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Morphological characteristics of mouse incisor enamel

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ABSTRACT

Maxillary and mandibular incisors of mice aged 5 wk were sectioned and ground along various planes, acid-etched and observed by scanning electron microscopy (SEM). The general design of the enamel structure resembled rat incisor enamel with an uniserial lamellar pattern of prisms in the inner enamel and incisally directed parallel prisms in the outer enamel. The centrolabial thickness of the enamel was about 60 μm in the maxillary and about 95 μm in the mandibular incisor. The angle between prism rows and enamel–dentine junction was about 70° in the maxillary and about 45° in the mandibular incisor, while the angle of decussation, which increased from the enamel-dentine junction towards the outer enamel, was 50–95° and 30–80° respectively. The angle between outer enamel prisms and enamel surface was about 12° in the maxillary and 5–15° in the mandibular incisor. The outer $\frac{1}{2}$–$\frac{1}{3}$ of the outer enamel contained iron and was more acid-resistant than the rest of the enamel. The superficial 3–5 μm was prismless with a Fe/Ca ratio of about 25/75 in the maxillary and about 10/90 in the mandibular incisor. The latter concentration of iron was insufficient to give visible pigmentation to the enamel. The extreme mesial and lateral enamel was neither typical of inner nor of outer enamel. Assuming that the length of the zone of enamel secretion is half the corresponding length in the rat, it could be calculated that ameloblasts in mouse mandibular incisors produce enamel at a rate of about 6 μm per day, about half the corresponding rate in the rat. In spite of this, the mouse mandibular incisor has a relatively thick layer of enamel, since the ameloblasts spend a relatively long time in the zone of enamel secretion due to a fairly slow eruption rate.

Key words: Teeth; dental enamel; prism pattern; iron pigmentation.

INTRODUCTION

The tooth is a convenient model for studying basic biological phenomena such as cell generation, cell differentiation and interaction, synthesis, secretion, and organisation and mineralisation of extracellular matrices (ECM). Rodent incisor teeth grow continuously and exhibit all stages of tooth formation at any time. This characteristic makes them ideal models for the study of enamel formation, which occurs in several distinct stages along the tooth axis (e.g. Pindborg & Weinmann, 1959; Suga, 1959; Warshawsky & Smith, 1974; Smith & Warshawsky, 1976; Leblond & Warshawsky, 1979). The rat incisor has for many years been extensively used for this purpose. Its normal enamel structure is well established (e.g. Tomes, 1850; Korvenkontio, 1934; Warshawsky, 1971; Risnes, 1979*a*). No fundamental differences exist in the basic structure and mode of formation between rat and human enamel (Warshawsky et al. 1981).

Over the last decade methods for generating transgenic mouse lineages and gene knock-outs have established the mouse as the most widely used animal model for the study of genetics, embryogenesis, organogenesis, histogenesis, tumorogenesis, and for testing drugs. Recent advances in mouse molecular genetics (e.g. Slavkin et al. 1992; Chen et al. 1994; Lyngstadaas et al. 1995; Matzuk et al. 1995; Thesleff et al. 1995) have shed new light on the molecular biology of tooth formation. In order to be able to interpret and evaluate the effects of biomolecular

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interventions, it is necessary to have a thorough knowledge of the normal morphology of an organ or a tissue. However, a detailed survey of the normal morphology of mouse enamel is lacking. We describe here the structure of mouse incisor enamel in different ground and etched planes as observed in the scanning electron microscope, with special emphasis on similarities and differences as compared with rat incisor enamel.

MATERIALS AND METHODS

Balb/c Albino mice, aged 5 wk, were killed and their upper and lower jaws dissected and fixed in 70% ethanol. After fixation for 24 h, a segment of the erupted part of the incisors was cut off with a water-cooled diamond wheel, air-dried and glued to brass cylinders with a cyanoacrylate glue (Risnes et al. 1995). The incisor segments were sputter-coated with a 50 nm layer of gold-palladium in order to protect the enamel surface from the subsequent acid etching. All segments were ground transversely (at the incisal end), some also longitudinally, tangentially, or oblique transversely (at the apical end), using 3M waterproof silicone carbide paper and a specially designed apparatus (Risnes, 1985) operated under a stereomicroscope. After grinding, the specimens were cleaned by light brushing under running tap water and etched for 10 s × 3 in 0.1% nitric acid. The specimens were air-dried, sputter-coated with 30 nm gold-palladium and observed in a Philips SEM 515 operated at 15 kV, using a specially designed holder allowing multiangular viewing of the specimens (Risnes, 1982).

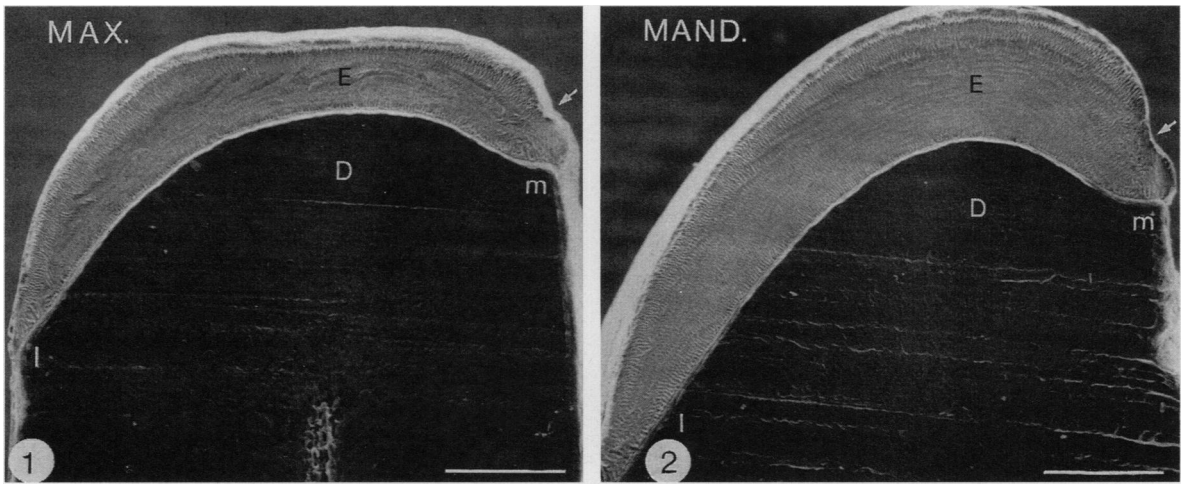
The SEM was equipped with an EDAX ECON2 detector and PV9900 analyser. Semiquantitative energy dispersive x-ray (EDX) analyses of calcium and iron were performed at 15 kV and 0° tilt using the SuperQuant program and normalising by element to 100%.

RESULTS

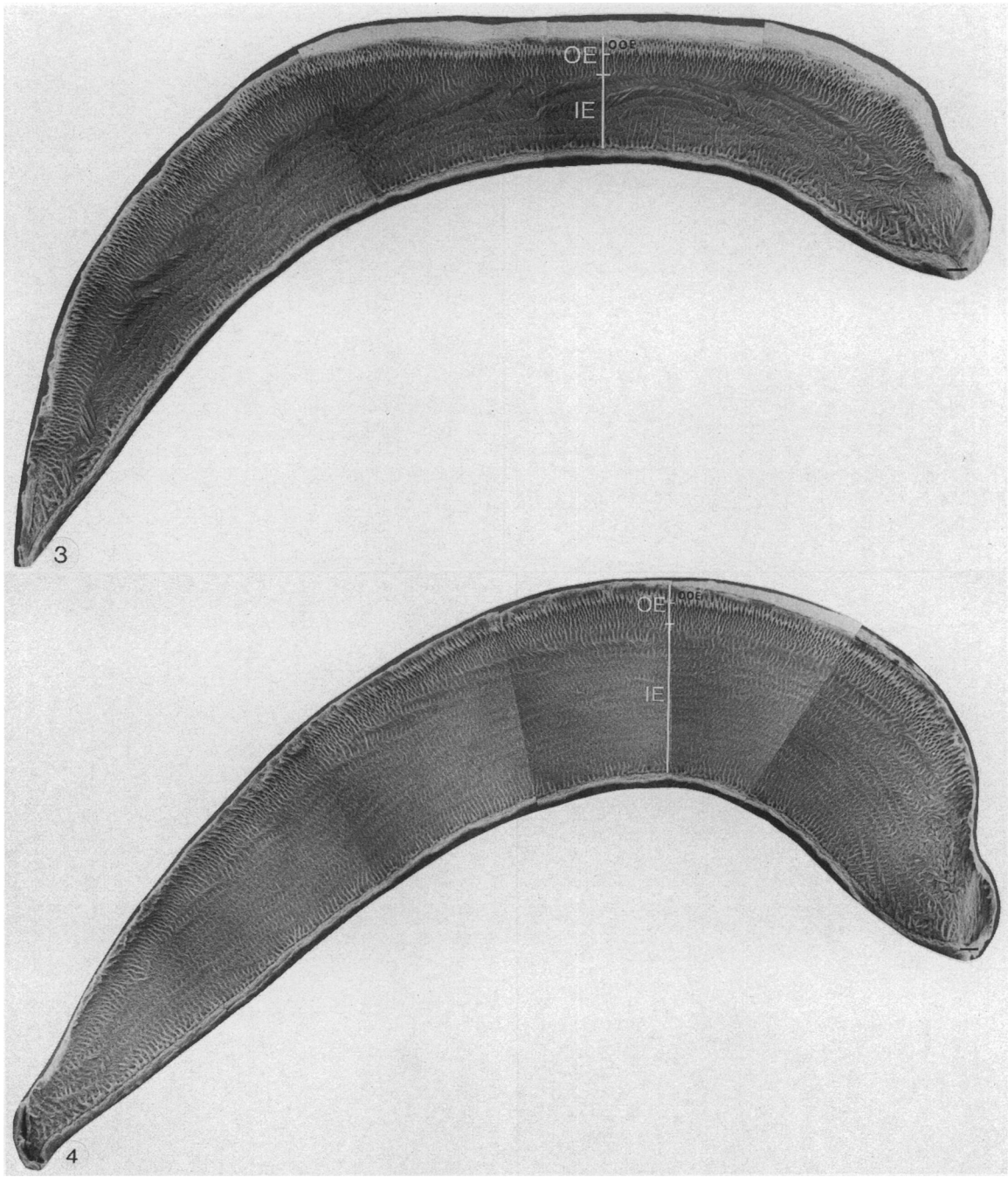
When observed under the dissecting microscope, the enamel of mandibular incisors was not appreciably pigmented. The enamel of maxillary incisors, on the other hand, exhibited a distinct yellow–brown pigmentation which faded away towards and was completely lost before the mesial and lateral cemento-enamel junctions.

The extent and outline of the enamel layer was well demonstrated in transverse sections (Figs 1–4). The enamel covered the labial part of the incisors, reaching further in the lingual direction on the lateral than on the mesial aspect. In the maxillary incisor the transverse enamel contour was flat in the central labial region. In consequence, the enamel thickness of the maxillary incisor was greater at the mesial (+17%) and lateral (+30%) angles than centrolabially. The thickness of the enamel in the centrolabial region was about 60 μm in the maxillary and about 95 μm in the mandibular incisor. Adjacent to the mesial concavity in the enamel-dentine junction the enamel surface showed a distinct notch, representing a longitudinal furrow running parallel with the mesial cemento-enamel junction. Laterally a corresponding notch and furrow was only faintly expressed.

The mouse incisor enamel can be divided into 2 main layers, inner enamel and outer enamel.



Figs 1, 2. Transverse sections of mouse incisors, incisal view. D, dentine; E, enamel; m, mesial; l, lateral. Arrow points at furrow mesially on the enamel surface. Bar, 100 μm. (Fig. 1) Maxillary (MAX.) right incisor. (Fig. 2) Mandibular (MAND.) left incisor.

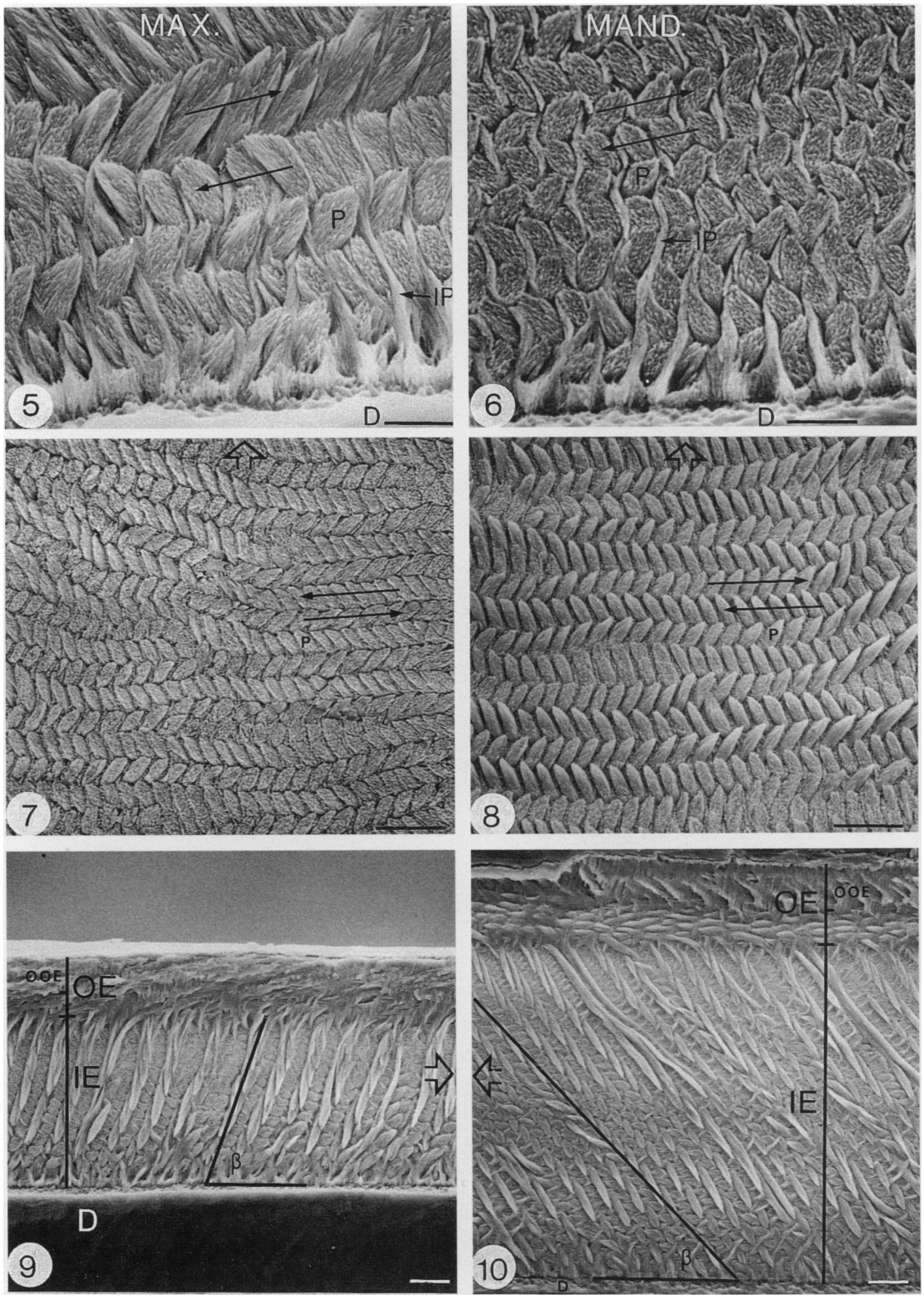


Figs 3, 4. Composite micrographs of enamel of mouse incisors shown in Figures 1–2. IE, inner enamel; OE, outer enamel; OOE, outer part of outer enamel which contains iron and is more acid-resistant. Bar, 10 μm. (Fig. 3) Maxillary right incisor. (Fig. 4) Mandibular left incisor.

Inner enamel

In the inner enamel, prisms were arranged in single-layered rows (lamellae), which were oriented transversely to the long axis of the tooth (Figs 3–12). Prisms of adjacent rows were inclined in opposite directions, i.e. mesially and laterally, and consequently crossed each other (decussation).

The appearance of the cut prism profiles in the transverse plane (Figs 3–6), with more oblong profiles in the maxillary than in the mandibular incisor, indicated that the prism rows were less incisally inclined in the former than in the latter. This was confirmed in the longitudinal plane, where the angle between prism rows and enamel-dentine junction was found to be about 70° in the maxillary incisor and about 45° in the mandibular incisor (Figs 9, 10). Prism row inclination varied somewhat within the same tooth, an the course of the prism rows in the longitudinal plane was often somewhat sinusoidal (Figs 9, 10). The angle of decussation (angle between crossing prisms open towards the surface and dentine)



Figs 5–10. Mouse incisor enamel sectioned along various planes. Maxillary (MAX.) incisors to the left, mandibular (MAND.) incisors to the right. D, dentine; IE, inner enamel; IP, interprism; OE, outer enamel; OOE, outer part of outer enamel; P, prism. (Figs 5–6) Transverse sections of inner enamel in incisal view showing obliquely cut prisms arranged in transverse rows (unlabelled arrows). Bar, 5 μm. (Figs 7–8) Tangential sections of inner enamel showing obliquely cut prisms arranged in transverse rows (unlabelled arrows). Open arrows show incisal direction. Bar, 10 μm. (Figs 9–10) Longitudinal sections showing incisal inclination of prism rows in the inner enamel (represented by the angle β). On entering the outer enamel all prisms run parallel with each other in an incisal direction (open arrows) and with an increased incisal inclination. The outer part of the outer enamel is iron-containing and more acid-resistant, as evidenced by a slope in the etched surface from this to the subjacent part of the outer enamel (seen more clearly in stereo-pair micrographs not shown here). Bar, 10 μm.

could be assessed in the oblique transverse plane (Figs 11, 12). Due to a somewhat curved prism course the angle of decussation increased from the enamel-dentine junction towards the outer enamel; in the inner, middle and outer parts of the inner enamel the angle of decussation was about 50°, 75°, and 95° respectively in the maxillary incisor and about 30°, 60°, and 80° respectively in the mandibular incisor.

Aberrations from an ideal uniserial lamellar prism pattern were observed, including variations in length of prism lamellae, fusion and bifurcation of lamellae, adjacent lamellae with parallel prisms, prisms changing direction, and variations in size and shape of prism profiles (Figs 5–12).

Outer enamel

In the outer enamel all prisms became parallel with each other, and ran in an incisal direction (Figs 9–14). Their incisal inclination was considerably increased (Figs 9, 10). However, it was difficult to measure the angle accurately since even minor deviations of the plane of section from the prism direction reduced the length of the prisms, hampering determination of prism orientation. Nevertheless, we assessed the angle between the prisms and the enamel surface to be about 12° in the maxillary incisor (Fig. 9). In the mandibular incisor this angle seemed to increase from about 5° near the inner enamel to about 15° near the enamel surface (Fig. 10). In accordance with this, the cross-cut prism profiles in the transverse plane appeared to increase somewhat in height from the inner to the outer part of the outer enamel in the mandibular incisor (Fig. 14), but not in the maxillary incisor (Fig. 13).

In the transverse plane the interprism defined a characteristic honeycomb pattern in the outer enamel (Figs 3, 4, 13, 14). In the outer $\frac{1}{2}$–$\frac{1}{3}$ of the outer enamel the interprism was more abundant, encompassing smaller (predominantly in the maxillary incisor) (Fig. 13) or fewer (predominantly in the mandibular incisor) (Fig. 14) prisms. This part of the outer enamel, including a superficial prismless layer of about 3–5 μm, was more acid-resistant than the rest of the enamel, evidenced by an abrupt slope in the etched transverse plane from the outer to the inner part of the outer enamel. The same effect was obtained when etching longitudinal planes (Figs 9, 10). EDX analyses revealed the presence of iron in this part of the outer enamel with a gradient of increasing concentration towards the surface. The iron content was higher in the maxillary than in the mandibular incisor. In analysed areas of 5 × 5 μm of the superficial prismless layer the Fe/Ca-ratio was about 25/75 in the former and about 10/90 in the latter.

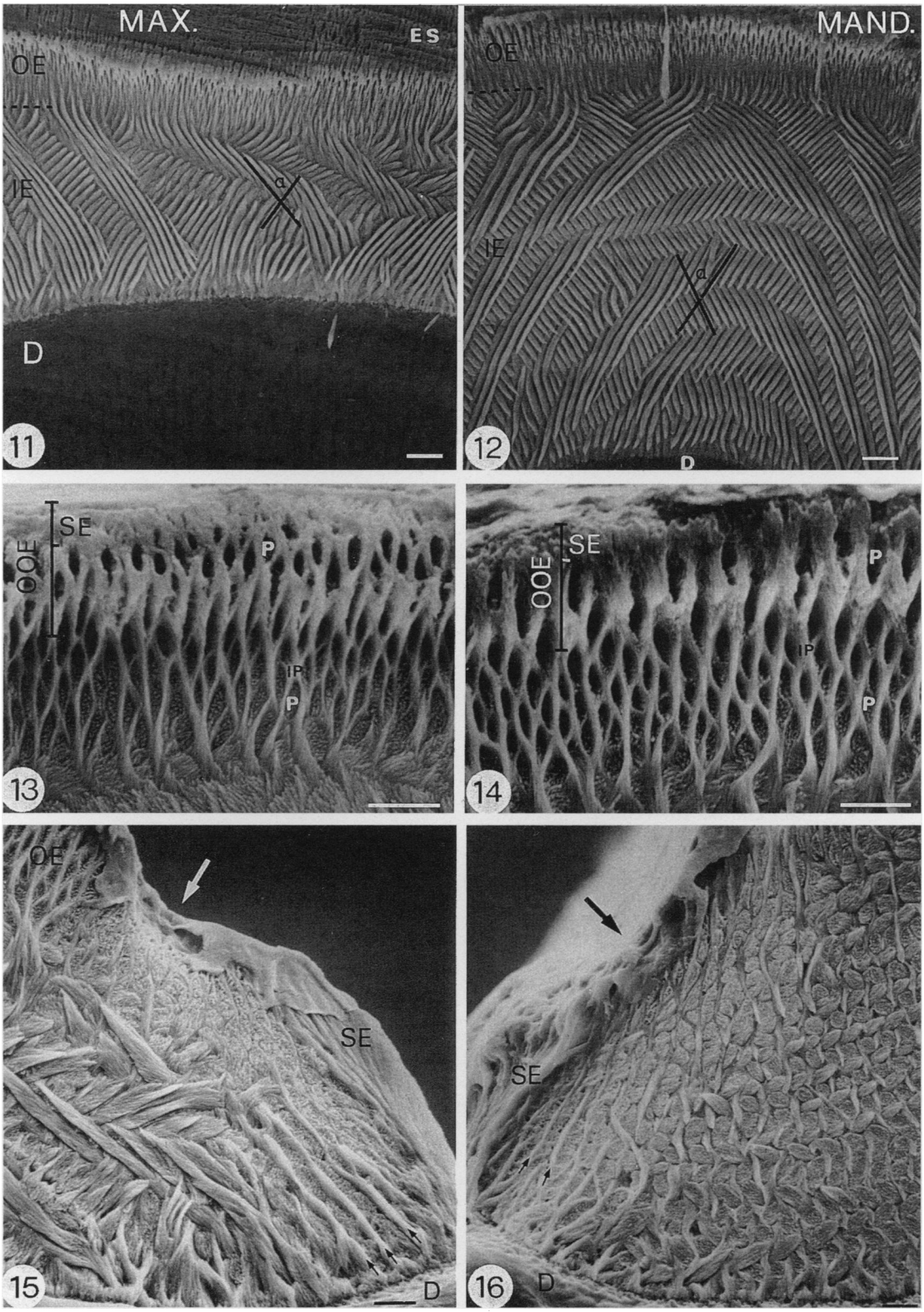
The thickness of outer enamel in the central labial region was about 20 μm in the maxillary incisor and about 22 μm in the mandibular incisor, giving thickness ratios between outer and inner enamel of 0.5 and 0.3 respectively.

Mesial and lateral enamel

Towards the mesial and lateral cementoenamel junctions (last 30–35 μm) the division into inner and outer enamel became less apparent (Figs 3, 4, 15, 16). The outer enamel with its characteristic architecture ended at the mesial notch and at a corresponding distance from the lateral cementoenamel junction. The acid-resistant part of the outer enamel terminated shortly before the outer enamel disappeared. In the enamel bulge between the mesial notch and the mesial cementoenamel junction distinct strands of interprism delimited radial lines of nondecussating prisms (Figs 15, 16). A conspicuous feature was a superficial prismless enamel layer where the constituent crystals apparently belonged to the interprism system and were oriented parallel with the surface and perpendicular to the subsurface prisms. The extreme mesial enamel appeared to be somewhat more susceptible to acid dissolution than the rest of the enamel.

DISCUSSION

As in the rat and other rodents, the enamel covers only the labial part of the mouse incisors (Korvenkontio, 1934). The enamel covers a smaller part of the incisor circumference in the mouse than in the rat. The centrolabial thickness of the enamel relative to the tooth diameter is, however, greater in the mouse than in the rat, especially in the mandibular incisor. According to Korvenkontio (1934) the enamel thickness of the mandibular incisor constitutes 1/9 of the labiolingual tooth diameter in the mouse and only 1/19 in the rat, which fits well with our own observations. At 5–6 wk of age the weight ratio between mice and rats is about 16 g/135 g. This means that the linear dimensions in the mouse are generally about half the length of those in the rat ($16/135 = 2.5^3/5.1^3$), which fits well with observed incisor length and diameter but, as we have seen, not with the observed enamel thickness. The solution to this apparent paradox lies in the slow eruption rate of the mouse incisors compared with rat incisors, for the mandibular incisor about 160 μm (Ness, 1965;



Figs 11–16. Mouse incisor enamel sectioned along various planes. Maxillary (MAX.) incisors to the left, mandibular (MAND.) incisors to the right. D, dentine, ES, enamel surface; IE, inner enamel; IP, interprism; OE, outer enamel; OOE, outer part of outer enamel; P, prism: SE, superficial enamel. (Figs 11, 12) Oblique transverse sections, apical view, showing angle of decussation (α) between prisms of adjacent rows in the middle part of the inner enamel. This angle increases from the enamel-dentine junction to the outer enamel due to a curved prism course. Bar, 10 μm (Figs 13, 14) Transverse sections, incisal view, showing outer enamel with prisms in a honeycomb pattern. The outer part of the outer enamel contains iron, has more abundant interprism, and is more acid resistant than the inner part of this enamel, as evidenced by a slope in the etched surface from this to the subjacent part of the outer enamel (seen more clearly in stereo-pair micrographs not shown here). In the mandibular incisor the number of prisms decreases from the inner to the outer part of the outer enamel concomitant with an increase in their profile height. The superficial enamel is prism-free. Bar, 5 μm. (Figs 15, 16) Mesial enamel in transverse sections showing

Beertsen, 1975) and 445–540 μm per day (Risnes, 1979*b*; Risnes et al. 1995) respectively. Although the zone of enamel secretion in the lower incisor of the mouse may be only half as long as in the rat, i.e. about 5.200 μm/2 = 2.600 μm (Warshawsky & Smith, 1974; Warshawsky, 1979), the ameloblasts will spend a longer time in enamel secretion in the mouse than in the rat, 16 and 10–12 d respectively, due to the slow eruption rate. The thickness of the finished enamel layer does not only depend on the rate of incisal movement of ameloblasts and the length of the zone of enamel secretion, but also on the appositional secretion rate of ameloblasts. Based on a measured enamel thickness of 95 μm and an assumed secretion period of 16 d, the appositional secretion rate of ameloblasts in the mouse mandibular incisor can be estimated to about 6 μm/d. This is only half of the rat value of 12–13 μm/d (Risnes, 1979*b*; Smith & Nanci, 1989) and contradictory to a common 16 μm/d apposition rate for rat and mouse incisors proposed by Schour & Hoffman (1939). The suggested difference in enamel apposition rate between mouse and rat is conspicuous. However, further studies are needed for confirmation. Relative to its size, the mouse mandibular incisor gives a high yield of enamel, which should be an important point to consider when choosing an animal model for studying the morphology, biochemistry and molecular biology of enamel formation. The mice used in the present study were fairly young (5 wk) and the thickness of enamel will probably increase somewhat with age, as it does in the rat (Schour & Massler, 1967). The thickness found in the present study corresponds well with the findings of Korvenkontio (1934). In rodent species mandibular incisors often have thicker enamel than maxillary incisors, which may be mechanically and functionally favourable (Korvenkontio, 1934). In the present mouse material the ratio between the enamel thickness of maxillary and mandibular incisors was about 0.6 compared with about 0.7 in the rat (Korvenkontio, 1934; Schour & Masseler, 1967; Risnes, 1979*b*).

Although rodent and human enamel contains the same basic structural elements, prisms and interprism, the rodent enamel is unique in its extreme prism decussation and also shows a characteristic division into 2 distinct layers. Rodent molar enamel exhibits the same features, but it is more variable (Risnes, 1979*c*; Lyngstadaas et al., unpublished results). The mouse incisor enamel exhibits the same basic architecture as the rat incisor enamel (Tomes, 1850; Korvenkontio, 1934; Warshawsky, 1971; Risnes, 1979*a*) with a uniserial lamella prism pattern in the inner enamel and an outer enamel where all the prisms run parallel. The ratio between the thickness of outer and inner enamel was found to be 0.5 in the maxillary incisor and 0.3 in the mandibular incisor, while Korvenkontio (1934) found ratios of 0.3 and 0.2 respectively. A compilation of data from the literature gives corresponding ratios for the rat of 0.5 and 0.2 (Risnes, 1979*b*).

The incisal inclination of the prism rows as seen in the longitudinal plane differed considerably in the 2 incisors, the angle between prism rows and enamel-dentine junction being about 70° in the maxillary incisor and about 45° in the mandibular incisor. The difference between maxillary and mandibular incisors is much smaller in the rat, where the corresponding angles are 55° and 45°–50° (Risnes, 1979*b*; Risnes et al. 1995). An experimental study on accelerated eruption of rat mandibular incisor indicated that there may be an inverse relationship between incisal and transverse inclination of prisms (Risnes et al. 1996); when the incisal inclination decreased (angle between prism rows and enamel–dentine junction increased) during accelerated eruption, the transverse inclination increased (angle of decussation increased). This may reflect a mechanism operating to maintain a constant vertical rate of ameloblast movement and hence enamel apposition (Risnes, 1979*b*). The differences in angular parameters between maxillary and mandibular incisors in the mouse may reflect the same relationship; going from the maxillary to the mandibular incisor the incisal inclination of prisms increases, while their transverse inclination decreases. The same relationship, although not of the same magnitude, exists in the rat (Korvenkontio, 1934; Risnes, 1979*b*) and in some other rodents with uniserial lamellar prism pattern (Korvenkontio, 1934).

The same types of prism pattern aberrations as those observed in rat incisor enamel (Risnes, 1979*a*) were found in the mouse. These aberrations probably reflect adaptations of ameloblasts to the continuously changing spatial conditions in the ameloblastema related to the complex movements of the ameloblasts (Risnes, 1979*a*; Risnes et al. 1989) and the increasing surface of the developing enamel.

The iron-containing outer part of the outer enamel, encompassing a zone of prismatic enamel with rather

notch in the enamel surface (large arrows). The outer enamel terminates at the notch. In the enamel bulge between the notch and the cementoenamel junction the prisms are nondecussating and arranged in radial lines delimited by radial strands of interprism (small arrows). In the superficial enamel the crystals appear to be parallel with the surface. Bar, 5 μm.

coarse interprism and the superficial prismless layer, was more acid-resistant than the rest of the enamel. The same phenomenon has been observed in the rat (Heap et al. 1983; Risnes et al. 1996). The finding that the acid-resistance was lost when the iron was lost during accelerated eruption (Risnes et al. 1996), indicates a possible relationship between iron content and etching properties. From the present study it appears that the iron content of the superficial enamel of the mandibular mouse incisor, with a Fe/Ca-ratio of about 10/90, was too low to give visible pigmentation. This is in accordance with observations made during accelerated eruption of rat lower incisor (Risnes et al. 1996) where reduced amounts of iron persisted in the superficial enamel of the accelerated erupting incisor for some time after the pigmentation had been lost. It thus seems that the iron concentration must exceed a certain and rather high value in order to be visibly perceived as pigmentation. The increase in interprism combined with a reduction in number of prism profiles occurring in the outer enamel towards the surface in mandibular incisors, is in accordance with observations on the developing surface of rat lower incisors (Salomon et al. 1991).

In the extreme lateral enamel of the mouse incisor the prism patterns of inner and outer enamel seem to merge into a pattern of a less characteristic architecture. In the extreme mesial enamel, i.e. in the enamel bulge adjacent to the enamel notch, the prism pattern is different from the rest of the enamel. The pattern resembles the prism pattern seen in regions of molar enamel, both in the rat (Risnes, 1979*c*) and the mouse (Lyngstadaas et al. unpublished results), where radial strands of interprism delimit radial lines of nondecussating prisms. The characteristic prism pattern of the outer enamel is absent in the enamel bulge, meaning that the ameloblasts here do not change their direction of movement when approaching the surface. A conspicuous feature was the superficial prismless layer consisting of crystals probably belonging to the interprism system and which are oriented parallel with the surface. The loss of the acid-resistant part of the outer enamel towards the mesial and lateral cementoenamel junctions is associated with an absence of iron. This is in accordance with the disappearance of pigmentation from the enamel surface towards the cementoenamel junctions.

In conclusion, a close resemblance between mouse and rat incisor enamel morphology has been established. Certain differences exist, such as in enamel extent and outline, relative enamel thickness, geometry of the prism pattern, degree of pigmentation, and deduced enamel apposition rate. The mouse incisor is a convenient model for studying various aspects of enamel formation; it is not too small to handle, but its relatively small size makes it easier and quicker to section histologically. The relatively thick enamel layer in the mandibular incisor makes it suitable for chemical and biochemical analyses (e.g. Robinson et al. 1979, 1995).

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