The microbiology of the acute dental abscess

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The acute dental abscess is frequently underestimated in terms of its morbidity and mortality. The risk of potential serious consequences arising from the spread of a dental abscess is still relevant today with many hospital admissions for dental sepsis. The acute dental abscess is usually polymicrobial comprising facultative anaerobes, such as viridans group streptococci and the Streptococcus anginosus group, with predominantly strict anaerobes, such as anaerobic cocci, Prevotella and Fusobacterium species. The use of non-culture techniques has expanded our insight into the microbial diversity of the causative agents, identifying such organisms as Treponema species and anaerobic Gram-positive rods such as Bulleidia extracta, Cryptobacterium curtim and Mogibacterium timidum. Despite some reports of increasing antimicrobial resistance in isolates from acute dental infection, the vast majority of localized dental abscesses respond to surgical treatment, with antimicrobials limited to spreading and severe infections. The microbiology and treatment of the acute localized abscess and severe spreading odontogenic infections are reviewed.

Introduction

The acute dental abscess is frequently underestimated in terms of its morbidity and mortality. The acute dental abscess usually occurs secondary to dental caries, trauma or failed root treatment. After the intact pulp chamber is breached, colonization of the root canals occurs with a diverse mix of anaerobic bacteria. The walls of the necrotic root canals become colonized by a specialized mixed anaerobic biofilm (Chavez de Paz, 2007). While asymptomatic necrosis is common, abscess formation occurs when these bacteria and their toxic products enter the periapical tissues via the apical foramen and induce acute inflammation and pus formation (Nair, 2004). The root canal microbiota is the main stimulus for the development of acute symptoms. The main signs and symptoms of the acute dental abscess (often referred to as a periapical abscess or infection) are pain, swelling, erythema and suppuration usually localized to the affected tooth, although the abscess can frequently spread causing a spreading odontogenic infection which can be accompanied by sepsis syndrome. The role of bacteria in the pathogenesis of the lesion is undisputed but modern diagnostic techniques have not identified a single causative pathogen. The dentoalveolar abscess is polymicrobial comprising various facultative anaerobes, such as the viridans group streptococci and the Streptococcus anginosus group, and strict anaerobes, especially anaerobic cocci, Prevotella and Fusobacterium species. The presence of anaerobes both cultivable and uncultivable tends to predominate. The vast majority of dental abscesses respond to surgical treatment, such as drainage of pus and elimination of the source of infection, with antibiotic use limited to severe spreading infections. The microbiology of the acute dentoalveolar abscess and its treatment in the light of improved culture and diagnostic methods are reviewed.

Background

Historically, the potential for a dental abscess to spread causing severe sepsis and death has been known since antiquity although the role of bacteria in this process was not recognized until the turn of the 20th century (Turner Thomas, 1908). When the Bills of Mortality (London) began listing the causes of death in the early 1600s, ‘teeth’ were listed as the 5th or 6th leading cause of death (Clarke, 1999). By the turn of the 20th century, dental infections were associated with a mortality rate of 10–40% (Turner Thomas, 1908). Collecting appropriate current epidemiological data is difficult due to differences in the methods of reporting throughout the world but the evidence suggests that it is still a significant clinical problem. In Scotland there were 3500 hospital admissions between 2000 and 2005 for acute dental infections while hospitals in England saw a doubling of admissions for surgical treatment of dental abscesses over a similar period.
Aspiration is 4 with a range of between 1 and 7.5 (Fazakerley et al., 1993; Khemaleelakul et al., 2002; Reader et al., 1994).

Facultative anaerobes

The most commonly found facultative anaerobes belong to the viridans group streptococci and the *anginosus* group streptococci. Difficulties lie in interpretation of the literature on the relative contributions of individual species from these two major groups of organisms due to taxonomic changes and accuracy of identification. The viridans group streptococci comprise the *mitis* group, *oralis* group, *salivarius* group, *sanguinis* group and the *mutans* group (Facklam, 2002). The *anginosus* group (formerly referred to as ‘*Streptococcus milleri*’ or *Streptococcus anginosus*) is also identified and reported with varying degrees of accuracy ranging from just beta-haemolytic streptococci down to species level.

Historically, *Staphylococcus* species have not been considered members of the oral flora or to play a major role in the pathogenesis of oral infections. However, a number of more recent studies have indicated that staphylococci may indeed be a more frequent colonizer of the oral tissues than previously thought (Smith et al., 2001). The recovery rates using conventional culture of *Staphylococcus aureus* from the acute dental abscess range from 0.7 to 15% (Brook et al., 1991; Goumas et al., 1997; Kulekci et al., 1996; Kuriyama et al., 2002b; Roche & Yoshimori, 1997; Siqueira et al., 2001d) although some workers have noted higher recovery rates of 47% (Mangundjaja & Hardjawinata, 1990). Interestingly, *Staphylococcus aureus* has been reported to occur more frequently in severe dental abscesses from children (Brook et al., 1991; Coticchia et al., 2004; Coulthard & Isaacs, 1991; Dodson et al., 1989; Tan et al., 2001).

Recovery rates of coagulase-negative strains of staphylococci (usually reported as *Staphylococcus epidermidis*) are generally higher with figures ranging from 4 to 65% (Gorbach et al., 1991; Goumas et al., 1997; Khemaleelakul et al., 2002; Kuriyama et al., 2002b; Lewis et al., 1995; Mangundjaja & Hardjawinata, 1990; Sakamoto et al., 1998; Storoe et al., 2001). *Staphylococcus* species may also be associated with refractory infections not responding to endodontic treatment (Reader et al., 1994).

Anaerobes

Similar difficulties exist for cross-study comparisons of identification and prevalence of strict anaerobes. The most commonly isolated genera include anaerobic streptococci, *Fusobacterium* species and the black-pigmented anaerobes such as *Prevotella* and *Porphyromonas* species (Sunqvist et al., 1989).

The nomenclature and recent changes in taxonomy have complicated the comparison of more recent studies with older studies due to the renaming of several species, specifically the *Prevotella*, *Bacteroides* and *Porphyromonas*
species. An important group of pathogens that has undergone much in the way of taxonomic rearrangement, this group, often referred to as the 'oral Bacteroides' and black-pigmenting anaerobes group, has been reclassified. The Bacteroides species have been divided into the saccharolytic genus Prevotella and the asaccharolytic genus Porphyromonas. The genus Bacteroides has been restricted to the fermentative Bacteroides fragilis and its closely related species. B. fragilis, a more common isolate from intra-abdominal infections, has only infrequently been reported from acute dentoalveolar infections and is not regarded as an oral commensal. The member of the Bacteroides genus most likely to be recovered from an acute dental abscess is Bacteroides forsythus (newly classified as Tannerella forsythia) (Gomes et al., 2006).

The most commonly reported anaerobic Gram-negative bacilli from acute dental alveolar infections are species from the pigmented Prevotella intermedia group (comprising Prevotella intermedia, Prevotella nigrescens and Prevotella pallens), Porphyromonas endodontalis and Porphyromonas gingivalis (Jacinto et al., 2006). The Prevotella species are the most frequent isolates, found in 10–87% of dentoalveolar abscesses (Baumgartner et al., 2004; Fazakerley et al., 1993; Kolokotronis, 1999; Kulekci et al., 1996; Kuriyama et al., 2005; Lewis et al., 1993; Riggio et al., 2006; Roche & Yoshimori, 1997; Sakamoto et al., 1998; Siqueira et al., 2001b, d; Wade et al., 1994). The genus Fusobacterium is frequently reported in infections of the head and neck with reports indicating that Fusobacterium species can be detected in up to 52% of specimens (Gill & Scully, 1990; Gilmore et al., 2001b, d; Lewis et al., 2000a, b, 2005, 2006; Roche & Yoshimori, 1997). Workers have recovered Fusobacterium nucleatum, F. nucleatum subsp. animalis, F. nucleatum subsp. vincentii and F. nucleatum subsp. fusiforme) are frequently detected with F. nucleatum recovered most frequently from the acute dental abscess (Dzink et al., 1990; Chavez de Paz Villanueva, 2002; Sassone et al., 2008). Studies utilizing non-culture techniques for analysis of the dental abscess for the presence of F. nucleatum have reported a prevalence of 73% (Baumgartner et al., 2004).

The Clostridia are infrequently reported from odontogenic infections either as a sole pathogen or as part of the abscess flora. Workers have recovered Clostridium species from 2–20% of specimens (Gorbach et al., 1991; Goumas et al., 1997; Khemaleelakul et al., 2002; Roche & Yoshimori, 1997). Where speciated, these isolates have included Clostridium histolyticum, Clostridium histolyticum, Clostridium perfringens, Clostridium subterminale and Clostridium clostridiforme (Khemaleelakul et al., 2002; Roche & Yoshimori, 1997). Although other Clostridium species such as Clostridium sporogenes, Clostridium biformentans, Clostridium botulinum, ‘Clostridium oedonatis’ and ‘Clostridium welchii’ have been recovered from carious dentine, they appear to be infrequent pathogens in the oral cavity (Van Reenan & Coogan, 1970).

**Analysis of the microflora of the acute dental abscess using molecular biological techniques**

Close attention to specimen collection and processing on selective and non-selective agars under appropriate atmospheric conditions has improved the routine diagnostic yield from acute dental abscesses. However, despite meticulous attention to detail, it is apparent that many genera of bacteria have yet to be cultured from many infectious diseases including the acute dental abscess (Siqueira & Rocos, 2005). The use of culture-independent or molecular diagnostic techniques has expanded our insight into the microbial ecology of the dental abscess. There is an increasing reliance on genetic methods of identification with 16S rRNA gene sequencing frequently being used for research purposes. Broadly speaking, the molecular analysis may take one of two approaches. Firstly, the use of molecular cloning and sequencing techniques to identify uncultivable micro-organisms using 16s rRNA or rDNA has led to the identification of several novel species (Dymock et al., 1996). The second approach utilizes PCR or DNA–DNA hybridization chequerboard techniques (Siqueira et al., 2001d, 2002a) and more recently 16S rRNA gene sequencing and species-specific primers searching for the presence of specific microbes (Dymock et al., 1996; Riggio et al., 2006; Rocos & Siqueira, 2005; Sakamoto et al., 2006; Siqueira et al., 2001b, c, 2002b, 2003). This approach has demonstrated the higher prevalence of more fastidious organisms such as Treponema species in the acute dental abscess.

*Treponema* species are strictly anaerobic, motile, helically shaped bacteria. Within the oral cavity they are more usually associated with diseases of the periodontium. There are a number of different species described from the oral cavity including Treponema amylovorum, Treponema denticola, Treponema maltophilum, Treponema medium, Treponema pectinovorum, Treponema socranski and ‘Treponema vincentii’ (Chan & McLaughlin, 2000). The treponemes are difficult to cultivate and differentiate and only T. denticola, T. pectinovorum, T. socranski and ‘T. vincentii’ have been readily cultivated. Recent work using PCR detection has indicated a surprisingly high prevalence of *Treponema* species within the acute dental abscess. Siqueira & Rocos (2004c) found that T. denticola was present in up to 79% of dental abscesses, with lower detection rates reported by other workers (Baumgartner et al., 2003; Siqueira et al., 2001a, c; Gomes et al., 2006; Cavrini et al., 2008). Other *Treponema* species were found in lower numbers, including *T. socranski* (in 26% of aspirates), T. pectinovorum (14–21% of aspirates), T. amylovorum (16% of aspirates) and T. medium (5% of aspirates).
aspirates). Other species such as *Treponema lecithinolyticum*, *T. vincentii* and *T. maltophilum* were not detected. Despite the possession of a number of potential virulence factors, the precise role of these poorly understood and under-reported organisms in the pathogenesis of the acute dental abscess is unclear.

**Unfamiliar species**

Improvements in sampling, culture and identification have led to a greater insight into the diversity of the microbial flora in an acute dental abscess. This has resulted in the reporting of micro-organisms which are probably more accurately described as ‘unfamiliar’ rather than ‘new’ implying their recent appearance. These include members of the genus *Atopobium* (Gram-positive strictly anaerobic coccobacilli), for example *Atopobium parvulum* and *Atopobium rimaec*. Anaerobic Gram-positive rods include *Bulleidia extructa, Cryptobacterium curtum, Eubacterium sulci*, *Mogibacterium timidum* and *Mogibacterium vescum* (Sakamoto et al., 2006), *Pseudomonabacter bacloctyticus* and *Slakia exigua* (Siqueira & Rocas, 2003c).

Other unfamiliar species include anaerobic Gram-negative rods such as *Filifactor alois* (Siqueira & Rocas, 2003a, 2004b; Gomes et al., 2006) and *Dialister pneumosintes* (Siqueira et al., 2005; Siqueira & Rocas, 2003b, 2004b). *Centipeda periodontii* and *Selenomonas spgutengena* are multi-flagellated, motile, anaerobic, Gram-negative rods also found recently in the acute dental abscess (Siqueira & Rocas, 2004a). *Catonella morbi*, a Gram-negative anaerobe formerly known as Bacteroides D42, was found in 16% of 19 aspirates, and *Granulicatella adiacens*, a facultative anaerobic Gram-positive coccus formerly known as nutritionally variant streptococci, was present in 11% of 19 aspirates (Rocas & Siqueira, 2005; Siqueira & Rocas, 2006).

The detection of these unfamiliar species has opened up a whole new area for possible study into the virulence factors possessed by these bacteria and their relative influence on the pathogenesis of the acute dental abscess and interactions with more commonly isolated and better understood pathogens. These techniques are not without their limitations and meticulous asepsis is required throughout the sampling and analysis procedure to avoid contamination due to the sensitivity of these methods. Furthermore, until recently these techniques could only give semiquantitative analysis of aspirates and indeed some papers cited above can only show the presence or absence of the species in question. This will improve with the advent of quantitative real-time PCR. The use of species-specific primers targeting the 16S rRNA gene or similar is also limited by the fact that they cannot distinguish between transcriptionally active viable cells and those non-vital bystanders. Advanced molecular techniques using reverse transcriptase are finding methods of overcoming these limitations currently. Finally, molecular techniques can give little useful information to guide the clinician in the choice of antibiotic if required.

**Antibiotic resistance**

The antibiotics most commonly prescribed in the management of acute dental abscesses in the UK are amoxicillin, penicillin, metronidazole and erythromycin (Palmer et al., 2000). Antibiotic resistance in microbes recovered from the acute dental abscess has been reported to be increasing (with the exception of metronidazole) in some populations studied over the last few decades (Kuriyama et al., 2006; Lewis et al., 1989, 1995; Storoe et al., 2001). Care must be taken in interpretation of studies due to differences in details of the identification of isolates, selection of appropriate breakpoints and their relevance to oral infections and lack of details on MICs (for example, not all studies report MIC₉₀ data). This is illustrated by reports of resistance rates for amoxicillin ranging from 9 to 54% of common isolates from acute dental abscesses (Baumgartner & Xia, 2003; Gilmore et al., 1988; Khemaleelakul et al., 2002; Kuriyama et al., 2000a, 2002a, 2005; Lewis et al., 1993, 1995; Smith & Jackson, 2003).

However, analysis of a number of reports does reveal a trend that the least susceptible isolates from an acute abscess are more likely to be black-pigmented *Prevotella* species, such as *Prevotella intermedia, Prevotella melaninogenica, Prevotella denticola* and *Prevotella loescheii*, followed by the non-pigmenting *Prevotella* species, such as *Prevotella oralis, Prevotella buccae, Prevotella disiens* and *Prevotella bivia*. The most common mechanism of antimicrobial resistance detected is production of beta-lactamase, probably related to the group 2e class of beta-lactamases (Valle et al., 1998). This group of beta-lactamases demonstrates a major activity on cephalosporins rather than penicillins and retains susceptibility to inhibition by clavulanic acid and tazobactam. The presence of beta-lactamase production in other anaerobes from acute dental infections, such as *Porphyromonas* and *Fusobacterium* species, appears infrequent.

Studies have reported that resistance from the *anginosus* group of streptococci is rare with 1 of 43 isolates (2.3%) having a penicillin MIC greater than 1 mg l⁻¹ and 7 of 45 (15.5%) ‘viridans group’ streptococci having a penicillin MIC greater than 1 mg l⁻¹ (Lewis et al., 1995). More recently, this group has failed to detect penicillin resistance by NCCLS breakpoints in 64 streptococcal isolates (Kuriyama et al., 2005). Reduced susceptibility to penicillin is more prevalent in the *mitis* group streptococci than in the *anginosus* group (Smith & Jackson, 2003).

Resistance to macrolides appears to have a higher prevalence in the ‘viridans group streptococci’, anaerobic streptococci and *Prevotella* species (Kuriyama et al., 2000a, 2001, 2002b). This is linked to penicillin resistance. The erythromycin MIC₉₀ of 139 streptococcal isolates was 1.0 mg l⁻¹ for penicillin-susceptible isolates and 2.0 mg l⁻¹ for penicillin-resistant isolates (Kuriyama et al., 2000a). For pigmented *Prevotella* species (n=93), the erythromycin MIC₉₀ for penicillin-susceptible isolates was 8 mg l⁻¹ and for penicillin non-susceptible isolates was 64 mg l⁻¹ (Kuriyama et al.,...
Both penicillin-susceptible and -resistant isolates of *Fusobacterium* species (n=90) had an MIC$_{90}$ of 64 mg l$^{-1}$ for erythromycin. Macrolide resistance is most commonly due to acquisition of one of a number of ern genes (erythromycin methylases resulting in reduced binding of macrolides to the 50S ribosomal subunit). The prevalence of resistance to lincosamides, such as clindamycin, is low. For example, Kuriyama et al. (2000a) reported on 664 isolates from 163 patients and found a clindamycin MIC$_{90}$ of 2 mg l$^{-1}$ for 15 strains of penicillin-resistant anaerobic streptococci, with all the remaining isolates (649) having a clindamycin MIC$_{90}$ less than 0.5 mg l$^{-1}$. Similar low levels of clindamycin resistance have been found in the UK (Kuriyama et al., 2005) and elsewhere (Kuriyama et al., 2001).

### Severe odontogenic infection

Deep neck and mediastinal abscesses are a rare complication of the dental abscess but spread of odontogenic infections accounts for up to 57% of deep neck abscesses (Mihos et al., 2004; Sancho et al., 1999). With the potential for infection spreading to the interpleural space and mediastinal tissue, the mortality rate of mediastinitis continues to be 17–50% despite aggressive use of antibiotics and advances in intensive care facilities (Corsten et al., 1997; Marty-Ane et al., 1999). Death usually occurs due to sepsis and multi-organ failure although airway occlusion is also a significant complication and requires early management by tracheostomy. Host factors affected by the patient's general health condition play a significant role. Specific at-risk groups are diabetics (Jimenez et al., 2004; Tung-Yiu et al., 2000) and the elderly (Wang et al., 2003). Most studies report that males are affected more often by severe odontogenic infections than females in both adult (Flynn et al., 2006; Sancho et al., 1999) and paediatric (Dodson et al., 1989) groups.

The bacteriology of the spreading odontogenic infection appears subtly different from that of the more localized dental abscess with *anginosus* group streptococci and *Fusobacterium* species forming the predominant flora isolated (Han & Kerschner, 2001; Heimdahl et al., 1985; Schuman & Turner, 1999). Recent work suggests a significant role for *Prevotella* species in the spreading odontogenic infection with these species accounting for 50% of clones analysed from samples of pus aspirated from spreading odontogenic infections (Riggio et al., 2006). Deep neck infections in the paediatric population also appear to be significantly different bacteriologically, with an increased involvement of *Staphylococcus aureus* (Brook, 1987; Cotichia et al., 2004; Coulthard & Isaacs, 1991; Dodson et al., 1989; Tan et al., 2001) and group A streptococci (Cotichia et al., 2004).

### Treatment of the acute dental abscess

There is no consensus over gold standard treatment as evidenced by the wide variety in endodontic and surgical protocols and antibiotic prescribing (Kuriyama et al., 2005). This ongoing controversy is a result of a lack of sufficient evidence to support the use of one antibiotic regimen over another or to indicate one treatment modality over another. Clinical trials in the treatment of the dental abscess are often flawed in design, limiting validity and applicability of results. Many studies are inadequately blinded and have not adequately controlled inclusion criteria. This has resulted in patients receiving multiple surgical and medical interventions making it impossible to analyse the relative contributions of each intervention to the success of treatment (Adriaenssen, 1998; Davis & Balcom, 1969; Fazakerley et al., 1993; Foud et al., 1996; Gilmore et al., 1988; Hanna, 1991; Kuriyama et al., 2005; Lewis et al., 1986, 1993; Mangundjaja & Hardjawinata, 1990). In one study, a total of six antibiotic regimens were prescribed with patients also receiving either incision and drainage or drainage through the tooth (Kuriyama et al., 2005). Other difficulties include a lack of standardization in how the primary outcome is measured, with some studies relying on clinical assessment of relatively crude measures, i.e. failure, slight improvement, cure (Adriaenssen, 1998; Gilmore et al., 1988; Hanna, 1991; Kuriyama et al., 2005), and others a combination of both patient responses and clinical examination with well-defined but subjective criteria (Fazakerley et al., 1993; Foud et al., 1996; Mangundjaja & Hardjawinata, 1990; Paterson & Curzon, 1993; Schuen et al., 1974, von Konow et al., 1992).

The above criticisms highlight the need for good-quality clinical trials to be held of sufficient size and scientific rigor to answer the question about the ideal treatment of the acute dental abscess. Nonetheless there are a number of recommendations which can be suggested based on the current evidence. Antibiotics should only be prescribed in patients exhibiting signs of local spread or systemic involvement. There is currently insufficient evidence to advocate the use of one regimen over another; however, a high dose used for as short a course as is consistent with a clinical cure has been shown to be effective and may reduce the development of resistance (Lewis et al., 1986). If empirical antibiotics are required, the following may be considered. Amoxicillin remains the antimicrobial of first choice. If local patterns of antimicrobial resistance indicate a high prevalence of resistance to amoxicillin then the use of either metronidazole (Roche & Yoshimori, 1997) or amoxicillin in combination with clavulanic acid (Lewis et al., 1993) should be considered as alternatives. Clindamycin remains an alternative in individuals who are allergic to the penicillin group of antibiotics (Gilmore et al., 1988; Mangundjaja & Hardjawinata, 1990; Schuen et al., 1974).

### Conclusions

With the advent of molecular diagnostic techniques, our insight into the diversity of the polymicrobial collection that comprises the dental abscess is expanding. Factors
influencing the process of bacterial succession from the saccharolytic cariogenic flora to the more anaerobic and proteolytic flora of the dental abscess remain unknown. Determination of factors that influence the spread of infection from a localized collection at the apex of a tooth to a cellulitis and life-threatening sepsis would aid treatment decisions. There are surprisingly few well-controlled studies into the most appropriate treatment regimen for the acute dental abscess, with most of the evidence pointing towards a key role for prompt surgical intervention and timely review. Antimicrobials should be reserved for patients with evidence of cellulitis and signs of sepsis. Although comparing different studies on antimicrobial susceptibility from dental abscesses is difficult, available data suggest that at present most isolates are still susceptible to first-line beta-lactam agents. In current times where the overuse of the prescription pad has eroded the antimicrobial arsenal, more effort could be placed on appropriate antimicrobial prescribing for the treatment of acute dental infections. Alternatively, strategies to improve oral health and reduce the incidence of dental caries, the main cause of the dental abscess, would maximize use of resources.

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