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Microbial Influence on the Development of Periapical Disease- Literature Review

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Abstract: *Periapical disease caused by the colonization of microrganisms in the root canal system. Microbiology implicated in endodontic disease is diverse and varied. Mircobial testing of periapical lesions can be traced back to 1890. The changes in balance of the microbiota along with other factors host resistance and viral infection can also affect the periapical disease. The various microbiology involved in periapical disease is reviewed in this article.More research needs to conducted on the bacteria involved and their interactions in order to improve the diagnosis and treatment of periapical lesions*.

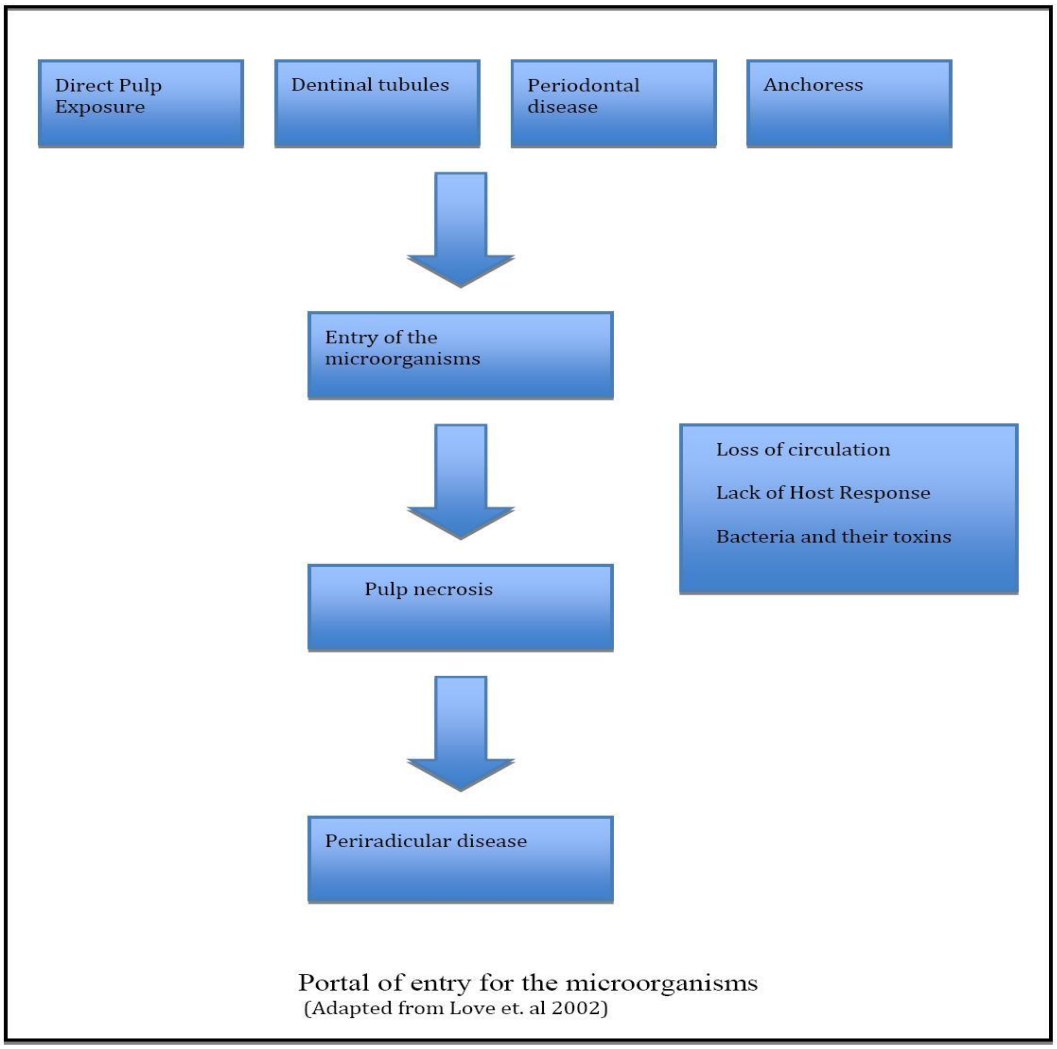
I. Introduction

Most Periapical pathologies are caused by bacterial invasion into the underlying pulp, most commonly occurring through the exposed dentinal tubules due to caries or traumatic injuries.The microbial testing of apical periodontis can be traced back to 1890[1]. W.D Miller (1890) demonstrated cocciand rods invaded the dentinal tubules of carious and non-carious teeth. Pulpal inflammation takes place due to the interactions between the bacteria and their toxins with the defense mechanism of the pulp[1].

In 1965 Kakehashi et al established an important relation between microorganisms and endodontic pathosis. They found that exposing dental pulp to oral environment in rats with normal flora caused the development of periapicalpathosis, while the gnotobiotic free animals on the other hand showed minimal inflammation [2]. The study highlighted the importance of microorganisms in the development of periapicalpathosis. The use of germ-free animals mimics the development of disease of the process but in reality the existence of gnotobiotic animals is questionable.

Moller (1981) studied the difference in apical response of necrotic pulps after they contaminated aseptically or with oral micro flora in monkeys. They found sterile pulps did not develop apical periodontis where as an infected pulp canal developed apical periodontis[3].This study helped dispel the common belief in those days that pulpal necrosis caused apical periodontis. It also provided a key to future investigators by proving that endodontic pathogens are Polymicrobial in nature and they lived in communities rather than single species.The use of animal models however raises ethical questions.Human teeth are similar anatomically to certain monkey teeth thus in studies where other animal models are used the results need to be interpreted with care[4].

Portal of entry for microorganisms



Portal of entry for the microorganisms
(Adapted from Love et. al 2002)

Dental caries is one of the most common portals of entry for microorganisms. The dentinal tubules usually vary between 0.9µm-2.5µm where as the microorganisms such as streptococci vary between 0.5-07 µm thus allowing unrestricted entry of bacteria[1].In the case of trauma or in those cases where the cementum is lost the dentinal tubules are exposed and serve as direct pathway for bacteria. The dentinal tubules are wider near the pulp than the dentino-enamel junction or the cement-enamel junction thus the potential for pulpal irritation may increase with the increase of dentine removal[4] . The bacterial movement through the tubules may be inhibited by dentinal fluid, odontoblastic processes and mineralized crystals and salivary immunoglobulin[15].

Nagaoka et al (1995) studied the difference in bacterial invasion in dentinal tubules between vital and non-vital teeth in 19 bilateral molars. They found that vital teeth were more resistant to bacterial invasion as compared to non-vital teeth[5]. The odontoblastic processes in the vital teeth may act as physical barriers thus inhibiting the bacteria. In non-vital teeth there are no such physical barriers thus making bacterial invasion easier. The antibodies present in the dentinal fluid in vital teeth protect dental pulp. The same study reported the rate of bacterial invasion was directly proportional with the passage of time[5].

Periodontal disease involving the apex of the tooth may cause pulpal necrosis thus allowing the bacteria to penetrate through lateral tubules and furcations[6]. The structural changes may take place in the cementum as a result of contact with crevicular fluid and bacterial enzymes increasing its bacterial permeability. Routine scaling causes stripping away of the cementum allowing easy bacterial penetration [4].

Anchoress is the chronic inflammation of the pulpal tissue by the blood borne bacteria. Some studies have found localized blood borne bacteria in inflamed canals of animals.However, this seems unlikely to occur in empty canals. Anchoress as a mechanism of pulpal and periradicular infections in humans seems unlikely[6].

Microbial flora of the root canals

Gram-positive cocci	Gram-positive rods	Gram-negative cocci	Gram-negative rod
Streptococcus *S.anginosus* *S.sanguinis* *S.mitis* *S.mutans*	Actinomyces *A.israeli* *A. naeslundii*	Capnocytophaga *C.orchea* *C.sputigena*	Fusobacterium
Enterococcus Faecalis	Eubacterium *E.alactolyticum* *E.lentum* *E.nodatum* *E.timidum*	*Veillonela parvula*	Prevotella *P.intermedia* *P.melaninogenica* *P.denticola* *P.buccae* *P.buccalis* *P.oralis*
Peptostreptococcus *P.anaerobius*	Propionibacterium *P.propinicum* *P.granulosum*	Campylobacter *C.rectus* *C.curvus*	Prophyromonas *P.gingivalis* *P.endodontalis*
Parvimonas *P.micra*	*Lactobacillus.spp*		*Bacteriodes gracalis*

Bacterial species commonly found in infected canals

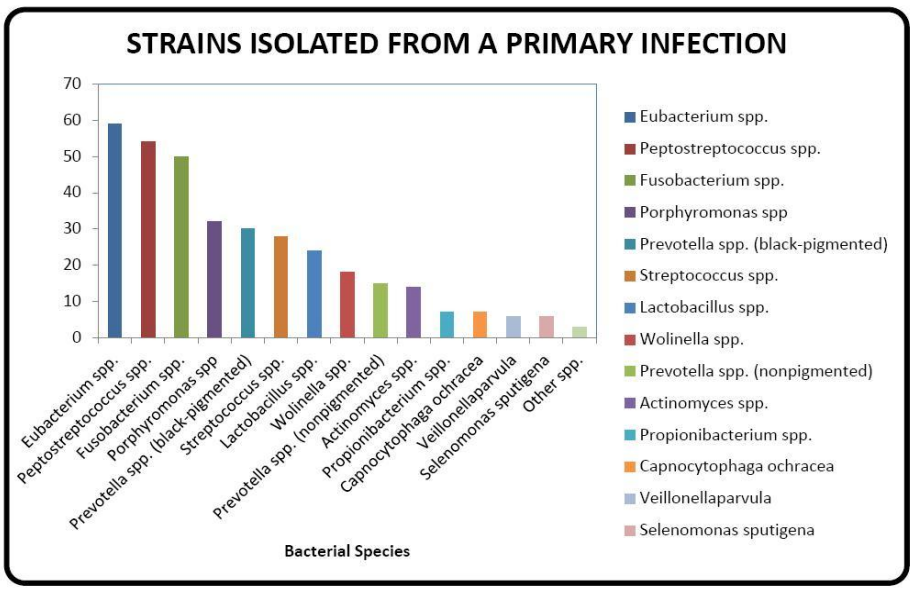
Adapted from Fouad AF. Endodontic Microbiology: John Wiley & Sons, 2009

Once the bacteria enters canal, it must utilize the available nutrient, cooperate or contend with other bacteria, battle the host defense mechanism before they can replicate and colonize the canal[4].

The oral cavity consists of more than 500 different types of microorganisms. Experimental evidence depicts that mono infection shows minimal periradicular infection and only certain bacteria like pseudomonas and enterococci are capable of surviving as single strain infections. Most periradicular pathologies occur as a result of 3-4 bacterial strains. [7]

Fabricus et al. (1982) inoculated sterile canals with 8 different bacterial species they found that mixed bacterial infections caused apical periodontis. The most pronounced lesions developed by the combination of all the eight strains[8]. Most endodontic infections are as a result of poly-microbial infections.However individual species may play different roles and dominate a particular period[9] .

Biofilms have been observed in parts of the root canal system.However, exact condition under which they exist is not known. They provide a safe a habitat for bacteria by hampering the effect of antimicrobials and host response, whilst allowing bacterial interactions to take place. The exact role of the of a biofilm in a poly-microbial environment like the root canal hasn't been completely investigated[4].



Graphical representation of Bacterial species isolated from primary endodontic infections.

Adapted from Sundqvist G, 1992. Oral Microbiol Immunol 7:257.

II. Factors Affecting Influencing Bacterial Survival

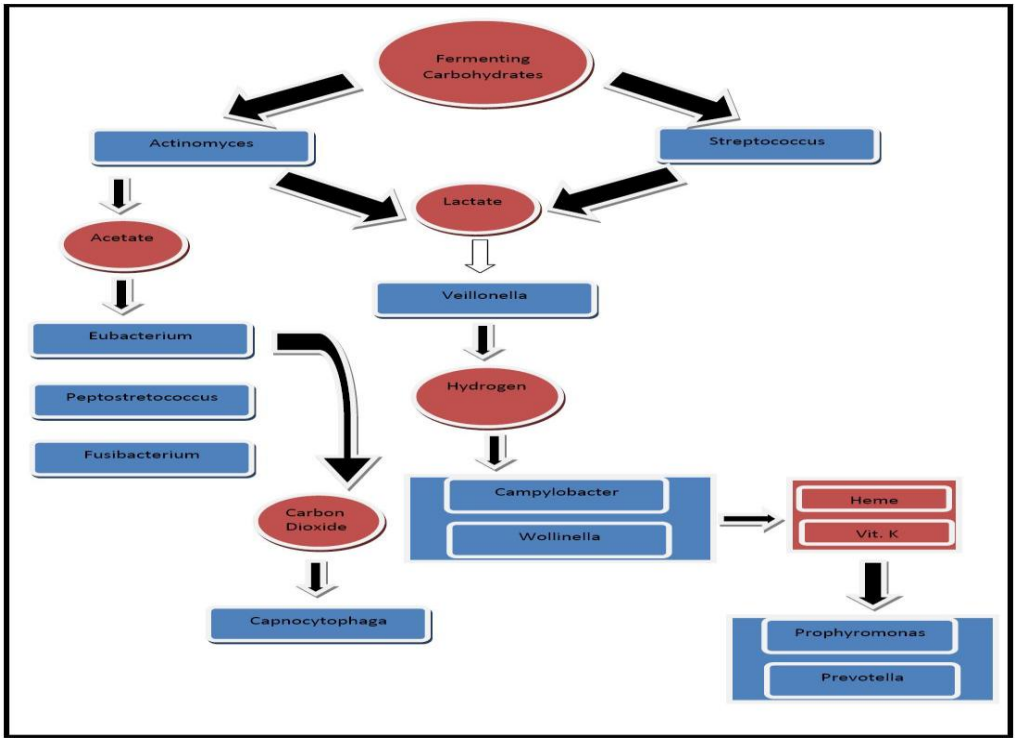
Effect of reduction -oxygen potential on the root canal environment

Abou –Rasset al. (1998) investigated the microbiology in closed periapical lesions and found 63.6% of the bacteria were obligate anaerobes while only 36.4 %were facultative anaerobes[10]. This experiment supports the concept of an endodontic milieu. The consumption of oxygen and the production of hydrogen and carbon dioxide by the early colonizers favors the growth of the anaerobic organisms [9]. The oxygen tension in necrotic canals is lowered thus reducing the redox potential[9].

As early as 1984, W.D. Miller observed that different bacteria were present in coronal middle and apical region due to the limitations in his sampling and culturing techniques although these observations couldn't be verified[9] .In another study, where the apical 5mm of a carious exposed canal was cultured, 68% bacteria were strict anaerobes[11].The bacterial flora in the apical third differs from the rest of the canal due to the difference in availability of oxygen and nutrients [9]. This is perhaps one of the reasons for the dominance of obligate anaerobes in the apical region. The apical third of the root canal is considered to one of the critical zone of the canal because the bacteria in apical third are in close contacts with the periradicular tissues through the apical foramen and accessory canals. In younger teeth the communication is wider thus the bacteria receive a better nutritional supply causing a more pronounced infection. The host defenses against apical pathogens are limited due to lack of circulation in the necrotic pulp[4].

Nutrition as an ecological driver

The type of nutrition available affects the growth of bacteria.The type of bacteria present will also vary depending upon on the stage of the disease[9]. The degenerating connective tissue and dentinal tubule contents are sources for nutrition for the micro biota. The exogenous nutrients such as carbohydrates affect the bacterial ecology in the coronal aspect of the canal and endogenous nutrients like glycoprotein and proteins encourage the growth of anaerobic bacteria. The bacteria capable of fermenting amino acids and peptides from the main canal are more predominant in the middle and apical third[12]. The root canal environment promotes anaerobic bacteria that are capable of fermenting amino acids and peptides as sources of energy and restricting the growth of bacteria that utilize carbohydrates as a source of energy[9]. This explains the dominance of facultative anaerobes in the coronal third of the canal and obligate anaerobes in the apical third of the canal. The decrease in direct contact with oral cavity limits the amount of carbohydrate available thus limiting the opportunity for survival for facultative anaerobes[13]. There is a transition that takes place in the canal during the stages of the disease from a period of nutritional abundance to a period of scarcity due to the difference in availability of carbohydrates causing the dominance of strict anaerobes[9].



Diagrammatic representation of bacterial interrelationships
Adapted from Sundqvist et al. 1992

Bacterial interrelationships

The growth of one bacterial species may depend on other bacteria to supply the essential nutrients for their survival. The antagonistic relationship exists amongst bacteria as well; some products metabolized by species may be toxic to other bacteria. Some gram -positive and gram-negative bacteria produce bacterial toxins like bacteriocins that are bacteriostatic or bactericidal to closely related species. The production of bacteriocins causes a selective advantage[4].

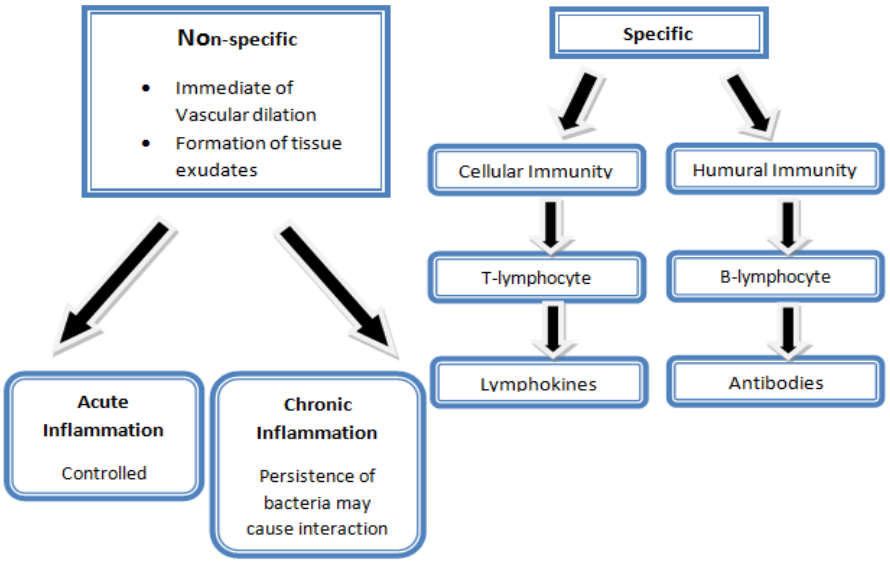
Sundqvist carried out a study on 65 single rooted necrotic pulps to study bacterial relationships[1214]. Bacterial cultures are more effective in evaluating the bacterial correlation as the growth of mixed bacterial populations depends upon the food chain in which one species provides essential nutrients for the survival other members. The culturing method depicts the quantity of bacteria isolated, allowing easy correlations to be made[4].

Host defense factors

Gram-negative bacteria like black-pigmented bacteriodes contain endotoxins that will attract neutrophils by chemotaxis to the periapical area. The neutrophils cause phagocytosis of the bacteria as well as release of leukutrines and prostaglandins, attracting more macrophages to site[7]

Specific and non-specific defense reactions have been implicated in the development and maintenance of periradicular lesion. The mechanisms vary minutely depending upon the microorganism present. Non-specific response is mediated by direct action of the microorganisms and their products on the immune system that causes phagocytosis of the microorganisms and confines them in the root canal[6]. Polymicrobial infection of the dental pulp induces an inflammatory response that causes bone destruction of the periradicular tissues. The immune responses involved in the pathogenesis of periapical lesions are complex .The main areas of difficulties are experienced in localizing the immunoglobulin's causing technical difficulties[15].

Some investigators think the host response acts harmfully against the irritants by causing destruction. The macrophages activate osteoclasts that cause bone resorbtion. This can be argued as this self-inflicted destruction prevents the spread of the infection to the other parts of the body[4].



Schematic diagram of immune reaction
Adapted from Color and Atlas of ENDODONTICS by Stock et al., 1995

III. Clinical Significance Associated With The Microbiology

Acute apical periodontis occurs as result of the immediate response of the host to the extension of the pulpal inflammation to the periradicular tissues. The bacteria in an acute lesion are characterized by increased metabolic activity and unregulated metabolism[4]. The advance of microorganisms to the apex may exacerbate a chronic lesion with reoccurrence of signs and symptoms. The bacteria are only able to exuberate the lesion when they are high in number and have the ability to overwhelm the local host response[4]. The body's main role is to prevent the spread of the infection thus forming an encapsulated fibrotic barrier (abscess).Antibiotics are indicated at this stage. Failure to control the spread of infection may result in a formation of a sinus tract[4] . Chronic lesions on the other hand are produced by bacteria in the dormant state and multiply at a very slow rate [4]. Existence of bacteria in the chronic lesions has been controversial.Histological samples failed to depict the presence of bacteria[6] whereas immunocytochemical methods have identified bacteria associated with chronic lesions[6].The use of molecular technique has improved the detection of bacteria associated with chronic lesions[4].

The microbiology symptomatic and asymptomatic tooth differs; studies have correlated the presence of certain symptoms with the presence of bacteria[4].

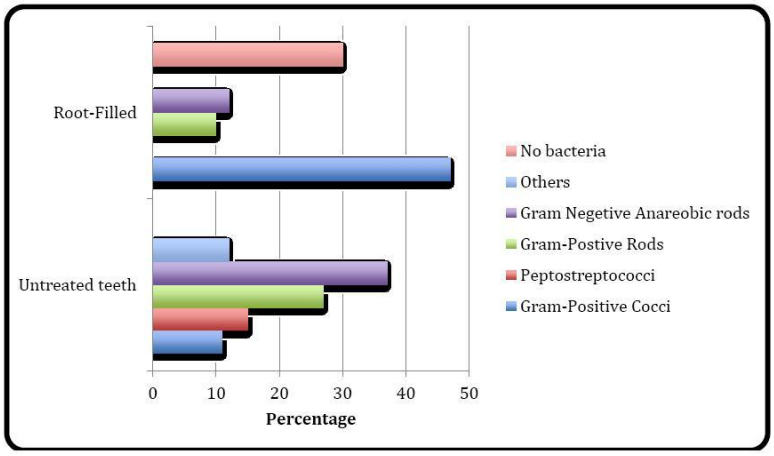
Most studies are in consort regarding the implication of anaerobic bacteria with acute phase of the disease. Different studies have found varied percentages of bacterial populations because of the difficulty to grow the bacteria as well as low sensitivity of the culture. Most bacteria that are found are anaerobic and require a pre-reduced culture medium making detection difficult. There have been studies depicting difference in bacterial populations related to different geographic areas as well[4].

IV. Microbiology Of Root Filled Canals

Periapical pathologies associated with root filled teeth persist for several years before they are accidentally discovered. The micro flora between unfilled canals and filled canals differs considerably[16]. Unfilled canals are characterized by poly-microbial microorganisms with a predominance of gram negative anaerobes, while filled canals are dominated by gram positive facultative and obligate anaerobes. In one study, complete periapical healing occurred in canals.Ninety eight percent of canals with a negative culture healed, whereas only 68% canals with positive cultures healed at the time of obturation, thus indicating the presence of an infection is more likely to cause failure to heal[16].

Most studies have found the predominance of Enterococcus,Eubacterium, Streptococcus, Fusibacterium and Prevotella[4]. Actinomyces have been implicated with extraradicular disease in cases of asymptomatic root treated teeth and Enterococci and Candida are opportunistic pathogens that are associated with interadicular disease[13]. Extraradicular microorganism like Actinomyces are inaccessible to endodontic disinfection, may establish periradicular disease after evading the body's immune response. Intradicular infections are the most common causes of persistent of infections.The reasons include lack of coronal seal, missed canal insufficient debridement and resistant bacteria[4].

Molander et al. conducted a study on 100 root filled teeth with apical periodontis and 20 without any periapical pathology. Molander concluded that the micro flora of an obturated canal differed from an untreated canal quantitatively as well as qualitatively[17]. Enterococci were most frequently implicated in failed root canals these findings were confirmed by another study carried out by Siquera[419]. The species that persists in root filled teeth requires a range of properties to survive; they have to have ability to with stand high PH and antimicrobial treatments. The bacteria need to with stand high periods of starvations and utilize periapical transudation as a form of nutritional supply[9]. Microbiology of poorly treated canals was similar to unfilled canals and was poly-microbial in nature[13] .



Comparison of (%) Microbial Composition between Untreated teeth (Sundqvist 1992) and Root- filled teeth (Molander et al.1998).
Adapted from Fouad AF. Endodontic Microbiology: John Wiley & Sons, 2009

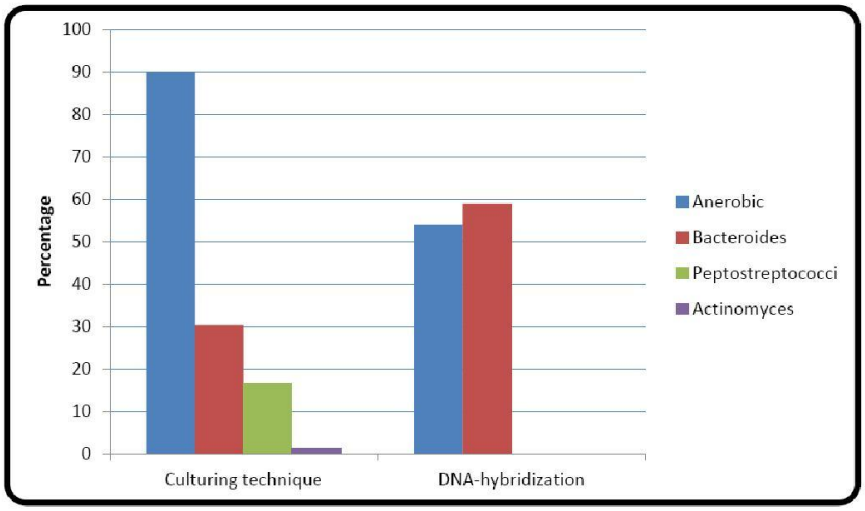
V. Identification Of The Bacteria

Most of the present knowledge is based on microbial culturing techniques. The culturing technique has provided important information regarding the correlation of bacteria with clinical situation and the effect of the various treatments on bacterial elimination[418].

One of the major disadvantages of the culturing technique is that the artificial media cannot be used to cultivate many of the microorganisms because of the difference in the physiologic and nutritional demands[4]. Culturing technique requires a strict protocol for the transportation of the specimen as well as immediate processing, though these precautions may be taken only the few organisms survive. Phenotype identification as

used in culturing technique is dependent on the physical and biochemical properties of the microorganism at times this may lead to misidentification of the bacteria. [4]

The newer molecular biology techniques are able to identify rare and uncultivable, uncharacterized bacteria. These techniques have helped identify BacteriodesForsythus, which have never been identified with endodontic infections before[19]. Culturing techniques showed the predominance of gram-negative bacteria however the molecular techniques have shown an increase presence of gram-positive bacteria [4].The Polymerase Chain Reaction (PCR) has some disadvantages.It not only identifies the active bacteria but also the bacteria that entered the canal and did not survive. This is because the PCR technology relies on reconization of gene sequence; the DNA still persists after the death of bacteria causing the identification[9].



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Comparing the % microorganism detected via Culturing (Sundqvist et. al, 1989) vs. DNA hybridization (Siqueira et.al ,2001)

VI. Effect Of Bacteria On The Management Of Periapical Disease.

Endodontic therapy aims at the complete elimination of the bacteria before obturation. The use of biomechanical preparation along with antimicrobial therapy helps eliminate the bacteria from the canal[16]. The preparation of flared root canal with minimal transportation of the canal allows maximum disinfection of the root canal. Differences in bacterial invasion between the apical third and coronal aspect suggests the moderate apical preparation because of minimal bacterial invasion in the area and heavily infected cervical and mid-root should be prepared with a coronal flare[4].

Difficulties are encountered in the elimination of bacteria because most canal have several lateral and accessory canals forming hospitable environments for the bacteria[4].In an abscess, bacteria penetrate the apex, making bacteria present on the apex difficult to reach by intracanal medicaments[4]. Biofilms increase the resistance of the bacteria to antimicrobial agents. Some bacteria are able to resist extremely harsh conditions. Gram-positive bacteria are better survivors compared to gram-negative bacteria[4].

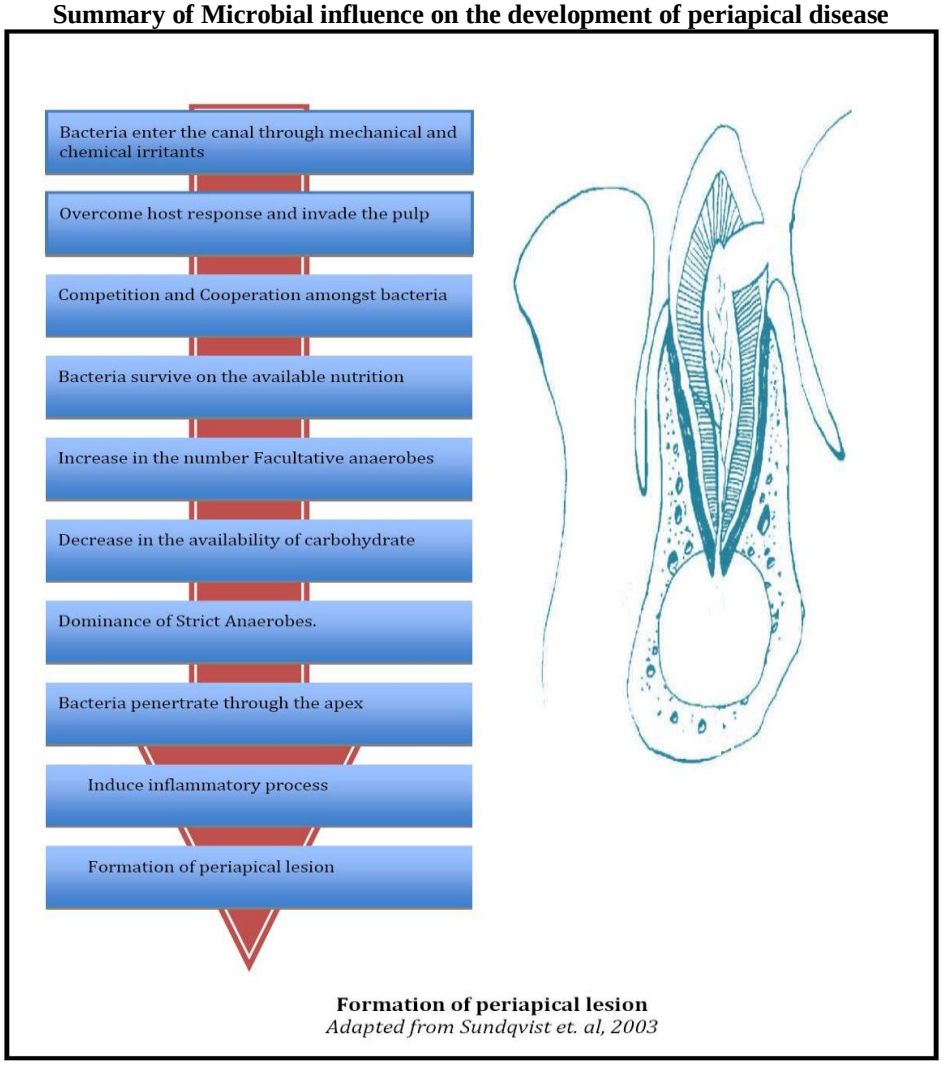
VII. Conclusion

The microorganisms associated with endodontic infections are diverse and varied. They include several cultivable and some uncultivated pathogens. Bacteria have a crucial role in the pathogenesis of endodontic lesions[16].

A diabetic host may be affected by more virulent bacteria, further compromising the host response causing delayed healing[4]. Contrary to common belief, T-cell deficiency as in the case HIV does not affect the ability of the host to mount an effective response against endodontic infections[4].

Molecular methods may improve the present knowledge, however the changing taxonomic classification and names may prove to be confusing. Studies have found fungi and virus associated with endodontic infections; the exact aetiology in the formation of periapical pathology needs to be clarified[4].

Summary of Microbial influence on the development of periapical disease



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