Tooth microstructure tracks the pace of human life-history evolution

M. Christopher Dean*

Department of Anatomy and Developmental Biology, University College London, Gower Street, London WC1E 6BT, UK

A number of fundamental milestones define the pace at which animals develop, mature, reproduce and age. These include the length of gestation, the age at weaning and at sexual maturity, the number of offspring produced over a lifetime and the length of life itself. Because a time-scale for dental development can be retrieved from the internal structure of teeth and many of these life-history variables tend to be highly correlated, we can discover more than might be imagined about fossil primates and more, in particular, about fossil hominids and our own evolutionary history. Some insights into the evolutionary processes underlying changes in dental development are emerging from a better understanding of the mechanisms controlling enamel and dentine formation. Our own 18–20-year period of growth and development probably evolved quite recently after ca 17 million years of a more ape-like life-history profile.

Keywords: life history; enamel; dentine; incremental markings; hominid; evolution

1. INTRODUCTION

Some of the most informative things about our own evolutionary history have emerged from an understanding of how morphological adaptations relate to the ways hominoids lived their lives. Variation in life-history strategy is dependent on a broad set of biological rules that govern the balance between fertility and mortality rates. Some apply across many organisms, others are characteristic of particular phylogenetic lineages and some are specific to local ecological circumstances. At one end of the spectrum, for example among eusocial insects, there are large differences in lifespan between the well-protected queens that experience low mortality rates and the more exposed and vulnerable workers (Keller & Genoud 1997). Generally among animals when mortality rates are low, reproductive success can be maximized by postponing age at first reproduction for as long as possible and by spreading reproductive output into adulthood over as long a period as possible (Ashmole 1963; Charnov 1991, 1993; Harvey & Nee 1991; Stearns 1992). In an environment where adult mortality rates are high, the greater costs to the mother of early and more frequent reproduction are outweighed by the need for increased reproductive effort to maximize reproductive success (Harvey & Zammuto 1985; Promislow & Harvey 1990, 1991). At the other end of the spectrum, however, especially when studying more closely related groups of animals such as primates, there are additional influences on life-history variables to consider (Harvey & Clutton-Brock 1985; Charnov & Berrigan 1993). Life-history strategy is also about optimizing available energy resources over a lifetime and primates exploit diverse diets and habitats in very different ways (Kozlowski & Weiner 1997; Gurven & Walker 2006; Dirks & Bowman in press). Among primates, orang-utans (Pongo pygmaeus) for example, are remarkable for their later age at weaning, later age at first reproduction, long inter-birth intervals (6–9 years) and lower mortality rates compared with chimpanzees (Pan troglodytes) and gorillas (Gorilla gorilla) (Hill et al. 2001; Wich et al. 2004). In the case of the orang-utan, food availability, home range and foraging strategy are thought to underlie these life-history traits as well as just differences in mortality rates (Wich et al. 2004).

While on the one hand there is huge life-history diversity among primates, one life-history trait, the period of growth and development, appears to have undergone just three major grade shifts (Schultz 1940, 1969). Among lemurs, irrespective of body size (Schwartz et al. 2002), growth is fast. Both New and Old World monkeys, despite differences among and between them, have a much more prolonged period of growth than prosimian primates and major differences exist in the period of development between monkeys and apes (Harvey & Clutton-Brock 1985; Kelley 1997, 2002). Similarly, the modern human growth period is greatly prolonged with respect to that of apes. Long periods of relative stasis in the general pace of development seem, therefore, to characterize primate evolution. This begs questions about the evolutionary origins of the major shifts between monkey-like, ape-like and modern human-like patterns of development.

A complex hierarchy of interrelated factors has contributed to the evolution of primate development, growth and lifespan. While much of this evolutionary history is unknowable, given only the fossil record of bones and teeth, teeth have to grow within whatever period of development is available. As such their growth is a reflection of the time determined by natural selection acting on key life-history variables (Godfrey et al. 2001; Dirks 2003).
2. ENAMEL AND DENTINE FORMATION

The developmental processes that control the rates of enamel and dentine formation ultimately hold the key to a better understanding of how the timing of dental development comes to track evolutionary change in life-history timing. Enamel and dentine, while fundamentally different tissues, are both extremely hard and never remodel. Dentine is secreted by odontoblasts. These differentiate from the mesenchymal neural crest cells of the dental papilla or future pulp through a long process involving reciprocal inductive signals between oral ectoderm and peripheral dental papilla cells (Lesot et al. 2001; Thesleff et al. 2001). Odontoblasts secrete a proteoglycan-rich organic matrix, part of whose function is to delay mineralization for several days until collagen fibre growth and orientation within the matrix is complete (Jones & Boyde 1984; Linde 1984, 1985; Boyde 1990), and then to induce hydroxyapatite formation at the predentine–dentine boundary (Irving 1963; Veis et al. 1977; Wauthier 1984). Several growth factors, including Insulin-like Growth Factor (IGF-1, IGF 11), Fibroblast Growth Factor (FGF-1) and members of the Transforming Growth Factor beta family (TGF-βs and Bone Morphogenetic Protein, BMP-2) may act synergistically to induce terminal odontoblast differentiation and stimulate the synthesis of dentine matrix formation. Importantly, some of these (e.g. TGF-β1) remain sequestered and potentially active throughout life within mineralized dentine (Tziafas et al. 2000; Sloan et al. 2000; DenBesten et al. 2001).

Enamel matrix is secreted by ameloblasts that differentiate from the inner enamel epithelium of the tooth. Unlike dentine, enamel contains no collagen and is even harder. IGF-1 and IGF-11 are known to increase rates of enamel matrix secretion and are associated with increased expression of genes for the enamel matrix proteins involved in mineralization, such as enamelin and amelogenin (Catón et al. 2005). The onset of enamel matrix secretion is delayed with respect to dentine matrix secretion by at least 30 hours, as continuing inductive epithelial–mesenchymal signalling occurs between these tissues (Gaunt 1967), but then mineralization, unlike dentine, begins almost immediately (Rosser et al. 1967).

3. CIRCADIAN INCREMENTAL MARKINGS IN TEETH

It is the incremental record of tooth growth that provides a time-scale for reconstructing life history. Circadian rhythms are almost universal among living organisms and the mineralizing systems of teeth, shells and corals are no exception. Fossil coral sequences preserve a record of the slowing of the Earth’s rotation over 350 million years (Wells 1963; Scrutton 1964) and fossil teeth contain a record of the daily secretory rhythms of the cells that formed them (Dean 1987).

The experimental evidence for circadian incremental markings in enamel rests largely on a number of labelling experiments, where either sodium fluoride or certain fluorescent markers have been administered at known intervals while enamel was still forming (Schour & Poncher 1937; Okada 1943; Bromage 1991; Smith 2006). There is also evidence for both shorter- (intradian) and longer-period increments in enamel and dentine (Shinoda 1984; Dean 1987, 1995; Boyde 1989; Ohtsuka & Shinoda 1995; FitzGerald 1998; Smith 2006).

No rhythms are known for growth factor synthesis in tooth germs, but circadian rhythms clearly exist in predentine matrix synthesis, dentine mineralization, odontoblast cell process morphology (Boyde 1990) and during tooth eruption (Risinger & Profitt 1996). Both mineralization and eruption rhythms have been shown to be maximal at the end of the light (or active) period and to be linked, respectively, with peak adrenal cortex activity and the late evening secretion of growth hormone and thyroid hormone (Miani & Miani 1971; Risinger & Profitt 1996; Craddock & Youngson 2004). All of this is likely to be controlled by the suprachiasmatic nucleus, and temporary...

Figure 1. Calcospheritic mineralization of root dentine is shown on the left with fluorescent labels seen with confocal microscopy (fieldwidth 130 microns), in the middle with SEM of a mineralizing root dentine front (fieldwidth 70 microns) and on the right in a ground section of a ~1.6 million year old fossil hominid root (fieldwidth 125 microns).
or permanent obliteration of this nucleus results in the loss of a circadian rhythm during dentine formation (Ohtuka-Isoya et al. 2001). However, it is highly likely that there are one or more as yet unidentified intracellular clocks operating during enamel and dentine formation of the kind that regulate intradentinal, circadian and developmental timing (e.g. Smith et al. 1987; Moore 1999; Adoutte 2000).

The circadian mineralizing lines in dentine are distinguished by their characteristic appearance that is described as calcospheritic (see figure 1). Small spheres of mineralizing dentine increase in size until they eventually coalesce with each other. It is the mineralizing increments in dentine that are especially well preserved in fossils (Boyd 1990; Furseth-Klinge et al. 2005). Okada (1943) summarized a series of elegant experiments that together suggest that the mechanism underlying the appearance of mineralizing lines in dentine is the daily change in acid-base balance that accompanies alternating periods of activity and rest (see also Lutz & Rhoads 1977; Boyd 1979). Ultimately, this is manifest as regions of differing refractive index that appear lighter or darker in transmitted light microscopy, and as light or dark bands under back-scattered scanning electron microscopy that reflect regular shifts density of mineral laid down (Boyd 1979, 1989).

5. HOW TOOTH ROOTS GROW IN LENGTH

A clearer understanding of the comparative processes involved in root growth is allowing us to recover more information about the timing of dental development in living and fossil hominoids. It is the cells of the internal layer of the epithelial root sheath that induce the peripheral cells of the dental papilla to differentiate into odontoblasts and go on to form tooth roots (figure 2). Initially, preodontoblast cells of the dental papilla align themselves along the basal lamina that separates them from the epithelial root sheath. A gradient of differentiation then begins that may initially be regulated by signals from the epithelium and subsequently by a lateral relay mechanism between odontoblasts (Lesot et al. 2001; Thesleff et al. 2001). This process ends with final polarization of the root odontoblasts, predentine secretion and mineralization (Thomas 1995).

The rates of odontoblast differentiation and rates of dentine formation can still be determined from longitudinal ground sections of tooth roots (figure 2). Daily incremental markings in the root indicate that mineralization rates begin slowly close to the root surface and that for at least the first 200 µm of dentine formation, the gradient of increasing rate is comparable in both living and fossil hominoids (Dean 1993, 1998). Based on the average spacing of daily mineralizing lines, the first 200 µm of root dentine takes ca 80 days to form. Longer-period accentuated incremental markings in the root reflect the former position and orientation of the odontoblast cell sheet at any one time during root formation. The angle these longer-period lines make to the root surface reflects the rate of differentiation of new odontoblasts during root development (Dean & Wood 1981). For example, in

Figure 2. The rate at which odontoblasts differentiate determines the rate of root extension. The original angle of alignment of the fully differentiated odontoblasts to the root surface (the cementum) can be reconstructed (black arrows) from the orientation of the incremental markings in roots to the root surface. In ground sections of Proconsul heseloni tooth roots, the incremental lines in a deciduous second molar root (the middle image) are near parallel in their orientation to the root surface (extension rate ca 18 µm d−1), while in a permanent premolar root (image on far right) they form a greater angle to the root surface (extension rate ca 8 µm d−1). In both cases, the origin of the arrow begins 200 µm (ca 80 days) deep to the root surface.
80 days, a wave of differentiation proceeding at $10 \, \mu m^{-1}$ will extend $800 \, \mu m$ down the root, whereas a differentiation rate of just $4 \, \mu m^{-1}$ will extend only $320 \, \mu m$. The rate of odontoblast differentiation determines the rate of root elongation, and this relationship has been formally described and referred to as the root extension rate (Shellis 1984). Calculating the changing root extension rates from ground sections of fossil primate tooth roots allows us to compare their growth with living primates.

A number of studies present data for rates of root extension in humans. Stack (1967) measured the increase in length of deciduous incisor tooth roots, which appear to grow linearly at $ca \, 19 \, \mu m^{-1}$. This is likely to be as fast as human tooth roots ever grow. Root growth in permanent teeth is, however, characteristically nonlinear and more complex. Human permanent tooth roots can take up to 7 years to complete, and all the evidence suggest that rates of molar root extension begin slowly, reach a peak and then reduce in rate again as the apex of the root closes (figure 3). Gleiser & Hunt (1955) estimated initial rates of root extension to be $ca \, 4 \, \mu m^{-1}$ for first permanent molars. Feasby (1981) and Inoue & Suzuki (1992) all present data for other permanent tooth roots that initiate with comparably slow rates, but then rise to maximal rates of between $ca \, 8$ and $18 \, \mu m^{-1}$ (Gleiser & Hunt 1955; Takeshima et al. 2004).

There is a consensus that eruption rates come to exceed rates of root growth as a tooth approaches occlusion (Gleiser & Hunt 1955; Schumaker & El Hadary 1960; Ando et al. 1965; Darling & Levers 1976; Feasby 1981; Inoue & Suzuki 1992; Takeshima et al. 2004). The spurt in root growth and the eruption surge are far from equal in magnitude, and eruption rates can exceed root growth by as much as $4.6 \, mm \, yr^{-1}$ in humans (Feasby 1981), and can to some extent be predicted from the height of the jaws (Takeshima et al. 2004).

It is clear that root extension and tooth eruption are independent processes and that only root length at the time of gingival emergence is a useful comparator for gauging differences in developmental timing. Total tooth height at gingival emergence is made up of similar proportions of root and crown height in great apes and modern humans (figure 4). Hence, the proportions in living taxa allow us to calculate the likely amount of root formed at gingival emergence in fossil primates on the basis of measurements of crown height.

6. LIFE HISTORY AND THE EARLIEST APES

Many Miocene apes were a morphological mosaic of characters that we recognize today as specific to either modern apes or monkeys. Great apes have a prolonged life-history profile compared with Old World monkeys. They have reduced rates of mortality, longer gestation.
periods, mature more slowly and have and much later ages at first reproduction (Harvey & Clutton-Brock 1985; Kelley 1997, 2002). Kelley (1997) suggested that besides studying their morphological attributes, M1 emergence times in Miocene fossil apes might, in addition, identify the first evidence of a shift to a modern ape-like life-history profile.

Age at first permanent molar emergence has been calculated for several fossil apes now, using the various daily and longer-period increments preserved in fossil enamel. These include Sivapithecus parvada (Kelley 1997, 2002), a 10 million year old ape from the Siwaliks of Pakistan, Afropithecus turkanensis (Kelley 2002; Kelley & Smith 2003), a 17 million year old ape from Moruorot in northern Kenya, Dryopithecus laietanus from Can Llobateres, a 9.5 million year old site in Spain (Kelley et al. 2001) and two species of Proconsul, dated to 17.5–17.9 million years ago, Proconsul heseloni and Proconsul nyanzae from Rusinga Island, Kenya. The consensus is that Sivapithecus, Afropithecus and Dryopithecus had mean age of M1 emergence times that place them firmly within the known range for modern chimpanzees (Kelley 2004).

Harrison (1987) has argued that the various species of Proconsul were stem catarrhines. Owing to the potential phylogenetic implications that a modern Old World monkey-like or modern great ape-like life-history profile might therefore have, an age for M1 emergence in Proconsul has been viewed as more controversial that in other Early Miocene apes. Proconsul heseloni and P. nyanzae were both arboreal quadrupeds, with long narrow trunks that showed few signs of any forelimb suspensory behaviour, but possessed frontal sinuses and a larger than expected cranial capacity for their body size (Walker 1997). Kelley (1997), on the basis of cranial capacity estimates, cautiously proposed that M1 emergence in the smaller siamang-sized 9–12 kg P. heseloni may have been close to 20.6 months and interpreted this as being later into development than might be expected in an Early Miocene catarrhine. This age for M1 emergence can now be matched using data for enamel and dentine growth combined with data for M1 crown height in P. heseloni.

Histological data for M1 crown formation times suggest that this took between 1 and 1.2 years (Beynon et al. 1998), but estimates for M1 root extension rates and of how much root might have been formed at gingival emergence have been harder to make (Walker & Shipman 2005). Smith et al. (2006) concluded that the method described by Shellis (1984) for calculating extension rates and used by Beynon et al. (1998) is prone to error when used on teeth with short, rapid periods of development. Reanalysis of the P. heseloni M1 roots reveals average extension rates of 9–10 \( \mu \text{m} \text{day}^{-1} \) over 7 mm of root formation. Two M1 crowns are each ca 4 mm tall (Beynon et al. 1998). Assuming crown height to be the same proportion of total tooth height as it is in modern chimpanzees (62–68%), then root length formed at gingival emergence (figure 4) will be 32–38% of total tooth height or 47–61% of crown height. It follows, therefore, that between 1.88 and 2.45 mm of root is likely to have been formed at M1 emergence in P. heseloni. At an average of 9.5 \( \mu \text{m} \text{day}^{-1} \), this translates as 198–258 days of root formation in P. heseloni. Even adding the shortest enamel formation time estimate of 1 year to this (Beynon et al. 1998) gives a likely age at M1 emergence as 18.5–20.4 months, a remarkably close match with Kelley's previous estimate of 20.6 months (Kelley 1997). Even though the small body size of P. heseloni makes it awkward to make direct comparisons with living apes (especially with so little data for living gibbons and siamangs; Dirks 1998), this age for M1 emergence suggests a more prolonged life history than would be expected for an Early Miocene catarrhine of the same body mass (Kelley 1997) and certainly contrasts with the faster enamel and dentine formation rates of the first known fossil Old World monkey, Victoriapithecus macimensi (Dean & Leakey 2004). The larger small chimpanzee-sized Proconsul nyanzae upper M1 crown analysed by Beynon et al. (1998) is 6 mm tall and took 2 years to form its enamel in the crown. Only 540–690 microns of the root are preserved either buccally or lingually in this M1. It now seems likely, by the same argument, that root length at gingival emergence would have been 47–61% of crown height and therefore, that 2.83–3.66 mm of root would have been formed at gingival emergence. Extension rates in this root average 6.25 microns/day, which compares well with those known for modern chimpanzees. Similar calculations for the sum of crown and root formation time give an age for M1 emergence at between 3.26 and 3.6 years, which is well within the age range known for M1 gingival emergence in modern chimpanzees.

All these data for Miocene apes suggest that ca 18 million years ago in the hominoid lineage there was a prolonged life-history profile that broadly matched that of living great apes. It is important to recognize, however, that within this profile a fast–slow dental/life-history continuum remains even today that reflects both the apportionment of available energy resources and population mortality rates (Godfrey et al. 2001; Dirks 2003; Kelley 2004; Nargolwalla et al. 2005; Dirks & Bowman in press). How this might have evolved is a more complex issue, perhaps as an adaptive prolongation of a shorter life-history profile in an as yet unidentified catarrhine ancestor, or as a simple extension of a prolonged life-history profile in a small bodied ancestor that simply kept pace with increasing body size (Kelley & Smith 2003).

7. WHEN AND WHY DID OUR MODERN LIFE-HISTORY PATTERN EVOLVE?

Modern humans have big brains, walk on two feet and have small teeth and jaws. The earliest bipedal fossil hominids from Chad and Kenya are dated at between 6 and 7 million years ago, but for at least the first 4 million years of hominid evolution there is little evidence for an increase in brain size. Brain size and body proportions seem to have changed significantly with the emergence of the genus Homo at about 2 million years and changes in brain size are closely linked with many life-history traits (Smith 1989; Allman & Hasenstaub 1999). Initially, it was thought, almost by definition, that the earliest hominids would show evidence of a human-like life-history profile, but it is now generally accepted this cannot be substantiated (Bromage & Dean 1985; Smith 1986). There are several lines of evidence that allow us to track the evolution of life-history traits among fossil hominids. Various incremental markings in enamel have been used to estimate an age at M1 emergence, as have their relatively small cranial capacities, and both approaches conclude
deciduous tooth wear early in life may have been linked to early first intake of supplementary food, early weaning and shorter inter-birth intervals. Significant adaptive changes in reproductive strategy and life history may have kept up with pressure to survive over millions of years. After 2 million years, only the ‘robust’ australopithecines (P. boisei from East Africa and P. robustus from South Africa) remain in the fossil record and these were extinct by 1 million years ago.

Cumulative trajectories describing enamel growth over time in monkeys, apes and humans (figure 5a,b) appear to show evidence of the major grade shifts in the pace of general somatic growth (Dean et al. 2001). All early hominin enamel growth trajectories fall among the African great apes and have shorter enamel crown formation times compared with those in modern humans (Beynon & Wood 1987; Dean et al. 2001; Reid & Dean 2005; Lacruz et al. in press). This alone suggests that dental development as a whole took less time than in modern humans. M1 emergence times for Homo erectus have been predicted from average cranial capacity estimates (Smith 1992; Smith & Tompkins 1995) and are a close match for those derived from dental histology. The combined evidence from both the enamel and the root extension rates in a single H. erectus specimen from Java (S7-37) indicates that M1 emergence times were close to 4.5 years rather than 6 years in modern humans and that M2 emergence times were nearer to 8 years than 12 years (Dean et al. 2001). On the one hand, this is the first evidence for a significant change from the broadly ape-like life-history profile for ca 17 million years. On the other hand, it seems that even at this relatively late stage of human evolution there was still on average a faster life-history profile than in modern humans today, but one that had slowed in parallel with a significant increase in brain size.

The link between brain size, tooth development and a slower life-history profile is a clear one but a curious one (Smith 1989; Allman & Hasenstaub 1999; Godfrey et al. 2001). Kelley (2004) has argued that the whole changing life-history profile during primate evolution has influenced brain growth and that it is this that has ultimately facilitated cognitive evolution. Longer periods of embryonic development have extended many phases of human brain growth, including glial cell mitosis, dendritic growth, synapogenesis, dendritic pruning and myelination (McKinney 2002). Just three or four extra days of embryonic development between E40 and E43 result in three or four more rounds of founder cell mitosis in the brain, which is enough to account for the 10-fold larger human cortex than of a macaque monkey (Rakic 1995; Hill & Walsh 2005). Brain size as well as brain complexity is, therefore, time dependent as is dental development and simply yet another part of the life-history package (Allman & Hasenstaub 1999). Brain size might not then have been driven solely by selection for cognitive ability. The sequence of events may have begun with a shift in life-history strategy and growth of a bigger more complex brain, which then increased the likelihood of selection for increased cognitive ability. And in the end, increased cognitive ability is bound to contribute towards a further reduction in adult mortality rates (Kelley 2004).

What then of Neanderthals whose brains were bigger than modern humans, but whose life-history profile is described either as at the lower limit of the modern human range on the basis of shorter enamel formation times...
(Dean et al. 1986; Stringer et al. 1990; Tompkins 1996; Guatelli-Steinberg et al. 2005) and patterns of molar tooth wear (Wolpoff 1979; Caspari & Lee 2004) or as being distinct and 15% shorter than modern humans (Ramirez Rozzi & Bermudez de Castro 2004)? Clearly, the late surviving Neanderthals were under considerable demographic pressure from both sudden colder, drier climatic conditions and from incoming biologically and behaviourally modern human populations ( Mellars 2006). Neanderthals are likely to have experienced high levels of infant and adult mortality. It makes no biological sense for any primate to take 18–20 years to grow up only to die as a young adult ( Trinkaus & Tompkins 1990), but then again the Neanderthals did not survive. Understanding the demise of the Neanderthals may ultimately come from a better understanding of our own survival.

At present, it is simply not clear when and where a prolonged modern human-like growth period evolved, nor, as with large brains, if this arose independently in Neanderthals and modern humans ( Dean 2000). The evidence from life-history theory suggests that a reduction in adult mortality rates is likely to have played a big role, but providing evidence for this in the fossil record is fraught with difficulty. Caspari & Lee (2004) calculated the ratio of older to younger adults in successive time periods through the hominin fossil record. They concluded that while there was a significant and successive increase in longevity between all the groups they examined, adult survivorship was a significant and successive increase in longevity. Moreover, the better we come to understand the processes involved in controlling rates of enamel and dentine formation, the closer we get to defining the mechanisms that underlie evolutionary changes in developing primate dentitions.

I am grateful for the helpful comments of three referees. I thank The Leverhulme Trust and The Royal Society for grants awarded to me for research on comparative dental development. I am grateful to the National Museums of Kenya for access to fossil primate material in their care.

REFERENCES
Boyle, A. 1979 Carbonate concentration, crystal centres, core dissolution, caries, cross striation, circadian rhythms and compositional contrast in the SEM. J. Dent. Res. 58b, 981–983.


