States, was established in 1998 to monitor the safety of treatment products and to collect a uniform set of clinical treatment and outcomes data that could be used to inform activities directed at preventing complications of bleeding disorders [14, 15]. Data have been collected from more than 18,000 people with bleeding disorders who receive care in these centers. The goal of this study was to use data from this large database to describe the incidence of and risk factors for joint infections and to evaluate the impact of septic arthritis on joint function among males with haemophilia.

METHODS

The details of eligibility and recruitment for the UDC project have been reported previously [16]. Briefly, persons with bleeding disorders are enrolled in UDC, and a standardized set of clinical data and plasma specimen are collected each year at participating HTCs. Participation is voluntary, and patients (or parents of minor children) are required to give informed consent. The study has received approval from the Human Subjects Institutional Review Boards of CDC and all participating HTCs. This report is based on data obtained from males with haemophilia A or B.

Data collection

Demographic, treatment, and clinical outcome data were collected from UDC participants during the annual comprehensive care visit. Date of birth was used to calculate age. Subject race and ethnicity, based on participant self-report, was categorized in accordance with census reporting. Haemophilia severity was based on the percentage of normal clotting factor activity and categorized as mild if the deficient factor activity was 6 – 30 IU/ml, moderate if 1 – 5 IU/ml, and severe if less than 1 IU/ml of a normal reference range.

Clinic records were used to determine if the participant had health insurance and to identify the treatment regimen used. If the person infused clotting factor on a regular basis (e.g., every other day) to prevent bleeding, and the infusions were expected to continue

indefinitely, he was considered to be on prophylaxis treatment. Data on the placement of a long-term CVAD for factor infusion and any complications (e.g., infections) occurring in these devices were also obtained from clinic records.

Participants with a measured inhibitor titer (to FVIII or FIX) of more than 0.5 Bethesda Units at any time during the year before the comprehensive care visit were classified as having an inhibitor. As part of the UDC project, a blood specimen is tested annually for serologic evidence of infection with HIV and hepatitis C (HCV). The results of this testing were used to determine the patient's status at baseline with regard to these infections.

UDC participants are routinely instructed to keep a log of all bleeds that occur between clinic visits, including its severity, location and treatment. HTC staff review available logs and record on the data form the number of bleeds by site (joint, muscle, or other) during the 6-month period before the comprehensive care visit. For participants who do not submit a complete log (approximately 75% of subjects), information about bleeding is based on patient and/or parent recall.

During the visit, the participant's height and weight were measured and used to calculate body mass index (BMI). Thirteen measurements of range of motion (ROM) were assessed bilaterally at the hips, knees, shoulders, elbows and ankles by a physical therapist or other trained health care provider using a standard goniometer according to detailed guidelines provided in a reference manual and training video supplied by CDC. ROM was not measured in joints in which a bleed had occurred within 24 hours or whose motion was restricted for another medical reason (e.g., recent surgery, presence of an immobilization device such as a splint or brace).

A joint in which recurrent bleeding had occurred on 4 or more occasions during the 6 months before the clinic visit was designated a target joint. Clinic and hospital records were reviewed to determine whether or not orthopedic surgery had been performed on 1 or more joints during the previous year, including arthrodesis (joint fusion), synovectomy (surgical or radioisotopic), and arthroplasty (joint replacement).

Study design

We used surveillance data collected during multiple visits on patients receiving care in HTCs in two types of analyses. The first, a retrospective cohort analysis, used data from all visits to calculate an overall incidence rate of septic arthritis. The second, a nested case-control analysis to investigate the risk factors associated with septic arthritis, used data collected only at the visits before and after the joint infection for the cases and data collected only at the two most recent visits for the controls. Baseline characteristics of all cases used data collected during the UDC visit before the visit when the joint infection was reported. Baseline characteristics for the controls were based on data collected at the visit prior to the most recent visit in the database.

Possible septic arthritis cases were identified on the basis of an affirmative response to the question “Has the patient had a joint infection during the past year”. To verify these surveillance data, a second questionnaire was sent to the participating HTC center as part of the current study to confirm the case status and to collect additional information about the infection, including diagnostic methods, causative organism(s), and treatment. In addition, data were collected about previous surgery or procedures involving the infected joint, the presence of a prosthetic joint or central venous access device (CVAD), the occurrence of any preceding joint hemorrhage or trauma, and any recent history of dental or urologic procedures.

Based on data from the second survey, cases were confirmed to have had a joint infection only if they had a microbial overgrowth on cultures of either synovial fluid aspirate or fluid drainage from the affected joint, or a positive blood culture with clinical symptoms of infection in a joint (e.g., fever, swelling, pain, tenderness, and increased warmth). All potential cases that could not be thus confirmed were included in the control group.

Data analysis

Joint infection rates were calculated by dividing the number of joint infections by the number of person-years of follow-up and reported as cases per 100,000 person-years. Each visit for a patient was counted as one person-year because the data collection tool asked about any joint infections that had occurred during the year prior to the visit. All UDC visits for controls and all visits until the index visit for cases were included in the calculation of person-years.

Differences in the distribution of demographic and clinical characteristics between the cases and controls were examined for statistical significance using chi-square tests. Logistic regression was used to identify independent risk factors for joint infection. All studied risk factors were entered into the regression model, and variables that were not statistically significant were removed one at a time until the most parsimonious model was achieved.

To compare changes in joint ROM before and after the joint infection, we first calculated an overall joint index for each participant, which was the sum of all flexion and extension (including hyperextension) measurements taken on all 10 joints. The total amount of joint ROM limitation in degrees was calculated as the difference between the normal overall joint index value [17] and the participant's overall joint index. The percent overall joint ROM limitation was determined for each person by dividing his total amount of joint ROM limitation by the normal overall joint index value and multiplying by 100. For the cases, the change in percent ROM limitation was calculated by subtracting the limitation at the visit during which the joint infection was reported from that measured at the baseline visit. For controls, the change between the 2 most recent visits was calculated. Using multiple linear regression analysis, the average change among cases was compared with that among controls adjusting for differences in BMI, haemophilia severity, race/ethnicity, presence of target joint, history of recent invasive surgery, and the presence of an inhibitor. All analyses were performed using SAS Version 9 statistical software (SAS Institute, Cary, NC).

RESULTS

Between January 1, 1999, and June 30, 2005, 8950 males with haemophilia participated in the UDC project. Of those, 8026 (90%) had 2 or more UDC visits with a cumulative 36,015 person-years of follow-up; these individuals formed the study population. Among the 114 patients whose data forms initially indicated the occurrence of a joint infection during the year before the UDC visit, 30 (26 %) were confirmed to have had a documented joint infection and were designated as cases. Of the remaining 84 patients, data about joint infections were incorrectly coded on the original data collection form for 20 (24%) and review of medical and clinic records by HTC staff in response to the second survey found no objective evidence of joint infection for the remaining 64 patients. These 84 patients and the remaining 7912 patients formed the control group.

The knee was the most commonly affected joint occurring in 67% of the patients and 3 (10%) patients had more than one joint infected at the time of presentation (Table 1 and appendix 1). The diagnosis of a joint infection was confirmed by a positive culture from a joint aspirate or fistula drainage in 83% of cases and gram positive organisms were identified in 77% of those cases. Twelve (40%) patients had experienced hemarthrosis in the

joint within 2 weeks of presentation with a septic arthritis. Two (6.7%) patients had either joint aspiration or trauma of the affected joint within two weeks of the joint infection. Eighteen patients (60%) had prior surgery in the affected joint, of which 13 (72%) were arthroplasties. The median duration from joint arthroplasty to joint infection was 60 months (range 1–216 months). Ten of these 13 (77%) individuals underwent surgical removal of the infected prosthesis. Of the 8 patients with multiple prosthetic joints, 2 had concurrent infections in more than one prosthetic joint. The median duration of antibiotic therapy was 42 days (range 5–918). Six individuals (20%) subsequently developed a recurrent joint infection.

The overall incidence rate of joint infections for the 7-year period was 83 cases per 100,000 person-years and varied from 26 to 129 cases per 100,000 person-years annually. Participant demographic and clinical characteristics by case-control status are shown in Table 2. The average age of study subjects was 23.3 years, 80% had haemophilia A, and the proportions of participants with mild, moderate, and severe haemophilia were 21%, 22%, and 57%, respectively. Two thirds of the subjects were white, 13% were black, 12% were Hispanic, and the rest were other races. A significantly higher proportion of cases than controls were older, non-white, and on home infusion and were more likely to have severe haemophilia, non-traditional or no health insurance, an inhibitor, a higher frequency of joint bleeds, at least one target joint, and a recent invasive procedure. In addition, cases were more likely than controls to be HIV and HCV positive.

When all of the patient characteristics were examined in a multivariate model, several were independently associated with case status (Table 3). Cases were 6.0 times more likely to be 30–39 years old and 9.4 times more likely to be 40 years or older than they were to be younger than 30 years of age. Cases were also 3.9–5.0 times more likely to be some other race or ethnicity besides white. Finally, cases were 2.7, 3.2, and 3.9 times more likely to have had an invasive procedure, at least 1 target joint, or an inhibitor, respectively, during the year in which the infection occurred. In the multivariate model, severity of haemophilia, HIV and HCV status were no longer significantly associated with case status.

After adjusting for differences in age, BMI, haemophilia severity, race/ethnicity, the presence of a target joint, recent invasive surgery, and an inhibitor, the cases had an average increase in overall ROM limitation of 2.4%, whereas the corresponding value for controls was only 0.5% ($p = 0.04$) over a similar period. ROM measures decreased in the infected joints of 72% of the case patients with an average 11.6% ROM limitation change in the affected joint vs. 0.6% in that of the contralateral joint ($p = 0.052$).

DISCUSSION

We found that the incidence of septic arthritis in haemophiliacs is 15–40 times higher than the reported incidence in the general population, 3–4 times higher than that seen among people with rheumatoid arthritis, [18–20] and similar to that reported in patients with prosthetic joints [21, 22], Several factors are likely responsible for the high incidence of septic arthritis in the haemophilia population, including a higher prevalence of pre-existing joint damage from repeated hemarthrosis and the high rate of joint replacements performed in this population.

As reported in other studies [1, 2], increasing age was associated with a higher risk of septic arthritis in haemophiliacs. We speculate that with increasing age, there is progression in the degree of joint disease from repeated hemarthrosis, thus setting up the joint for bacterial seeding. Hemophilic joint disease characterized by chronic synovitis, articular cartilage damage, and subchondral cysts, may facilitate colonization following intravenous

cannulation for factor replacement or other sources of transient bacteremia, such as an invasive orthopedic procedure, which was also associated with a higher incidence of joint infection in our study. The associations we found between septic arthritis and the presence of either a target joint or an inhibitor may reflect inadequate treatment of hemarthrosis leading to prolonged joint exposure to blood, a medium for bacterial growth.

Compared with whites, we found that blacks, Hispanics, and persons of other races were significantly more likely to develop septic arthritis. The reasons for these differences are not entirely clear, but it is possible that minorities have decreased access to health care compared with whites and may also delay seeking medical attention for either hemarthrosis or localized or systemic infection. Although we accounted for differences in health insurance type in our analysis, there are other factors that lead to delayed treatment, including cost, transportation issues, and knowledge and attitudes about illness [23]. These differences could also reflect residual confounding from other unknown factors that were not included in the model but we are unaware of other factors that may be related both to race or ethnicity and the risk of septic arthritis.

Even though the proportion of patients that were HIV positive was higher among cases than among controls, HIV infection was not an independent risk factor for septic arthritis in our study. Similarly, in a prospective study of septic arthritis among hospitalized patients in Africa, a higher proportion of septic arthritis cases were HIV positive compared with a control group even though there was no difference in the septic arthritis prevalence between HIV-positive and HIV-negative patients [24]. Much of the evidence for the apparent association between HIV infection and septic arthritis in haemophilia comes from small case series in single institutions in which a high proportion of the cases were HIV positive. In contrast, studies that compared outcomes of surgery in patients with haemophilia found no difference in infection rates between HIV-positive patients without AIDS and those who were HIV negative [5, 25, 26].

In our study, the presence of a central venous access device (CVAD), typically used more in children than in adults for prophylaxis, was not a risk factor for septic arthritis. A somewhat smaller proportion of cases than controls had a CVAD, and none of the cases had a CVAD infection at the time of their joint infection. On the other hand, all but one of the cases infused factor at home. Home infusion, made possible by the advent of factor concentrates, has been shown to improve quality of life [27] and reduce hospitalizations for bleeding complications [28]. However, intravenous infusions conducted under less-than-ideal conditions may increase the risk of infection from improper sterile technique. The majority of the organisms cultured from our patients were skin pathogens that likely were introduced during factor infusions. Further evidence for infusions as the source for these infections is the fact that, among patients infected with HIV, septic arthritis caused by these organisms occurs among intravenous drug abusers but not among homosexuals [29]. At least one investigator has proposed that the increasing prevalence of home infusion, not HIV infection, is responsible for the apparent increase in septic arthritis during the past 2 decades [8].

In a community-based study of 154 consecutive patients in the Netherlands, the morbidity associated with septic arthritis was substantial, especially among individuals with pre-existing joint disease, those with prostheses, and the elderly [30]. In that study, 10% of patients died and nearly 50% of adults had a poor outcome defined as limb amputation, removal of prosthesis, or much worse self-reported function of the affected joint. Among 29 patients with an infected prosthesis, 20 (69%) underwent removal of the joint in that series. In our study, based on joint ROM measurements made during annual visits before and after the joint infection, we found a 5-fold greater increase in overall ROM limitation among our

haemophilia patients with septic arthritis than among the control group over a similar period. The average ROM limitation change in the infected joint was 11.6% vs. 0.6% in that of the contralateral joint ($p = 0.052$). These findings provide evidence that the difference between cases and controls was a result of the septic arthritis. This change in ROM following joint infection might impact the activities of daily living. Finally, just as in the Dutch study, a high proportion (77%) of the infected prosthetic joints in our patients with haemophilia required surgical removal.

Several limitations should be considered when evaluating the results of this study. First, the septic arthritis cases were initially identified on the basis of a yes response to the data form screening question “Has the patient had a joint infection during the past year.” As a result of our second survey for this study, we found that there were more cases of joint infection reported on the data forms than could be confirmed by objective criteria present in the medical record. One possible explanation is that the initial response provided on the UDC data form was based on patient recall rather than by a review of the medical record. Although we are confident that the cases we report truly did have an infection, it is possible that other patients who had a joint infection may have been missed since we could not practically seek confirmation of control status. In addition, to be captured by our surveillance, patients who had septic arthritis must have survived long enough to have a clinic visit during which the septic arthritis was reported. Patients who died as a result of their septic joint would have been missed. For these reasons, we may have underestimated the rate of septic arthritis in this population. In addition, we did not specifically evaluate the incidence and risk factors for septic arthritis in female Haemophilia carriers or individuals with other bleeding disorders.

A second limitation of our study's retrospective design is that concomitant medical issues that may have contributed to the joint infection may have been overlooked and, therefore, were not documented in the medical record. Thus, we may have incorrectly specified the risk factors present for patients, which would have had the overall effect of decreasing the apparent associations we observed. However, the risk factors that we studied, such as prior urologic procedures, HIV infection, and CVAD placement, were unlikely to have been omitted from the medical record.

In conclusion, septic arthritis in an uncommon complication, but it occurs at a higher rate in individuals with haemophilia than in the general population and may lead to an accelerated decline in joint range of motion. Age greater than 30 years, history of a recent invasive procedure, and the presence of either an inhibitor or a target joint were associated with increased risk for septic arthritis among patients with haemophilia after adjusting for potential confounders. Our finding of greater risk among minorities warrants further study. Septic arthritis should be included in the differential diagnosis in patients with haemophilia with localized joint pain and swelling, especially if there is associated fever and refractoriness to appropriate factor replacement therapy.

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Table 1

Infected Joint Characteristics

Characteristic	Cases (n = 30)	Percentage
Joint infected *		
Knee	20	66.7
Ankle	6	20.0
Elbow	3	10.0
Hip	3	10.0
Wrist	1	3.3
Organism isolated		
Polymicrobial	4	13.3
Gram positive	23	76.7
Staphylococcus species	15	50.0
Staphylococcus aureus	7	23.3
MRSA	2	6.7
Staphylococcus coagulase negative	2	6.7
Streptococcus species	7	23.3
Streptococcus viridans	3	10.0
Streptococcus pneumoniae	1	3.3
Beta hemolytic streptococcus	1	3.3
Enterococcus faecalis	1	3.3
Streptococcus bovis	1	3.3
Gram positive bacilli	1	3.3
Gram negative	6	20.0
Escherichia coli	2	6.7
Enterobacter cloacae	1	3.3
Pseudomonas aeruginosa	2	6.7
Serratia marcescens	1	3.3
Filamentous fungi	1	3.3
Prior joint surgery	18	60.0
Joint replacement	13	43.3
Synovectomy	2	6.7
Debridement	1	3.3
Fusion	2	6.7
Recent joint aspiration of the affected joint	2	6.7
Recent trauma of the affected joint	2	6.7

* 2 patients had an infection in more than one joint

Table 2

Characteristics and Associations With Joint Infections Among 8026 Males With Haemophilia in the United States, 1999–2005

Characteristic	Controls (n = 7996)		Cases (n = 30)		
	n	%	n	%	p value
Age					
2–19	4428	55.4	6	20.0	<0.001
20–29	1269	15.9	1	3.3	
30–39	816	10.2	7	23.3	
≥40	1483	18.5	16	53.3	
Race/ethnicity					
White	5568	69.6	12	40.0	0.001
Black	999	12.5	10	33.3	
Hispanic	971	12.1	5	16.7	
Other	465	5.8	3	10.0	
BMI					
Underweight (<18.5)	1964	24.9	6	20.0	NS
Normal (18.5–24)	3069	38.9	8	26.7	
Overweight (25–29)	1698	21.5	11	36.7	
Obese (≥30+)	1164	14.7	5	16.7	
Insurance type *					
Commercial	1198	15.1	4	13.8	0.05
HMO/PPO	2757	34.6	5	17.2	
Medicare/Medicaid	2295	28.8	8	27.6	
Other/None	1707	21.5	12	41.4	
Haemophilia Type					
A	6359	79.5	27	90.0	NS
B	1637	20.5	3	10.0	
Severity					
Mild	1662	20.8	1	3.3	0.02
Moderate	1794	22.4	5	16.7	
Severe	4540	56.8	24	80.0	
Treatment Type					

Characteristic	Controls (n = 7996)		Cases (n = 30)		
	n	%	n	%	p value
Episodic	5487	68.6	21	70.0	NS
Prophylaxis	2509	31.4	9	30.0	
Home Infusion					
Yes	6165	77.1	29	96.7	0.01
No	1831	22.9	1	3.3	
CVAD					
Yes	942	11.8	2	6.7	NS
No	7054	88.2	28	93.3	
CVAD infection					
Yes	99	1.2	0	0	NS
No	7897	98.8	30	100.0	
Number of joint bleeds					
0 bleeds	3427	42.9	3	10.0	0.003
1–2 bleeds	1557	19.5	8	26.7	
3–6 bleeds	1401	17.5	10	33.3	
7+ bleeds	1610	20.1	9	30.0	
At least 1 target joint					
Yes	1788	22.4	18	60.0	<0.001
No	6208	77.6	12	40.0	
Invasive procedure					
Yes	424	5.3	8	26.7	<0.001
No	7572	94.7	22	73.3	
HIV status					
Positive	1140	14.3	12	40.0	<0.001
Negative	6856	85.7	18	60.0	
HCV status					
Positive	3267	40.9	21	70.0	0.001
Negative	4729	59.1	9	30.0	
Inhibitor					
Yes	462	5.8	6	20.0	0.001

Characteristic	Controls (n = 7996)		Cases (n = 30)		p value
	n	%	n	%	
No	7534	94.2	24	80.0	

Columns may not sum to n or to 100% because of missing data

* Patients may have more than one insurance type.

Table 3

Independent risk factors for a joint infection among males with haemophilia based on multivariate analysis.

Risk factor	OR	95% CI	p-value
Age (30–39 vs <30 years)	6.1	2.1 – 17.9	0.001
Age (40+ vs <30 years)	9.4	3.7 – 23.8	<0.001
Black race (vs white)	5.0	2.1 – 11.9	<0.001
Hispanic (vs white)	3.9	1.3 – 11.4	0.01
Other race (vs white)	4.5	1.2 – 16.3	0.02
Invasive procedure	2.7	1.1 – 6.4	0.03
At least 1 target joint	3.2	1.5 – 6.8	0.004
Inhibitor	3.9	1.5 – 9.9	0.004

Appendix 1

Characteristics of Patients with Joint Infection

	Age	Hem[1] type	Severity	Infected joint(s)	Microbe	Surgery within 3 months	Recent aspiration of the infected joint	Recent trauma of the infected joint	Prior surgery of infected joint	Type of surgery	Infected joint prosthetic?	Interval between arthroplasty & infection (months)	Joint hemorrhage within 2 weeks	Recurrent infection
1	56	A	Moderate	Right hip	*Staphylococcus*	No	No	No	Yes	Joint replacement	Yes	84	No	Yes
2	46	A	Severe	Right knee	Gram positive bacilli	No	Yes	Yes	Yes	Joint replacement	Yes	60	No	No
3	39	A	Severe	Right knee	*Streptococcus viridans*	No	No	No	No	n/a	No	-	Yes	No
4	42	A	Severe	Right knee	*Enterococcus faecalis*	No	No	No	Yes	Joint replacement	Yes	2	No	Yes
5	45	A	Severe	Left knee Left elbow,	*Escherichia coli*	No	No	No No	No Yes	n/a Joint replacement	No	L elbow: 1;	Yes	No
6	30	A	Severe	Left hip	*Staphylococcus aureus*	Yes	Yes		(both)	(both)	Yes (both)	L hip: 24	No	No
7	44	A	Severe	Right knee	n/a *Staphylococcus, Enterobacter cloacae,*	No	No	No No	Yes	Joint replacement	Yes	60	No	Yes
8	55	A	Moderate	Left knee	*Pseudomonas aeruginosa* *Staphylococcus*	Yes	No	No	Yes	Joint replacement	Yes	1	Yes	No
9	71	A	Severe	Right knee	*epidermidis*	No	No		Yes	Joint replacement	Yes	84	No	Yes
10	52	A	Severe	Right ankle	*Staphylococcus aureus*	No	No	No	Yes	Debridement	No	-	No	Yes
11	22	A	Severe	Right elbow	*Staphylococcus aureus*	Yes	No	No	No	n/a	No	-	No	No
12	10	A	Severe	Right ankle	*Staphylococcus aureus*	No	No	Yes	Yes	Synovectomy	No	-	Yes	No
13	36	A	Severe	Right ankle	*MRSA*	No	No	No	No	n/a	No	-	Yes	n/a
14	56	B	Moderate	Left knee Right knee,	*Staphylococcus aureus*	No	No	No No	Yes Yes	Joint replacement Joint replacement	Yes	216 R knee: 48;	No	No
15	42	A	Moderate	Left knee	*MRSA* *Staphlococcus epidermidis*	No	No	No	(both)	(both)	Yes (both)	L knee: 60	No	No
16	36	A	Severe	Right knee	*Streptococcus viridans* Filamentous fungus,	No	No	No	Yes	Joint replacement	Yes	60	No	No
17	6	A	Severe	Left knee	*Staphylococcus*	No	No		No	n/a	No	-	Yes	No
18	40	A	Severe	Right knee	n/a	No	No	No	No	n/a	No	-	Yes	No
19	45	B	Severe	Right knee	*Streptococcus salivarius*	Yes	No	No	Yes	Joint replacement	Yes	72	No	No
20	38	A	Severe	Right knee	*Escherichia coli*	Yes	No	No	Yes	Joint replacement	Yes	192	No	Yes
21	34	A	Severe	Left ankle	*Streptococcus viridans* Non-group A or B Beta	No	No	No No	No	n/a	No	-	Yes	No
22	52	A	Severe	Left knee Left ankle,	hemolytic *Streptococcus*	No	No	No	Yes	Joint replacement	Yes	24	No	No
23	31	A	Severe	Right elbow	*Streptococcus pneumonae* *Serratia marcescens,*	No	No	No	No	n/a	No	-	Yes	No
24	41	B	Severe	Left ankle	*Staphylococcus aureus*	No	No		Yes	Fusion	No	-	Yes	No
25	56	A	Mild	Right wrist	*Staphylococcus*	No		No	Yes	Fusion	No	-	No	No

	Age	Hem[1] type	Severity	Infected joint(s)	Microbe	Surgery within 3 months	Recent aspiration of the infected joint	Recent trauma of the infected joint	Prior surgery of infected joint	Type of surgery	Infected joint prosthetic?	Interval between arthroplasty & infection (months)	Joint hemorrhage within 2 weeks	Recurrent infection
26	11	A	Severe	Left knee	n/a	No	No	No	No	n/a	No	-	No	No
27	16	A	Severe	Right knee	n/a	No	No	No	Yes	Synovectomy	No	-	No	No
28	8	A	Severe	Right knee	*Staphylococcus aureus*	No	No	No	No	n/a	No	-	Yes	No
29	7	A	Moderate	Right hip	*Pseudomonas aeruginosa*	No	No	No	No	n/a	No	-	Yes	No
30	50	A	Severe	Right knee	n/a	No	No	No	No	n/a	No	-	No	No

Legends: Hem[1]: Haemophilia