QUESTION 6: B-6 (G-32) Does Mycobacterium tuberculosis form a biofilm on implants?

Authors: Sendi, Parham; Burastero, Giorgio; Komnos, Georgios

Response/Recommendation:
Few data from experimental in vitro and in vivo studies and a limited number of case reports indicate that M. tuberculosis has a slow, albeit significant, ability to form biofilm on metal surfaces. The group suggests that management of M. tuberculosis implant-related infections should be treated using the same principles as that of other implant-related infections.

Level of Evidence: Strong
Delegate Vote: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

Rationale:
A search of the English language literature on the question published during the period 1966–May 20, 2018 was conducted. The search strategy in PubMed used the terms Mycobacterium tuberculosis AND biofilm, and identified 177 articles. All articles were reviewed for the response to the question. The vast majority of articles were categorized as basic sciences articles focusing on the components for tubercular biofilm formation in vitro. There were no randomized controlled trials, no controlled clinical studies. A systematic review to answer the provided question is not meaningful. Hence, the response of the question is answered as a summary of a narrative review.

In the laboratory, M. tuberculosis shows peculiar aggregated growth, or in other words, can form organized pellicle-like structures. The hallmark of biofilms is the self-production of the extracellular polymeric substance that holds the mycobacterial community together and confers phenotypic heterogeneity to the genotypically identical cells. Several studies have highlighted extracellular components within M. tuberculosis aggregation, including mycolic acids, complex sugars, cellulose, proteins, lipids and DNA. In addition, M. tuberculosis residing within organized pellicle-like structures exhibits drug tolerance to antitubercular agents. Thus, criteria of a structure to what is interpreted as biofilms are given.

The clinical role of M. tuberculosis biofilms in humans is not fully understood. Basaraba and Ojha provide convincing arguments that extracellular M. tuberculosis, in necrotizing lesions, likely grow as biofilms and may participate in the process of casseous necrosis and cavitation formation in lung tissue. The vast majority of studies investigating M. tuberculosis biofilms uses polystyrene plates. Ha et al. compared the adherence and the biofilm formation of Staphylococcus epidermidis with those of M. tuberculosis on four types of metal segments. In contrast to S. epidermidis, M. tuberculosis rarely adhered to metal surfaces and showed discrete biofilm formation. Similar results were reported by Chen et al. who compared S. aureus and M. tuberculosis in vitro and in vivo. Adetunji V et al. analyzed M. tuberculosis biofilm formations on cement, ceramic, or stainless steel coupons. The experimental settings in this study are difficult to transfer in an in vivo implant model (e.g., more biofilms were formed when media containing 5% liver extract was used). However, more biofilms were formed on cement than on ceramic and stainless steel coupons. Taken together, the few available data from in vitro and in vivo...
studies indicate that biofilm formation of *M. tuberculosis* on metal segments is poor in comparison to *Staphylococcus* spp.

Among the 66 cases reported by Veloci et al. 12, 13 (19.6%) were treated with antitubercular agents only. Hence, in these cases no surgical intervention was performed to reduce the mycobacterial load or to remove mechanically the biofilm adhering to the implant. One patient died because of far-advanced tuberculous meningitis, miliary tuberculosis of the lungs, femoral osteomyelitis and extended cold abscesses along the femoral shaft 13. In the other cases, no failure was reported. Though, only in 6 (50%) of 12 cases, a follow-up results of ≥18 months after the end of therapy was available. Treatment duration ranged from 6 to 18 months. These data indicate that tubercular biofilm eradication is possible chemotherapy only. Whether this is due to poor biofilm formation on metal implants or due to effective anti-biofilm activity of antitubercular agents cannot be assessed.
References:


