The Physiology of BONE

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Preface to Third edition

SINCE the first edition of this book in 1970 there has been increasing interest in the problems that are raised for many different disciplines in an attempt to understand the physiology of bone. The present volume is intended for readers who want a bird's-eye view of the subject and directions as to where they can find more detailed information on particular aspects. It does not attempt to give a complete account or even a full bibliography of the many exciting and often controversial questions that are covered by specialist journals and monographs. It can only hope to provide some signposts to both the past and the present, and perhaps the future.

Oxford J.M.V.
May 1980

Preface to Second edition

CERTAIN aspects of the physiology of bone have advanced with amazing rapidity since the first edition of the book with this title appeared in 1970. This is particularly true of our understanding, still incomplete, of the behaviour of vitamin D and of the complicated story of the effects of parathyroid hormone and calcitonin on calcium homeostasis. An attempt is now made to bring our knowledge of the physiology of bone up-to-date without increasing the length of the book. This has necessitated a complete rewriting of some sections though others are little changed. The bibliography represents an attempt to include mainly references to papers and monographs that have appeared since 1969. On the other hand, mention is made of classical papers of an earlier date and in some cases knowledge is dependent on older work entirely. Again I must apologize to authors who have received inadequate mention. The bibliography is personal rather than complete.

It is hoped that this new edition will be useful to both medical students and their teachers.

Oxford J.M.V.
May 1975

Preface to First edition

THE skeleton, for purposes of the present monograph, is taken to include both bone and the cartilage closely related to bone. The teeth are excluded. The anatomical structure and the supporting function of the skeleton is not discussed in any detail, nor is the haemopoetic marrow, a tissue which in some ways it is difficult to dissociate from consideration of bone. Emphasis is laid rather on the complex mechanisms involved in enabling the skeleton to play its essential role in mineral homeostasis.

Attention is given to the most recent work available, particularly that in journals and symposia. The bibliography does not attempt to be comprehensive. Certain questions are discussed at greater length than others for the reason that at the moment they are arousing lively interest and therefore new knowledge is available. No attempt is made to replace standard works such as *Mineral metabolism: an advanced treatise*, by Comar and Bronner, or *The biochemistry and physiology of bone*, edited by Bourne. It is certainly presumptious for one individual to attempt to survey a field which today occupies the attention of specialists from many different disciplines. However, it is hoped that a bird's-eye view of an exciting and expanding subject may be of use to medical students and their teachers.

Acknowledgements

I AM grateful to many people who have helped me in different ways in preparing this edition. My special thanks must go to John Loutit for exciting discussions and for having read the whole manuscript. I am also much indebted to Dr G. E. Harrison for his advice and help over Chapter 8. Once again I must take sole responsibility for the pattern of the book, the views expressed, and for the omission of many important references.

Thanks are due to the editors and publishers of the following journals, symposia, and books for permission to use new figures and tables. I regret that in two cases no permission has been obtained as I have not been able to trace the origin of the picture, which I had in my files: Fig. 2.3 and Fig. 1.14. *The biochemistry and physiology of bone* (2nd edn), Academic Press; *Histopathology of cartilage, bone and joints*, J. B. Lippincott Company; *Human growth*, Cassell Ltd; *Nature (London)*; *Calcified tissue Research*; *Annals of Human Biology*; *The New England Journal of Medicine*, Pergamon Press; *The Journal of Cell Biology*; *Proceedings of the Royal Society*; *Professional and Scientific Publications*, Springer Verlag.

I am also grateful to my photographer, Richard McAvoy, for his careful work. This revised edition has only been made possible because of the devoted work and patience of my secretary, Janet Judge.

Contents

1. Bone as a Tissue

BONE is a highly specialized form of connective tissue. It is distinguished from other forms of connective tissue by the fact that it is extremely hard, owing to the deposition within a relatively soft organic matrix of a complex mineral substance, largely composed of calcium, phosphate, and carbonate.

1. DEVELOPMENT

Bone is often described as developing by two different methods: intramembranous (in membrane), and endochondral (in cartilage). The fundamental process is, however, similar. An organic matrix, the osteoid, is laid down by cells, the osteoblasts. This becomes calcified with the deposition of amorphous and crystalline apatite. The bones of the calvarium of the skull are formed by intramembranous ossification, the basal bones of the skull and the majority of bones of the skeleton by endochondral ossification.

1.1. Intramembranous ossification

In early foetal life a condensation of mesenchyme cells occurs in the case of both membrane and endochondral bone formation. In the former a group of cells differentiate into osteoblasts, so forming centres of ossification (Ham 1974). These cells secrete osteoid and in so doing some of them become surrounded and become osteocytes lying in their lacunae. Others continue to form osteoid and surround ingrowing capillaries which will bring in the haemopoietic cells of the future marrow (Ham 1974), (Fig. 1.1). Spicules of bone are found radiating out from the ossification centre as a result of matrix formation by the osteoblasts lying on the surface of the condensation, thus creating a spongy type of bone. Calcification of the osteoid proceeds by the same process of vesicle formation as is seen in trabecular bone (see p. 37) (Bernard and Pease 1969). In early foetal life, in human or long gestation species, resorption and apposition begin to take place, so that the spongy or cancellous bone occupies the centre of the mass while a layer of compact bone is formed on each surface by the continuous addition of new sheets of bone by the active osteoblasts.

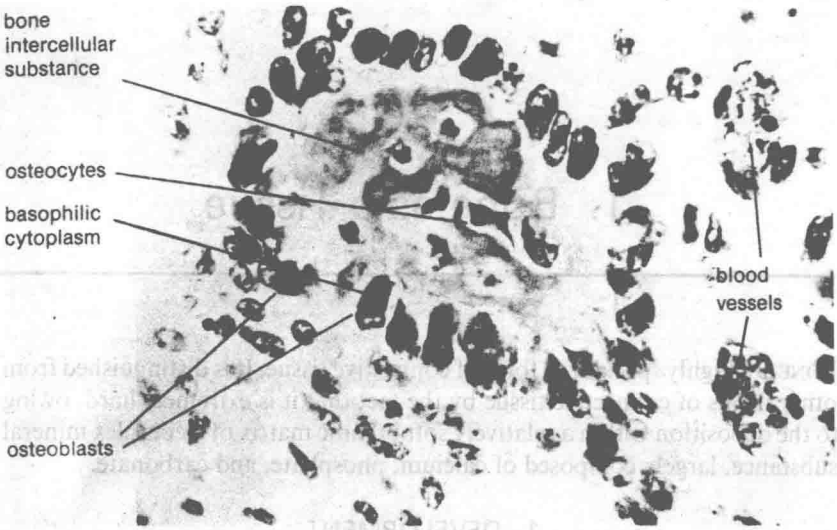

FIG. 1.1. High-power photomicrograph of a transverse section of a forming trabecula of bone, in the developing skull of a pig embryo. Osteoblasts arranged around its periphery are laying down intercellular substance of bone. Some bone cells have entirely surrounded themselves with intercellular substance so as to become buried as osteocytes in it; these reside in lacunae. (From Ham and Cormack (1979) by courtesy of authors and publishers.)

1.2. Endochondral ossification

In an area of mesenchymal condensation, in the case of endochondral ossification, cells with oval or round nuclei appear packed together forming a model of the future bone (Fig. 1.2). These cells surround themselves with an intracellular matrix or ground substance which is largely composed of glycoproteins peculiar to cartilage (see p. 58). The cells at the periphery of the original condensation become orientated to form, which is described as a perichondrium. The inner layer of cells of this perichondrium differentiate and can be shown to contain alkaline phosphatase, the *sine qua non* of the osteoblast. These differentiated cells lay down a layer of osteoid, i.e. the matrix characteristic of bone. This immediately calcifies, so becoming a collar of periosteal bone directly in contact with the cartilaginous model. The cartilage cells in the centre of the model have in the meantime undergone degenerative changes which are associated with some calcification (Fig. 1.3). Capillaries from outside the perichondrium push through the perichondrium and the periosteal bone and invade the degenerating cartilage cells carrying with them stromal cells from the inner layers of the perichondrium which will form the marrow stroma (Jotereau and Le Douarin 1978) (Fig. 1.3). The vessels arborize and ultimately, together with their stromal cuff derived from