

Culture Negative Orthopedic Biofilm Infections

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1. Auflage 2012. Buch. x, 146 S. Hardcover
ISBN 978 3 642 29553 9
Format (B x L): 15,5 x 23,5 cm
Gewicht: 403 g

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Preface

Because orthopedic infections often involve inert fixation and prosthetic devices and almost always involve sequestra of dead bone that act as foreign bodies, they are predominantly caused by bacteria living in biofilm communities. The first clinical consequences of this communal lifestyle of the causative bacteria were that these infections were not cured by host defenses or by systemic antibiotic treatment, and orthopedic surgeons have quickly developed the very effective strategy of aggressive debridement followed by very high dose antibiotic therapy. But the biofilm paradigm is complex, and the change from the acute paradigm of planktonic infections is profound, and these elaborate communities of bacteria living as highly integrated societies had one more surprise hiding up their tiny sleeves!

As Patrick DeMeo's Department of Orthopedic Surgery began to cooperate with Garth Ehrlich's Center for Genomic Sciences, several individual cases were identified and published as case reports, in which bacterial biofilms could be seen in infected tissues, but traditional cultures were negative. The routine hospital lab that provides services to Allegheny Hospital is accredited, but it does not incubate specimens anaerobically or keep cultures for more than 5 days, so the rates of positive culture are not as high as the more advanced labs at the Mayo Clinic. However, this level of microbiological service is typical of that available to most orthopedic surgeons in the USA. It was abundantly clear that DNA- and RNA-based molecular methods would be needed to replace cultures in the detection and identification of bacteria in orthopedic infections, but, initially, the "water was muddied" by the use of single species PCR methods that were nonquantitative and hypersensitive. Bill Costerton came to Allegheny Hospital just as the new universal DNA-based Ibis methods were being refined in Garth Ehrlich's lab, and he began to work with colleagues in Orthopedics to compare cultures with Ibis data and to confirm the results using RNA-based FISH probes and deep 16S sequencing.

The first Ibis study of infected total joints (with Fen Hu, Sandeep Kathju, and Nick Sotereanos) and the second study of infected nonunions (with Dan and Greg Altman) indicated that the universal Ibis technique improved the detection of bacteria from <25 % (cultures) to >80 %. Because this technology and several parallel platforms can provide results in 6 h and also give data on antibiotic

sensitivity, we judged that we should announce this dramatic improvement in diagnosis in a special meeting (May 2011) attended by 100 colleagues who would be instrumental in demanding and managing this transformation. We have incorporated several presentations from this meeting, in the form of chapters in this book, ranging from parallel studies of modern detection techniques (Thomsen, Kennedy, and Shirliff) to statements of how the modern methods will impact clinical practice (O'Toole, Sotereanos, and Parvisi). Perhaps the culmination of the book is a special chapter by Heinz Winkler, of Vienna, whose one-stage revisions of infected prostheses inspired much admiration at the May meeting and whose faithful adherence to the biofilm concept has served hundreds of patients as a gold standard in the treatment of orthopedic biofilm infections.

The difficulty of detecting and identifying biofilm bacteria by culture methods is, of course, not limited to orthopedic infections. Less than 1 % of the bacteria growing predominantly as biofilms in natural ecosystems can be recovered by culture methods. Culture methods have been so insensitive in the detection of bacteria in major biofilm infections, like otitis media and prostatitis, that the bacterial etiology of these infections has been questioned and the polymicrobial nature of mixed species infections (e.g., diabetic foot ulcers) has been ignored when cultures grew very few species. The demonstration that modern molecular methods can detect and identify all of the bacterial species present in affected tissues in Orthopedics may have two salutary outcomes in all medical areas. First, the etiology of many chronic disease conditions will be better understood when all of the power of modern molecular diagnostics is brought to bear on them. Thus, elusive connections between infections and clinical problems such as nonunions at fracture sites will be resolved one way or the other. Second, clinicians will know the species identity of the infecting bacteria and their antibiotic sensitivities, as they design surgical or medical interventions, without any limitations imposed by the biofilm mode-of-growth or by the reluctance of certain species to grow in culture. It should be seen as simple justice as it was the orthopedic surgeons, who first understood the basic biofilm paradigm and modified their practice accordingly, that they benefit from the best diagnostic technologies that modern microbiology can provide.

3 March 2012

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