QUESTION 1: What is the recommended time interval that would divide acute and chronic periprosthetic joint infection (PJI) (4 weeks, 90 days, etc.)?

RECOMMENDATION #1: There is no evidence-based time interval that divides acute from chronic PJI. The natural history of infection is a continuum from initiation to chronicity. Surgical treatment for patients with infection should not solely be based on the duration of symptoms or the time from implantation of the prosthesis. Other factors should also be considered such as implant stability, presence of sinus tract, virulence of the infective organism and the general health of the patient. It is important to note that the efficacy of surgical intervention, involving retention of the prosthesis, is more likely to fail as one moves past four weeks from the index arthroplasty and/or duration of symptoms of infection.

LEVEL OF EVIDENCE: Limited
DELEGATE VOTE: Agree: 84%, Disagree: 15%, Abstain: 1% (Super Majority, Strong Consensus)

RECOMMENDATION #2: We recommend moving away from the traditional division between acute and chronic infection based solely on time from index arthroplasty or duration of symptoms. Periprosthetic infection is a continuum that leads to establishment of biofilm.

LEVEL OF EVIDENCE: Limited
DELEGATE VOTE: Agree: 60%, Disagree: 34%, Abstain: 6% (Super Majority, Weak Consensus)

RECOMMENDATION #3: Should we have a specific time limit cutoff between chronic and acute infection?
DELEGATE VOTE: Agree: 60%, Disagree: 37%, Abstain: 3% (Super Majority, Strong Consensus)

RATIONALE

According to the Oxford Advanced Learner’s Dictionary, the term “acute” in the case of illness is defined as “coming quickly to the most severe or critical stage” and the term “chronic” as “lasting for a long time, happening continually.” In the case of an acute PJI, this would be translated as a sudden onset of severe joint pain and/or swelling in a priorly symptom-free prosthetic joint, and in case of chronicity, as the presence of mild or moderate pain in which its exact onset is hard to establish. In our opinion, this is the most accurate definition to differentiate acute from chronic PJs, and reflects the virulence of the microorganism(s) causing the infection. The reason that a certain time frame was subsequently introduced in the world of PJI to divide acute from chronic infections was primarily based on clinical grounds to identify those patients with a high and low success rate when treated with debridement, antibiotics and retention of the implant (DAIR) [1–15].

One of the factors associated with DAIR failure is the presence of a mature biofilm in which embedded bacteria are unresponsive to antibiotic treatment due to multiple phenotypic and genotypic changes [16,17]. In such a condition, a PJI cannot be cured with antibiotics alone without removal of the implant. In which time frame a biofilm reaches maturity is not clear. In vitro studies indicate that biofilm start to form within just hours after inoculation of bacteria [18], but these experiments are performed under “optimal” circumstances for bacterial growth and do not include the complexity of the host’s environment and the protective effect of its immune system [19]. Carli et al. observed in a mouse model with a proximal tibial implant infection, using a high initial bacterial inoculum (3x10^5 CFU) that a biofilm is evident after two weeks of infection, but extends and is covered by fibrous tissue and multiple host cells after six weeks [20]. A recent mouse model of knee PJI using a low infecting inoculum of S. aureus (10^3 CFU) (which is similar to the expected inoculum during surgery [21]) demonstrated that after a two-weeks incubation period, antibiotic combinations including rifampin were able to eradicate the infection [22]. These studies suggest that a mature biofilm develops within two to six weeks. However, the process of biofilm formation varies greatly among bacterial species, its inoculum and the host [23,24]. Accordingly, it has been demonstrated that the efficacy of DAIR in acute infections is highest when the DAIR is performed as soon as possible after the onset of symptoms [25–36]. Moreover, it is important to note that, since the success of DAIR is determined by many factors, the decision to perform a DAIR procedure should not solely be based on symptom duration and/or time from index surgery in acute PJs, but should include host related factors, causative microorganism and the stability of the implant. For this reason, we propose not to include a time interval in the definition of acute and chronic PJI since the natural history of an infection is a continuum from initiation to chronicity.

REFERENCES