Understanding failures is a key to success

P.N. Ramachandran Nair

A tropical paradise

The human mouth with a balmy temperature of 37°C and a steady influx of food and moisture is a *tropicl paradise* teeming with life and consisting of trillions of microorganisms belonging to bacteria, fungi and protozoa. However, when a baby is born, its mouth is sterile. Within seconds after birth the infant's mouth is inoculated with a sample of microorganisms from the mother's body surface, mouth and environmental surroundings. Subsequently a busy and continuous procession of objects loaded with microorganisms come in and out or pass through the baby's mouth (such as its own fingers, food, and anything that can be imagined of) and will thus increase the variety and numerical load of the oral flora until an equilibrium is achieved. However, the body's mouth remains free of those organism that belong toan important bacterial species of adult human mouth, namely of *Streptococcus mutans*. These sphere shaped bacteria, discovered in 1920, are found only in the human mouth. They are highly adapted to enamel surface for perching there so that *Streptococcus mutans* are unable to establish themselves in a toothless human mouth. Further, they live entirely on sugar. *Streptococcus mutans* start colonising the baby's mouth during the period of tooth eruption. By age three, most infants have a full set of primary teeth and an oral microbial community estimated to be composed of 200 to 400 species. While most of these microbes are simple residents, some of them can be harmful to our health and general well being. Many oral diseases result from the constant conflict between those microbes and our body. The widespread tooth decay (caries) and gum rotting (periodontitis) are diseases of microbial origin. These and other tooth and gum diseases are the consequences of a series of biological chain reactions that are initated by oral microbial colonisation.

P.N. Ramachandran Nair Ph. D.
Department of Oral Structural Biology, Centre of Dental and Oral Medicine, University of Zurich, CH-8028 Zurich, Switzerland.
Phone: +41-1-634 31 42.
Fax: +41-1-312 32 81.
E-mail: nair@swissonline.ch.

Fossilised communities under climax vegetation

The starting point of the chain reaction is the establishment of microbial communities on tooth surfaces, fissures and gum lines. Bacteria attach themselves to those sites and rapidly build themselves into colonies. Even after few hours following a thorough brushing, a tooth is swarming with spheroid and filamentous bacteria. After a day, the teeth will be shrouded with a carpet of microbial colonisers that give a creamy yellow colouration to the teeth and a slimy feeling when touched with the tongue. This is a type of biofilm commonly known as plaque (figure 1).If undisturbed, the plaque can grow into several mm of thickness. Such old plaques on teeth and gum lines are also known as dental calculus, which is nothing but a succession of fossilised ecological communities of microbes. Each community of organisms having successively been replaced by its predecessors until an equilibrium of climax vegetation is established on top.

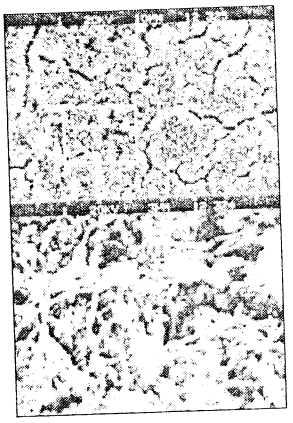

Figure 1: A scanning electron microscopic view of a bacterial plaque on human tooth surface (a). The rectangular demarcated area in (a) is magnified in (b). Note the mixed microbial flora consisting of cocci (CC), rods (RD) and filamentous (FI) organisms. Magnifications: a x 1'500, b x 6'000

Healthy human Tooth

In order to appreciate our story of chain reaction in the mouth, it is advantageous at this stage to understand the basic architecture of the human tooth. The bulk of our teeth is made up of dentine, the rigid ivory like material which encapsultes an inner soft connective tissue called dental pulp. Human dentine is covered on its root region by cement and the crown region by a harder substance called enamel. Enamel is the hardest, highlymineralised (96%) and

extremely conherent substance in the human body. It is essentially a tightly packed mass of crystalline calcium phosphate which can be easily dissolved in an acidic solution. The inner soft core of teeth, the pulp, is rich in blood vessels and nerves and is essentially responsible for the production and nourishing of dentine. The dentine is penetrated by millions of tiny canals or tubules which radiate outward from the pulp to the periphery of dentine. In a healthy tooth the dentinal tubules contain the long arms or processes of the cells called odontoblasts which are bathed in tissue fluid. This architecture of dentine has much to do with the progression of the chain reaction in the mouth.

'Worm-tooth' has nothing to do with worms

The next stage in the chain reaction is the formation of holes in tooth enamel and a gradual decaying of the tooth substance, what the oral health professionals call rampant caries. Even today, in almost all traditional world communities, a carious tooth is referred to as worm-tooth based on the earlier belief that tooth decay is caused by worm infestation. However, researchers have long reduced the 'tooth worms' to the unicellular size of microorganisms and elaborated the process of dental caries into the acidogenic concept. The current view of tooth decay can be summed up as follows: Human food is rich in various nutrients particularly carbohydrates. The dietary carbohydrates are taken up by the plaque bacteria, breaking them down to simple sugars which they use in turn for their nourishment. Some bacteria, particularly the *Streptococcus mutans* live entirely on common sugar. Bacteria not only metabolise dietary sugars for their growth but also release organic acids as byproducts. It is these acids that destroy tooth enamel as calcium ions dissociate from the enamel crystals and diffuse out into the oral cavity, a process what the researchers call demineralisation that creates holes beneath the plaque covered tooth surface.

Highways if invasion

Once the enamel is destroyed by formation of holes, bacteria invade en mass the underlying dentine. The dentinal tubules inadvertently act as highways for the invaders and oral bacteria can rapidly reach the inner soft core of teeth, the pulp tissue. Unlike enamel and dentine, dental pulp is highly vascularised and innervated soft connective

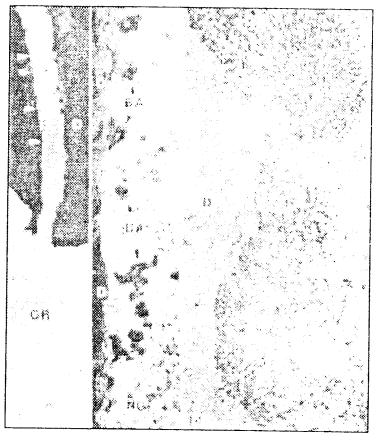

Figure 2: The microbial flora in the root canal of a human tooth with apical periodontitis (GR). The areas in between the upper two and the lower two arrowheads in (a) are magnified in (b,c), respectively. Note the dense bacterial aggregates (BA) sticking (b) to the dentinal (D) wall and also remaining suspended among neutrophilic granulocytes (NG) in the fluid phase of the root canal (c). The NG appear to form a defensive wall against the advancing bacterial front. A transmission electron microscopic view (d) of the pulpo-dentinal interface shows bacterial condensation on the surface of the dentinal wall forming thick layered plaque. Magnifications: a x 46; b x 600; c x 370; d x 2350

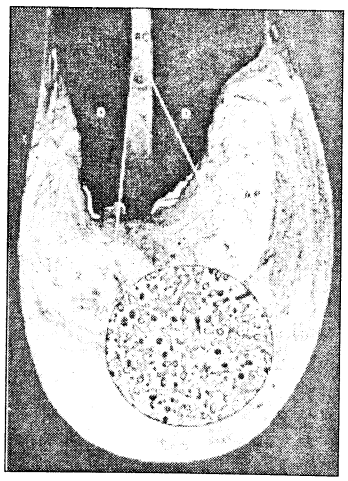

Figure 3: Necrotic root canal (RC) provides a selective habitat for the development of a predominantly anaerobic polymicrobial flora (inset). Apical periodontitis (AP) is body's defence response against the hostile microbes living in the sanctuary of apical root canal. The body defence at periapex is largely successful in preventing microbial invasion into periradicular tissues. D = Dentine. Magnifications: x60, inset 12'000. (Figure reprinted from: Nair P.N.R. Endodontie, 3: 169-179, 1995).

tissue that 'explodes' with an inflammatory response against the incoming waves of foreign invaders. The condition is described as acute pulpitis and the patient will eperience excruciating tooth pain and belatedly seek the help of a dentist for pain relief!

A dynamic encounter

In effect, the tooth pulp gets infected and killed by an autogenous oral microflora. A sample of oral microorganisms consisting of potentially by hundreds of species can gain access into the pulp and root canal (Figure 2). These microbes now face an environment that is considerably different from that of the oral cavity. As for instance, the availability of oxygen in the necrotic pulp is substantially lower and the nutritional resources are protein rich (necrotic tissue) rather than carbohydrate dominated. Such an endodontic environment provides a new ecological habitat that favours the selective growth and establishment of a microflora consisting of species that are oxygen haters (anaerobes). In due course an anaerobes-dominated flora comes to stay in the dead pulp and the root canals (Figure 3). Such a polymicrobial community has collectively several biological and pathogenic properties such as antigenicity, mitogenic activity. chemotaxis, enzymatic histolysis and activation of host cells. The microbial invaders residing in the pulp chamber and the root canals can advace or their toxic and harmful products can leak into the jaw bone through the apical foramen.

In response, the host tissue mounts an array of defence consisting of cells, of intercellular messengers an chemical weapons. Several classes of body cells participate in this defence. Some of them (fibroblasts, osteroblasts) are stationed locally forming part of the physiological architecture of the periapex but give a 'helping hand' in local defence. Some others are embryonic remnants of the tooth germ (epithelial rests of Malasse) which get involved in the local turbulence. But the great majority of the cell participants in apical periodontitis are 'professional' recruits from the defence systems such as neutrophils, lymphocytes, plasma cells and macrophages.

The hostile microbial and the host defence forces join battle at the root up around the apical foramen. This results in the formation of a disease complex known as the apical periodontitis which are inflammatory lesions well barricaded in tough collagenous capsules. In spite of the formidable defence, the body is unable to destroy and eliminate the microbes well entrenched in the sanctuary of the necrotic root canal. The apical periodontitis, therefore, is not self-healing. However, the periapical inflammatory host response, functioning as a defence enclosure, largely prevents the root canal infection from spreading into jaw bones and beyond. This is because the inflammatory cells that congregate around tooth apex are generally able to destroy the microbes that invade beyond the apical foramen. Therefore, early researchers were unable to locate the microbial presence within the inflamed periapical tissue. This lead to the assumption that apical periodontitis is caused not necessarily by microorganisms alone but by othe primary and independent co-factors such as the decomposition products of necrotic pulp. Using the very precise and convincing technique of correlative light and electron microscopy, this author was able to document the disease germs *within teeth*, the strategic location of the germs *in the apical part of the root canal* (Figures 2 & 3) and the structural contiguity of the diseased tissue existing beyond the toodth apex into the jaw bone.

'Treating nerves' that no more exist

The treatment of the disease is intended to eliminate infection from the root canal and to prefgent re-infection by sealing off the root canal from the oral environment. This is done by removal of the dead tissues and the morobial infection using special instruments, rinsing solutions and antibacterial medicaments. Finally, the root canal will be sealed off from the oral cavity with a speically processed and medicated rubber known as the gutta percha. The damaged crown will be restored by an artifical one. The specialists dentists, who treat diseased ental pulps and

root canals ae Endodontists and the procedure is endodontic therapy or root canal treatment. Some dentists erroneously claim such a treatment as 'treating nerves' although the nerves have been dead long before and cannot be treated! A great majority of diseased tooth-apices heals after root canal treatment and the teeth usually become normally functional.

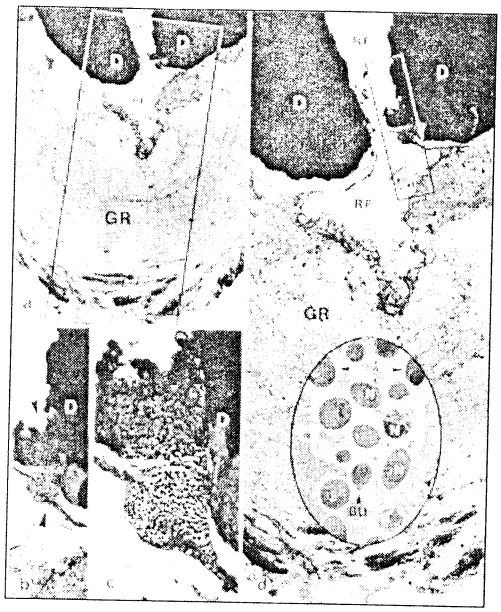

Figure 4: Fungi as a potential etiological agent in the perpetuation of human apical periodontitis lesions even after proper root canal treatment. Figure a is an overview of a root-filled (RF) tooth with a non-healing apical periodontitis lesion (GR). The rectangular demarcated areas in a and d are magnified in d and b, respectively. Note the two microbial clusters (arrowheads in b). They are further magnified in c. The oval inset in d is a transmission electron microscopic view of the organisms. They are about 3-4 um in diameter and reveal a cell wall (CW), nuclei (N) and budding forms (BU). Magnifications: a x 35; c x 330; d x 60; oval inset x 3400. (Figure adapted from Nair P.N.R. et al. Journal of Endodontology, 16: 589-595, 1990

Treatments are not infallible

Even when the highest standards and the most careful procedures are followed, failures still occur and the causes of such failures remained a mystery for several decades. In order to find out the potential causes of root canal treatment failures, the unhealing root tips together with the attached diseased tissue have to be removed by careful aseptic surgery and processed so that the apical portion of the root canals and the diseased tissues can be examined thoroughly under light and electron microscopes. Early investigations of periapical biopsy material have been limited by the use of unsuitable specimens, inappropirate methodology and criteria of analysis that failed to yield relevant etiological information. This author's studies that have taken into account appropriate case selection and investigative methods have helped to identify several etiological agents that contribute to the perpetuation of the disease even after proper root canal treatment (Figure 4). It should be pointed out that there are root canal regions that cannot be cleaned adequately of necrotic tissues and microbial infection with existing instruments, materials and techniques.

This is because root cancel anatomy varies widely among teeth and the canals ramify extensively at the root tip in analogues to a large river forming deltas before entering an ocean. We were able to show that even when the main canals are cleaned, medicated and sealed off, microbes can survive for more than a decade in these ramifications (!) and continue to irritate and inflame the bone beyond the tooth apex.

Further, our studies found that infection persisting in the apical root canal is not the only potential cause of failures after endodontic treatment. Other factors, so far identified, include extraradicular infection, generally in the form of peripical actinomycosis, extuded root cancel filling or other materials that cause a foreign body reaction; a massive accumulation of cholesterol crystals and peripherals cysts.

Beyond failures!

It is obvious that the major goal of the clinical management of pulp and periapex diseased teeth is the elimination of root canal infection and the prevention of reinfection. Therefore, much of the on going research attention in this area centres around resolving those problems. It is, thus, not surprising that instrumentation and root canal sealing techniques, with mere mechanistic view, have come to dominate the debate about treatment. However, basic research pertaining to the actiology and pathogenesis is not only necessary to understand the biological mechanisms behind the disease process but also helpsd to open new unconventional therapeutic avenues. This author had the privilage and opportunity to participate actively in basic research on apical periodontits and to elucidate the cause of its failed treatments. These advances are of considerable benefit to dental patients as they provide a sound biological rationale for succesfull clinical management of the disease.

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