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Dental diseases – are these examples of ecological catastrophes?

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It is important to realize that the oral microflora is very diverse, and we can now recognize over 500 different types that can inhabit the mouth. This makes finding associations between particular types and disease very challenging and often very frustrating. Oral diseases do not seem to follow a simple paradigm that we see with many classical medical infections, and in my presentation today I'd like to give you a viewpoint or a philosophy, that may help make some sense of this complexity, and if you accept some of these principles I think it can lead to new opportunities for prevention and control and also new ways of communicating very complex ideas to patient groups.

In my talk today I'm going to describe the relationship between the microbes that inhabit our body and describe the mischief and benefits that they bring, and I'm going to describe the dynamic relationship that exists between the host as an environment and these organisms, and then put forward an ecological approach to dental disease and the implications for control. But first of all I want to pose a question to you. Which of the following examples is the odd one out: Is it the effect of acid rain on the forests of Scandinavia caused by pollution from Great Britain? Is it the growth of algae across the ponds and lakes because of the run-off of the phosphate and nitrogen fertilizers from agricultural use on the land that cause the algae to grow and consume all the oxygen and kill the aquatic life? Is it the loss of the dinosaurs when a meteorite impacted and altered the climate on Earth? Or is it dental diseases? My point is that all the principles that apply behind these examples are the same; they are all examples, albeit on a different scale, of ecological catastrophes.

It has been estimated that the human body is made up of over 10^{14} cells, but only 10% of them are mammalian and the

rest are the micro organisms that naturally inhabit all of the environmentally exposed surfaces of the body, and these micro organisms are natural and are important to us (1). Without them, the host's physiology and the immune system do not develop properly, absorption of nutrients is impaired; the resident microorganisms also function with the host defences to act as a barrier to exclude the organisms that we come into contact with on a daily basis. This phenomenon has been termed 'colonization resistance'.

If you examine the different sites on the body the predominant organisms vary (2), and this is in spite of regular throughput of organisms from one site to another. People are licking their fingers and putting them in their mouth, and yet few of the organisms that predominate on the skin are able to establish successfully in the mouth. Likewise when studies are done on the gut only 29 species which are found in the mouth are regularly isolated from the gastrointestinal tract, despite the fact that these organisms are constantly being passed into this area. This site variation means that certain key factors control which organisms are able to grow and dominate at a site. The habitat is able to select which organisms grow, so it's the physical and chemical properties of each of these sites that determines the composition of these characteristic microbial communities.

If we look into the mouth itself, the main types of microorganisms that dominate at distinct surfaces also vary, and again this is in spite of these organisms having the opportunity, through saliva, to colonize each of them. So the habitat, because of its biological properties at each of these sites, determines which organisms colonize successfully (2). Thus, distinct surfaces such as fissures and the gingival crevice, have radically different groups of bacteria dominating. In fissures we have many streptococcal species and very few Gram-negative bacteria, whereas the reverse is true in the gingival crevice, where obligately anaerobic species are common, many of which are Gram negative. There has to be reasons to explain these biological differences, and in my view, it is due to the properties of the habitat. Fissures are influenced by the properties of saliva, whereas in the gingival crevice the flow of gingival crevicular fluid brings in not only components of the host defences but also host molecules that can act as novel nutrient sources for the bacteria that grow there. So the microhabitat can also select.

The interpretation of these findings is that the place where organisms grow (the habitat) is selective, it's hostile to many organisms (so some organisms are just unable to colonize), and there is a direct relationship between the environment and the organisms.

Dental plaque in health and disease

Dental plaque is now described as a biofilm and a microbial community – in other words it's a mixture of organisms growing and interacting together (3). The consequences of a biofilm style of growth is that it's now being shown that when organisms attach to a surface they change their patterns of gene expression, so they turn off genes they don't need when they're floating around in a liquid and they turn on those genes that are needed for life on a surface. The organisms are not randomly distributed, they're spatially organized to maximize functional activities, and they're embedded in a matrix of extracellular polymers. Because the cells are relatively close together, there is cell–cell communication, which involves signalling and gene transfer. The microbial community aspects means that bacteria growing together can often (a) inhabit a broader habitat range, so they can survive conditions that on their own they wouldn't be able to tolerate; (b) they have a more efficient metabolism, they can use nutrients which on their own they couldn't break down; (c) they are more able to cope with environmental stresses, including anti-microbial agents and (d) in certain situations, they can display enhanced virulence, such as occurs with abscesses (4). Consequently, the organisms growing in a biofilm have a novel phenotype, they coordinate their activities, they are functionally organized and they have increased tolerance to antimicrobial agents. Indeed some people are regarding biofilms, particularly mixed species biofilms, as a primitive example of a multicellular organism.

Scientists are beginning to rethink their ideas about dental plaque, as we now believe that the organisms are not indifferent to one another, because they have cell–cell communication systems, so that some bacteria will produce molecules that are detected by neighbouring cells. This may result in altered patterns of gene expression by the recipient, perhaps in response to a stress. The bacteria in plaque interact metabolically, including synergism and antagonism, and they use cell–cell signalling strategies. The signalling molecules are now being identified; streptococci use peptides whereas Gram-negative anaerobes use a different class of molecules. In biofilms such as plaque, there is also the opportunity for horizontal gene transfer between different species.

One of the clinical features of increased significance is the fact that biofilms are more tolerant to anti-microbial agents, and there are a number of reasons behind this (5). It may be that the anti-microbial does not penetrate far into the biofilm; the bacteria within there may induce a stress response when they detect the presence of anti-microbial agents, also the environment within the biofilms can be radically different from

that on the outside, and this environment may mean that some anti-microbials don't work properly, and there's a new phenomenon where there may be some cells that are slightly genetically different to their neighbours – they're called persisters and they don't divide until there is a dramatic impact on the biofilm. Again, on occasions, there is opportunity for gene transfer.

In terms of knowing what bacteria are present in plaque, the conventional approach has been to use selective and non-selective agar plates, which are incubated under a range of environmental conditions, often for prolonged periods to discern different colony types. Our views of plaque are now being changed radically by the introduction of molecular techniques (6). DNA can be extracted from dental plaque from a site, and it can be cloned and amplified, followed by sequencing, enabling databases to be searched for homology, which gives a presumptive identification. These studies have shown that there may be >700 different types of microorganisms found in the mouth, at least half of which cannot be cultivated in the laboratory at present. Researchers have found nearly 50 unculturable spirochaetes, and there are some organisms which are found in periodontal disease that (sadly) have no name. These can be numerous, and one group that may be of increasing relevance to periodontal disease is termed as 'TM7' (7). This molecular approach to define the microbial composition of a site results in increasingly fearsomely long lists of bacteria found in plaque samples, and when one attempts to correlate certain types or certain microbial profiles with disease it clearly becomes a challenging objective.

As dental plaque develops as a biofilm, eventually all of these resident microorganisms strike a sort of balance with each other, where the numbers remain relatively constant over time, but this constancy should not be regarded as any biological indifference by the organisms. This balance is maintained despite a range of minor perturbations each day depending on our diet, the integrity of our host defences and the sort of organisms we come into contact with. This balance is maintained by a series of dynamic interactions among the multitude of organisms. A consequence of this balance is that in the host, with someone who has a normal diet and reasonable oral hygiene, de- and re-mineralization can be in equilibrium and there is little inflammation so that the flow of gingival crevicular fluid is minimal. However, in people who do not have a good diet and who don't clean their teeth well, then we start to lose the balance in terms of de- and re-mineralization and we start to get inflammatory reactions around our gums. So we can describe this as saying that we may get an environmental overload at a site, for example, through diet, which can cause an ecological catastrophe of some sorts. It may result in the microbial community undergoing rearrangement resulting in outgrowth of organisms that were only minor components before, but now are able to become dominant and perhaps initiate disease.

This is the situation that I described in rivers and lakes, and it's what is believed to happen in certain medical conditions, so acne is associated with growth and activity of a bacterium, *Propionibacterium acnes*, on the skin in response to hormones released during puberty, and likewise colitis can be caused by antibiotics removing most of our natural organisms and letting others grow up. Could these same type of theories explain what we see in dental disease?

So, we have dental plaque on teeth, it's natural, we all have it – even dentists – and the sort of organisms we find, we could argue, are quite benign. However, in caries if one takes samples we find increased numbers and proportions of certain organisms like *Streptococcus mutans* and lactobacilli, and the factors that we regard as being important in disease include the ability to make acid rapidly from dietary carbohydrates, and the production of extracellular and intracellular polysaccharides, but perhaps most importantly is the ability of the organisms to tolerate the low pH they generate from their metabolism. In contrast, in periodontal diseases we see a different, more diverse microflora, so we see far more Gram-negative anaerobic organisms, including those classed as unculturable, and the significant factors they produce include proteases and the ability to deregulate the inflammatory response, so we get an undesirable uncontrolled inflammatory response.

We use the term 'pathogen' to describe the organisms associated with disease and as we are using more and more sensitive techniques, we have the uncomfortable finding that we can detect these organisms far more commonly in health than we used to, albeit in very low numbers. So if we look at the organisms implicated in caries, the mutans streptococci, using different techniques, they are reasonably common at healthy sites. If we apply molecular techniques such as PCR and look for some of the very difficult to grow anaerobic organisms, again they can be present in quite high proportions of individuals including, surprisingly, young infants (8). So these organisms (pathogens?) are there but they're present at very, very low levels and as such are clinically insignificant.

Where do they come from? Studies have shown that there is transmission from mother to child, and on occasions with some of the periodontal organisms between spouses. There are two possibilities; either these organisms are there in very, very small numbers most of the time and, as such, are not capable

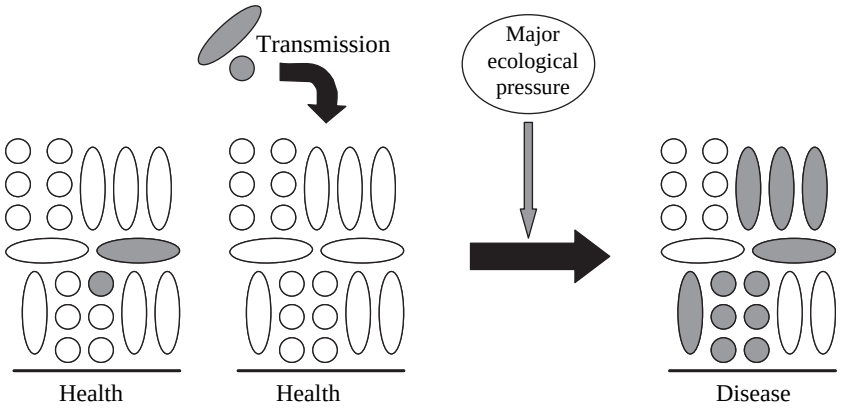

Fig. 1. Relationship of oral pathogens to disease in dental plaque. The microflora of dental plaque is distinct in health and disease. Potential pathogens (shown in grey) may be present in low numbers in plaque at healthy sites or transmitted in low numbers from other sites. A major ecological pressure is necessary for such pathogens to outcompete other members of the resident microflora and achieve the numerical dominance needed for disease to occur. Adapted from (12).

of causing disease, or we acquire them from some other person. However, for disease to occur, these organisms have got to increase in numbers to reach a level where they are capable of causing damage to the host, and for this to happen I believe there has to be some major ecological change at that site for these organisms to suddenly escape from the natural homeostatic mechanisms that keep them at low numbers (Fig. 1). So it could be changes in diet, it could be in response to an inflammatory response where not only do we get the host defences but also these novel compounds that can be nutritional sources. It could be that the host defences are impaired, thereby letting organisms escape the normal host control, or a pH change following sugar metabolism.

Let us move on to try and explain the relationship between the host and dental plaque. If one looks at other habitats, the type of factors that can cause upsets in bacterial composition of sites include a change in nutrient source, a change in pH, the host defences being altered, the introduction of an antimicrobial agent, or a change in the gaseous atmosphere (i.e. whether it is anaerobic or aerobic), and in this instance we are going to concentrate mainly on nutrients and pH.

In terms of nutrients, oral organisms generally live on endogenous nutrients; saliva provides proteins and glycoproteins, while gingival crevicular fluid can additionally introduce molecules, for example, those that contain haemin which many of the black pigmented anaerobes require for their growth. Superimposed on that are the exogenous sources of nutrients provided by the diet, and sugar is a key factor. In caries, we know that there is a shift from the natural pH of around neutrality (which is maintained by saliva) to conditions of acidity, while during inflammation the pH of the gingival crevice rises slightly and becomes alkaline.

Traditionally, the way microbiologists investigate bacteria is to study them in pure cultures. From the era of Pasteur, the way the properties of organisms were discovered was to separate them from their natural neighbours and look at their properties in isolation. So you would take an organism and look at how it behaved in terms of growing at different pH values, or in the presence or absence of sugars, and then compare it with a different type of organism in pure culture and see how that did and decide that one was more 'dangerous' or unpleasant than the other one.

What we have done is to grow some of these oral bacteria together as communities, as they do in dental plaque, and look at the effects of pH and sugar on these organisms growing together as dynamic mixtures. What we are looking at is not just phenotypic properties, e.g. whether they make more or less acid, or produce more or less protease, but we're determining what the impact of these changes are on the competitiveness of these bacteria, when they start to out-compete one another, and therefore begin to understand the impact of environmental change on the structure (composition) of the community.

So to summarize, in these studies, we found that an organism like *Strep. mutans*, when there is excess carbohydrate present, some of the sugar uptake systems are repressed, others are induced, and likewise when there is very little carbohydrate, they shut down other systems and induce high affinity transport systems (9). But the factor I want to focus on is the influence of the low pH generated by sugar metabolism. *Strep. mutans*, which is implicated in caries, loves growing at low pH, whereas if you take an organism that we associate more with health, such as *Strep. sanguinis*, we find that it really grows very poorly at low pH, and makes very little acid under these conditions.

If we look at other groups of organisms, such as those implicated in periodontal disease such as *Porphyromonas gingivalis*, when we introduced more haemin into its environment (it has an absolute requirement for haemin and haemin can be present in many of the molecules found in gingival crevicular fluid), we found that its potent proteases (e.g. arg-gingipains) were up-regulated (10). Thus, enzymes that are considered to

help deregulate the inflammatory response are increased, and we get a shift in the ratio of certain patterns of enzyme. If we grow *P. gingivalis* at different pH values, we find that the peak activity of arg-gingipains is around pH 7.5, and in fact when we grow the organism at 7.5 and then measure the enzyme activity at different assay pHs, we get a massive up-regulation of gingipain.

If we look at the range of growth in terms of pH range for many of the organisms found in the periodontal pockets we can see that the optimum is generally around neutrality or shifting slightly towards an alkaline pH (10), whereas, in contrast, the optimum pH is towards the acidic side for the organisms associated with dental caries.

What we see from these studies is that we can make cases that the environment changes during disease and that the oral bacteria can respond to these environmental changes. In addition, the sort of environmental changes we associate with disease favour the growth, survival and metabolism of these so called pathogens, and that many of the genes that are related to their virulence are up-regulated under these conditions, so they become fitter and are more able to grow and exploit these circumstances.

To explore these theories, we grew some of these organisms together, imposed some of the critical environmental changes associated with disease, such as shifts in pH and changes in nutrients. In this model system, we were able to see cause and effect relationships when we grew either nine or 10 organisms together in a chemostat; we grew the bacteria on a mucin-based medium that simulated the type of nutrients that are supplied by saliva. We could add nutrients into this vessel or we could transfer the organisms into a second vessel and alter the environmental parameters in there. We were able to add surfaces to grow them as biofilms or we could connect the system up to another model system that allows us to grow biofilms of particular depths. We included organisms associated with health and organisms associated with caries and some organisms that are implicated with periodontal disease, and we looked at factors such as increasing sugar frequency and conditions of low pH to review the factors important in caries, and in terms of periodontal disease tried to simulate the increased flow of gingival crevicular fluid and the rise in pH that has been reported to occur.

In the first study, we grew 10 organisms together and we looked at the effect of a fermentable substrate – glucose – and we gave this system daily pulses of glucose over 10 days, but we could exploit the properties of this system by not letting the pH change (11). These organisms would be making acid from the glucose, but this acid was neutralized by the automatic addition of alkali to keep the pH constant at 7.0. We compared the microbial composition of the community at the end with a parallel system where we did the pulsing again, but where we let the pH change naturally under bacterial metabolism for 6 h. We found that when we were growing the community on the artificial saliva, that mutans streptococci and lactobacilli were not competitive when they have to metabolize glycoproteins and proteins. When we pulsed in glucose, even though there is a fermentable carbohydrate to utilize, if we kept the pH constant at pH 7 the microflora was unchanged, so the mutans streptococci and lactobacilli were still <1% of the microbial community. Where we let the pH change after each glucose pulse, gradually after each pulse we got a change in the microflora and after the 10th pulse over half of the community was now made up of these acidogenic and cariogenic bacteria (mutans streptococci and lactobacilli), and the bacteria associated with health were reduced. There was a dose-dependent response – the lower the pH the greater the proportions of mutans streptococci and lactobacilli. We investigated this further by repeating the study but when we let the pH fall we only let it fall to a certain degree, so we would have an independent culture and let the pH fall but only to pH 5.5. In a second independent culture we would let the pH fall, but let it go further to 5.0, and in a third one it would go even lower to 4.5 but not lower than that (12). After daily pulses of glucose for 10 days, the proportions of *Strep. mutans* and lactobacilli increased depending on how low the pH was allowed to fall; thus, these organisms became more competitive at lower environmental pH values, at the expense of those species associated with health. We learnt that some organisms are very pH sensitive, and the lower the pH falls the fewer their numbers were. This study showed that a low pH can really distort the composition of these communities.

We concluded that low pH rather than the carbohydrate itself selects the cariogenic bacteria and there is a relationship between pH and the levels of these bacteria, which begs the question: could inhibitors of acid production prevent this selection? We investigated the effects of fluoride; fluoride has beneficial enamel effects, but it can also inhibit bacterial metabolism and slow down acid production. We repeated the above study design, but introduced low levels of fluoride (10 or 20 parts per million) with the glucose. We found that the terminal pH where we had no fluoride was around 4.41, but in the presence of low levels of fluoride it was higher, at 4.81 (13). Although that change does not seem very dramatic, the impact on the competitiveness of *Strep. mutans* was very marked. Before the glucose pulsing, levels of *Strep. mutans* were around 4% of the total community; when we did the glu-

cose pulsing without pH control, but in the absence of fluoride, it reached over 20% of the flora. However, when we pulsed glucose with fluoride, the proportions of *Strep. mutans* stayed at prepulsing levels (13).

We developed a system with colleagues in The Netherlands where we could measure the pH in mixed culture biofilms using pH sensitive dyes. When glucose was added, the pH changed over time (*c.* 20 min) to around pH 5. When we repeated the study but with the presence of even low levels of fluoride, the pH in the biofilms is in the range of pH 7 to 6, so there was a marked inhibition of pH change in the biofilm itself when even low levels of fluoride were there (14).

Moving on to periodontal diseases, as I stressed, in gingival crevicular fluid there are a number of molecules that bacteria can use as nutrient sources, and a number of studies have used serum as a surrogate for gingival crevicular fluid to look at the effects of this on bacterial metabolism. This was a study many years ago, again done in The Netherlands, where three samples of dental plaque taken from patients to determine the presence of a black pigmented anaerobe that was implicated in periodontal disease, now called *Prevotella intermedia* (15). They could not detect this organism in two of the samples and found very low levels of it in the third. They grew these plaque samples in repeated aliquots of fresh serum. After the first enrichment, again they could not detect *Prevotella intermedia*, but gradually as they carried on with these enrichments the *Prevotella* was detectable and it eventually reached considerable proportions within the sample, which proves that if you change the nutrient status at a site you can distort the bacterial community – organisms that were minor components can suddenly be more competitive and increase in number.

We have conducted a similar study with our mixed culture where we have also looked at the effect of serum (to simulate gingival crevicular fluid) as a nutrient source. During the start of the experiment, we keep the pH constant at around pH 7, and the culture is anaerobic (the redox potential is −330 mV). The proportions of the periodontal pathogen, *P. gingivalis*, were low, and it was not very competitive in this system; it was metabolizing salivary type molecules, and the overall protease activity was low. When we introduced serum, we got significant changes in a number of parameters over time. Through bacterial metabolism, the pH immediately started to rise and reached around pH 7.5, which has been recorded in inflamed periodontal pockets, and the redox potential fell even lower. We also saw a change in the composition of the community of bacteria, so that by the end of the experiment, *P. gingivalis* became far more competitive and reached 80% of the community, and the protease activity was also high, so again a change in the nutrient status caused a massive change in the balance and competitiveness of the organisms. When we did an experiment where we just grew three black pigmented anaerobes together and investigated the influence of pH, we found that even a shift from pH 6.7 to 7 (measured in healthy gingival crevices) towards 7.25 and up to 7.5 (inflamed pockets) invoked changes in the proportions of these bacteria (10). At neutral pH or below, *P. gingivalis* was just not competitive with these organisms and it was dominated by the one we find in health (*Prevotella melaninigenica*), but a small rise in pH first enabled *Prevotella intermedia* to dominate, and then above pH 7.25, *P. gingivalis* became more competitive and dominated the culture. These are the pH changes that occur during inflammation.

The point I want to stress is that this relationship between the environment and the microflora is active and dynamic and that if you get a change in local conditions, then the organisms will respond, but the key point is: can this relationship be managed, or manipulated for our benefit? These studies led me to propose an ecological approach to disease. In the past we've had various hypotheses put forward to try and explain plaque and its role in disease, and the field was taken a long way forward. Walter Loesche proposed a 'specific plaque hypothesis', because it meant that out of the vast range of organisms that we see in plaque, disease was due to just one or two particular types, and we could focus on those (16). However, an alternative view was that many of the organisms in plaque may have a role which may actually be of a beneficial nature, and so we should consider the activity of all of the organisms; these views were captured in the non-specific plaque hypothesis (17). More recently, I tried to gain the benefits of both of these hypotheses by putting forward an 'ecological plaque hypothesis' (Fig. 2)(18). In this hypothesis, it is not necessary for the aetiology to be mono-specific; many organisms could contribute, and there are examples of this in terms of abscesses and various other infections, which we call 'pathogenic synergism'. It is also consistent with this hypothesis that you can 'carry' pathogens, so you could have organisms that we associate with disease, which we can now detect with sensitive molecular techniques, at healthy sites, but they are at levels that are clinically insignificant.

The important thing is that disease can be preventable not only just by directly inhibiting the causative organisms but by maintaining the normal and natural favourable microbial balance, the homeostasis, by interfering with the factors driving the deleterious shifts in the microflora. In the example of dental caries, in subjects who consume sugar frequently, plaque bacteria produce acid, and this causes an environmental stress which results in a change in the pH of plaque dropping from neutral to a low pH more regularly, so we get an environmen-

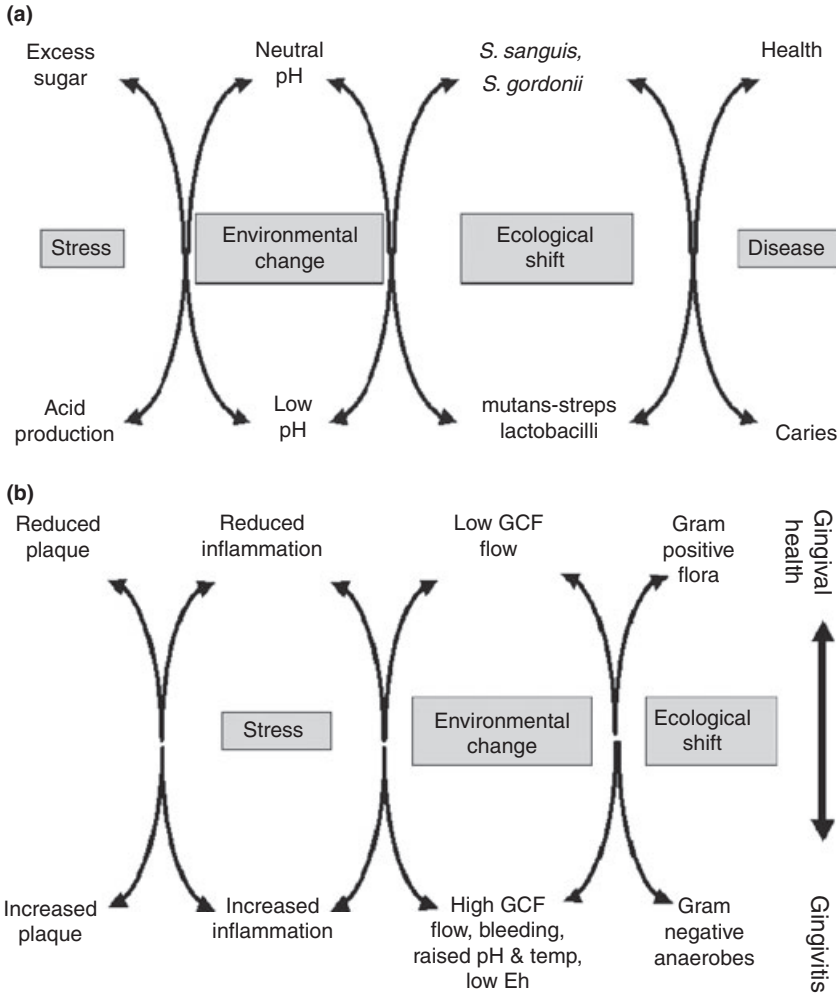

Fig. 2. The ecological plaque hypothesis and the prevention of (a) dental caries and (b) periodontal diseases. The postulated dynamic relationship between environmental cues and ecological shifts within the biofilm implies that disease could be prevented not only by direct inhibition of the putative pathogens, but also by interfering with the key environmental factors driving the ecological shifts (18).

tal shift, and this will tend to select for those organisms that prefer to grow under acidic conditions (Fig. 2a). Thus, we inhibit those bacteria we associate with health and enrich those that we associate with disease (because their physiology makes them more competitive under these acidic conditions), resulting in a change in the balance of the organisms. So we get an ecological shift, and this is tending to bias the system more towards caries and demineralization, and away from health.

This process is selecting organisms with properties that are acidogenic and those that like and can tolerate the acidic conditions they generate. My point is that you could prevent caries by having a 'magic bullet' that would inhibit these organisms directly, but you could also achieve the same effect if you interfere with the processes that are driving the selection of these organisms, i.e. frequent periods of acid production. So, although the traits of acid production and acid tolerance are associated with mutans streptococci, they are not uniquely so, and there are other acid-tolerating streptococci now identified and other bacteria that produce almost as much acid as *Strep. mutans*, and these organisms will all be part of the burden that determines whether we get caries or not. We could reduce this threat by various strategies. Fluoride obviously plays a role, not only on its influence on enamel but also by inhibiting bacterial metabolism. We could have dietary control to avoid sugar in our snacks, and we could use food products that contain sugar substitutes. In addition, chewing sugar-free gum that stimulates saliva flow in the absence of a sugar challenge will help reduce the ecological stresses on the system, while some of the anti-microbial agents in oral consumer products (toothpastes, mouthwashes) even at sublethal levels can inhibit glycolysis.

In gingivitis, when plaque accumulates there is a stress to the system and we can get inflammation, and this causes environmental changes. There is an increased flow of gingival crevicular fluid, bleeding, the local pH and temperature rises, and this is going to cause an ecological shift by affecting the competitiveness of the subgingival plaque bacteria (Fig. 2b). We get a shift away from the normal Gram-positive flora to one

where there are more Gram-negative anaerobic bacteria, and again this is more likely to provoke more inflammation (gingivitis). Again, my point is that you could have specific inhibitors to prevent the growth of these bacteria, but you could have the same effect if you can reduce or inhibit the processes that drive their selection and growth. These environmental changes select for those bacteria with properties that are proteolytic and like growing under alkaline conditions, and these traits again are associated with some of the main putative periodontal pathogens, but not uniquely so.

We can try to interfere with the key processes, for example by introducing oxygenating or redox agents to try and make the environment less suitable for growth by the anaerobes. Reducing inflammation will also reduce the flow of gingival crevicular fluid, which switches off the nutrient supply for these bacteria, and again some anti-microbial agents at sublethal levels inhibit the proteases, for example, that are driving the inflammatory response.

Therefore, it is possible to take a more ecological or holistic approach to dental diseases. If you go to a conference of microbiologists all we talk about are the micro organisms being important. If you go to other conferences where they are interested in the host defences, then that will be the big issue, but essentially all these factors are inter-related. The micro organisms will respond to changes in saliva flow, they'll respond to changes in our diet or lifestyle, whether we smoke or don't smoke, whether we're on medications that influence the host defences or not, and so all these parameters are inter-related and unless we understand the inter-relationship, patients will keep returning with dental disease because we're only treating the consequence of the micro organisms, we're not dealing with the underlying biological parameters that are causing them to be able to cause this mischief. So I think it should be possible to identify risk factors for individual patients and make sure that one deals with the specific underlying events for that particular patient.

In summary, dental plaque is a biofilm and a microbial community, remember that it is natural and beneficial to health, we cannot eliminate it, but the diseases are due to changes in the local environment which cause an enrichment of previously minor bacterial populations, so although you may not agree that they're ecological catastrophes perhaps they are examples of very micro-ecological catastrophes. An understanding of this process means that an ecological concept can offer novel therapeutic approaches by interfering with the factors driving the selection of these bacteria and offers educational and communication opportunities, because this is a concept that is much easier for patients to accept.

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