**Introduction**
Aseptic prosthesis loosening resulting from bone loss is a major problem associated with orthopedic implants. Although bone loss may arise as a result of biomechanical stress around the implant, a distinct type of osteolysis exists which appears to arise from a biological rather than mechanical process. This biological process affects some, but not all patients and to date, a clinical indicator of which patients are prone to osteolysis is unknown. More than likely, this is because the exact mechanism of bone loss is still unclear. However, many in vitro and in vivo studies carried out have implicated increased expression of cytokines that are capable of inducing bone resorption as a possible causative factor [1, 2]. Interleukin 1 beta (IL-1ß) and interleukin 6 (IL-6), both of which are known to cause bone resorption, are two cytokines thought to play a major role in the mechanism of loosening. Elevated levels of these cytokines have been demonstrated at the site of bone loss [1, 2]. We have recently identified a polymorphism in the human IL-6 gene which may affect expression levels of this cytokine [3]. Polymorphisms which affect expression levels of IL-1ß and TNFα have also been identified. [4, 5].

Recently, these polymorphisms have been linked to the clinical outcome of several disease states, namely cerebral malaria and periodontitis [6, 7]. We put forward the hypothesis that patients who possess the high secretory phenotype for bone resorbing cytokines may be more susceptible to developing osteolytic prosthesis loosening, and as a consequence cytokine polymorphism typing may be used as a predictive marker for the development and severity of aseptic prosthetic joint loosening. As part of a study investigating the link between cytokine gene polymorphisms and the development of prosthetic joint loosening, we examined the association between IL-6 and IL-1 ß polymorphisms in patients undergoing revision arthroplasty for osteolysis. We present the preliminary data from this project in this report.

**Methods and Materials**
Peripheral blood was taken from 20 patients attending the pre-operative clinic for revision arthroplasty. In all cases, the indication for revision was prosthesis loosening resulting from periprosthetic bone loss. DNA was extracted from the lymphocytes using a salting out method [8] and amplification of the relevant cytokine DNA was carried out with PCR primers designed in house. For the IL-1ß +3953 polymorphism analysis [4], a 10µl aliquot of the PCR product was incubated with 5 Units of Taq I overnight and the digest products run out on a 1.5% agarose gel. IL-6 polymorphism analysis [3] was carried out with PCR primers designed in house. For the IL-1ß +3593 polymorphism typing may be used as a predictive marker for the development and severity of aseptic prosthetic joint loosening. As part of a study investigating the link between cytokine gene polymorphisms and the development of prosthetic joint loosening, we examined the association between IL-6 and IL-1 ß polymorphisms in patients undergoing revision arthroplasty for osteolysis. We present the preliminary data from this project in this report.

**Results**
20 revision patients, 51 primary arthroplasty patients and 102 healthy controls were typed for IL-1ß +3953 and IL-6 -174 polymorphisms respectively. No statistically significant difference in allele frequency between the patient and control population groups was observed for these cytokines, either independently or in combination (Table 1).

**Discussion**
This study presents the preliminary data on the distribution of polymorphisms in several cytokines implicated in the development of prosthetic joint loosening. Our hypothesis is that these polymorphisms play a role in the process. However, we were unable to demonstrate any difference in the distribution of IL-1ß and IL-6 polymorphisms, two potent bone resorbing cytokines, between patients undergoing revision arthroplasty and both primary arthroplasty patients and normal healthy controls. This preliminary data suggests that the elevated levels of IL-1ß and IL-6 at the site of bone loss, which has been demonstrated by several studies, does not appear to be a result of genetic predisposition to increased expression of these cytokines owing to the presence of these polymorphisms. This observation may be accounted for by the small number of revision patients presently in our study and as a result we are expanding the study by recruiting more patients. However, despite the fact that these particular gene polymorphisms were not associated with osteolysis, it is still possible that other polymorphisms in the gene construct result in altered responses to stimuli such as particular wear debris present in humans. Further work with other cytokine gene polymorphisms that may be relevant to the pathogenesis of prosthetic joint loosening is ongoing and will determine if this is true.

**Table 1: Allele frequency of cytokine polymorphisms in samples.**

<table>
<thead>
<tr>
<th>Secretory Phenotype</th>
<th>IL-6 Taq I genotype</th>
<th>IL-6 -174 genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type</td>
<td>Revisions</td>
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<td>Low</td>
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<td>Intermediate</td>
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**References**

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