QUESTION 18: Is there a distinct microbiome in the joints?

RECOMMENDATION: It remains unclear whether the native joint or a joint after arthroplasty can be considered a microbiological niche in which specific organisms reside without causing any manifestation of infection. However, given the innocuous character of microorganisms (such as coagulase-negative Staphylococcus, Cutibacterium species) recovered from clinical specimens in the context of aseptic loosening it appears plausible to hypothesize that chronic colonization of devices can occur and be of long-lasting nature before signs and symptoms of clinical infection occur, if they occur at all. Further studies are needed to determine the clinical relevance of microorganisms or microbial dysbiosis detected within joints, without apparent clinical features of infection, ensuring clinical correlation, long-term follow-up and multicenter validation.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 80%, Disagree: 7%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

The term microbiome (or microbiota) is defined as the entity of microorganisms that colonize the human body. It is well-known that defined ecological niches (e.g., the gut, the skin, the oral cavity) can carry groups of microorganisms that differ dramatically in their specific composition [1,2]. There is growing evidence that the specific microbiome composition might be associated with defined clinical pictures or even support the development of illness, but without causing invasive disease [3].

However, in most cases the microbiome/microbiota would be considered to be beneficial for the host [4,5]. This commensal microbiome is expected to be found in niches of the human body traditionally regarded as non-sterile. In contrast, detection of commensal bacteria in sterile body sites (e.g., joints) would be regarded best as an artifact resulting from sample contamination or as evidence for a pathology evolving under certain predisposing conditions (e.g., immune suppression, foreign material implantation). Thus, in the current understanding, detection of single or multiple species originating from human microbiota in sterile body compartments would be primarily regarded as mono- or poly-microbial infection rather than as evidence for colonization. The physiologic or non-pathogenic presence of bacteria within the joint would therefore represent a groundbreaking change of current dogmas in microbiology.

In the face of these considerations, the general question under review comprises several distinct sub-questions: (1) Is there chronic microbial colonization in the joint, and can colonization occur without presence of foreign devices (i.e., an artificial niche)? (2) Can microorganisms establish chronic joint colonization without inducing infectious pathology or sequelae? (3) If so, are joints colonized by one or more species? (4) Can patterns of colonization be identified that predict defined clinical characteristics?

(1) Without doubt, there is chronic persistent colonization of joints in the presence of an implanted device. In fact, this is a basic characteristic of almost all infections caused by more innocuous (less virulent) organisms derived from the skin microbiota and able to form a biofilm [6]. There is limited data available as to which extent native joints also can also harbor such microorganisms. Evidence supporting this hypothesis comes from studies in which joint fluids from apparently uninfected individuals were microbiologically analyzed. Furthermore, some studies identified bacteria by culture or the strict protocols of molecular techniques from shoulder joint fluids [7–9]. Here, a relevant number of samples taken from patients without evidence for infection grew C. acnes. Unfortunately, in most of these studies it remains unclear if detection of C. acnes indeed represents colonization of the joint or rather was a consequence of contamination by skin flora due to insufficient skin washing procedures [10]. Moreover, since joint aspirates were performed for medical reasons, it is unclear if detection of bacteria would also be possible in individuals without any clinical evidence of infectious shoulder pathology.

(2) A hallmark of device-associated infection is a chronic persistent course with only low-grade inflammation. This course is most likely a direct consequence of biological traits related to microorganisms derived from resident skin microbiota – namely mechanisms that support persistence on the skin without inducing a relevant inflammatory response. In such a scenario, chronic colonization of foreign devices indeed could potentially occur through masking of the pathogen from effectors of the host immune system [11,12]. Some studies investigating explanted prosthetic devices from patients with periprosthetic joint infection (PJI ) or aseptic loosening of a joint found small numbers of cases in which bacteria were unambiguously identified from the sample but that didn’t show any sign of infection according to current standards (e.g., elevated C-reactive protein (CRP), elevated erythrocyte sedimentation rate (ESR), polymorphonuclear (PMN) cell tissue infiltration) [13–17]. However, of major importance, it is questionable if indeed such cases can be truly regarded as valid evidence for asymptomatic colonization of a device since assignment to the aseptic failure group is based on current algorithms to define PJI. While it remains open whether loosening of the implant can potentially be the only evident sign for an infection, it certainly is unclear if these patients would not have developed disease or PJI according to current case definitions if they remained untreated [18–20]. The relevant control group to test the hypothesis of chronic asymptomatic implant colonization has not yet been investigated, but would be completely asymptomatic patients with implants in situ.
Importantly, in future investigations and especially those applying molecular techniques strict protocols for sample processing, application of DNA-free consumables and process analysis (i.e., inhibitor controls) need to be applied.

(3) and (4) Building on the aspects discussed above, at present it remains unclear if the term “microbiome” is appropriate to describe microorganisms in native joints or after arthroplasty. Some evidence suggests, nevertheless, that more than one organism can potentially colonize artificial surfaces. It will be of major importance to unravel the extent of polymicrobial colonization and the potential importance of interspecies cooperation in future projects (making use of next-generation/metagenomic sequencing techniques and advanced microscopy methods [21]).

REFERENCES