INTRODUCTION
The process of dental caries is now well-understood, although there are many details yet to be determined. Studies over approximately the last 20 to 30 years have clarified the mechanisms of demineralization and remineralization and also elucidated a great deal of the complex microbiology of the process (Loesche, 1986; ten Cate and Featherstone, 1991). However, clinical trials are still conducted with the endpoint being frank cavitation as measured and examined by standard criteria (Radike, 1972). This endpoint of the caries process comes after months or years of decay progression and is itself a rather crude measure. A great deal of time and effort has been spent in modeling dental caries, both in the laboratory and utilizing the human mouth as a laboratory, as well as in a range of animal models (ten Cate and Featherstone, 1991; Featherstone, 1995; ten Cate and Mundorff-Shrestha, 1995; Zero, 1995). The definitive proof, of course, of any product designed to intervene or reverse caries is the so-called "clinical trial". With the in-depth understanding that we now have of the dental caries process, it is possible to design measures for the detection of dental caries at a much earlier stage and to assess the efficacy of therapeutic procedures to prevent progression or, even better, reverse the process. However, there has been debate about whether early caries turns into eventual cavitation, whether the different types of caries are comparable, and whether the various modeling methods are predictive (Featherstone, 1995). The purpose of the present paper is to present a brief review of the continuum of dental caries and the evidence for caries being a dynamic disease process.

CATEGORIES OF DENTAL CARIES
The categories of dental caries that are mostly considered by clinicians and researchers are smooth-surface caries, pit and fissure caries, enamel caries, dentinal caries, secondary caries, early childhood caries, and root caries. Other subdivisions may also be considered and described clinically or histologically. The basic mechanism of dental caries, as described in the next section, is the same for all of these so-called "types of caries". Mineral is lost through attack by acid generated by bacteria. This is demineralization. If demineralization continues, a cavity eventually occurs in whatever form and in whatever position on the teeth in the mouth. The natural body repair mechanism for dental caries is remineralization related primarily to minerals from saliva diffusing back into the porous subsurface region of the caries lesion (Featherstone, 2000). The physical treatment methodologies for restorative dentistry are obviously different, depending on the location, extent, and seriousness of the decay. However, the basic mechanistic principles are the same for all of the above-mentioned categories of dental caries.

CARIES MECHANISM
Dental caries is a simple process in concept, but complicated in detail. In outline, the caries mechanism can be described as follows (Featherstone, 2000):

1. Acidogenic (acid-producing) oral plaque bacteria ferment carbohydrates that are taken into the mouth, thereby producing organic acids, including lactic, formic, acetic, and propionic.
2. These acids diffuse into the enamel (Featherstone, 1983), dentin, or cementum, partially dissolving the mineral crystals (composed of carbonated hydroxyapatite (LeGeros, 1991) as they travel.
3. Mineral (calcium and phosphate) diffuses out of the tooth, leading eventually
Remineralization has been demonstrated in the laboratory for all types of caries listed above, but of course, the deeper the caries lesion, the harder it is for remineralization to be effective (ten Cate and Featherstone, 1991). Whether a lesion will progress, stay the same, or reverse is determined by the balance between protective factors and pathological factors (Featherstone, 2000). This balance is illustrated in Fig. 1. If the pathological factors predominate, then caries progresses. If the protective factors predominate, then caries is halted or reversed. In simple terms, the pathological factors are cariogenic bacteria, salivary dysfunction, and frequency of ingestion of fermentable carbohydrates. Once established in a particular person's mouth, these cariogenic bacteria are very difficult to manage. Protective factors include most of the components in saliva (such as calcium), phosphate, fluoride, protective proteins that form the pellicle, proteins that maintain supersaturation of the mineral in saliva and plaque, and antibacterial substances naturally in saliva but also supplied extrinsically (e.g., chlorhexidine), salivary fluoride, fluoride from external sources, and substances (e.g., chewing gum) that stimulate salivary function. Fig. 1 conceptually summarizes the dynamic process of dental caries as being a balance, or imbalance, between demineralization and remineralization that occurs numerous times daily in the mouths of most humans.

**PREVENTION AND INTERVENTION**

Prevention, intervention, and reversal of dental caries can be enhanced by either reducing the pathological factors or enhancing the protective factors.

**Bacteria**

Antibacterial therapy such as treatment by chlorhexidine gluconate mouthrinse has been shown to be effective in reducing the cariogenic bacteria (Krasse, 1988). If the bacterial challenge is reduced, then the protective factors have a greater chance of taking over and halting or reversing dental caries (Featherstone, 2000). The natural antibacterial substances in saliva, such as lactoferrin and the immunoglobulins, are obviously not sufficiently active in cases where caries progresses.

**Fermentable Carbohydrates**

One of the most significant contributions to dental caries is the frequency of ingestion of fermentable carbohydrates. Reducing the frequency of ingestion is a behavioral matter. However, substituting non-cariogenic sweeteners such as xylitol for the fermentable carbohydrates such as glucose, sucrose, and fructose has been shown to be effective in reducing the pathological challenge (Hildebrandt and Sparks, 2000; Söderling et al., 2000).

**SALIVARY FUNCTION**

In the case of reduced salivary function, there are fewer protective factors provided by the saliva, and less ability for the saliva to enhance remineralization, remove bacteria, or inhibit bacterial action. Xerostomic patients have rampant caries if intervention strategies are not put in place (Mandel, 1974, 1989). These subjects illustrate, in a few months, the progression from smooth-surface caries to cavitation and rapid breakdown of the teeth on all surfaces, related directly to the lack of salivary function and the ability of the bacteria to take over and produce mineral-destruction acids very rapidly (Dreizen et al., 1977).

**FLUORIDE**

It is very well-documented that, in clinical trials assessed by conventional visual-tactile detection methods (Jenkins, 1985), fluoride products such as toothpaste, mouthrinse, and office topicals have been shown to reduce caries between 30 and 70% compared with no fluoride therapy. Fluoride in the drinking water has also been shown, of course, to be effective in reducing the severity of dental decay in entire populations. However, it has become obvious that where the bacterial
challenge is too high, it is not possible for fluoride to overcome this challenge completely. Again, this is an illustration of the continuum of dental caries and the ability or inability to balance the outcome according to the schematic diagram in Fig. 1.

**THE CONTINUUM OF DENTAL CARIES**

As described above, demineralization and remineralization occur in the mouth several times daily as a dynamic process, with progression or reversal of dental caries being the end result. The site at which the caries occurs is determined by the acidogenic bacteria at that site and access to either pathological factors and/or protective factors. Caries begins to manifest itself at the atomic level as soon as a diffusing molecule of organic acid reaches a susceptible site on a crystal surface of carbonated hydroxyapatite down inside the tooth (Featherstone, 1983). This has been shown, by laboratory experiments, to cause preferential loss of calcium, phosphate, and carbonate from specific sites in the crystal. This process was visualized by Featherstone and co-workers approximately 20 years ago (Featherstone et al., 1979, 1981). The reversal of demineralization also occurs at the atomic level when calcium, phosphate, and fluoride come together to build a new surface onto the existing crystal remnants that have remained following demineralization. This again has been visualized at the atomic level, at the ultrastructural level, and in chemical experiments by numerous researchers (Featherstone et al., 1981; ten Cate and Duijsters, 1983; ten Cate and Featherstone, 1991; ten Cate and Mundorff-Shrestha, 1995).

The process of dental decay can be modeled in the laboratory in chemical or microbiological systems to produce the early manifestation of caries, namely, the white spot lesion, decay around orthodontic brackets, secondary decay around restorations, decay on smooth surfaces or on occlusal surfaces, root caries, and dentinal caries. In general, in the mouth, the process takes much longer than in the laboratory models. The advantage of the models is that much can be learned about processes involved in a much shorter period of time (Featherstone, 1995; ten Cate and Mundorff-Shrestha, 1995). The thousands of experiments that have been conducted and reported in the literature for both in vitro and in vivo experiments readily confirm that the caries lesion is formed by a continuous process starting at the atomic level on the crystal surface in the subsurface of the tooth, and progressing deeper and deeper into the enamel, or, in the case of root caries, starting in the cementum and eventually ending up in the dentin.

The dynamic nature of the process has been modeled in numerous laboratories by various pH cycling models (ten Cate and Duijsters, 1982; Featherstone et al., 1990). To review these studies is beyond the scope of the space of the present article. Suffice it to summarize that these models can produce a continuum of the dental decay process with end results ranging from an almost imperceptible white spot to a cavity. For example, a recent study (unpublished) in our laboratory examined pH cycling (alternating demineralization/remineralization) over a period of 3 wks with 6 hrs of demineralization daily in a pH 4.3 partially saturated calcium and phosphate demineralizing solution and 17 hours of remineralization during every 24 hours, according to methods reported previously (Featherstone et al., 1990). In between each of the de- and remineralization steps, the crowns were subjected to treatment in dentifrice slurries made from a range of products containing, respectively, 2800 ppm F, 1100 ppm F, 250 ppm F as NaF, and a placebo product with no added fluoride. At the end of the experimental time, the teeth were semi-sectioned and assessed by cross-sectional micro-hardness (Featherstone et al., 1990). The relative mineral loss (volume % x µm) as ∆Z was linearly related to the negative logarithm of the fluoride content of the products (p < 0.01). The lesion profiles are shown in Fig. 2. The placebo product contained less than 1 ppm F. In the case of the treatment by the placebo, cavitation occurred in some parts of some lesions, the lesions were deep (∆Z approximately 4000) for the period of treatment, and the mineral content remaining in the outer portion of the lesion was on the order of 30% volume mineral (Fig. 2). On the other hand, the group treated with the 2800-ppm-F product produced lesions that were barely visibly perceptible as white spots, with a low ∆Z value (approximately 500). This model clearly illustrates the continuum from almost no effect of the strong acid challenge when treated with the high-F product, to major demineralization and cavitation with the placebo dentifrice. These results parallel those of clinical trials involving similar products.

Similarly, the caries process can be modeled in the mouth with in situ studies, as demonstrated over the last 30 years by numerous laboratories, as reviewed in a recent conference (Featherstone, 1995). Several models have been used, and these have been reported in many papers. Most of the models involve utilizing extracted teeth and placing enamel and/or dentin samples in the mouth and observing subsequent demineralization or remineralization. Again, these models have produced product efficacy indications similar to those found in laboratory in vitro pH cycling studies. A model that is one step closer to what might be considered 'natural caries' is one that uses orthodontic appliances. In this case, true caries occurs on the smooth surfaces surrounding these orthodontic appliances. For example, O'Reilly and Featherstone (1987) reported such a model and based the development of a pH cycling model on the results that they found in the human mouth. Øgaard and co-workers have used orthodontic models, particularly bonding, to show severe caries challenge and rapid progression of lesions in the mouth in a high-challenge situation with poor access for remineralization (Øgaard and Rolla, 1992). There is no reason to believe that caries around orthodontic brackets is any different from any other of the forms of caries described above.

Since it has been established that the caries process is a continuum, albeit one that is interrupted numerous times daily, it is therefore possible to intervene at any stage with a therapeutic product or an intervention methodology. If detection methods are accurate and objective enough, then the disease can be followed over time, the rate of progress measured, or the rate of reversal measured (Stookey, 1999).

In summary, dental caries covers the continuum from the first atomic level of demineralization, through the initial white spot (or its equivalent in the tooth root), often through dentinal involvement, to eventual cavitation. All of the steps can be modeled in the laboratory or in the mouth. The dynamic balance between demineralization and remineralization, as determined by pathological factors and protective

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**Figure 2.** Plot of volume % mineral vs. depth from the surface for 4 groups in a pH cycling study. Each group was treated between demineralization and remineralization by a dentifrice containing, respectively, (a) no added fluoride, (b) 250 ppm F, (c) 1100 ppm F, and (d) 2800 ppm F each as NaF. Error bars are standard deviations for the data at each depth from the surface. Each group is statistically significantly different from every other group (p < 0.05).
factors, determines the end result. The disease of dental caries is reversible, if detected early enough. It may be necessary to use antibacterial methods as well as methods that enhance remineralization or inhibit demineralization. With the sophisticated knowledge we now have of the dental caries mechanism and our ability to quantify demineralization at early stages, rather than wait for frank cavitation, intervention methods can be tested by short-term clinical trials.

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REFERENCES


