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Infections in Hip and Knee Arthroplasty: Challenges to and Chances for the Microbiological Laboratory

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1. Introduction

Comprehensive algorithms have been devised to improve the management of periprosthetic joint infections of the hip and the knee (Gomez & Patel, 2011a, 2011b; Peel et al., 2011). There is still no single best method for diagnosis, as stressed for instance in a guideline published recently by the American Association of Orthopedic Surgeons (AAOS) (Della Valle et al., 2010). An important reason for this is lacking consensus on how to define arthroplasty infection accurately. Nevertheless, it is beyond dispute that microbiologic techniques play a key role in assessment for these infections.

The chapter consists of three sections. Firstly, a general introduction to the special nature of arthroplasty infection is given, which highlights the necessity of reliable microbiological diagnostics. Secondly, a critical appraisal of the various technical and interpretive aspects of microbiologic procedures is featured. Thirdly, our own diagnostic approaches are presented, and a prospect on probable useful developments in the future is offered.

2. Identification of infected implants: The need for microbiological testing

2.1 Epidemiology

Periprosthetic joint infections are a feared complication of hip and knee arthroplasty. Infection is supposed to be the underlying cause in about 15% of hip revision arthroplasties and 25% of knee revision arthroplasties (Bozic et al., 2009, 2010). Depending on the onset of infection after the primary implantation, periprosthetic infections have been defined as "early" (up to 3 months), "delayed" (3-24 months), and "late" (more than 24 months) after surgery (Zimmerli et al., 2004). However, a different classification makes more sense from the therapeutic point of view. According to this, infections which occur within 4 weeks after arthroplasty implantation are recognized as "early". These are most often caused by highly virulent organisms (e. g. *Staphylococcus aureus*) acquired during or shortly after implantation and can be treated with the prospect of survival of the implant. In contrast, infections which become manifest after more than 4 weeks ("late" infections) require removal of the

prosthesis. Late infections are low-grade infections due to less virulent agents belonging to the normal skin flora (e. g. coagulase-negative staphylococci, *Propionibacterium* species, coryneform bacteria), which are mostly also attained during the operation procedure or are infections which result from hematogenous spreading from remote sites (Cui et al., 2007; Hanssen & Osmon, 2002; Virolainen et al., 2002).

2.2 Pathogenetic aspects

The characteristics of arthroplasty infection reflect a unique pathogenesis which is ultimately marked by two features: biofilm development and manifestation of a periprosthetic membrane.

2.2.1 Biofilms

Biofilm-forming bacteria share the ability to colonize foreign implant materials by initial attachment to the surface, followed by agglomeration in multi-cellular layers. During the accumulation process the bacteria excrete matrix substances into which the infectious agents themselves become embedded. Due to alterations in cellular metabolism, regulated by complex signal pathways within the biofilm, the bacteria switch from the planktonic state to a sessile condition in which proliferation rates are extremely low (Costerton et al., 1999; Donlan & Costerton, 2002; Donlan, 2005; Gristina & Costerton, 1985).

Infections involving biofilm formation are both difficult to identify and to treat. On one hand, the biofilm matrix provides a substantial barrier to host defense mechanisms and to diffusion of antibiotics. On the other hand, the low proliferation levels of the sessile organisms may dramatically impair their antibiotic susceptibility, especially to bactericidal agents (Jones et al., 2001; Monzon et al., 2002; Stewart & Costerton, 2001), and their cultivation for diagnostic purposes in vitro.

As biofilm formation is a gradual process, this mechanism is the characteristic feature of late, low-grade infections. Implants with an established biofilm are definitely subject to removal although the causative agents are less virulent by themselves than the bacteria which cause early arthroplasty infections.

2.2.2 Periprosthetic membrane

The periprosthetic membrane is the histomorphologic hallmark of joint implant failure. It is a seam of connective tissue which develops at the interface between the bone and the implant in the course of the inflammatory process that leads to septic or aseptic prosthetic loosening. Interestingly, there are four morphologic types which can be linked to different etiologies of inflammation. Of these, the infectious type (type II) is particularly often associated with periprosthetic infection. It is characterized by predominant infiltration with neutrophilic polymorphonuclear leukocytes (Krenn et al., 2011; Morawietz et al., 2006).

As the periprosthetic membrane must be removed if the surgical revision procedure is to be successful, it is ideal sample material for characterizing the type of inflammation by histology, thus providing valuable evidence for the underlying cause of implant loosening.

2.3 Inflammation parameters: Utility to detect infections

Early periprosthetic infections are mostly associated with typical clinical signs of infectious disease. However, in low-grade (late) infections the clinical symptoms and radiologic signs are often unspecific and therefore not suitable for ruling out aseptic implant failure

(Virolainen et al., 2002). Nuclear imaging techniques used to detect periprosthetic inflammation are generally regarded as optional tests which may be of use if the diagnosis cannot be established otherwise, but they are not recommended for routine application (Della Valle et al., 2010). In contrast, the following procedures do play important roles in patient assessment for arthroplasty infection.

2.3.1 Blood laboratory markers

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level are the parameters most widely used for preoperative evaluation of patients with suspected arthroplasty infection. While sensitivity is mostly high, specificity is limited, especially in patients with systemic inflammatory diseases (e. g., rheumatoid arthritis) (Bottner et al., 2007; Della Valle et al., 2007; Fink et al., 2008; Greidanus et al., 2007; Kamme & Lindberg, 1981). Nevertheless, from the studies with reliable data the AAOS strongly recommends testing of both ESR and CRP in all patients assessed for arthroplasty infection (Della Valle et al., 2010).

Other inflammation markers (interleukin 6, procalcitonin, tumor necrosis factor α) are evaluated increasingly for periprosthetic infections, but at present there seems to be no advantage over CRP testing (Berbari et al., 2010; Bottner et al., 2007; Di Cesare et al., 2005).

2.3.2 Microscopic detection of inflammatory cells

Joint aspiration fluid. Total and differential white blood cell counts in synovial fluid are routinely determined in many settings. Some studies of knee patients have reported that total leukocyte counts or neutrophils percentages which exceed a certain cutoff level are highly indicative of arthroplasty infection. However, the thresholds differ considerably between studies (Della Valle et al., 2007; Ghanem et al., 2008; Trampuz et al., 2004).

In contrast, there are less data available for hip patients because aspiration of this joint is more prone to complications and is therefore only recommended if there is substantial clinical or laboratory evidence for infection (Della Valle et al., 2010; Schinsky et al., 2008).

Frozen tissue sections. Neutrophils are the predominant histomorphologic factor in periprosthetic infection (Krenn et al., 2011; Morawietz et al., 2006). As a consequence, the histologic diagnosis of probable infections is based on the tissue neutrophil concentration, as defined by i) the number of neutrophils in a high-power (400x) microscopic field, and ii) the minimum number of fields (usually 10) containing that concentration of neutrophils. The available studies report 5 or 10 neutrophils per high-power field as suitable thresholds for diagnosis of arthroplasty infection (Banit et al., 2002; Della Valle et al., 2007; Fehring & McAlister, 1994; Fink et al., 2008; Frances Borrego et al., 2007; Ko et al., 2005; Lonner et al., 1996; Nunez et al., 2007; Schinsky et al., 2008). Patients with inflammatory arthropathy, which often display tissue infiltration by neutrophils in the absence of infection, were excluded in some of these investigations (Fehring & McAlister, 1994; Ko et al., 2005; Pandey et al., 1999; Schinsky et al., 2008). However, all in all there is not enough information to enable a clear-cut preference of the lower or the higher threshold.

Despite the considerable advances in recent years with respect to the histomorphologic characterization of periprosthetic infections, it is not possible to treat affected patients sufficiently unless the causative microorganisms are identified precisely. Thus, customized local and systemic antibiotic therapy of a known infectious agent is inherently superior to calculated therapy because treatment failure arising from antibiotic resistance can be avoided (Bejon et al., 2010).

3. Microbiological diagnosis: Pros and cons of different approaches

Adequate microbiological procedures must reflect the special character of periprosthetic infections in order to identify the causative agents accurately. Although largely interdependent, eight issues which may influence the significance of microbiologic testing are addressed separately in the following: i) patient-specific factors, ii) the sample character, iii) the logistic interface between the clinic and the laboratory, iv) the method of sample processing, v) the means of identification, vi) the culture conditions, vii) the means of discriminating between infection and contamination, and viii) the stage at which sample materials are drawn (pre-operatively versus intra-operatively).

3.1 Patient-specific factors

3.1.1 Sample origin (hip versus knee)

Joint aspiration prior to revision arthroplasty is widely utilized. For knee patients the procedure is comparatively straightforward, whereas hip aspiration may impose a higher risk of iatrogenic infection. Thus, it is often argued that invasive diagnostic samples from hip patients should be obtained only if a there is a high probability of infection (Bozic et al., 2009, 2010).

Regarding periprosthetic tissue biopsies, the diagnostic sensitivity of pre-operative sampling may be lower in hip infections compared with knee infections (Fink et al., 2008; Meermans & Haddad, 2010; Williams et al., 2004), possibly because infected tissue is more difficult to assess without dislocating the joint.

3.1.2 Underlying systemic diseases

The definitive identification of microorganisms is especially important in patients with systemic inflammatory diseases because, as mentioned before, inflammation markers can be elevated in aseptic implant failure. At the same time, the differentiation between an infecting and a contaminating agent is challenging in these patients (see 3.7).

3.1.3 Previous antibiotic therapy

False-negative results of microbiological cultures and even PCR tests have been reported in patients who received antibiotic therapy within 2 weeks prior to obtaining intra-articular sample material (Achermann et al., 2010). Furthermore, it is also suggested that peri-operative antibiotic prophylaxis should be withheld if possible until samples for microbiological analysis have been obtained, but that the risk of false-negative sample results also should be weighed against the protective effect of pre-operative administration of antibiotic prophylaxis (Achermann et al., 2010; Engesaeter et al., 2003; Jämsen et al., 2009; Trampuz et al., 2007).

3.2 Sample character

3.2.1 Tissue swabs

In a report on hip and knee patients organisms cultured from swabs of sinus tracts showed no concordance with the culture results from specimens obtained intra-operatively (Sadiq et al., 2005). There are limited data which suggest that the results of superficial swabs show a reasonable correlation with culture yield from intra-operative tissue biopsy material (Cune et al., 2009). However, other studies have rated results from swab material as both insensitive and unspecific (Font-Vizcarra et al., 2010; Levine & Evans, 2001). Swabs cannot

absorb nearly as much material as can be harvested from tissue biopsies or joint fluid, which alone would account for inferior sensitivity. Furthermore, as most etiologic agents of arthroplasty infections belong to the normal skin flora, it is hardly possible to discern between infectious strains and contaminants using swab material. In summary, tissue swabs cannot be recommended to assess prosthetic infections reliably.

3.2.2 Joint aspiration fluid

The overall significance of culture from pre-operative synovial fluid to detect periprosthetic infection is valued as high. However, sensitivity may be reduced if the infection does not involve the synovia or if the concentration of planktonic bacteria in the fluid is limited due to a mature biofilm. Furthermore, false positive results from skin flora occur (Barrack & Harris, 1993; Della Valle et al., 2007; Eisler et al., 2001; Fink et al., 2008; Lachiewicz et al., 1996; Malhotra & Morgan, 2004; Williams et al., 2004).

3.2.3 Periprosthetic tissue biopsies

Analysis of tissue biopsies offers the advantage that multiple samples can be obtained from different locations within the suspicious area. Repeated isolation of bacteria (e. g., isolation of the same organism in at least 2 tissue samples) increases the probability of infection. Thus, there are several reports in which higher sensitivity of tissue culture compared with synovial fluid culture is observed (Fink et al., 2008; Meermans & Haddad, 2010; Roberts et al., 1992; Sadiq et al., 2005; Williams et al., 2004).

3.3 Logistics between clinic and laboratory

Pre-analytical sampling errors have been claimed to contribute significantly to false-negative culture results, with highly sensitive PCR techniques being a means to overcome these drawbacks (Achermann et al., 2010). Guidelines devised by the German Society of Hygiene and Microbiology have proposed that periprosthetic sample material intended for microbiological cultivation should be processed within one hour post-drawing. Although such stringent demands are not realistic for the routine setting, it is indeed crucial to establish a standardized work flow between the clinic and the laboratory regarding the procedures of sample drawing, transportation to the laboratory, and specimen processing. The organizational structure in our laboratory comprises a courier service as well as evening and weekend laboratory duty, which ensures that over 95% of culture samples are processed within 6 hours post-operatively (see 4.1.1).

3.4 Sample processing

The efforts made to obtain significant sample material are futile if the laboratory process is not optimized. However, costs and benefits should be well-balanced.

3.4.1 Native material

The simplest way of tissue sample processing is mincing by a scalpel. This allows efficient investigation of multiple samples from each patient (see 3.2.3). If carried out under a laminar air flow workbench it is not highly prone to contamination (Atkins et al., 1998; Schäfer et al., 2008; Trampuz et al., 2006, 2007).

Some authors favor scraping the surface of the explanted material. This has been reported to be more sensitive than tissue culture but also liable to contamination (Bjerkan et al., 2009; Neut et al., 2003).

3.4.2 Blood culture vials

Automated incubation and fluorometric detection of bacterial growth improves sensitivity compared with conventional liquid culture broths (Font-Vizcarra et al., 2010; Levine & Evans, 2001). However, there are potential drawbacks. Firstly, the possibility to determine leukocyte counts is lost if no native material is saved. Secondly, if the sample volume falls short of three milliliters, standard aerobic and anaerobic blood culture bottles may lack sensitivity. Pediatric vials are optimized for culture of lower sample volumes, but it is possible that some anaerobic bacteria are missed due to the composition of the medium (Morello et al., 1991).

3.4.3 Sonication of explants

Sonication of explanted prosthesis components to disrupt bacterial biofilms has been assessed by several authors (Achermann et al., 2010; Kobayashi et al., 2006; Trampuz et al., 2003, 2007; Tunney et al., 1998). Culture of the sonication fluid appears to be more sensitive than native sample processing. However, it is cumbersome and not suitable for high-throughput analysis. The possible destruction of planktonic bacteria is an issue that has not been raised systematically to date, but may be of importance in cases of prosthetic infection caused by bacteria which do not establish classical biofilms (Sampedro et al., 2010). There also may be an increased risk of contamination (Holinka et al., 2011; Trampuz et al., 2006).

3.4.4 Bead mill processing of tissue biopsies

The bacterial yield using a bead mill is probably enhanced due to facilitated tissue disruption (Roux et al., 2011). However, careful evaluation of conditions for different bacterial species is necessary in order to avoid overheating of samples and mechanical disruption of planktonic bacteria. At present it cannot be decided whether bead mill processing offers significant advantages.

3.5 Identification of infectious agents

3.5.1 Conventional microbiological detection

Direct gram staining of periprosthetic samples is insensitive and therefore not recommended as a routine test (Banit et al., 2002; Parvizi et al., 2006; Spangehl et al., 1999). However, it can be useful in certain cases of early infection, where prompt treatment of agents which show characteristic morphology (e. g. *Clostridium perfringens*) is enabled.
Classic microbiologic culture confirms the presence of viable bacteria and permits testing for antibiotic susceptibility.

3.5.2 PCR strategies

Universal bacterial detection by PCR-based amplification of the 16S rRNA gene allows the identification of bacteria or fungi which are not viable by conventional culture methods. The overall sensitivity may be higher compared with culture (Bergin et al., 2010; Dempsey et al., 2007; Ince et al., 2004; Levine et al., 1995; Panousis et al., 2005; Tunney et al., 1999). On the other hand, singular specific PCR assays (Kobayashi et al., 2009; Piper et al., 2009; Tarkin et al., 2003) or multiplex assays (Achermann et al., 2010) are sensitive but limited to the organisms included in the test panel.

Although important antibiotic resistance mechanisms like methicillin resistance can be identified genotypically with PCR (Kobayashi et al., 2009; Tarkin et al., 2003), for most substance classes phenotypic susceptibility testing will be necessary in the foreseeable future.

There is no straightforward method to determine whether microbial DNA as detected by PCR reflects living organisms. On the other hand, it cannot be ruled out that previous therapy with antibiotics hampers the sensitivity not only of culture, but also of PCR (Achermann et al., 2010).

3.6 Culture conditions

3.6.1 Culture media

A combination of solid (usually blood agar, chocolate agar, and Schaedler agar) and liquid media (e. g. brain-heart infusion broth and Schaedler broth) is used by standard for aerobic and anaerobic cultivation. Solid media alone lack sensitivity to detect low-grade infections because because the medium eventually dries out. On the other hand, infections involving more than one agent can be overlooked if only broth media are utilized because slower-growing organisms may be inhibited in the presence of fast-growing bacteria.

3.6.2 Culture duration

"Standard" cultivation periods (mostly ≤ 7 days in the literature) are generally questionable in infections where biofilms are involved, due to low cell counts of planktonic bacteria and impaired growth rates of sessile organisms in the biofilm. However, the issue was not addressed for a long time. Prolonged cultivation for 14 days was described sporadically (Ince et al., 2004) and even included as a standard recommendation into German practice guidelines, but not assessed under controlled conditions. Thus, our group systematically evaluated a 14-day culture period with periprosthetic tissue samples from hip and knee patients (Schäfer et al., 2008).

Using the algorithm described under 3.1.1 to distinguish infecting agents from contaminating strains, only 74% of the infections (caused by "early" agents) were found within the first week of cultivation (Schäfer et al., 2008). In the second week we not only identified a significant amount of additional infections, but also a completely different spectrum of causative ("late") species (Table 1).

	isolated organisms	frequency (%)	median time to detection (days)
early species	*Staphylococcus aureus*	8.9	2
	coagulase-negative staphylococci	55.4	4
	Enterococcus species	3.8	2
	Streptococcus species	3.8	1.5
	Enterobacteriaceae	1.9	5
late species	coryneform bacteria	7.6	10
	Propionibacterium species	13.4	11
	Finegoldia species	3.2	8
	others	1.9	9.5

Table 1. Spectrum of bacteria detected over a 14-day cultivation period.

Regarding the late species, the sensitivity would have been merely 27% if cultures had been monitored for only 7 days (Fig. 1).

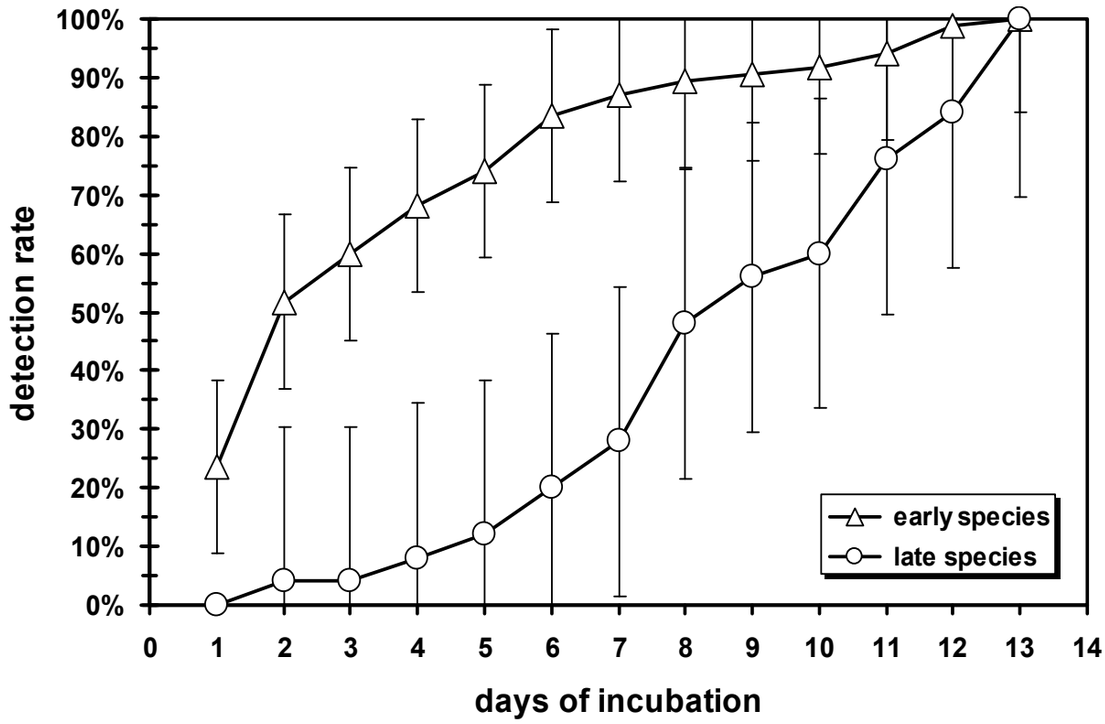

Fig. 1. Detection rates of early and late species depending on the cultivation period. Whisker bars span the Hall-Wellner 95% confidence intervals.

3.7 Discrimination between infection and contamination

There is no standardized procedure which would define infection over contamination accurately. Regarding tissue samples, usually a combined algorithm of neutrophil infiltration scores (2.3.2) and culture detection of identical organisms from multiple tissue samples is used. However, due to the missing consensus criteria the approaches vary considerably between studies (Atkins et al., 1998; Bori et al., 2007; Fink et al., 2008; Ko et al., 2005; Mirra et al., 1976; Pandey et al., 1999).

A problem we encountered was that the algorithms we have adopted to define infections (Atkins et al., 1998; Pandey et al., 1999; Virolainen et al., 2002) were evaluated in the context of "standard" microbiological cultivation periods. Thus, with prolonged culture duration (3.6.2) a larger amount of contaminants might have impaired the significance of this algorithm. However, our findings allowed us to refute the concern that prolonged culture of tissue biopsies could lead to over-proportional contamination rates (Schäfer et al., 2008). It became clear that among both the "early" and the "late" agents (Table 1) a highly significant correlation existed between positive histology and the number of culture-positive tissues (Fig. 2).

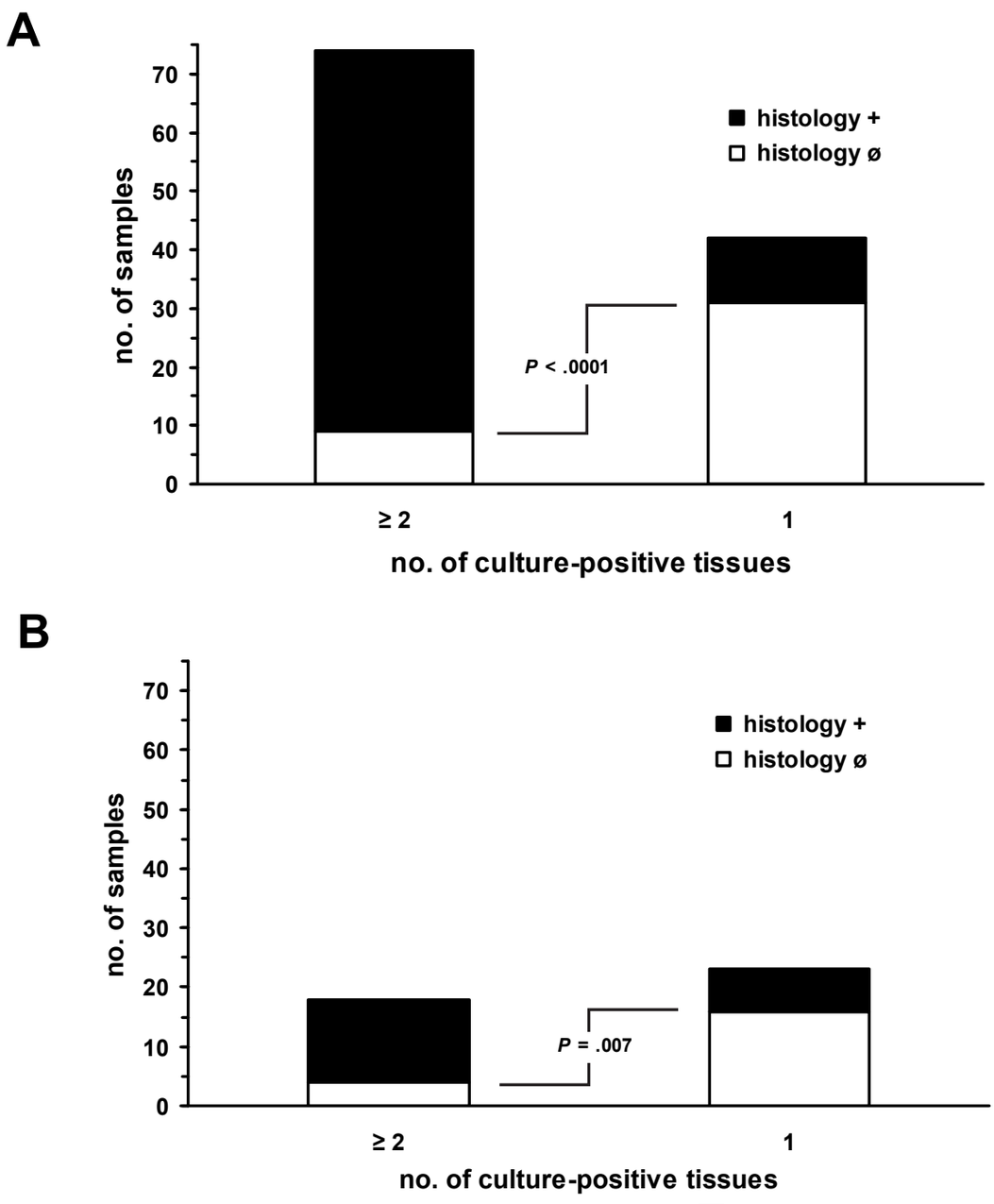

Fig. 2. Correlation between positive histology and the number of culture-positive tissue biopsies. (A) early species. (B) late species. Statistical significance was demonstrated by the χ^2 test.

3.8 Stage at which samples are attained

Although an additional risk and cost factor at first glance, preoperative evaluation of tissue samples in addition to joint aspiration can be helpful to identify the causative agent of arthroplasty infection accurately before the revision is carried out (Fink et al., 2008). This enables a one-stage replacement procedure, if clinically viable. Moreover, it allows to design

an individual regimen of systemic and localized antibiotic treatment for two-stage approaches using cement spacers supplemented with antibiotics (Fink et al., 2011). However, the utility of pre-operative biopsies is controversial between studies, mainly due to differences regarding the number of biopsies obtained and the definitions of infection (Fink et al., 2008, 2009; Meermans & Haddad, 2010).

4. Our own approach and future prospects

4.1 The value of both pre-operative and intra-operative sampling

We are convinced that pre-operative identification of the causative agent is a key factor for successful eradication of arthroplasty infections. It enables the design of individualized systemic and localized antibiotic therapy, while intra-operative tissue samples confirm the diagnosis and allow modification of the systemic antibiotic regimen if necessary. The diagnostic workflows we have established to identify hip and knee infections are outlined below.

To minimize the effect of false-negative results, we call for an antibiotic-free interval of 4 weeks before sampling for microbiological diagnosis. At our clinic we withhold peri-operative antibiotic prophylaxis until samples have been drawn, and we have not experienced adverse outcomes.

4.1.1 Samples and diagnosis

An overview of the laboratory procedures is given in Table 2.

sample material	storage	detection method	processing method	no. of samples	definition of infection
synovial aspiration fluid	room temp.	14-day automated culture	pediatric blood culture vial		
tissue biopsies	4°C	14-day aerobic and anaerobic culture	native	5	identical organisms in ≥ 2 samples
		sheep blood agar chocolate agar Schaedler agar brain-heart infusion broth Schaedler broth			
	-20°C	histological staining	frozen sections	5	≥ 5 neutrophils per 400 x field in 10 fields

Table 2. Overview over the laboratory methods used to detect arthroplasty infection.

The definitive diagnosis of arthroplasty infection is established with multiple tissue biopsies taken from the periprosthetic membrane and other macroscopically conspicuous sites

during revision surgery. We have experienced that the inflammation process can be assessed with high reliability if 5 samples each are obtained for culture and for histologic analysis. The definition that i) growth of indistinguishable bacteria in ≥ 2 specimens or ii) microbial growth in one specimen combined with a histology score of 3+ (≥ 5 neutrophils per high-power field in 10 fields) (Atkins et al., 1998; Pandey et al., 1999; Virolainen et al., 2002) has proven feasible with respect to the clinical outcomes (Fink et al., 2008, 2009).
Until now we use native tissue biopsies for culture. Tissue mincing is simple to perform and not too prone to contamination if carried out under a laminar air flow workbench. In our opinion, the prolonged incubation period of 14 days we carry out before cultures are cleared is a decisive measure. The persuasiveness of this approach has been shown in detail in 3.6.2. Although it would be interesting to compare the allegedly most sensitive sonication culture method directly with prolonged tissue cultivation, we doubt that the cumbersome and potentially contamination-prone sonication concept would prove significantly superior to our own approach.
As we are convinced that prolonged cultivation over 14 days is the key to detecting infecting organisms with optimal sensitivity, we also currently refrain from using PCR techniques on a routine basis.
If overnight storage of unprocessed samples is necessary, which occurs in less than 5% of cases in our setting, tissue specimens are kept at 4°C and processed at the laboratory the next morning with highly reproducible results. Synovial fluid, when inoculated into pediatric blood culture vials immediately post-drawing, is stable for at least 24 hours at room temperature. Subsequent supplementation with the appropriate enhancing medium, which is necessary to cultivate blood-free sample fluids, can then be done at the laboratory.
Taken together, our diagnostic measures have contributed significantly to the high eradication rates we observe with the treatment of both hip and knee arthroplasty infections (Fink et al., 2008, 2009).

4.1.2 Hip infections

By default, we carry out two-stage revisions of infected hips in our clinic (Fink et al., 2009). Localized antibiotics applied via cement spacer and systemic antibiotics are customized for administration at the time of revision surgery (Fink et al., 2011).
The general sampling algorithm is depicted schematically in Fig. 3. In addition, we obtain pre-operative tissue biopsies for culture and histology if the joint aspiration culture is negative but the risk assessment suggests indicates septic implant failure.

4.1.3 Knee infections

We perform pre-operative tissue biopsies rather than joint aspiration if it is clear that revision operation is necessary due to an unstable implant (Fig. 4). Five biopsies for culture are obtained in a blind fashion without instillating fluid in the intra-articular space (to avoid possible losses in sensitivity due to sample dilution). Afterwards standard arthroscopy is performed to rule out possible joint damage, and during this process 5 additional tissue samples are obtained for histological analysis.
We define infection using the same combined culture and histology algorithm as in biopsy samples taken during revision surgery. Our experience is that pre-operative biopsies are more sensitive than culture from aspirated synovial fluid (Fink et al., 2008).

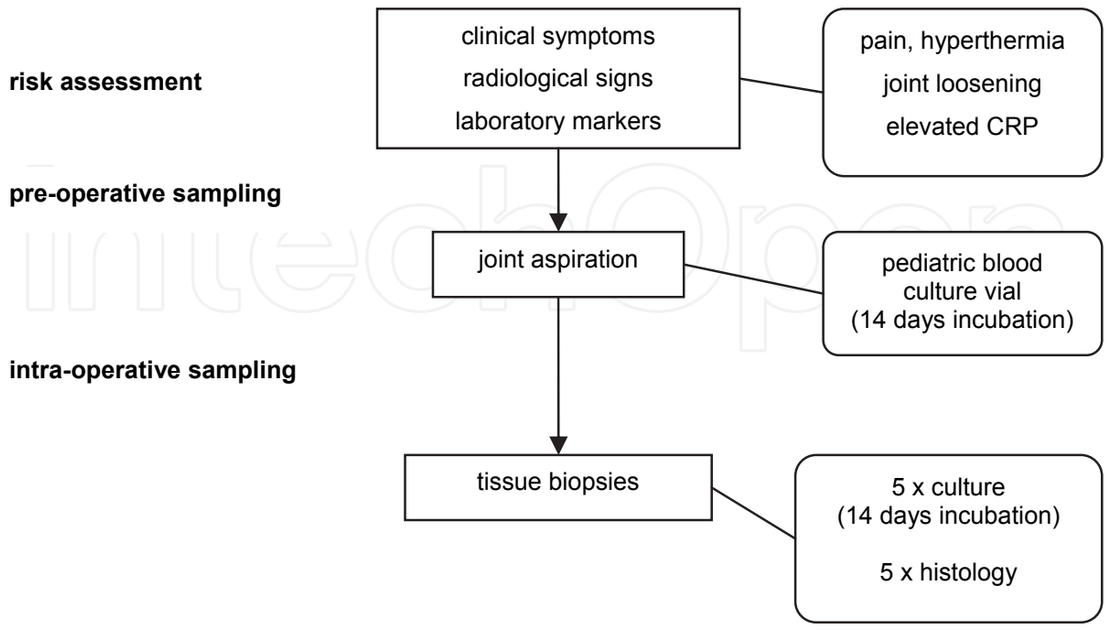

Fig. 3. Sampling algorithm for suspected periprosthetic hip infection. If joint aspiration cultures are negative but the risk assessment suggests indicates septic implant failure, pre-operative tissue biopsies are drawn additionally for culture and histology.

In stable implants, we do not undertake the risk of causing joint damage by blinded tissue biopsy. Instead, joint aspiration culture is performed, which has shown accuracy of 89% (Fink et al., 2008).

The pre-operative diagnostic approach of combined tissue culture histology has shown an accuracy of 98.6% compared to the definitive results obtained during revision surgery (Fink et al., 2008).

4.2 Future prospects

The detection of bacterial RNA rather than DNA by reverse transcription PCR is a potentially useful new approach to arthroplasty infection (Bergin et al., 2010). On one hand, RNA should be present only in viable bacteria and therefore indicate infections more accurately than DNA. On the other hand, the much shorter half-life of RNA should make its presence as a contaminant less likely. It remains to be seen whether this concept will prevail.

Rapid identification of bacteria and fungi to the species level by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry is utilized increasingly. There are already promising data on the detection of *Staphylococcus epidermidis* in tissue samples of patients with periprosthetic joint infections (Harris et al., 2010). It appears that it should even be possible in the near future to prove clonal identity of strains from the same species isolated from different tissue samples with this technique. This should facilitate the decision whether bacteria isolated from multiple tissue biopsies are likely to be involved in infection or rather reflect contaminating strains.

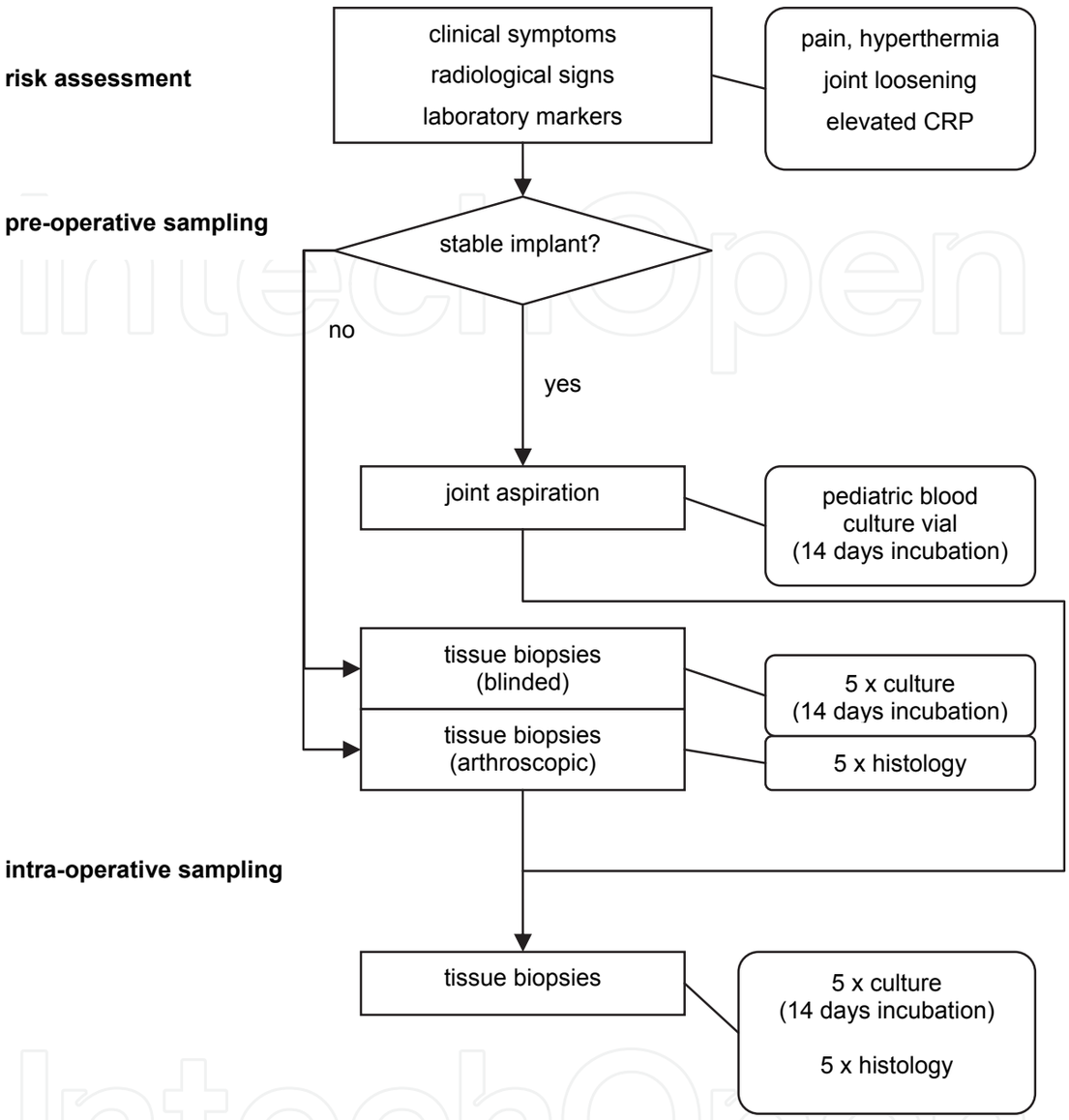

Fig. 4. Sampling algorithm for suspected periprosthetic knee infection.

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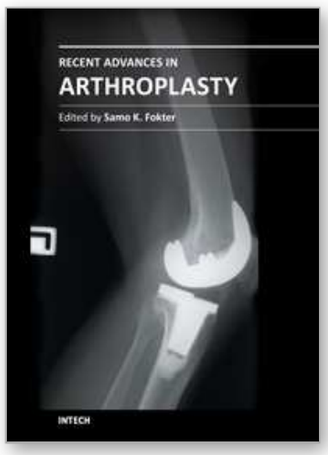

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The purpose of this book was to offer an overview of recent insights into the current state of arthroplasty. The tremendous long term success of Sir Charnley's total hip arthroplasty has encouraged many researchers to treat pain, improve function and create solutions for higher quality of life. Indeed and as described in a special chapter of this book, arthroplasty is an emerging field in the joints of upper extremity and spine. However, there are inborn complications in any foreign design brought to the human body. First, in the chapter on infections we endeavor to provide a comprehensive, up-to-date analysis and description of the management of this difficult problem. Second, the immune system is faced with a strange material coming in huge amounts of micro-particles from the tribology code. Therefore, great attention to the problem of aseptic loosening has been addressed in special chapters on loosening and on materials currently available for arthroplasty.

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