Enterococcus faecalis and Dental Implants

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Enterococcus faecalis appears in many tooth root infections and is not eliminated by root canal therapy. It can reside in tooth root canals and the surrounding bone. This species may vegetate in bone after extraction of an infected tooth and colonize a dental implant after placement in the healed site. A colonization may cause fixture loss or marginal bone loss. These colonizations are generally multibacterial and pathogenic properties can be shared via plasmids. However, *E faecalis* is not detectable with some culture techniques and thus can be missed. It is usually not a dominant species in these infections. Nonetheless, *E faecalis* may be a "keystone" player in dental implant bone loss or peri-implantitis. That is, *E faecalis* may be the pathogenic determinant for any particular peri-implantitis infection of a multiple-species infection.

Key Words: biology, cell biology, implant dentistry, maxillofacial pathology

Introduction

Dental mplants can fail to successfully integrate whether placed immediately after a tooth extraction or after ridge healing, or failure can occur long after initial placement. There are several reasons that may cause the failure or loss of integration: inadequate bone volume or quality, occlusal overload, micromovement during healing, foreign body type immunologic rejection and bacterial colonization.[1] Bacterial colonization can be a factor in implant failures.[2,3]

Enterococcus faecalis is found in the osseous environs of infected teeth and implants.[4] *E faecalis* is so pervasive in dental infections that it is used to test composite fillings, endodontic sealers, and implant abutment seals of implant designs.[4–6]

The object of this article is to review the bacterial species *E faecalis* and its pathogenic activities related to dental implants.

Materials and Methods

A Medline PubMed online search was made using the terms "*Enterococcus faecalis* AND dental implant," yielding 1 related article, serendipitously by this author.[2] *E faecalis* as a dental implant pathogen is not well studied. A subsequent search "*Enterococcus faecalis* ONLY" yielded 1904 articles that were vetted for bacterial pathophysiology that may relate to dental implant colonization.

Results

Thirty-two related articles were found and are reviewed below, along with other articles that were deemed interesting, related, and appropriate.

Discussion

Taxonomically, *E faecalis* is in the bacteria domain, Eubacteria kingdom, Fermicutes phylum, Cocci class, Lactobacillales order, Enterococcaceae family, Enterococcus genus, and the species *Enterococccus faecalis* (Figure).[7]

E faecalis is a gram positive, nonmotile, commensal, spherical bacteria. It appears in planktonic form, in pairs and chains.[7] It ferments glucose. It generally resides in the gastrointestinal tract of humans and other mammals.[7] *E faecalis* is capable of causing life-threatening infections, especially in a hospital setting. Hospitals generally are where sick people go with infections that do not respond favorably as outpatients[7]; these patients go to a hospital for more intensive treatment. Thus, the hospital is where virulent and antibiotic resistant bacteria accumulate.[7] *E faecalis* is one of the top three pathogens of nosocomial infections.[7] *E faecalis* can cause septicemia, meningitis, urinary tract infections, and a multitude of other infections.

E faecalis has been found to colonize dental implants to cause peri-implantitis.[8] Peri-implantitis has a different and more diverse pathogenic microflora as compared to periodontitis.[8] The microbiologic profile harbored in peri-implantitis is generally variable, opportunistic, and composed mostly of complex gram-negative species.[8] The members of this profile are associated with and reside with the Epstein-Barr virus and nonsaccharolytic anaerobic gram-positive rods.[8] Also found is a high incidence of enteric species, which include *E faecalis*.[8]

One recent study found *E faecalis* in 14% of adequately treated root canals with persistent apical periodontitis.[9] However, it was predominant in 2 of 27 cases. Streptococcus species were the most prevalent bacterial species.[9]

The *E faecalis* genome contains 3.22 million base pairs (Mbp) with 3113 protein-coding genes; as much as 25% of these are acquired via plasmids.[10] Thus, virulence and antibiotic resistance can be shared among these bacteria.

E faecalis are very often found in and around the roots of root canal treated teeth.[11–13] There is a prevalence of *E faecalis* in and about failed endodontically treated teeth.[14] In fact, *E faecalis* is the most common microorganism found with failed endodontic treatment with most detection methods.[12,15,16] *E faecalis* is susceptible to various antibiotics, but there are virulence factors that allow this species to survive.[14] Nonetheless, many *E faecalis* strains are sensitive to amoxicillin, which is bactericidal. Conversely, some strains of *E faecalis* are resistant

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DOI: 10.1563/aaid-joi-D-16-00069

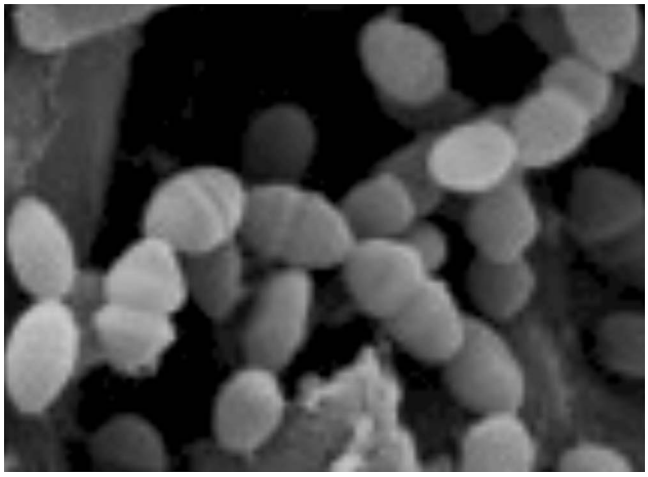

Figure 1. A scanning electron microphotograph of *Enterococcus faecalis*.

to rifampicin, erythromycin, and azithromycin.[14] *E faecalis* is highly correlated with persistent intraradicular infections.[17]

E faecalis has unique characteristics. They are facultative anaerobes and can survive extreme alkaline pH as high as 9.6 and high salt concentrations.[11] *E faecalis* can successfully compete with other microorganisms, invade dentinal tubules, and resist nutritional deprivation.[12] Unlike other pathogens, *E faecalis* can colonize the root canal space. It is capable of being the only infectious organism and survive without the support of other bacteria.[15,16]

E faecalis is found in root-filled teeth associated with periradicular lesions and is detected by culture and polymerase chain reaction analysis (PCR).[14] *E faecalis* has been found in these failed cases in a range of 0–70% by culture[18,19] and 0–90% by PCR.[19,20] The differences in research findings may be caused by geographic differences, different dietary intake, variations in clinical sampling, and analysis methods.[19,20]

PCR analysis methods enable rapid identification of both uncultivable and cultivable microbial species with high specificity and sensitivity. PCR is more effective in detecting *E faecalis* than other analytical tools, such as culturing.[14] This may explain why *E faecalis* is not routinely found in some studies.[14] Conventional PCR assays detect only the presence or absence of a microorganism and not the quantity.[21] Detection may depend on the quality of the laboratory technique and personnel.[21]

Bacterial resistance to antibiotics has been increasing over time, and oral Enterococci have become resistant as well. It has been noted that erythromycin is ineffective against *E faecalis*.[22] Azithromycin was found to be even less effective against Enterococci than erythromycin. *E faecalis* is less susceptible to chloramphenicol, tetracycline, and ciprofloxacin.[14] Chlorhexidine may not be effective against *E faecalis*.[23]

E faecalis isolated from failed endodontically treated canals have virulence factors that are related to adherence to surfaces.[14] The surface adherence factor of these strains contributes to the persistence of these strains even after extraction. That substrate surface can be bone trabeculae.[14] *E faecalis* possesses collagen-binding proteins which enables it to bind to dentin.[24] Blood serum helps *E faecalis* to bind to type I collagen, which is the organic component found in bone.[12] Additionally, the adhesive virulence factor gelatinase E (gelE) is identified in almost all (91.6%) *E faecalis* strains isolated from cases of failed endodontic treatment.[12,25] GelE is a hydrophobic metalloprotease with the capacity of cleaving insulin, casein, hemoglobin, collagen, gelatin. and fibrin.[25] GelE enhances biofilm formation by *E faecalis*.[26] The ability to form a biofilm and gelE is the reason *E faecalis* can form a periapical lesion.[27] In one study, aggregation substance (ASA) was found in 83.3% of *E faecalis* isolates.[28] ASA is a pheromone-responsive, plasmid-encoded bacterial adhesin that mediates efficient contact between donor and recipient bacterium, facilitating plasmid exchange. ASA was also found to mediate binding to extracellular matrix proteins, including type I collagen. Binding to type I collagen by bacteria may be of particular importance with respect to endodontic infections since this is the main organic component of the dentin and bone.[29] The Enterococci surface protein (ESP) is encoded by the ESP gene and may be involved in colonization and persistence of *E faecalis* during infections.[30] The enterococcal gene ESP, which encodes the high-molecular-weight surface protein ESP, has been abundantly detected among bacteremia and endocarditis isolates. Nonetheless, it is rare in stool isolates from healthy individuals.[31]

Cytolysins are a class of proteins and lipid surfactants that cause cell lysis are produced by many *E faecalis* strains and are important for pathogenesis.[14] One study determined that 16.6% of *E faecalis* strains carry the cytolysin (*cylA*) gene.[14] Cytolysin can induce tissue damage through the lysis of erythrocytes and destruction of host cells. The genes in the cyl operon encode cytolysin, where *cylA* is the only reading frame necessary for the expression of component A, a serine protease. Therapeutic inactivation of bacterial cytolysins may be instrumental in reducing bacterial pathogenesis. Sedgley et al determined that 36% of the *E faecalis* endodontitis-associated strains are capable of producing the red blood cell membrane destroyer, hemolysin.[32,33]

E faecalis resists bile salts, detergents, heavy metals, ethanol, azide, and desiccation.[34] It can survive and grow in a temperature range of 10–45°C and survive for 30 minutes at temperatures of 60°C.

E faecalis is successfully inactivated after 40 minutes of exposure to 5.25% sodium hypochlorite (SHC). *E faecalis* is capable of surviving an exposure to SHC in less than 40 minutes and less than 5.25% concentration.[35,36] This robust nature makes this species a relatively persistent culprit in implant failures.[2]

There are generally many species involved in a dental infection. Bacterial colonization or vegetation may occur when there are residual planktonic or biofilms in the osseous ridge.[37] Nonetheless, the presence of a biofilm may not be the most important factor, but the virulence and pathogenicity of a species may be the prime factor in colonization.[37] *E faecalis* may be a prime suspect for a dental implant colonization.[38] *E faecalis* can act in concert with other species, but it is also capable of a solo infection.

Viable *E faecalis* can persist in treated root canals as shown by m-RNA analysis.[37] Enterococcus species can remain meta-

bolically active in a vegetative form during periods of starvation and later resume growth and division when conditions become more favorable.[39] Vegetative starved cells recover by utilizing serum from surrounding bone and periodontal ligament.[12] Because of its ability to change into a vegetative form, *E faecalis* can exist without causing signs or symptoms of disease. An osteotomy in an edentulous site arouses the vegetative form. When a dental implant is placed in the osteotomy, it provides a surface for the bacteria to colonize. Thus, the vegetative organism can reactivate, alter its metabolism, and form a biofilm on the implant surface.[37] Additionally, the implant displacement itself blocks complete access to the biofilm by serum antibodies and antibiotics.

Nonpathogenic peri-implant symbiotic species are similar to those in a pathogenic flora. There is no clear pathogenic profile associated with peri-implantitis.[8] The pathogenic species profiles of periodontitis and peri-implantitis are different.[8] Peri-implantitis infection is composed of multiple dysbiotic species, but there may be a "keystone" species that is the primary pathogenic determinant.[40] This means that *E faecalis* may work in concert with other species with *E faecalis* as the primary enabler of the infectious process.

Ozone is an effective antimicrobial and has been found to be effective in removal of *E faecalis* biofilm.[41] The combination of ozone and SHC can enhance the action against the *E faecalis* biofilm.[41] Repeated ozone treatments are required to substantially eliminate a *E faecalis* biofilm.[41] Thus, removing an *E faecalis* biofilm can be challenging.

Lasers have been shown to eliminate 100% of *E faecalis* on rough surface implants in vitro.[42] The Nd:YAG laser irradiation is able to reduce *E faecalis* on implants. The GaAlAs laser used at 3 watts showed 100% bacteria elimination on implant surfaces.[42]

People who have a chronic fingernail biting habit usually have a significantly higher *E faecalis* oral population as compared to non-fingernail biters.[43] Although there is no data, dental implant patients who are fingernail biters may have a higher risk for peri-implantitis or implant failure due to the higher *E faecalis* load. Bacteria are transmitted among close relationships. and *E faecalis* may be transmitted as well among a family.[44]

After an extraction, thorough debridement of the socket is crucial even if an implant will not be immediately placed—crucial because of the vegetative talents of *E faecalis*. Irrigation of an extraction socket or osteotomy with an antimicrobial agent may be appropriate, but the effective use of irrigants is not established.[45] One-hundred percent complete removal of any bacteria from any osseous site is improbable. Theoretically, a single planktonic bacterium left in the site can proliferate into a colonization of a dental implant. The prudent clinician can only debride as diligently as clinically possible.

Bioactive glass implant coatings may act to reduce an *E faecalis* population due to the action of pH and the liberation of calcium ions.[46]

Dental implant dealers in international venues have been known to resell sterilized previously placed implants.[47] In one study, *E faecalis* was detected on the abutments of a set of these.[47]

Additional study is required to demonstrate the species that could be an accurate predictor for or diagnostic of peri-implantitis. Peri-implantitis is a complex infection. Recently, *Parvimonas micra* has been implicated as a potential predictor of peri-implantitis.[48] This species may be a harbinger, but it does not discount the potential enabling activity of *E faecalis*.

Conclusions

E faecalis is a bacterial species that can persist in bone after endodontic therapy. It is found in many dental infections, has a vegetative capacity, and adheres to type 1 bone collagen. Thorough debridement of extraction sockets is crucial for any potential implant site to remove this and any other pathogenic species that may subsequently colonize an implant surface. Complete removal of all bacterial species may be practically impossible. This and other species are capable of surviving in a vegetative state that allows the bacteria to survive in healed bone and be reactivated upon dental implant placement. There can then be bacterial colonization of the implant. Because *E faecalis* is not detected in some culture techniques, it will not be reported in some studies. It is usually not found as a predominant species in most studies. Nonetheless, *E faecalis* may be a keystone species; that is, *E faecalis* may be an enabling pathogenic determinant for peri-implantitis infection and bone loss.

Abbreviations

ASA: aggregation substance
cylA: cytolysin gene
ESP: Enterococci surface protein
PCR: polymerase chain reaction
SHC: sodium hypochlorite

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