

Preface

The first few paragraphs and bullet list are taken pretty much verbatim from the Preface to *Developmental and Cellular Skeletal Biology* (Hall, 1978a in references). Their durability attests to the wide number of disciplines for which the skeleton was and remains central.

The skeleton has fascinated humankind ever since it was realised that, aside from one or several sets of genes, bare bones are our only bequest to posterity. The skeleton is more than an articulated set of bones, however. In human skeletons, the following hold true:

- three-dimensional conformation establishes the basis of our physical appearance;
- formation and rate of differentiation determine our shape and size at birth;
- postnatal growth orders us among our contemporaries and sets our final stature; while its
- decline in later life is among the primary causes of loss of the swiftness and agility of youth.

Not surprisingly, the skeleton is a central focus of many scientific and biomedical disciplines and investigations.

For developmental or cell biologists, the skeleton provides an ideal model for studies of gene action in normal and abnormal development, cell differentiation, morphogenesis, polarised growth, epithelial–mesenchymal interactions, programmed cell death and the role of the extracellular matrix. The skeleton supplies geneticists with a permanent record of the vicissitudes of its growth, whereby the phenotypic expression of genetic abnormalities can be studied. Orthopaedic surgeons earn a livelihood from correcting abnormalities and breaks, while orthodontists and oral surgeons use their knowledge of bone resorption to correct the position of teeth displaced consequent to alveolar bone dysfunction. Physiologists, biochemists and nutritionists are concerned with the skeleton's store of calcium and phosphorus and its response to vitamins and hormones, while haematologists find that the skeleton houses the progenitors of the blood cells. Pathologists endeavour to understand the disease states that result from abnormalities in skeletal cellular differentiation or function; surgeons want to prevent formation of skeletal tissues in the wounds that bear witness to their work. Vertebrate palaeontologists make their living from the analysis of the skeletons of

extinct taxa. Veterinarians, physical anthropologists, radiographers, forensic scientists ... the list goes on.

Bones come in all shapes and sizes. There are long bones, flat bones, curved bones, bones of irregular and geometrically indefinable shapes, large and small bones. Bones exhibit bumps, ridges, grooves, holes and depressions where they articulate with other bones or attach to tendons and ligaments, and where nerves and blood vessels course through them. Some bones and cartilages arise within the skeleton and are integral parts of it. Others arise outside the skeleton, some as sesamoids or ossifications within tendons or ligaments, others as pathological ossifications in what otherwise would be soft tissues. Bones and cartilages may develop during embryonic or fetal life, in larval stages or in adulthood – often late in adulthood – during normal ontogeny, wound repair or regeneration. Bones modify themselves in response to injury, disease or parasitic infection, in the aftermath of surgery, as a defensive response to predators, as a consequence of domestication or hibernation and through evolutionary adaptations.

The previous edition of this book was published in 2005. It and this second edition are concerned with the nature of bones and cartilages and the cells that make them: how skeletal cells, tissues and organs are made, develop and age, and how they evolved. In the preface to the first edition I set out some 20 questions concerning skeletal development and 11 questions concerning skeletal evolution^A. I will not list those questions again. Many have been answered in the intervening 10 years (the literature for the first edition went into 2004), but many have not. The aim in this as in the previous edition is to analyse and evaluate studies of the development, growth and evolution of the skeleton and of skeletal tissues to provide a synthesis of the field of **Developmental and Evolutionary Skeletal Biology**.

A. I was stimulated to prepare this list by the Agenda of 45 questions used by Gavin de Beer to conclude his *Development of the Vertebrate Skull* (de Beer, 1937, pp. 512–515). I answered several of de Beer's questions in my own Ph.D. research and hoped a similar list would stimulate other skeletal biologists to do the same.

ORGANISATIONAL CHANGES

I have kept the same organisation in this edition as in the first. Every chapter has been revised and updated extensively and the single chapter in Part XV (Evolutionary Skeletal Biology) is now two (44 and 45) devoted to the origin of skeletal variation and organismal variability in producing changes to the skeleton. Because the flow is the same, I will not provide a detailed outline of the organisation of the book here. Rather, I (a) have added introductions to each of the 15 parts that outline the topics of the chapters in each of those parts, and (b) summarise below (and on the back cover) some of the major advances in understanding.

The literature from 2004 to around August 2014 has been analysed and integrated into the book. In doing so I have reduced the number of references by 8% to 6,182. I was able to do this by including only key references to older studies by individuals or from individual laboratories, marking those with an asterisk in both the reference list and in the text. For more complete lists of earlier studies, refer to the first edition. Major reviews also are identified with an asterisk. Additionally, and for ease of working from the reference list, I have added the chapter (s) in which a particular reference is cited in square brackets at the end of the citation in the reference list. A random example is: * Anderson, H. C. (1985). Matrix vesicle calcification: Review and update. In *Bone and Mineral Research/3* (W. A. Peck, ed.), pp. 109–149. Elsevier Science Publishers B. V., Amsterdam. [22].

Most figures from the first edition have been retained and 45 new figures have been added. Major terms and concepts are placed in **bold** or in *italics* in the text. As in the first edition, references, comments and elaborations (and a few asides) are in endnotes at the end of each chapter. A detailed single subject and taxonomic index is provided. Acknowledgements to individuals who generously commented on sections of text are included as endnotes in the appropriate chapters.

CONCEPTUAL CHANGES

The back cover contains a list of some of the changes in content from the first edition. Here I highlight some of the substantive changes in our understanding of skeletal development and evolution from research over the past decade.

We now have an appreciation of the integrated and coordinated functioning of the vascular, haematopoietic and skeletal systems in whole organism physiology.

Although known since Thomas Huxley's time (Huxley, 1859), our understanding of the fundamental differences in vertebral development between teleost fish and tetrapods has been expanded greatly. In fish, vertebral development is initiated by mineralisation of the sheath of the notochord, which also is responsible for vertebral

segmentation. In tetrapods, vertebral development is initiated by chondrogenesis of sclerotomal cells, and segmentation is a function of the sclerotomal mesenchyme. One consequence is that relationships among notochord, chondroid and cartilage have been reevaluated in the context of whether notochord is a form of cartilage.

The evolutionary origins of cartilage have been reinterpreted on the basis of new phylogenetic, cellular and genetic data, including the importance of gene regulatory networks in chondrogenesis (and osteogenesis).

Dedifferentiation of osteoblasts has been identified as the source of blastemal cells in regeneration of fin rays in zebrafish.

Recent data on a mesodermal rather than neural crest origin of teleost fin rays and scales are analysed. One of many consequences is a reevaluation of the proposal by Smith and Hall (1993) of the recognition of the exoskeleton and the endoskeleton on the basis of their origin in neural crest or mesoderm, respectively. The division into exo- and endo- remains valid, but not on the basis of germ layer of origin.

There is increased discussion of dinosaur bone based on palaeohistology and evaluation of whether skeletal growth is ever indeterminate.

Discovery of 'avian' secondary cartilage in dinosaurs is discussed in relation to dinosaur origins of birds and the evolution of secondary chondrogenesis.

There has been expanded treatment of stem cells in embryos and adults, including mesenchymal stem cells and their use in genetic engineering of cartilage, and the concept of the stem cell niche.

There is enhanced discussion of resolution to hurdles associated with *in vitro* culture of articular cartilage and repair *in vivo*.

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