

## Should Gram Stains Have a Role in Diagnosing Hip Arthroplasty Infections?

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### Abstract

**Background** The utility of Gram stains in diagnosing periprosthetic infections following total hip arthroplasty has recently been questioned. Several studies report low sensitivity of the test, and its poor ability to either confirm or rule out infection in patients undergoing revision total hip arthroplasty. Despite this, many institutions including that of the senior author continue to perform Gram stains during revision total hip arthroplasty.

**Questions/purposes** We assessed the sensitivity, specificity, accuracy, and positive and negative predictive values of Gram stains from surgical-site samplings taken from procedures on patients with both infected and aseptic revision total hip arthroplasties.

**Methods** A review was performed on patients who underwent revision total hip arthroplasty between 2000 and 2007. Eighty-two Gram stains were performed on patients who had infected total hip arthroplasties and underwent revision procedures. Additionally, of the 410 revision total hip arthroplasties performed on patients who were confirmed infection-free, 120 Gram stains were performed. Patients were diagnosed as infected using multiple criteria

at the time of surgery. Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated from these Gram stain results.

**Results** The Gram stain demonstrated a sensitivity and specificity of 9.8% and 100%, respectively. In this series, the Gram stain had a negative predictive value of 62%, a positive predictive value of 100%, and an accuracy of 63%.

**Conclusions** Gram stains obtained from surgical-site samples had poor sensitivity and poor negative predictive value. Based on these findings, as well as those of other authors, we believe that Gram stains should no longer be considered for diagnosing infections in revision total hip arthroplasty.

**Level of Evidence** Level III, diagnostic study. See Guidelines for Authors for a complete description of levels of evidence.

### Introduction

Infections in THA continue to present challenges for the orthopaedic surgeon. There is sometimes uncertainty concerning the best method for the diagnosis of infections and the most optimal treatment modalities. Since there is no one gold standard for the diagnosis of periprosthetic hip infections, preoperative assessments may include the patient's clinical presentation (pain, erythema, the presence of a draining sinus tract, swelling), laboratory tests (erythrocyte sedimentation rate, Westergren C-reactive protein, leukocyte count), and analysis of hip aspirates (leukocyte cell count, cell differential, and Gram stain and cultures) [2, 5, 6, 7, 15, 22, 23]. While no one serologic test is considered confirmatory, some authors have determined criteria that involve combinations of these markers that are more suggestive of infection than a single positive test

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Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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[19]. Intraoperatively, gross signs of infection and histologic frozen sections with signs of acute inflammation are often used to confirm the diagnosis of periprosthetic joint infection. Traditionally, Gram stains have been used either preoperatively, in samples taken from aspirated synovial fluid, or intraoperatively, from tissue swab samples [5, 6].

Although the Gram stain has been commonly used to help diagnose periprosthetic infections associated with total hip arthroplasty, various authors have observed the sensitivity of the test is extremely low, with only a single report of a sensitivity greater than 20% [1, 2, 8, 13, 17, 21]. Recent reports of the effectiveness of Gram staining in diagnosing periprosthetic infection continue to report low sensitivities, and suggest this test does little to aid the surgeon in making a definitive infection diagnosis [2, 8, 9, 23]. Despite this, it has been hard to convince our own institution of their low utility. This may be because of their low cost, fast turnaround time, and ease with which the test can be performed. In addition, Gram stains have advantages over more conventional laboratory evaluation methods and are often used as the primary diagnostic tool for many other types of infections. For these reasons, it appears difficult to change the thought processes of our own and other institutions in terms of utilizing Gram stains for periprosthetic infection diagnosis.

To confirm past reports, we determined the sensitivity, specificity, accuracy, and positive and negative predictive values of Gram stains using two groups of patients undergoing revision total hip arthroplasties: (1) hips with definite periprosthetic infections; and (2) hips being revised for aseptic reasons.

## Patients and Methods

We reviewed a database of all patients treated at a single center between 2000 and 2007 to identify those patients treated for infected total hip arthroplasties. Gram stain samples were obtained from two groups of patients: patients who were definitively infected at the time of surgery and those who were revised for aseptic reasons. The infected group consisted of 97 patients (98 infected hips) surgically treated for a periprosthetic hip infection. Many of the patients underwent multiple irrigation and débridement procedures alone, or as part of a two-stage revision. The Gram stain from the first procedure on an infected joint was the only Gram stain considered for this analysis. Additionally, during the reimplantation procedure for two-stage revision hip arthroplasty, if the patient was considered free from infection, as outlined below, then the Gram stain from this procedure was considered a Gram stain obtained from an aseptic total hip arthroplasty revision procedure. Six patients presented after six months of

reimplantation total hip arthroplasty with recurrent signs of infection. These were considered new infections, and the Gram stains from their initial procedure following reinfection were included in the group of infected patients. The group without infection consisted of 407 patients (410 hip revisions). Gram staining was not required for each revision total hip arthroplasty procedure for aseptic reasons, and consequently we did not perform a Gram stain on every aseptic total hip revision arthroplasty procedure. Using these criteria, there were 82 Gram stains performed on patients with confirmed periprosthetic infections after total hip arthroplasty and 120 Gram stains performed on patients who were confirmed infection-free. Approval for this study was obtained from our Institutional Review Board.

The diagnosis of periprosthetic hip arthroplasty infections was determined using the Leone and Hanssen criteria [19], which was originally described for determining infection in patients with total knee arthroplasty. Consequently, one of the following criteria was required for the diagnosis of periprosthetic infection: (1) two or more positive cultures with the same organism; (2) histological evidence of acute inflammatory response seen on intraoperative frozen section; (3) gross purulence; or (4) a draining sinus tract that communicates with the joint space. Additionally, at the senior author's institution, if greater than 10 polymorphonucleocytes were seen on any intraoperative histological section, the patient was considered to have a periprosthetic infection [3, 10, 20].

All tissue swabs were taken intraoperatively. After initial surgical exposure, multiple swabs (between 1 and 4) of the most infected appearing tissue were taken for culture and Gram stains. The tissue swab was then handed to the surgical scrub technician, who then passed the sample to the circulating nurse. After transportation to the laboratory using aseptic technique, Gram stains were performed using the standard laboratory technique at our institution. All specimens were evaluated by a trained technician. A Gram stain was considered positive when either gram-positive or gram-negative organisms were visualized. The presence of polymorphonuclear leukocytes was not considered a positive Gram stain.

The regular followup intervals were at 3, 6, 12, and 24 months, as well as annually thereafter. The patients without infection were followed for a minimum of 24 months so that changes in their clinical status could be investigated. If any patients presented with new symptoms suggestive of infection, they would be evaluated for multiple clinical signs and symptoms (swelling, redness, increased pain), laboratory findings (Westergren sedimentation rate, C-reactive protein), and aspirate fluid analysis (leukocyte count, cultures, neutrophils count) to ascertain if they had an infection. Of the 410 hips that underwent

aseptic revision, 2 patients presented with acute infections within 30 days of their revision surgery. There had been no signs suggestive of infection at the time of the initial revision surgery (negative frozen sections, permanent sections, and cultures). Both of these patients were treated with two-stage revisions, and were free of infection at their most recent followup of 24 months.

Gram stains were compared against a diagnosis of infection, using the above criteria, to determine sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. SigmaStat (SyStat, San Jose, CA) was used for statistical analyses. The Wilson score method was used to calculate 95% confidence intervals for the sensitivity and specificity.

## Results

Eight infected patients had a positive Gram stain and 74 infected patients had negative Gram stains. There were 120 infection-free patients with negative Gram stains. Of these, 67 were from patients at the time of reimplantation of components following a two-stage revision total hip arthroplasty, once the patients were confirmed infection-free. The remaining 53 patients with negative Gram stains were obtained during revision total hip arthroplasty on patients for aseptic causes.

The sensitivity and specificity for Gram stains in diagnosing periprosthetic hip infection were 9.8% (95% confidence interval, 5%–18%) and 100% (95% confidence interval, 97%–100%), respectively. The positive predictive value was 100%, and the negative predictive value was 62%. Additionally, the accuracy of Gram stain tests in this population was calculated to be 63.4%.

## Discussion

Infection in total hip prostheses can be a devastating outcome for the patient, a challenge for the surgeon, and a burden on the healthcare provider. Much work has been done in an attempt to make preoperative diagnosis of periprosthetic infections easier, and the treatment more straightforward [4, 6, 9, 12, 14, 15]. Authors have used clinical evaluations, laboratory tests (C-reactive protein, Westergren sedimentation rate), and aspiration values (complete blood count with differential) to help make the diagnosis. For example, in 2008 Ghanem et al. reported on the determination of cutoff values ( $> 1100$  leukocyte count, and  $> 64\%$  neutrophils in the differential of the aspirated hip fluid in patients who are suspected of having an infected total hip arthroplasty) in an effort to provide the surgeon an opportunity to make the preoperative diagnosis

of infection [14]. At the senior author's institution, Gram stains are frequently performed when intraoperative tissue samples are sent for culture to the laboratory. It has been our experience, and the experience of prior authors, that these Gram stains rarely offer any confirmatory evidence to aid in the diagnosis of periprosthetic infection, and this study is to further iterate that these tests should not be performed for the diagnosis of periprosthetic hip infections.

There were several limitations of this study. First, a limited number of Gram stains were available for review, as there was no specific protocol in place to ensure that every patient undergoing revision total hip arthroplasty (for septic or aseptic reasons) had a Gram stain performed intraoperatively. Second, because of the nature of Gram staining and how the cultures are taken, there are several opportunities for contamination that exist between procurement of the sample from the surgeon to the operating room scrub technician or scrub nurse, to the transfer to the nonsterile circulating nurse, and finally during handling in the laboratory prior to analysis of the sample. However, we identified no false positives. Although it is certainly possible that an infected hip from the presumed aseptic group eluded our detection, we believe that our followup, as described above, minimized this possibility. Third, it is also possible that the two infections diagnosed in the followup period may not have been present during the initial revision procedure; however this could not be definitely ascertained, although all the evidence indicates there was no infection at the initial revision (negative pathology and cultures). Another limitation is that Gram stains were not conducted on all procedures, such as in patients where there was no concern for infection. Fourth, the criteria used in this study to confirm infection or no infection was originally described by Leone and Hanssen for infections in periprosthetic total knee arthroplasty [19]. Although the validity of these criteria has not been evaluated in its application to diagnosing periprosthetic infections following total hip arthroplasty, the authors believe these criteria are generic enough to be easily applied to any periprosthetic infection. Additionally, we added the criteria that if any frozen histologic section had 10 or greater neutrophils per high power field, the patient was considered to have an infection. Although there has been debate in the literature as to the number of neutrophils per high power field that correlates with infection, there are several reports that support the use of 10 neutrophils as an appropriate cutoff value when considering infection [3, 10, 20].

Our findings from a total of 202 Gram stains (82 Gram stains taken from patients with known periprosthetic infection, 53 from patients undergoing aseptic revision, and 67 from patients receiving reimplantation of components after successful two-stage revision), showed, despite having a strong positive predictive value (100%) and

**Table 1.** Previously published sensitivities and specificities for Gram stain as a diagnostic tool for infected total hip arthroplasty

Study	Year	Number of infected total hip arthroplasties	Sensitivity (%)	Specificity (%)
Kraemer et al. [17]	1993	20	23	100
Athanasou et al. [1]	1995	16	25	100
Chimento et al. [8]	1996	11	0	0
Atkins et al. [2]	1998	41	12	98
Spangehl et al. [24]	1999	35	19	98
Della Valle et al. [11]	1999	68	15	99
Pandey et al. [21]	1999	79	21	100
Ko et al. [16]	2005	34	0	0
Ghanem et al. [13]	2009	150	31	100
Mont [current study]	2010	82	10	100

specificity (100%), the sensitivity and negative predictive value were poor predictors, at 10% and 62%, respectively. Our results fall within the range of previously reported values for Gram staining in infected total hip arthroplasty (Table 1). While some authors have reported a complete inability of Gram stains to diagnose infection [8, 16], other authors report sensitivity of Gram stain from tissue swabs between 19% and 36% [3, 4, 9, 14, 23]. These studies also all report specificities and positive predictive values at or near 100%. In a review of diagnostic procedures by Della Valle [9], the authors concluded Gram stains should only be conducted when gross purulence is present to aid in the empirical selection of antibiotic therapy. In a study by Lachiewicz et al. [18], the sensitivity and specificity of preoperative aspirates were 92% and 97%, respectively. In preoperative aspirates, Gram stains have largely been abandoned in favor of cell counts and leukocyte differentials, which have proven to have better overall sensitivities and specificities [13]. At our institution between 2000 and 2007, when hip aspiration was performed, we used microbiologic culture, leukocyte cell count, and differential for diagnostic criteria. More recently, Ghanem et al. [13] published a study of 150 infected THAs. They prospectively analyzed intraoperative Gram stain samples for both organisms and PMNs. When the presence or absence of organisms or PMNs were both used, the sensitivity increased to 43% and negative predictive value to 82%. While these numbers show moderate improvement compared to observation for organisms alone, they concluded the false-negative rate was still too high to safely exclude prosthetic infection. Similarly, because of our results, we have abandoned the use of Gram stains to diagnose periprosthetic hip arthroplasty infections at our institution, as we believe they provide little information.

In summary, although Gram stains have the potential to provide a quick and inexpensive means of diagnosing periprosthetic infections, we believe they are of little value in diagnosing infection in revision THA. While a positive Gram stain correlates well with the diagnosis of infected revision THA, the sensitivity and negative predictive value are consistent with prior reports, which have proven too low to provide any useful information regarding the ability to rule out periprosthetic hip infections. With Gram stains from intraoperative swabs resulting in a sensitivity of 10% and negative predictive value of 57%, we have abandoned Gram staining at our institution for the diagnosis of periprosthetic infections.

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