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Enterococcus faecalis, a dental point of view

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Abstract
Enterococcus faecalis is a bacterium prevalent in periodontal diseases and root canal infections. **Objective:** To analyze the existing literature about the epidemiology, diagnosis, treatment and clinical manifestations of *E. faecalis*. Methodology: PubMed, Web of Science and Google Scholar databases were searched with the following keywords: *E. faecalis*, bacterial resistance, epidemiology, diagnosis, treatments, and clinical manifestations and the information obtained was used to generate this review. **Results:** The oral cavity may constitute a reservoir for virulent strains of *E. faecalis,* which may have both biofilm formation capacity and antibiotics resistance. The diagnosis is by culture or PCR analysis on duct samples. The clinical manifestations are periapical lesions, pain on percussion and/or palpation, and radiographically deficient endodontics. The treatment for the elimination of *E. faecalis* consists in the instrumentation and the irrigation with NaOCl. Conclusions: In dentistry, continuous research on *E. faecalis* and its elimination from the oral cavity may improve results in root canal treatments.

Keywords: *E. faecalis*, diagnosis, treatment, epidemiology, clinical manifestations

1. Introduction
Enterococcus faecalis is a commensal bacterium that is generally found in the human oral cavity, digestive system, and the vaginal mucosa [1]. The prevalence of this gram-positive coccus is 60% in caries and 70% in endodontic infections [2]. This microorganism invades the dentinal tubules, forms biofilms, survives in an environment with few nutrients and is resistant to extreme environmental challenges. It is difficult to completely eliminate *E. faecalis* with chemomechanical instrumentation or intraconduct medication [3]. The most effective treatment against pathogens that cause endodontic infection microorganisms seems to be a combination of photodynamic therapy (PDT) and 5.25% Sodium hypochlorite (NaOCl) [4].
Failure of endodontic treatments is due to the presence of bacteria in the system of root canals and periradicular tissues. The role of *E. faecalis* in failure of endodontic treatment is polemic. Therefore, the objective of this article is to discuss the epidemiology, diagnosis, clinical manifestations and treatment for *E. faecalis.*

2. Materials and methods
In this article, important literature on the epidemiology, diagnosis, clinical manifestations and treatment of *E. faecalis* infection is reviewed through a comprehensive search of the PubMed, Web of Science and Google Scholar databases. To carry out the search, the following keywords were used: *E. faecalis*, diagnosis, root canal treatment, epidemiology, clinical manifestations.

3. Results & Discussion
3.1 Epidemiology
E. faecalis is prevalently found in human stool at 105-107 colony-forming units/g. The concentration varies with the geographical location and diet of the host. Stool samples from individuals from England, Scotland and the United States have lower concentrations of Enterococcus compared to samples from subjects from India, Japan and Uganda, who adopt a majority vegetarian diet [1].

A Mexican study at the National Institute of Pediatrics during 2016 revealed that amongst 149 antibiogram cultures, 68.5% were positive for *E. faecalis* and 31.5% for *Enterococus faecium* [5]. In the United States, *E. faecalis* was the fourth most common cause of nosocomial bacteremia [6]. The study on the diversity of genotypes of *E. faecalis* in multiple oral sites associated with endodontic failure through the polymerase chain reaction; observed 7 different genotypes of *E. faecalis* in different subjects and oral sites associated with endodontic failure [7]. In an Iranian study on 70 samples from canals of root-filled teeth from patients with apical periodontitis, *E. faecalis* was isolated from 22 samples; 91% of the isolates were susceptible to ampicillin and 73% formed biofilms, which seemed to be an important virulence factor [8]. Virulence factors converged in *E. faecalis* and *E. faecium*, which have been isolated in nosocomial infections, including resistance to antibiotics, extracellular proteins, genetic and extrachromosomal elements, cell wall components, biofilm formation, adhesion factors and colonization factor, such as bacteriocin [9]. In 2018, a study determined the effect of MTAD (mixture of Doxycycline, citric acid and a detergent) on the expression of the virulence factors of *E. faecalis* considering the role of Guttapercha/AH26 or Resilon/Real Seal SE. MTAD could inhibit the expression of some known virulence factors of *E. faecalis*. This may partly explain some of the mechanisms of antimicrobial efficacy of MTAD against this resistant microorganism, which is known as one of the main causes of failure of root canal treatment [10]. The survival of *E. faecalis* and the formation of biofilms under stress due to starvation of glucose can be attributed to an increase in the hydrophobicity of the cell surface and to the positive regulation of some genes involved in the response to stress and the formation of biofilms. These characteristics explain why *E. faecalis* is viable for a long time in an environment lacking in energy and why it is often isolated from persistently infected root canals [11].

The oral cavity can be a reservoir for virulent strains of *E. faecalis* that have traits of resistance to antibiotics and, at the same time, different biofilm formation capacities [12].

E. faecalis in endodontics is related to endodontic failure due to the ability to produce biofilms and to remain viable for a long time in root canals, maintaining root canal infection and periradicular lesion.

3.2 Diagnosis

Microbiological culture techniques have revealed that *E. faecalis* is the most common isolate in persistent infections or those associated with the failure of endodontic treatment [13].

Apart from the combination of microbiological culture techniques and the analytical profile index for biochemical identification [18], molecular biology techniques are common for diagnosis. For example, DNA extracted from root canals samples was PCR screened for the 16S rDNA of all the bacteria present in a number of root canals and was amplified by PCR and separated by denaturing gradient gel electrophoresis, generating patterns of bands representative of the structure of the microbiota. A specific PCR of the species was also carried out for the detection of *E. faecalis* [14].

Studies show that transmission of *E. faecalis* between patients may occur via the hands of healthcare personnel or after direct inoculation via medical devices, urinary or vascular catheters [5]. A simple, inexpensive and equipment-free colorimetric assay based on Bacterial Inhibition of GOX-catalyzed reaction (BIGR) has been successfully developed for the rapid detection of bacteria, achieving the detection of broad-spectrum bacteria such as *Escherichia coli, Staphylococcus aureus, E. faecalis, Streptococcus mutans* [15]. *E. faecalis* causes root canal treatment failure because of entry via microfiltration in defective restorations, direct exposure to the pulp and through the gingival sulcus [16]. Gene Capture Inc. developed a portable *in vitro* diagnostic platform that enables the rapid detection of seven common pathogens, including *E. faecalis*, from crude fragmented cell extracts [17]. A Russian study on 30,504 blood samples used a combination of culture, commercial biochemical API test systems and mass spectrometry for species identification [18]. If you do not have sophisticated rapid diagnostic methods, such as mass spectrometry, fluorescent in situ hybridization (FISH) offers an option for rapid differentiation for laboratories in resource-limited settings [19]. For the detection of antibiotic resistance, antibiograms obtained from the disc diffusion test are the gold standard [18].

In summary, the most outstanding methods for the diagnosis of *E. faecalis*. Include traditional microbiological cultures and biochemical API tests, novel BIGR-based colorymetry, and practical molecular biological techniques such as the Gene Capture and the FISH systems.

3.3 Clinical manifestations

The most frequent clinical manifestations are bronchopneumonia and other acute respiratory infections with bacteremia (21.5%), urinary tract infection, soft tissue infection (14.7%), bacteremia without focus (11.2%), and surgical wound infection (10.3%). Enterococci showed a high resistance *in vitro* to most of the antibiotics tested [20]. Apart from virulence genes involved in adherence, biofilm formation and host tissue invation [12], patient status and characteristics were important for pathogenic *E. faecalis* presence (ref missing). In endodontics, after a root canal treatment, restoration of the dental organ is important, because studies show that the interface of the dentin sealant undergoes degradation, which allows the proliferation of microbial biofilms, leading to the failure of the treatment of conduits. Saliva and cariogenic bacteria showed activities similar to esterases [21]. *E. faecalis* possesses a degradation activity similar to esterase towards the restoration materials of the dental methacrylate resin, which could accelerate the degradation of the interface of the dentin methacrylate resin, increasing the proliferation and penetration of bacterial biofilms in the system of root canals [21]. *E. faecalis* ex vivo formed biofilms and colonized dentin under stress due to alkaline and glucose starvation, but its ability to invade the dentin tubules decreased significantly [22]. One of the most important clinical characteristics of this bacterium is the capacity of production and colonization, as well as the production of biofilm. Although the most frequent clinical manifestation is bronchopneumonia. In endodontics, when the patient returns with pain after treatment, it is mainly due to the presence of bacteria, including *E. faecalis*.

3.4 Treatment

The treatment to eliminate *E. faecalis* from the root canals depends on the disinfection, the irrigating substances and the way in which they are administered and activated, although these have a limited capacity to reach all parts of the root canal system [23]. The use of a good aseptic technique, the increase of apical preparation sizes and the use of sodium hypochlorite are currently the most effective methods to combat *E. faecalis* within the systems of root canals of the teeth [24]. NaOCl in passive ultrasonic irrigation helps in chemo- mechanical preparation, contributing significantly to the reduction of microbial content during root canal treatment [25]. An *in vitro* study confirmed the high potential of photodynamic therapy (PDT) in the elimination of *E. faecalis* biofilm.

PDT not toxic for periapical tissues, while it is useful against endodontic pathogens as it effectively attacks the biofilm organization of microorganisms [26, 28]. The association of PDT with hypochlorite and reciprocal instrumentation provides an effective elimination of *E. faecalis* [27]. Er, Cr: YSGG laser was the most efficient tool in the eradication of biofilms from *E. faecalis* and *Candida albicans* [23]. The complementary PDT in combination with an irrigation protocol with NaOCl and chlorhexidine (CHX) was an effective method for the reduction of the bacterial biofilm within the root canals of the extracted teeth [27]. Photoactivated disinfection can be a useful complement to mechanical and antimicrobial agents to eliminate endopathogenic microorganisms in secondary or persistent endodontic infection [28]. A combination of calcium hydroxide and 2% CHX slightly improved microbial eradication rates [20]. The effectiveness of different disinfection protocols in the reduction of bacteria in an *E. faecalis* biofilm has been compared in teeth with large root canals. The most effective method for disinfecting broad root canals is with instrumentation with files 60-90 and irrigation with 2.25% NaOCl [29]. The effectiveness against *E. faecalis* was compared using CHX and NaOCl, concluding that NaOCl may be superior to CHX [30]. Studies have evaluated the effectiveness of experimental solutions containing silver and zinc nanoparticles and conventional endodontic irrigators which are effective against *E. faecalis* [31]. Endodontic sealants play an important role in the eradication of bacteria, reducing the failure of endodontic treatment [32]. The impact of calcium hydroxide on *E. faecalis* biofilms inside the root canal *in vitro* has been studied, it was observed that the biofilm is formed even in the presence of calcium hydroxide, in most cases, but that the drug it helps to reduce bacteria in the duct and, therefore, slows the formation of biofilm (33). Intraconduct medication is recommended as essential and equated in importance with adequate biomechanical instrumentation [34]. A new bioactive endodontic sealer with a strong antibiofilm activity was developed, against *E. faecalis* biofilm and high levels of Ca and P ion release for remineralization [35]. The obturation technique with gutta-percha stem showed a shorter microfiltration time of *E. faecalis* compared to cold lateral and vertical condensation systems with continuous heat wave [36]. The correlation between the molecular characteristics and the pharmacological resistance of *E. faecalis* isolates from local hospitals was investigated, detecting a high resistance to certain common antibiotics and the clonal propagation between isolates of patients in different hospital wards [36].

For the treatment, instrumentation and irrigation with NaOCl combined with the laser application resulted in a comparable bacterial reduction in the elimination of *E. faecalis* [37]. It has been shown that ultrasonic irrigation with sodium hypochlorite contributes to the reduction of microbial content. Endodontic sealants have a great role in this treatment, helping to eradicate bacteria from the duct system. The calcium hydroxide used in this type of treatment will not diminish the biofilm formation of this bacterium, but it helps to diminish pathogens associated with it, slowing the formation of biofilm.

4. Conclusions

E. faecalis in endodontics is related to endodontic failure due to the ability to remain viable for a long time in root canals, maintaining the infection within the root canals and the periradicular lesion. Different isolation techniques can be effective to diagnose *E. faecalis* among the most outstanding are: microbiological cultures, PCR, BIGR-based colorimetric tests, the Gene Capture system, spectrometry, and FISH system. When the patient returns with pain after treatment, it is mainly due to the presence of *E. faecalis*. Fortunately, with PDT along with sodium hypochlorite irrigation, instrumentation, and adequate restoration, it is the best technique for effective in the presence of *E. faecalis*.

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