Nonmammalian Synapsids

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Introduction to Nonmammalian Synapsids

The fossil record of Permo-Triassic Synapsida has been the source of important data for studying the origin and evolution of mammalian traits (e.g., Kemp 1982, 2005, Angielczyk 2009), terrestrial community structure (e.g., Roopnarine and Angielczyk 2015, Codron et al. 2017), survival from mass extinctions (e.g., Huttenlocker 2014, Smith and Botha-Brink 2014, Day et al. 2015, Botha-Brink et al. 2016) and macro-evolution (e.g., Sidor 2001, Laurin 2004, Roopnarine and Angielczyk 2012, 2016, Didier et al. 2017). Importantly, this group also produced many physiological innovations, providing some of the earliest evidence for rapidly forming fibrolamellar bone tissues, systematic skeletal remodeling, and, perhaps, endothermic thermotabolism. Synapsida includes all amniotes more closely related to mammals than to reptiles (Angielczyk 2009). The nonmammalian synapsids classically comprised two major radiations: a paraphyletic assemblage of basal synapsids commonly referred to as “pelycosaurs” and the more recent, monophyletic Therapsida. Synapsids arose during the Late Carboniferous and originally included two major clades: the extinct Caseasauria and the more diverse Eupelycosauria, which includes the therapsids (Huttenlocker and Rega 2012, Reisz 2014). These early synapsids were the dominant terrestrial vertebrates during the late Carboniferous to early Permian, but by the middle Permian they had essentially been replaced by the mammal-like therapsids. The Permo-Triassic Therapsida represent one of the most iconic evolutionary transitions in the fossil record. The first mammals evolved from therapsids by the Early Jurassic as tiny shrew-sized creatures. Despite some degree of ecological diversity, mammals remained relatively small (less than a few kilograms) until the extinction of the nonavian dinosaurs some 66 million years ago (Ma) (Kielan-Jaworowska et al. 2004).

The first researchers to document and describe the osteohistology of extinct synapsids included Moodie (1923), Gross (1934), Enlow and Brown (1957), Enlow (1969) and Ricqlès (1969, 1972, 1974a, b). However, the last two decades have seen a profusion of studies within a phylogenetic context (including, but not limited to those by Botha-Brink, Chinsamy-Turan, Huttenlocker, Jasinoski, Laurin, Ray, Shelton, among others; see below for detailed references), which have greatly improved our understanding of synapsid histology, growth, and physiology. These studies are summarized below in their phylogenetic context.
Non-therapsid Synapsids

Caseasauria

Caseasauria included small to very large-bodied (>200 kg) generalists and herbivores characterized by a recumbent snout with enlarged nares, some with an absurdly small skull compared to their body length (Olson 1968). During the Carboniferous-Permian transition (ca. 300 Ma), the caseasauria were among the first diverse group of large-bodied vertebrate herbivores, along with diadectomorphs (amniotes) and edaphosaurids (eupelycosaurs). They also included some of the latest surviving pelycosaur-grade synapsids, with some caseasauria recovered from middle Permian-aged rocks. Although their lifestyle is somewhat controversial, with some researchers suggesting a possible aquatic habitus (Lambertz et al. 2016), they have mainly been interpreted as terrestrial (Olson 1968, Felice and Angielczyk 2014).

The diversity of skeletal tissues in caseasauria is poorly known, as they have largely been neglected in histological studies. Our first insights into caseasaur histology were offered by Ricqlès (1974b), who sectioned and described the midshaft histology of a femur of a subadult caseasaur, Ennatosaurus tecton from the middle Permian of Russia. The short, robust femur showed a thin cortical wall and a poorly developed free medullary cavity; most of the medullary area is occupied by a spongiosa, flanked by occasional perimedullary erosion cavities. The thin cortex was dominated by inconsistently vascularized primary lamellar bone, with sparse longitudinal canals dorsally, oblique canals ventrally (associated with the adductor ridge) and was nearly avascular posteriorly. Overall, the predominance of lamellar bone with sparse, but highly ordered vascular canals, resembles that of contemporary diadectomorphs, and it may therefore reflect the primitive state of the amniote stem. Shelton (2015) and Lambertz et al. (2016) showed similar tissue textures in limb bones of other European and North American caseasauria, demonstrating the paucity of nonlamellar bone and sparse vascularity, even in purported juveniles. Lambertz et al. (2016) further suggested, controversially, the possible existence of a diaphragm on the basis of Sharpey’s fibers preserved in the ribs. Future histologic work on the basal eothyrids would continue to clarify the primitive condition for synapsids and for amniotes in general.

Eupelycosaurs

The highest diversity of sampled tissues comes from the Permo-Carboniferous eupelycosaurs, which exhibited considerably more diversity than contemporary caseasauria. Eupelycosaurs includes all synapsids more closely related to Dimetrodon and mammals than to caseasauria, and, by extension, includes therapsids as a subgroup. However, we will first discuss non-therapsid eupelycosaurs as their histology is distinctly different from therapsids and records motifs remarkably similar to modern reptile groups, notably to monitor lizards (varanids) and crocodylians. Varanopids, for example, represent an early eupelycosaur clade that shared many characteristics with extant monitor lizards, including long, slender limbs and sometimes recurved, ziphodont teeth (Evans et al. 2009). Few varanopid taxa have been examined histologically, including the varanodontine Varanops (Ricqlès 1974b, Huttenlocker and Rega 2012, Shelton 2015), and anecdotal observations from the varanodontine Watongia (Ricqlès 1976, Bennett and Ruben 1986) and a mycterosaurine from the lower Permian of Oklahoma (Huttenlocker and Rega 2012, Shelton 2015). Histologically, varanopid taxa show some degree of variation in tissue texture, vascularity and growth zone formation. In Varanops, the cortices of the radius and femur were generally thin and dominated by lamellar primary bone with occasional growth marks. Mycterosaurine femora were slightly thicker walled with combinations of parallel-fibered bone transitioning to lamellar bone (Figure 28.1A), and numerous growth marks and growth zones incorporating mainly longitudinal vasculature arranged in radial rows. Any transition to slowed growth into adulthood was subtle as there is little evidence of distinctive, avascular outer circumferential lamellae. The bone wall was generally dense and compact, but with a distinct medullary cavity sometimes bounded by well-developed inner (endosteal) circumferential lamellae. The well-differentiated medullary cavity of varanopids contrasts with some other early tetrapods, which tended to exhibit bones with a medullary region invaded and partly occluded by a dense spongiosa. The relative lightening of the skeleton in varanopids, and the well-defined tubular architecture of their bones, may be more consistent with a more efficient terrestrial locomotion.

Ophiacodontids exhibited a curious degree of histovariability compared to contemporary groups (Enlow and Brown 1957, Enlow 1969, Ricqlès 1974b, Laurin and Buffrénil 2016). The overall structure and compactness profile of Ophiacodon limb bones appear similar to other early tetrapods; an irregular perimedullary margin, thick bone wall and often, an occluded medullary cavity suggested the possibility of a primitively aquatic lifestyle (though this has been questioned by numerous authors; e.g., Felice and Angielczyk 2014). However, material referred to the Carboniferous ophiacodontid Clepsydrascoletees shows a remarkably thinner bone wall with an abrupt transition between medulla and cortex that is more like that of Varanops (Laurin and Buffrénil 2016). Both Clepsydras and Ophiacodon exhibit cortical bone tissues that are dominated by parallel-fibered and lamellar primary bone with varying degrees of vascularity. In the femoral midshaft of Clepsydras (as in varanopids and many early eupelycosaurs) the vascular canals are formed by longitudinal primary osteons and were nearly avascular posteriorly, with some other early tetrapods, which tended to exhibit bones with a medullary region invaded and partly occluded by a dense spongiosa. The relative lightening of the skeleton in varanopids, and the well-defined tubular architecture of their bones, may be more consistent with a more efficient terrestrial locomotion.

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FIGURE 28.1 Basal nonmammalian synapsid and dinocephalian osteohistology. A, Mycterosaurine varanopid femur UWBM 98580 showing relatively poorly vascularized lamellar-zonal bone. B, Ophiacodon humerus MCZ 5926 showing woven-fibered bone in a juvenile individual. C, Sphenacodon humerus CM91212 showing zonal parallel-fibered and lamellar bone and vascular canals in radial rows. D, Anteosaurid dinocephalian femur BP/1/5591 showing highly vascularized zonal fibrolamellar bone. E, Titanosuchid dinocephalian femur BP/1/7242 showing a laminar vascular arrangement. Arrowheads indicate growth marks. (B, courtesy of Shelton and Sander; D and E, courtesy of Shelton and Chinsamy.) Abbreviations: LB, lamellar bone; MC, medullary cavity; PFB, parallel-fibered bone.
extant crocodylians. These tissues are largely primary and there is no evidence of systematic cortical remodeling to the degree observed in domestic mammals, although there are perimedullary resorption cavities with concentric lamellae. Large individuals may exhibit less vascularized outer circumferential lamellae suggestive of slowed growth during adulthood (Shelton and Sander 2017).

The Permo-Carboniferous edaphosaurids were a predominantly Euramerican clade typified by a large, sometimes tuberculated, dorsal sail formed by hyperelongate neural spines. Like caseids, edaphosaurids tended toward herbivory and large body size (with the exception of the basal *lanthasaurus*, which may have exhibited an omnivorous or insectivorous juvenile stage (Mazierski and Reisz 2010) and preserved long bone cortices constructed by sparsely vascularized lamellar-azonal bone (Enlow and Brown 1957, Enlow 1969). Primary bone deposition was incremental, mostly lamellar, and most vascular canals (either simple or primary osteons) were confined to the perimedullary areas of the limb bones and spines. The sail-supporting struts formed by the elongated neural spines tended to be constructed as a hollow cylinder with a somewhat thick bone wall composed of lamellar-azonal bone that was nearly avascular in the outer cortex (Huttenlocker et al. 2011). Prominent, short bundles of Sharpey’s fibers are frequently confined to growth zones in the outer cortex. In *Edaphosaurus*, some degree of remodeling occurred in the inner third of the cortex in the spines as evidenced by large erosion cavities lined by multiple layers of concentric lamellae. Localized woven-fibered bone has been identified in *Edaphosaurus* spine tubercles, suggesting that tubercle growth was rapid in this taxon; pathologic woven bone has been identified in a fracture callus in a specimen of *Lupeosaurus* (Huttenlocker et al. 2011, Huttenlocker and Reba 2012). Among early eupelycosaurians, outer circumferential lamellae are most obvious in edaphosaurids, possibly due to the overall avascularity of their cortical bone and attainment of determinate growth.

Sphenacodontian synapsids form the sister group to edaphosaurids and include iconic predators such as the crested sphenacodontid *Dimetrodon* (Dimetrodon) and a paraphyletic group of generally small-bodied predators traditionally called “haptodonts”. Skeletal fragments from the Permian *Dimetrodon*, including pathological examples, were among the first eucynodont grade synapsid materials histologically studied (Moodie 1923, Enlow and Brown 1957, Enlow 1969). As in the edaphosaurids, much histological work has focused on the sail of *Dimetrodon* and its relatives—formed as an array of hyperelongated neural spines that were apparently covered by a webbing of soft tissue (Huttenlocker et al. 2010, Huttenlocker and Reba 2012, Rega et al. 2012). Histologically, however, the spines of sphenacodontids are formed by tissues strikingly different from those of edaphosaurids. The cortical bone records numerous growth zones composed of alternating lamellar and nonlamellar tissues occasionally with abundant primary osteons, especially in the lateral cortex. The medulla is completely occupied by cancellous bone, rather than forming a free, hollow cavity. Limb bones also show evidence of more rapid early growth, as large-bodied *Sphenacodon* and *Dimetrodon* tended to form large amounts of parallel-fibered and occasionally a woven-fibered matrix in juveniles (Huttenlocker et al. 2006, Huttenlocker and Rega 2012, Shelton et al. 2013). The numerous primary osteons are usually longitudinal and arranged in radial rows (Figure 28.1C), or sometimes more radially oriented in young individuals. Occasional fractures preserving pathologic woven bone have been documented, particularly in the neural spines (Enlow 1969, Huttenlocker et al. 2010, Rega et al. 2012). Some osseous lesions have been attributed to the oldest putative examples of osteomyelitis outside mammals (Moodie 1923).

**Nonmammalian Therapsids**

By the middle Permian (ca. 268 Ma), the diversity of basal synapsids was largely supplanted by a derived group of sphenacodontians called Therapsida (although some caseids and varanopids also survived into middle Permian times, but with low diversity and abundances). The clade Therapsida is defined as all synapsids more closely related to *Biarmosuchus* and mammals than to pelycosaurs such as *Dimetrodon* (Laurin and Reisz 1996). A considerable amount of research on therapsid histology has been published, particularly within the last decade (see Chinsamy-Turan 2012 for a detailed overview).

**Basal Therapsids and Dinocephalians**

Among the most basal therapsids, only the histology of biarmosuchians is known, based primarily on a representative sample from *Biarmosuchus* (Ricqlès 1974b). Limb bone histology of *Biarmosuchus* demonstrates that, even at this early stage, therapsids already expressed more densely vascularized and haphazardly organized osseous tissues that resembled those of some mid- to large-bodied mammals. More recent reports on cranial ornamentation in the “horned” burnetianmorph biarmosuchians have shown rapid-growing osseous tissues in the skull, as well as pachyostosis and the fusion of cranial sutures (Sidor et al. 2017). The latter study has important implications for dimorphism in early therapsids and further bears on the taxonomic issues inherent in species with ontogenetically variable cranial adornments.

Dinocephalians were among the first therapsids to appear during the middle Permian. They were large, heavily built animals with some having pachyostotic skulls thought to have been used for head-butting (Barghusen 1975, Benoit et al. 2017). The group came to dominate the terrestrial landscape before disappearing during the end-Guadalupian mass extinction some 260 Ma (Kemp 2005, Atayman et al. 2015, Day et al. 2015). Relatively few researchers have examined dinocephalian bone histology because the group requires a comprehensive taxonomic revision. However, Ricqlès (1972) briefly examined several bones of the basal carnivorous brithopians and the omnivorous/herbivorous titanosaurs and found that highly vascularized fibrolamellar bone was also present in these basal eutherapsids. A more recent study by Shelton and Chinsamy (2016) confirmed the initial findings of Ricqlès (1972) and found that representatives of both groups display rapidly forming, densely vascularized bone tissues interrupted...
by cyclical growth marks during early to midontogeny, after which the deposition of lamellar-zonal bone indicates a switch to slower growth and eventually growth cessation (Shelton and Chinsamy 2016). The vascular canals are numerous and large, and primarily arranged in a laminar or plexiform pattern (Figure 28.1D, E). This differs from what Ricqlès (1972) observed in *Biarrosuchus*, which displays fewer, smaller, mostly longitudinally oriented primary osteons arranged in circular rows with some short, thin anastomoses. A laminar or plexiform arrangement is typical of large-bodied mammals (e.g., ruminants, Köhler et al. 2012, hippopotamus and elephant; Botha, personal observation) and sauropod dinosaurs (Sander 2000) and may result in stronger, stiffer bones that are better at resisting shear stress compared to other bone vascular patterns (Margerie et al. 2002, 2004). Given their large body sizes (basal skull lengths [BSLs] up to 80 cm; Kemp 2005), this type of bone tissue arrangement may have helped to strengthen dinocephalian bones, an important factor in supporting their considerable weight.

**Anomodonts**

In terms of diversity and abundance, the most successful Permo-Triassic therapsid group was the Anomodontia. Their highly specialized herbivorous masticatory apparatus likely helped them to diversify into a range of body sizes, ecological niches and geographical regions. Many of the derived forms underwent further adaptations in which their dentition was largely replaced by a rhamphotheca (a keratinized beak), and modifications to the jaw hinge and musculature allowed them to produce a particularly powerful bite (Kemp 2005). They appeared during the middle Permian and survived both the end-Guadalupian and Permo-Triassic mass extinctions before finally going extinct during the Late Triassic (Ruta et al. 2013, Day et al. 2015). The majority of anomodonts fall into a group known as the Dicynodontia, but there are a few basal non-dicynodont anomodonts from South Africa and Russia. Little is known about the growth patterns of these basal taxa as only one specimen of the small-bodied anomodont *Galeops*, from the middle Permian of South Africa, has been sampled histologically (Botha-Brink and Angielczyk 2010). Although the presence of fibrolamellar bone in *Galeops* indicates that even the earliest anomodonts were capable of relatively rapid growth, the bone tissues are interrupted by wide regions of slow growing parallel-fibered bone (Figure 28.2A). The canals vary between small, narrow simple canals and longitudinally oriented primary osteons. These features differ from most other dicynodonts, which tend to have more complex vascular patterns in their limb cortices. The large-bodied basal dicynodont *Endothiodon* (BSL ~40 cm), and the relatively small *Diiictodon* (Figure 28.2B) and closely related Emydopoidea (BSL ~7–24 cm), tend to have randomly distributed, longitudinally oriented primary osteons or reticular arrangements (Ray and Chinsamy 2004, Ray et al. 2009, Botha-Brink and Angielczyk 2010). Within the more recent Bidentalia, the Cryptodontia, which include both medium (BSL < 30 cm) and large-bodied (BSL > 40 cm) taxa, exhibit longitudinally oriented primary osteons, often in circumferential rows and plexiform arrangements appear in patches (Figure 28.2C, D). However, mammal-like plexiform and laminar vascular arrangements begin to dominate in later ontogenetic stages only in Dicynodontioidea (Figure 28.2D) among anomodonts (Gross 1934, Enlow and Brown 1957, Ricqlès 1972, Chinsamy and Rubidge 1993, Ray and Chinsamy 2004, Botha-Brink and Angielczyk 2010, Green et al. 2010, Ray et al. 2010). Although these arrangements tend to be present in the larger bodied taxa (BSL > 40 cm), the variation in vascular patterns may not be related to body size alone, as the basal dicynodont *Endothiodon* and the cryptodont *Rhachiocephalus* are large dicynodonts and do not show this pattern. It is likely that phylogeny also plays an important role in the selection of vascular patterns as plexiform and laminar bone tissues become increasingly prevalent in the Dicynodontioidea, even in the relatively smaller bodied Triassic *Lystrosaurus* species (Figure 28.2E) (although it should be noted that fully grown Triassic *Lystrosaurus* specimens have yet to be recovered and thus, even Triassic species may have been relatively large once skeletally mature; Botha-Brink et al. 2016).

Growth marks are present in all anomodonts studied to date, but they are especially prevalent in Permian taxa (Figure 28.2A–D), indicating that cyclical growth is a primitive feature of the clade as a whole. Many dicynodonts grew rapidly to the subadult stage and only exhibit growth marks relatively late in ontogeny (generally more than 50% of the maximum known size; Ray and Chinsamy 2004, Botha-Brink and Angielczyk 2010). Growth decreased during later ontogeny, forming a relatively avascular outer circumferential layer (indicating that growth had essentially ceased and skeletal maturity had been attained). Examples have been demonstrated in the Triassic kannemeyeriforms *Kannemeyeria* and *Placerias* (Botha-Brink and Angielczyk 2010, Green et al. 2010), indicating that, like many other vertebrates, dicynodonts underwent asymptotic growth (*contra* Ray and Chinsamy 2004, Ray et al. 2005, Ray et al. 2010), and the absence of outer circumferential lamellae in specimens is more a reflection of the skeletal immaturity of the individual than an expression of an indeterminate growth strategy (Woodward et al. 2011, Lee et al. 2013). Haversian remodeling is present in the inner cortices of both small and large taxa, but it is more prevalent in larger bodied taxa. However, dense Haversian bone throughout the cortex has only been observed in adult Triassic kannemeyeriids such as *Kannemeyeria* and *Placerias* (Botha-Brink and Angielczyk 2010, Green et al. 2010).

Another histomorphometric feature characteristic of dicynodonts is the small size or infilling of the medullary cavity. Dicynodont bones generally have relatively thick cortices with a medullary cavity infilled with trabeculae, which produces broad transition zones between compact and cancellous bone. When the medullary cavity is open and free of trabeculae (Figure 28.2C), it tends to be very small (Botha-Brink and Angielczyk 2010). Long bones of larger dicynodonts generally have a medullary cavity infilled with trabeculae, but exceptions do occur, such as the basal dicynodont *Endothiodon*, in which a small, but open, medullary cavity occurs. It has been hypothesized that the infilling of the medullary cavity in dicynodonts is the result of an aquatic lifestyle (Ray et al. 2005, Canoville and Laurin 2010) as many extant aquatic tetrapods
have this feature. However, this feature is also found in active, pelagic animals, in which the development of extensive spongioseae spreading into periosteal cortices results in decreasing the skeletal mass and consequently reducing the inertia of the moving body (Ricqlès and Buffrenil 2001, Kriloff et al. 2008, Houssaye 2012, Houssaye et al. 2016). To date, no morphological adaptations have been found in dicynodonts to suggest that any were aquatic, particularly not fully aquatic, active swimmers. The trabecular infilling of the medullary cavity is more likely to have resulted in increasing skeletal and body mass. Infilled medullary cavities and/or thick compact cortices might even have been associated with their dual-gate mode of locomotion where the hind limbs were held in a more parasagittal plane compared to the forelimb (Ray and Chinsamy 2003, Kemp 2005). The trabeculae in the medullary region likely provided a biomechanical advantage by acting as buttresses against the high bending loads present in the larger taxa. This feature would have aided smaller taxa as well. For example, Lystrosaurus is a medium-sized burrowing animal and its limb bones would have been susceptible to high bending and torsional loads during digging (Botha-Brink 2017). Notably thick cortices have also been reported for smaller dicynodonts such as Dictodon and Cistecephalus, both of which are considered to be fossorial (Ray and Chinsamy 2004, Nasterlack et al. 2012) and would have experienced similar biomechanical loads to Lystrosaurus.

Gorgonopsians

The most striking and iconic carnivorous therapsids of the late Permian were the gorgonopsians. They are commonly referred to as the “saber-toothed cats” of the Permian due to their greatly elongated canines, and they ranged in size from a small dog up to the size of the largest extant mammalian predators (Kemp 2005). They form part of a collective group known as the Theriodontia, which also include the mammal-like theriocephalians and cynodonts. These theriodonts acquired increasingly mammalian features during their evolution, with improved locomotory and masticatory capacities. The extinction of the carnivorous dinoccephalians during the end-Guadalupian mass extinction opened up a new niche for the guadalupians, allowing them to become the apex predators during the middle Permian and diverged into a variety of body sizes and ecological niches, evolving into highly specialized herbivorous forms during the Middle Triassic. They survived both the end-Guadalupian and Permo-Triassic mass extinctions and were important components of the recovery ecosystems after both events. Their osteohistology was briefly examined by Ricqlès (1969), Ray et al. (2004) and Chinsamy-Turan and Ray (2012) who identified fast-growing cyclical fibrolamellar bone in all taxa studied. More recent comprehensive studies have revealed important patterns in theriocephalian life histories from the Permian to the Triassic (Huttenlocker and Botha-Brink 2013, 2014). Large-bodied Permian theriocephalians (BSL ~25–40 cm) exhibited abundant vascular canals in a variety of motifs, ranging from plexiform, to radiating and reticular networks interspersed with longitudinally oriented primary osteons. The bones of smaller taxa tend to exhibit a predominance of longitudinally oriented primary osteons. The middle Permian predator Lycosuchus exhibits highly vascularized plexiform tissues in its limb bone cortices (Figure 28.3C). Some Permian theriocephalians, however, showed unique tissue patterns with lower levels of vascularity and numerous, variably spaced growth marks, particularly the late Permian Theriognathus (Figure 28.3D). Regardless of body size, Permian theriocephalians generally experienced multiyear growth to asymptotic size, and some taxa like Theriognathus, achieved skeletal maturity quite late based on delayed fusion of neurocentral sutures, even in large specimens (Huttenlocker and Botha-Brink 2014, Huttenlocker and Abdala 2015). At the Permian-Triassic boundary, the clade experienced a “Lilliput effect” in which large-bodied taxa disappeared during a global mass extinction (Huttenlocker and Botha-Brink 2013, Huttenlocker 2014). Even the large-bodied Moschorphius, which is among the few known Permo-Triassic boundary-crossing theriocephalians, experienced within-lineage dwarfing. Despite a decrease in body size, however, Triassic Moschorphius grew more quickly than did its Permian counterpart, as evidenced by more densely vascularized bone tissues and fewer growth marks (Figure 28.3E, F) (Huttenlocker and Botha-Brink 2013). This is surprising because, within a given clade, large-bodied individuals tend to grow more quickly than their small-bodied relatives (Case 1978). The smaller Triassic survivors like Tetracynodon underwent relatively slower growth,
FIGURE 28.3 Gorgonopsian and theerocephalian osteohistology. A, Gorgonopsian indet. limb bone SAM-PK-K10622 showing highly vascularized fibrolamellar bone with a change from inner cortical radial canals (bottom right) to a more reticular vascular arrangement (top left). B, Cyonosaurus ulna SAM-PK-K10428 showing zonal fibrolamellar bone. C, basal theerocephalian Lycosuchus ulna SAM-PK-9084 showing rapidly deposited fibrolamellar bone interrupted by growth marks. D, Euthercocephalian Theriognathus femur NMQR 3375 showing growth marks. E, Permian euthercocephalian Moschorhinus humerus NMQR 3939 showing a mid- and outer cortex of rapidly forming fibrolamellar bone and three annuli. Note there is no growth deceleration at the subperiosteal surface, even after three growth cycles. F, Triassic euthercocephalian Moschorhinus humerus BP/1/4227 showing highly vascularized fibrolamellar bone, a midcortical annulus and two closely spaced annuli at the subperiosteal surface indicating growth deceleration. G, Baurioid euthercocephalian Tetracynodon humerus NMQR 3745 showing a wide region of lamellar bone. Arrowheads indicate growth marks, and arrows indicate radial vascular canals. Abbreviations: FLB, fibrolamellar bone; LB, lamellar bone; MC, medullary cavity.
but all experienced shorter growth durations (Figure 28.3G). Increased aridity and unpredictable rainfall regimes during the Early Triassic (Smith and Botha-Brink 2014, MacLeod et al. 2017) resulted in elevated mortality rates and rapid attainment of skeletal (and presumably reproductive) maturity, which would have been advantageous in taxa with shortened life expectancies (Botha-Brink et al. 2016).

**Nonmammaliaform Cynodonts**

The most recent and mammal-like nonmammalian therapsids are the nonmammaliaform cynodonts. They appeared relatively later in the fossil record than other therapsid clades, with the first documented record from the late Permian (Botha et al. 2007, Kammerer 2016a). They were relatively rare components of Permian ecosystems, although this may reflect a poor preservation probability rather than a genuine rarity in their biological community as these early taxa are all relatively small (BSL ~5–14 cm; Abdala and Ribeiro 2010, Kammerer 2016a). After the Permo-Triassic mass extinction, however, they flourished, radiating into a speciose clade with an increasingly mammalian morphology before finally evolving into the first true mammals by the Early Jurassic. Consequently, there have been numerous osteohistological studies on nonmammaliaform cynodonts as they hold the key to understanding the origin and evolution of mammalian growth patterns (e.g., Ricqlés 1969, Botha and Chinsamy 2000, 2004, 2005, Ray et al. 2004, Chinsamy and Abdala 2008, Botha-Brink et al. 2012; in review, Veiga et al. 2018, Butler et al. 2018).

Rapidly forming fibrolamellar bone has been found throughout the clade, even in its most basal members such as the late Permian *Procynosuchus* (Ray et al. 2004). During the Early Triassic, nonmammaliaform cynodonts were still relatively small, reaching skeletal maturity within one to two years (Figure 28.4A). Two major lineages diverged at this time, the Cynognathia and Probainognathia. Within the Cynognathia, a group of large-bodied herbivorous taxa known as the Gomphodontia (named for their buccolingually expanded postcanines; Abdala and Ribeiro 2010) arose during the Middle Triassic. This clade includes the Traversodontidae, a family of diverse, globally distributed nonmammaliaform cynodonts that became highly abundant during the Late Triassic. The Gomphodontia exhibit high growth rates and multiyear growth to skeletal (and presumably reproductive) maturity, similar to large extant mammals. The bone tissues comprise rapidly forming fibrolamellar bone, with a variety of vascular arrangements, interrupted by narrow annuli and LAGs (Figure 28.4B, C) (Botha-Brink et al. 2012). Exceptions to this pattern are two basal traversodontids, *Andescynodon* and *Massetognathus*, where the dominant bone tissues are slower growing lamellar-zonal and parallel-fibered bone tissue, respectively (Chinsamy and Abdala 2008). These taxa are smaller than their more recent relatives (BSL approximately 13 and 20 cm, respectively; Chinsamy and Abdala 2008, Liu and Powell 2009), but other similar sized nonmammaliaform cynodonts, such as the Early Triassic *Thrinaxodon* and *Galesaurus*, exhibit faster growing bone tissues (in stressful conditions relating to a harsh, postextinction environment), thus factors other than body size are likely to have influenced the growth rates of these taxa. Chinsamy and Abdala (2008) proposed that there was an increase in growth rates within the traversodontids, as *Andescynodon* and *Massetognathus* exhibit slower growth rates than in more recent taxa such as *Exaeretodon*, *Gomphodontosuchus* and *Scalenodontoides* (Botha-Brink et al. 2012). This would imply a selection for slower growth rates in the basal traversodontids, as the more basal nontraversodontid gomphodontosuchines *Diademodon* and *Trirachodon* exhibit rapidly forming fibrolamellar bone during early and midontogeny (Botha-Brink et al. 2012).

The other major nonmammaliaform cynodont clade is the Probainognathia, which gave rise to the smaller bodied Prozostrodontia. The prozostrodontians exhibit increasingly mammalian characteristics such as more efficient locomotory and masticatory structures allowing for increased activity levels and energy assimilation, maxillary vibrissae indicating improved sensory capabilities and improved thermoregulatory and reproductive controls (implied from the loss of a pineal foramen) (Benoi et al. 2016a, b), as well as high growth rates (Figure 28.4D). They evolved into the tiny Mammaliaformes, which includes the crown group Mammalia, during the Late Triassic. The tritylodont and tritheledont prozostrodontians exhibit similar growth patterns to the Cynognathia, with highly vascularized, rapidly forming fibrolamellar bone being the dominant bone tissue type. Chinsamy and Hurum (2006) and Botha-Brink et al. (2012) suggested that the tritylodontid *Tritylodon* underwent sustained growth to skeletal maturity due to the presence of peripheral lamellar bone containing multiple LAGs in a radius and fibula. However, in the radius (Figure 28.4E), this region does not represent the outer circumferential lamellae, which indicates growth cessation because, although the LAGs are near the bone periphery, additional bone was deposited after these growth marks around most of the shaft, showing that the animal was still growing at the time of its death. The region containing the lamellar bone tissue is relatively wide and thus, could be mistaken for an outer circumferential layer. Multiple peripheral LAGs were also found in a fibula, but it is not known if this feature represents outer circumferential lamellae or just a temporary change in growth rate similar to the radius. Wide zones of slow-growing bone tissue have recently been found traversing the midcortex of the limb bones of a more basal prozostrodontian *Prozostrodon* (Figure 28.4D) and LAGs have been found in the tritheledontid *Irajatherium* (Botha-Brink et al. 2018). Therefore, without more material, it is difficult to determine whether *Tritylodon* underwent sustained or cyclical growth.

Recent work on the tiny brasiliodontid prozostrodontian taxa *Brasiliodon* and *Brasilitherium*, which are currently considered to be the sister taxa to Mammaliaformes, has shown that they grew relatively more slowly than the more basal nonmammaliaform cynodonts. The bones of these taxa contain a mixture of comparatively less vascularized fibrolamellar and parallel-fibered bone (Botha-Brink et al. 2018). This pattern is similar to those of the Early Jurassic mammaliaform *Morganucodon* and the Late Cretaceous multituberculate mammals *Kryptobaatar* and *Nemegthaatar* (Chinsamy and Hurum 2006). The relatively slower growth rates in these brasiliodontids compared to other nonmammaliaform cynodonts may be related to phylogeny and/or decreased body
FIGURE 28.4  Nonmammaliaform cynodont osteohistology. A. Basal eucynodont *Thrinaxodon* humerus BP/1/5208 showing rapidly forming fibrolamellar bone and peripheral slower forming parallel-fibered bone. B. Gomphodontosuchine *Diademodon* fibula UCMZ T448 showing zonal fibrolamellar bone. C. Gomphodontosuchine *Trirachodon* showing zonal fibrolamellar bone. D. Prozostrodontian *Prozostrodon* femur UFRGS-PV-248T showing a wide region of parallel-fibered bone. E. Tritylodontid *Tritylodon* radius BP/1/5167 showing an outer cortical growth mark with continued peripheral growth. F. Brasilodontid *Brasilitherium* femur UFRGS-PV-1043T showing a midcortical growth mark. Arrowheads indicate growth marks, and arrows indicate Sharpey’s fibers (muscle insertions). Abbreviations: FLB, fibrolamellar bone; MC, medullary cavity; PFB, parallel-fibered bone.
sizes as all these taxa were very small (BSL ~3–4 cm). When compared with similar-sized extant mammals, they may have grown more slowly to adult size than their osteohistology shows they took more than one year for growth to attain (as shown by the presence of a midcortical growth mark prior to growth deceleration), thus taking more than one year for these animals to reach skeletal maturity (Figure 28.4F). Thus, although the Prozostrodontia exhibit increasingly mammalian characteristics, including rapid juvenile growth, the small derived nonmammalian prozostrodontians still exhibit an extended growth period compared to similar-sized extant mammals.

Summary of Nonmammalian Synapsid Histology

Despite a great deal of histovariation due to the effects of phylogeny, biomechanics, body size and lifestyle, there are some osteohistological features that distinguish the derived therapsids from the more basal nonmammalian synapsids. For example most of the pelycosaur bone tissues studied to date exhibit relatively slowly forming parallel-fibered and lamellar bone tissues. There are exceptions to this pattern such as Ophiacodon and some sphenacodontids.

The predominance of fibrolamellar bone in even the earliest, most basal therapsids indicates that rapid growth rates are plesiomorphic for the clade. The high frequency of densely vascularized bone tissues among them indicate that therapsids grew rapidly to at least reproductive maturity. The dominance of fibrolamellar bone throughout the skeleton indicates that therapsids grew faster than their pelycosaur-grade ancestors, in which fibrolamellar bone is absent or, if present, limited to certain elements in isolated regions in some eupelycosaurans (Ophiacodon and some sphenacodontids). The implication is that pelycosaur generally exhibited a greater investment in individual growth spread out over their lifetimes, and possibly over a greater length of time than in similarly sized therapsids.

Therapsids for which the complete life history is known (i.e., osteohistology data from different ontogenetic stages is available) exhibit cyclical growth where growth decreased or ceased temporarily during the unfavorable season. Those for which growth marks have not been observed are represented by immature individuals, such as the nonmammaliaform cynodonts Cynognathus and Scalenodontoides, and thus, the occurrence of sustained growth to reproductive or skeletal maturity cannot be confirmed without the assessment of older individuals. However, the large size of the nonmammaliaform cynodont individuals studied (BSL 30 and 40 cm, respectively) indicates that they grew in a sustained manner to at least midontogeny (Botha-Brink et al. 2012). A few possible exceptions to this are Early Triassic eutheriodonts such as Thrinaxodon, which likely underwent rapid sustained growth to reproducitve maturity (Botha-Brink et al. 2016). However, the presence of a single annulus in one bone of Thrinaxodon shows that the capacity to produce growth marks existed (Botha and Chinsamy 2004). The widespread occurrence of growth marks among the Therapsida, a clade that lived in a variety of environmental conditions (middle Permian to Early Jurassic climates) and geographical regions indicates that this feature represents an endogenous circadian rhythm and not merely a response to random or even seasonal environmental stresses (Huttenlocker et al. 2013, see also Chapter 31). Some therapsid taxa, however, expressed growth marks relatively late in ontogeny. This is particularly noticeable in the dicynodont and eutheriodont clades, indicating that a greater part of their growth (mainly early ontogeny) occurred in a sustained manner compared to other taxa.

Although it may be possible to trace endothermic-like physiology in some therapsid groups on the basis of growth rates, bone remodeling and bioapatite isotopic ratios, it remains unclear as to whether these instances pinpoint the origins of true mammalian endothermy, some type of intermediary or independent evolution of mammal-like thermophysiology. These questions remain open ended because some early mammaliaform cynodonts preserved attributes of ectothermy, and some modern monotremes have been suggested to be mainly ectothermic or intermediate (Grady et al. 2014). These can only be further resolved by better taxonomic sampling and implementation of phylogenetic comparative methods within a well-sampled evolutionary framework (e.g., Huttenlocker and Farmer 2017, Olivier et al. 2017). However, it is likely, considering the combined morphological and osteohistological evidence, that therapsids had higher metabolic rates than did their predecessors. The increasingly mammal-like features acquired during therapsid evolution (e.g., improved locomotory, masticatory and ventilatory capabilities necessary for increased energy assimilation) suggest that high standard metabolic rates were likely a feature of some therapsid groups, especially in the later cynodonts (see Chapter 37).

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