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Crystal chemistry and dissolution of calcium phosphate in dental enamel

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ABSTRACT

The mineral component (at least 95 wt. %) of dental enamel is hydroxyapatite (hydroxylapatite) with multiple substitutions. The biogenic origin of enamel is reflected in the unusual ribbon-like morphology of the crystals, which are extremely elongated in the *c*-axis direction, and their organized arrangement within the tissue. The study of enamel dissolution has been driven by the very high prevalence of dental caries. In enamel caries, the initial demineralization results in subsurface dissolution of mineral. While the surface remains intact, reversal of the lesion by remineralization is possible. Problems of understanding the physico-chemical processes in enamel demineralization include the general problems concerning the structure and chemistry of apatites formed in aqueous media. Added to these are the general problem of dissolution in an inhomogeneous porous medium and the complication that enamel apatite has a naturally variable composition which changes during demineralization. The use of model systems in caries research is illustrated by reference to X-ray absorption studies of enamel and synthetic analogues.

KEYWORDS: enamel, apatite, caries, teeth, demineralization, microradiography, microtomography.

Introduction

Morphology and arrangement of crystals in dental enamel

DENTAL enamel is at least 95 wt. % impure hydroxyapatite (hydroxylapatite), with the balance being non-collagenous protein and water. The enamel is supported on dentine, a more resilient collagen-apatite composite, which forms the bulk of the tooth.

The biogenic origin of enamel mineral is reflected in the unusual morphology of the crystals and in their anisotropic arrangement. Aoba (1996) has given a detailed review of the regulation of enamel crystallization by amelogenins (matrix proteins) and the formation and growth of enamel crystals. In mature enamel the crystals are flattened hexagons in cross-section (typically 300 Å in width) and extremely elongated in the *c*-axis direction. This ribbon-like morphology has been taken as an indication that the original crystal template is triclinic octacalcium phosphate (OCP) rather than hexagonal apatite. Although the existence of an OCP precursor is not established, it would be consistent with the changes in morphology (an initial precipitation of thin ribbons, followed by overgrowth of apatite and the appearance of the hexagonal crystals) and the reduction in acid phosphate species observed during amelogenesis (Aoba, 1996). Synthetic model systems of enamel formation have been used to investigate the mechanisms of crystallization of ribbon-like non-stoichiometric apatite crystals having an OCP lamella or central planar inclusion parallel to the (100) apatite plane (Nelson and Barry, 1989; Iijima *et al.*, 1992) and the marked increase in apatite/OCP ratio of the lamellar mixed crystals with fluoride concentration (up to 1 ppm) in solution (Iijima *et al.*, 1996).

The crystals are arranged within enamel prisms that run from the enamel-dentine junction towards the tooth surface. The organization of the crystals

and the various arrangements of prisms in enamel have been described by Boyde (1965). To a first approximation, the crystals are aligned parallel to the long axes of the prisms, so that it is possible to prepare sections of enamel in which there is fair alignment of the apatite *c*-axes. The preferred orientation of the uniaxial apatite crystals leads to the intrinsic birefringence of enamel, but the total birefringence for the tissue includes a component of form birefringence if the pores contain a material with refractive index different from the mineral. The prismatic structure of enamel affects diffusion processes in the tissue. Tracer clearance studies by Dibdin (1993) have indicated that there is a biphasic distribution of diffusion pathways; fast, as at prism boundaries, and slow, probably within prism cores. The most commonly observed surface etching patterns produced by phosphoric acid are related to the prismatic structure of enamel (Silverstone *et al.*, 1975).

Dental caries

Dental enamel has been studied extensively because of the economic and social costs of restorative dental treatment attributable to dental caries, which is the most prevalent disease of civilised man. Caries is an infectious disease that involves demineralization of enamel by organic acids produced in the fermentation of dietary carbohydrate by plaque bacteria on the tooth surface and is influenced by salivary effects (van Houte, 1994). The demineralization in enamel caries is unusual in being subsurface. This has the important clinical consequence that remineralization of the lesion can occur with maintenance of the integrity of the surface. Restorative treatment is not required unless the lesion progresses into dentine and the enamel surface layer is breached, allowing massive bacterial invasion of dentine. An understanding of the mechanisms of de- and remineralization of enamel is therefore important as a basis for clinical and public health strategies for caries control.

The complexity of natural caries has led to the development of model systems: human models, with study of teeth scheduled for extraction; animal models; *in situ* models, in which sections or blocks of tooth tissue are worn by a volunteer in an intra-oral device but examined in the laboratory; and *in vitro* models. The role of microbiology (Marsh, 1995) and salivary factors (Hay, 1995) in caries models have been reviewed. Although *in vitro* caries models do not replicate intra-oral conditions, they are widely used for testing the efficacy of topical fluoride agents (e.g. toothpaste) and for the study of fundamental physico-chemical processes in de- and remineralization because the effects of single variables can be investigated under controlled conditions (White, 1995). The particular difficulty of understanding the physico-chemical mechanisms of enamel demineralization arises from the natural variability of enamel mineral, problems concerning the crystal structure and chemistry of apatites formed in aqueous media, and the effects of the structure of sound and demineralized tissue on diffusion processes.

Composition and structure of enamel apatite

Overall chemical composition and variability

As a consequence of developmental factors and the effects of exposure in the mouth, the composition of enamel is rather variable, between and within teeth. Minor constituents of whole enamel include typically 3.0 wt. % CO_2, 0.4 wt. % Cl, 0.2 wt. % Mg, 0.01 wt. % F and many trace elements (Elliot, 1994). Composition varies with depth within the tissue. For example, from the surface towards the enamel-dentine junction, there is an increase in carbonate and magnesium concentration that parallels a decrease in crystallinity (LeGeros *et al.*, 1996, and references therein). By contrast, the concentration of fluoride is highest at the surface and declines extremely rapidly with depth (Hallsworth and Weatherell, 1969). Based on published analyses, Margolis and Moreno (1990) calculated that substitution of 26% of hydroxyl ion sites by fluoride may be reached at the outer enamel surface.

The determination of total water in enamel and its distribution between the mineral and organic phases poses difficulties, in part from uncertainty of its constitutional role in the mineral. This problem affects the determination of the mineral mass and volume fractions; mean values of these are usually given as 95 wt. % and 86 vol.% (Angmar *et al.*, 1963), but have recently been recalculated as 98 wt. % and 96 vol.% (Elliott, 1997). Since water within the pores of enamel provides the medium for diffusion of ions in de- and remineralization, knowledge of the volume fraction is of fundamental importance.

In the early stages of caries, there is a preferential loss of carbonate (Hallsworth *et al.*, 1973) and Mg (Hallsworth *et al.*, 1972). An

increased fluoride concentration is found in lesions (Hallsworth and Weatherell, 1969), with variably elevated levels (maximum detected 21,700 ppm) in the surface zone (Pearce *et al.*, 1995). In old enamel, magnesium-containing whitlockite crystals, identified by SEM and electron probe microanalysis, found in lamellae have been associated with dissolution and reprecipitation of mineral in caries (Kodaka *et al.*, 1992).

Crystal structure

The crystals of enamel and of synthetic carbonate-containing apatites are too small for single crystal X-ray diffraction. X-ray powder diffraction gives lattice parameters, $a = 9.441 \pm 0.003$ and $c = 6.884 \pm 0.006$ Å (Trautz, 1955). The ~0.02 Å enlargement of the *a*-axis parameter relative to hydroxyapatite is probably due to structural water and/or hydrogen phosphate ions, rather than the effects of chloride or carbonate substitution which almost balance out (Elliott, 1994). Although Rietveld analyses of X-ray powder diffraction patterns have been undertaken, these have given little new structural information. [Note added in proof: However, recent work has shown direct structural evidence for CO_3^{2-} replacing PO_4^{3-} ions in the lattice (Wilson *et al.*, 1999).] Instead, understanding of the structure has been gained from other techniques, particularly infrared (IR) spectroscopy, and the study of analogous synthetic and mineral apatites. Detailed reviews of the numerous apatite substitutions have been made (LeGeros, 1991; Elliott, 1994).

Fluoride and chloride can substitute for hydroxyl ions in *c*-axis channel sites. Perturbation of hydroxyl ions by adjacent halide ions has been indicated by additional OH stretch bands in the IR spectra of deuterated enamel (Dykes and Elliott, 1971) and synthetic apatites (Fowler, 1974).

In the apatite lattice, there are two distinct sites for carbonate substitution. The principal carbonate substitution in enamel and other biological apatites is in phosphate ion sites. The polarized IR spectrum of francolite (carbonate-fluorapatite) is consistent with the plane of the carbonate ion in this site having a similar orientation to the face of the phosphate tetrahedron which is sloping with respect to the basal plane (Elliott, 1965). In enamel, the *c*-axis channel sites contain ~11% of the carbonate ions (Elliott *et al.*, 1985). However, if enamel is heated in dry CO_2 at 900°C, carbonate ions in the *c*-axis sites become the predominant substitution. The polarized IR spectrum of a thin (6 μm) section of such enamel cut approximately parallel to the long axis of the crystals showed the orientation of the plane of the ion was almost parallel to the *c*-axis (Elliott, 1965). This orientation has been confirmed by preliminary Rietveld powder diffraction analysis of monoclinic $Ca_{10}(PO_4)_6CO_3$ (Elliott, Young and Dowker, unpubl. data) and calculations using an *ab initio* crystal field method (Peeters *et al.*, 1997).

The amount and location of structural water is a general problem for apatites formed in aqueous media (Elliott, 1994). For example, the so-called Ca-deficient apatites, that are free of other substituents such as carbonate, can differ in their Ca/P ratio from 1.66 to 1.5, while having rather similar powder X-ray diffraction patterns. In these apatites, the substitution of water molecules for hydroxyl ions and of hydrogen phosphate ions for phosphate ions may both act as mechanisms of charge compensation for the calcium deficiency.

Dissolution of apatite and enamel powders

Hydroxyapatite and fluorapatite powders

The solubility product constant (K_{sp}) for fluorapatite is lower than that for hydroxyapatite. For example, in a series of fluor-hydroxyapatites equilibrated in dilute phosphoric acid at 37°C, K_{sp} was 3.19×10^{-61} and 7.36×10^{-60} $(mol.\ l^{-1})^9$ for the end-members fluorapatite and hydroxyapatite respectively (Moreno *et al.*, 1974). The reduction in K_{sp} for all solid solutions of fluorapatite and hydroxyapatite compared with hydroxyapatite (minimum at $Ca_5(PO_4)_3(OH)_{0.44}F_{0.56}$) was ascribed to effects of OH directional disorder and OH···F hydrogen bonding.

Studies of the kinetics of hydroxyapatite dissolution in non-stoichiometric solutions at constant pH and undersaturation (Christoffersen *et al.*, 1996) and under a range of conditions relevant to caries (Margolis and Moreno, 1992) indicate that the dissolution is controlled by surface processes rather than by diffusion of ions away from the crystallite surfaces. The rate of dissolution was found to be dependent on the sum of activities of the acidic species and the degree of saturation of the solution (Margolis and Moreno, 1992). The formation of HPO_4^{2-} in the surface has been shown to be the most important reaction controlling the rate of hydroxyapatite dissolution (Christoffersen *et al.*, 1996).

Non-stoichiometric apatite and enamel powders

Study of the solubility of enamel and of non-stoichiometric apatites is complicated by the uncertainty of their composition and defect structure, the possibility of heterogeneity (they may contain fractions with different solubilities), and the possible formation of other phases during dissolution. Ideally, the solubility of enamel should be defined by an ion activity product that takes account of all the substituent ions. As an approximation, enamel solubility has been calculated in terms of the ion activity product for hydroxyapatite, I_{HA}, $(Ca^{2+})^5(PO_4^{3-})^3(OH^-)$ (where brackets denote activity). However determined values differ by $>10^7$, suggesting a variability with experimental conditions, e.g. preferential dissolution of more soluble fractions or metastability resulting from control of solubility by the formation of other calcium phosphate phases (Shellis *et al.*, 1993, 1997). The preferential loss of carbonate, observed in the dissolution of synthetic carbonate-containing apatites and enamel, has also been attributed to the formation of a surface layer of dicalcium phosphate dihydrate ($CaHPO_4.2H_2O$) or other phosphate complex (Mayer *et al.*, 1988). The possible importance of other phases has also been indicated by an investigation of enamel and hydroxyapatite solubility conducted in CO_2-containing atmospheres, modelling biological conditions and recognizing the carbonate component of enamel apatite (Moreno and Aoba, 1991). In this study, the results could be interpreted in terms of the formation of a carbonate-containing apatite which, under these conditions, was more stable than hydroxyapatite.

The concept of metastable equilibrium solubility (MES) has been introduced as an approach to understanding the dissolution behaviour of synthetic carbonate-containing apatite powders over time-scales from seconds to days, before thermodynamic equilibrium is attained (Fox *et al.*, 1995*a*). The rate of dissolution in acidic solutions was initially rapid, but became extremely slow when the solution reached a degree of saturation still well below that needed for crystal growth. The MES ion activity product was defined as the product at the rapidly attained apparent equilibrium. Many synthetic carbonate-containing apatite powders were shown to exhibit a distribution of MES ion activity products. Possible explanations of this phenomenon include an inhomogeneous distribution of defects (e.g. carbonate ion substitution) within the crystal lattice (Fox, *et al.*, 1995*a*).

Demineralization of enamel

Additional problems in understanding the physico-chemical processes in enamel caries are caused by the natural porosity of enamel and the phenomenon of subsurface demineralization.

Polarized light microscopy of natural enamel lesions using a range of imbibition media demonstrated variation in porosity and indicated a molecular sieve effect to a varying extent within zones of the lesion and sound enamel (Darling *et al.*, 1961). Variation in porosity (and tortuosity) with position within a lesion and with time during demineralization complicates mathematical modelling of diffusion within the lesion. The influence on effective diffusion coefficient has been considered in relation to fluoride transport (Chu *et al.*, 1989). However the effect of ion transport in the pore system of demineralizing enamel on the rate of lesion progression is unclear.

There are a number of processes during demineralization that could be rate-controlling, particularly processes at the surfaces of the crystals at the advancing front of the lesion or transport processes to and from the advancing front. Vogel *et al.* (1988, 1997) studied perm-selectivity of enamel and have reported that the fluid within an *in vitro* caries lesion is saturated with respect to hydroxyapatite. These authors commented (Vogel *et al.*, 1988) that this finding was inconsistent with caries models which presumed that enamel demineralization is controlled by the rate of release of ions from the crystals (presumably they meant at the advancing front), so that diffusion in the enamel might be rate limiting. In support of this, some studies have reported a linear relation between the square or cube of lesion depth with time, which implies that transport processes may be limiting. However recent *in vitro* work shows that, at least under the conditions studied, lesion depth increases nearly linearly with time (Chow and Takagi, 1989; Gao *et al.*, 1993*a*), implying that the rate is not limited by diffusion within the lesion. Clearly it is not yet established what controls the rate of growth of a lesion and it may be that it is an oversimplification to seek only one mechanism.

Theories explaining the phenomenon of subsurface demineralization in enamel have been reviewed by Anderson and Elliott (1992). Four groups of theories were described: (1) chemical inhibition of dissolution of the surface enamel by salivary components or fluoride derived from the

oral environment; (2) anatomical variations in structure and composition of enamel; (3) chemistry specific to calcium phosphates, such as formation of dicalcium phosphate dihydrate or less soluble subsurface complexes; and (4) a more general phenomenon that may involve coupled diffusion. The theories are not mutually exclusive and the relative importance of the proposed factors might vary with clinical and experimental conditions.

Model systems

An approach to clinical conditions is provided by *in situ* experiments, in which sections or blocks of tooth tissue are worn by a volunteer in an intraoral device but the mineral content of samples is measured in the laboratory (Marsh, 1995). However *in vitro* models of enamel caries are required for precise control of de- and remineralization conditions (White, 1995). Although bacterial preparations can be used to produce demineralization *in vitro* (Marsh, 1995), the demineralizing agent is usually an acidified gel or organic acid buffer solution. Modelling has been further extended for the study of fundamental physico-chemical processes in subsurface demineralization by the use of blocks (Langdon *et al.*, 1980) and gel-stabilized suspensions (Featherstone and Cussler, 1987) of hydroxyapatite, and other permeable solids (Anderson and Elliott, 1992).

Ten Bosch and Angmar-Månsson (1991) have reviewed methods that have been used for measurement of demineralization in *in situ* studies (also applicable to *in vitro* studies). These included chemical analysis of microsamples, microprobe analysis, microhardness measurement, iodide penetration (an indirect measurement of porosity), microradiography, iodine X-ray absorptiometry, polarized light microscopy and light scattering. Infrared reflectance (Anderson *et al.*, 1996) and laser scanning confocal microscopy of demineralized enamel stained with a fluorescent dye (Fontana *et al.*, 1996) have also been investigated. Birefringence measurements have been widely used in caries studies, but Theuns *et al.* (1993) have now shown that quantification of mineral content is unsatisfactory because of the sensitivity of the method to form birefringence.

The important advantage of microradiographic methods is the direct measurement of mineral content without destruction of the specimen. Demineralization is usually studied in sections coated with an acid-resistant nail varnish leaving a window exposed to the acidic solution. Quantitative measurement of X-ray transmission by photon counting has several advantages over contact microradiography using photographic film, notably the measurement of a wider range of intensities (Elliott *et al.*, 1989). If both incident and transmitted intensities are measured and the mass attenuation coefficient of the mineral is known, the projected mineral mass per unit area can be calculated. (Absorption from the organic phase of enamel can be neglected at the X-ray energies used.) The fractional projected mineral mass is the projected mineral mass per unit area after demineralization divided by that before demineralization. This can be calculated from transmitted intensities alone.

In scanning microradiography (SMR), the environment in which demineralization occurs can be controlled and the changes in mineral content can be measured in real time (Elliott *et al.*, 1994). A section is stepped across a 10 μm X-ray beam and the absorption measured typically at 10 μm intervals while demineralizing solution is pumped through the cell (Fig. 1). In this way, series of directly measured profiles of projected mass can be obtained as demineralization proceeds (Fig. 2). Thus the influence of single variables on the progress of demineralization can be examined. For example, it has been shown that the rate and pattern of enamel demineralization is more influenced by the degree of saturation with respect to hydroxyapatite than the pH (range 2.5 to 4.5) of the demineralizing solution (Gao *et al.*, 1991).

Scanning microradiography has also been used to investigate the influence of anatomical variations in the structure and composition of enamel on its rate of demineralization. Usually (as in Fig. 2), the natural surface of enamel is exposed to the demineralizing solution which diffuses inwards, simulating caries. However it has been demonstrated that the phenomenon of subsurface demineralization is not specific to the natural surface (Anderson and Elliott, 1992). Sections of enamel were cut and varnished so that acid was presented to the inner surface (normally adjacent to dentine) and diffused outwards towards the natural surface. Subsurface demineralization occurred, although the surface layer was less pronounced. In a further experiment, instead of an edge being exposed, the entire flat surface of a section from the outside of the enamel through to

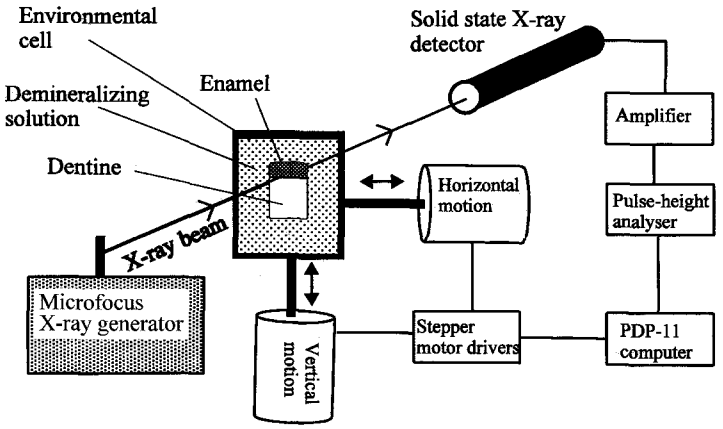

FIG. 1. Schematic of scanning microradiography (SMR) system.

the dentine was exposed to acid (Elliott *et al.*, 1994). The rate of demineralization was found to increase with distance from the natural surface.

In simpler model systems, synthetic aggregates have been used to overcome the problem of variation in enamel composition. The occurrence of subsurface demineralization in strontium hydroxyapatite (which has no dicalcium phosphate dihydrate equivalent) exposed to acid and in calcium hydroxide exposed to de-ionized water (Fig. 3) indicated that this is a physico-chemical phenomenon not restricted to calcium phosphates (Anderson and Elliott, 1992). Very uniform lesions can be produced in pellets of hydroxyapatite sintered after isostatic compression (Fig. 4), but there is limited control over their chemistry. We are therefore developing model systems based on well-characterized synthetic apatite powders which will allow control over the characteristics of the dissolving solid as well as the demineralizing

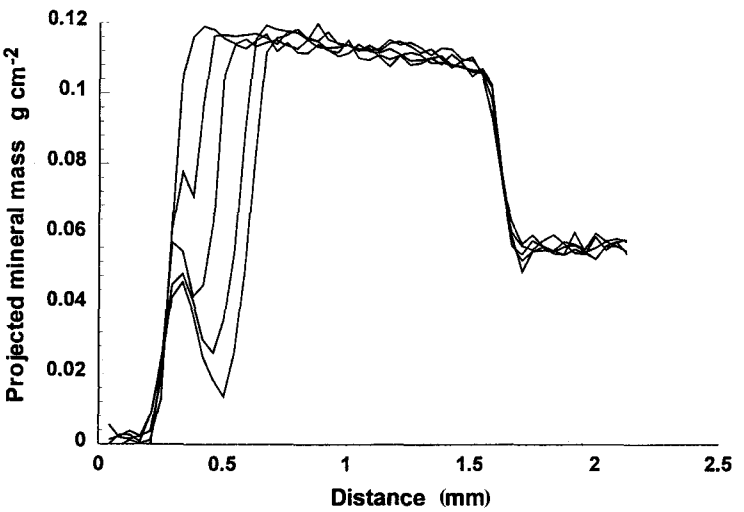

FIG. 2. Demineralization of enamel section from its natural surface by sodium acetate/acetic acid buffer at pH 4.0. Ag-K_α radiation, 10 s at each point, 100 points at 10 μm intervals, scan every 54 h.

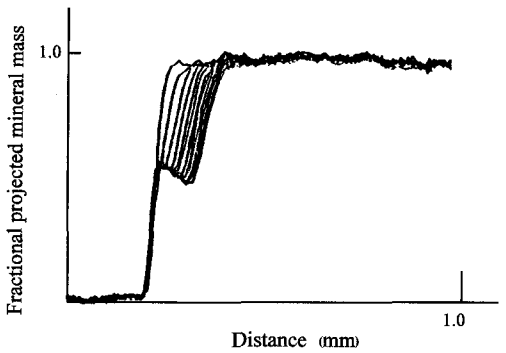

FIG. 3. Demineralization of $Ca(OH)_2$ aggregate by deionized water. Mo-K_α radiation, 10 s at each point, 101 points at 10 μm intervals, scan every 3 h (from Fig. 13 in Anderson and Elliott, 1992).

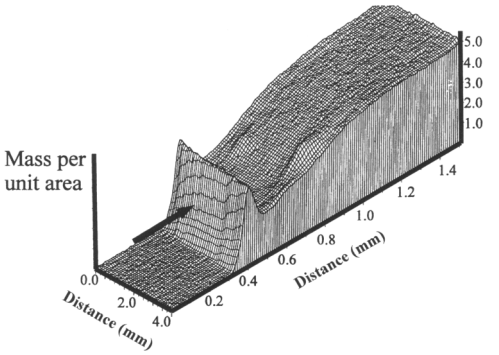

FIG. 4. SMR area scan of a developed lesion in a 200 μm section of permeable hydroxyapatite aggregate after exposure to a 0.1 mol l^{-1} lactic acid demineralizing solution at pH 4.0 (151 points at 10 μm intervals in the direction perpendicular to the surface, 40 points at 100 intervals in the direction parallel to the surface, 10 s per point.) The arrow indicates the direction of acid attack. (After Fig. 5.1.1.2 in Anderson, 1988).

solution (Morgan *et al.*, 1998). One system uses a tube with layers of powder separated by filter paper that can be disassembled, so that each layer can be studied for changes in apatite structure or formation of other phases. In experiments using the same apatite preparation in each layer, subsurface demineralization has been observed: the loss of mineral was most pronounced in the second layer and was successively reduced in deeper layers, but the surface layer was relatively well preserved. This system also allows the effect of variations in physico-chemical characteristics with depth to be studied by use of different powders in different layers.

Although subsurface demineralization can be produced in sections, these systems do not model the 3-dimensional spread of natural caries lesions. Smooth surface lesions are approximately conical, with the deepest penetration centrally, and exhibit variation in the thickness of the surface zone across the lesion (Bjørndal and Thylstrup, 1995). Model systems of 3-dimensional demineralization in blocks of enamel have been studied by X-ray microtomography (XMT), a miniaturized form of clinical CAT scanning (Gao *et al.*, 1993*b*; Elliott *et al.*, 1994). From the reconstructed volume data set of X-ray attenuation coefficients (resolution 10 μm cubic voxel sidelength), slices can be extracted for study of mineral content distribution (Fig. 5). As a nondestructive method, XMT has the advantage that repeated measurements can be made during the course of de- and remineralization, so there is potential for study of the kinetics of mineral loss and gain in three dimensions.

Fluoride

The influence of fluoride on de- and remineralization of enamel is an important theme running through caries research. The extensive work has

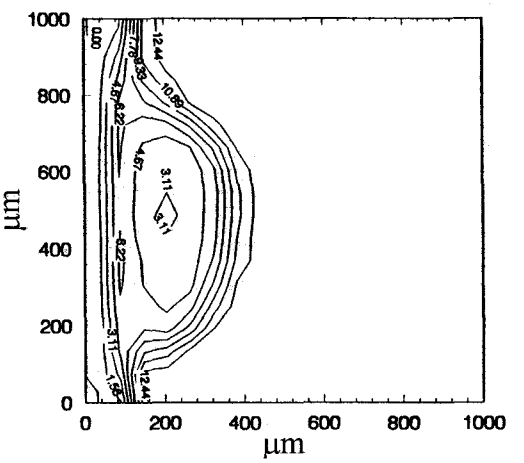

FIG. 5. Contours of X-ray attenuation coefficient (1.56 cm^{-1} intervals) in a 10 μm thick slice reconstructed from X-ray microtomographic measurement (Ag-K_α radiation) of a demineralized block of enamel, showing that the mineral concentration is lower in the central region of the lesion than towards the outer enamel surface (left) that was exposed to demineralizing solution (from Gao *et al.*, 1993*b*).

been reviewed by Margolis and Moreno (1990), Moreno (1993), Ingram and Edgar (1994), and Aoba (1997). The belief that incorporation of fluoride into the enamel during tooth development was the primary mechanism for reduced caries levels in regions with fluoridated water originated from epidemiological studies of caries experience in children, reviewed by Backer Dirks (1974). However there is now evidence that the topical effect of fluoride from water or therapeutic agents (e.g. toothpaste) is more significant than the systemic effect. The reduced solubility of surface enamel with very high fluoride content may provide some protection against caries, but the current thinking is that free fluoride available at the tooth surface during acid attack is usually more important. However the mechanism is uncertain.

The model of Margolis and Moreno (1985) proposes a dynamic process: in a solution undersaturated with respect to enamel, so that enamel dissolution occurs, the presence of fluoride may result in supersaturation with respect to fluoridated hydroxyapatite, so that a fluoridated apatite phase is precipitated in the place of dissolved enamel mineral in the surface. Thus the net demineralization can be decreased or completely inhibited, depending on the relative rates of dissolution and precipitation. Quantitative experimental results (Margolis *et al.*, 1986) were consistent with this model. Under the demineralizing conditions used in this study, solution fluoride concentration influenced the pattern of demineralization (cavitation of the enamel surface at 0.004 ppm F, subsurface demineralization at 0.024 ppm F, and no detectable mineral loss from most samples at 0.504 ppm F).

Fox *et al.* (1995*b*) have proposed a different model in which the adsorption of fluoride on the surface of crystals determines the microenvironment within the enamel pores. Calculations using a mathematical description of the model predicted experimentally observed patterns of demineralization.

Conclusions

The enormous body of research into dental caries reflects the economic and social costs of this extremely prevalent disease. The initial subsurface demineralization of enamel caries has profound clinical importance because it provides the possibility of reversal of the lesion by remineralization. The complexity of natural caries has been addressed through the use of model systems and by study of the atomic-scale structure and fundamental physico-chemical properties of enamel mineral and synthetic apatite analogues (see LeGeros (1991) and Elliott (1994) for extensive critical reviews). Outstanding problems include the structure, chemistry and dissolution of carbonate-containing apatites, including enamel mineral, formed in aqueous media. Additionally, understanding transport and dissolution processes in inhomogeneous porous solids is of fundamental importance to demineralization of enamel tissue. The mechanisms determining rate-control of dissolution and subsurface demineralization in enamel have not been established. However, it may be that the variety of mechanisms proposed to explain the dissolution behaviour of the tissue is essentially an expression of the inherent variability and complexity of the system.

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