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High Incidence of Metal Sensitivity

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It may not seem evident from the subtitle, but Yang et al. have reported a surprisingly high incidence of "varying degrees of lymphocytic infiltration in 17 (63%) of the 27 cases" of TKA patients with pain showing positive test results by LTT. When using >1 as the threshold lymphocyte infiltration score, this number increases to 22 of 27 (81%). However, this incidence of positive LTT falls to 6 of 27 (22%) for moderate to high combined ALVAL scores of >4. These high incidence levels of metal hypersensitivity among aseptic, persistently painful TKA patients indicate a relatively strong link between ALVAL (or local lymphocyte accumulations) and LLT results. Pathology related to implant-associated adaptive immune responses (i.e. hypersensitivity) can be clinically identified as activated lymphocyte accumulations (1,2), and histologically categorized as ALVAL.

However, there are several practical limitations that diminish the chances of identifying local lymphocyte accumulations (3,4):

- Not all peri-implant tissue is excised for examination.
- Only a portion of removed tissue is sent for pathological examination.
- Only a portion of tissue that is sent for examination is used to section for microscopic analysis, and
- Only a portion of all histological sections (5-10 μm in thickness) are examined for ALVAL.

Thus, the ability to determine ALVAL within any suspected peri-implant tissue is severely diminished by the statistical sampling error associated with practical limitations of histological analysis.

This was true in the current study, where tissue for analysis was chosen based on anatomical location ("anterior-lateral flange of the femoral component") and not where inflammation may have been more readily present. Exactly what the chances are of identifying ALVAL in peri-implant tissue known to be undergoing a hypersensitivity response has not been established. It is likely that there is less than a 10% chance of finding ALVAL in peri-implant tissues containing lymphocyte accumulations. ALVAL has not

been readily identified in TKA retrieval analysis studies compared to MOM THA since there is orders of magnitude less metal implant debris present (5-7).

The findings of Yang et al. that identify this type of histological pathology in vivo in a surprisingly high percentage of patients are thus strongly supportive of a relationship between lymphocyte accumulation/infiltration and diagnosis by LTT. Additionally, this relationship will likely strengthen over time when the data of Yang et al. are expanded upon in future studies, when researchers use improved histological examination (e.g., complete retrieved tissue analysis for ALVAL), and when more hypersensitivity-specific ALVAL measures (e.g., histologically quantifiable lymphocyte infiltration/activation) are analyzed.

Despite mounting evidence in case, cohort, basic science, and animal studies of the potential for metal hypersensitivity to induce implant pathology, the overall incidence remains low, with current estimates of 2% to 6%. That is based on the data of Yang et al. (10% to15% of the general orthopaedic population as metal sensitive pre-operatively and 20% to 60% of aseptic persistently painful well fixed TKA as indicated by Yang et al., together yielding a total of approximately 2% to 6% of orthopaedic patients). Thus, LTT seems inappropriate as a routine preoperative assessment for primary TKA, but it is supported by this study in cases of suspected elevated immune response-induced implant pathology.

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Conflict of Interest:
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