Question B4:

“What is(are) the best preclinical model(s) of orthopedic infection for the evaluation of diagnostic technologies?”

3rd Meeting of the International Consensus Meeting
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Edward M Schwarz

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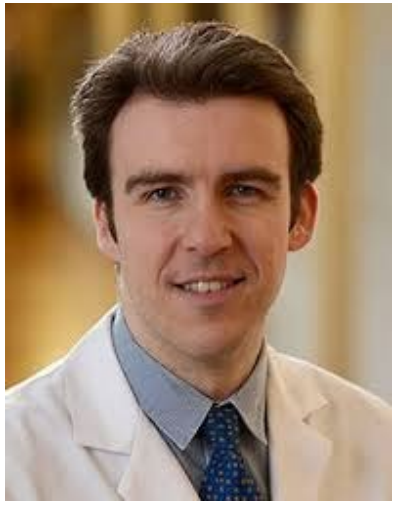

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- A Systematic literature review of PubMed and Ovid Embase databases identified 628 papers relevant to the question. A total of 38 papers were selected for extraction and review through Covidence.

- Murine, rodent models most common, ”first pass”

- Rabbits best fit for larger models. Reliable

- Porcine over murine as mirror human immunity better.

Diagnosis of infection in models

- Concordance in innoculms, antibiotics, sampling, advanced sampling PCR/RAPD etc.
- DNA sequencing, nucleic acid assays, cytokines, TNF etc….
- Imaging, FDG PET vs. MRI. SPECT/CT and radiotracers.
- Bioluminescence imaging, no euthanasia, correlates well with imaging modalities. Targeted fluorescent imaging and Photoacoustic imaging using ultrasound,

Recommendation

- As with all research on living organisms, the “best” model is primarily determined by the hypothesis to be tested, and general animal welfare rules apply (e.g. molecular/mechanistic and initial diagnostic index studies should be tested in small species, while clinically relevant hypotheses on human specific diagnostics might be appropriate for testing in larger or humanized species).
- With regard to animal models, the following should be declared in all studies, the translational potential ,ethical approval, model design, statistical analyses with prospective threshold of success and failure.
- Currently the industry standard for evaluating diagnostic potential is a receiver operating characteristic (ROC) curve analysis of the new technology vs. clinical cultures, clinical signs and symptoms or other FDA approved diagnostic of orthopedic infection.
- Potential researchers are directed to: *PREPARE (Planning Research and Experimental Procedures on Animals:Recommendations for Excellence) , https://norecopa.no/PREPARE*.
- Guidelines such as this should be mandated by publishing media.
- Studies should use standardised species-specific innocula of bacteria. Endpoints should be valid and diagnosis should involve quantative microbiological, radiological, serological, histological, as well as clinical observations.
- Newer diagnostic technologies can be correlated with the above modalities and should specifically aim to replicate accuracy and reduce invasiveness. Although validated in silico and in vitro models to assess diagnostics of orthopaedic infection do not currently exist, these technologies are rapidly emerging and may need to be considered in the near future

Level of Evidence: Expert Opinion

❖**Vote:**

Agree n=38; 93%

Disagree 0

Abstain n=3; 7%