

Contents

Contributors **xi**

Preface to the Ninth Edition of the *Primer*:

John P. Bilezikian **xxiv**

About ASBMR **xxv**

President's Preface: Michael J. Econs **xxvi**

About the Companion Website **xxvii**

Section I: Molecular and Cellular Determinants of Bone Structure and Function **1**

Section Editor: Karen Lyons

- 1 Early Skeletal Morphogenesis in Embryonic Development **3****
Yingzi Yang
- 2 Endochondral Ossification **12****
Courtney M. Karner and Matthew J. Hilton
- 3 Local and Circulating Osteoprogenitor Cells and Lineages **20****
Naomi Dirckx and Christa Maes
- 4 Osteoblasts: Function, Development, and Regulation **31****
Elizabeth W. Bradley, Jennifer J. Westendorf, Andre J. van Wijnen, and Amel Dudakovic
- 5 Osteocytes **38****
Lynda F. Bonewald
- 6 Osteoclast Biology and Bone Resorption **46****
Hiroshi Takayanagi
- 7 Signal Transduction Cascades Controlling Osteoblast Differentiation **54****
David J.J. de Gorter, Gonzalo Sánchez-Duffhues, and Peter ten Dijke
- 8 The TGF- β Superfamily in Bone Formation and Maintenance **60****
Ce Shi and Yuji Mishina

- 9 Recent Developments in Understanding the Role of Wnt Signaling in Skeletal Development and Disease **68****
Zhendong A. Zhong, Nicole J. Ethen, and Bart O. Williams

- 10 Mechanotransduction in Bone Formation and Maintenance **75****
Whitney A. Bullock, Lilian I. Plotkin, Alexander G. Robling, and Fredrick M. Pavalko

- 11 The Composition of Bone **84****
Adele L. Boskey and Pamela G. Robey

- 12 Assessment of Bone Mass, Structure, and Quality in Rodents **93****
Jeffrey S. Nyman and Deepak Vashishth

- 13 Skeletal Healing: Cellular and Molecular Determinants **101****
Alayna E. Loiselle and Michael J. Zuscik

- 14 Biomechanics of Fracture Healing **108****
Elise F. Morgan, Amira I. Hussein, and Thomas A. Einhorn

Section II: Skeletal Physiology **115**

Section Editor: Ego Seeman

- 15 Human Fetal and Neonatal Bone Development **117****
Tao Yang, Monica Grover, Kyu Sang Joeng, and Brendan Lee

- 16 Skeletal Growth: a Major Determinant of Bone's Structural Diversity in Women and Men **123****
Ego Seeman

- 17 Racial Differences in the Acquisition and Age-related Loss of Bone Strength **131****
Shane A. Norris, Marcella D. Walker, Kate Ward, Lisa K. Micklesfield, and John M. Pettifor

- 18 Calcium, Vitamin D, and Other Nutrients During Growth 135**
Tania Winzenberg and Graeme Jones
- 19 Mechanical Loading and the Developing Skeleton 141**
Mark R. Forwood
- 20 Pregnancy and Lactation 147**
Christopher S. Kovacs and Henry M. Kronenberg
- 21 Menopause and Age-related Bone Loss 155**
Carlos M. Isaacs and Ego Seeman
- Section III: Mineral Homeostasis 163**
Section Editors: David Goltzman and Harald Jüppner
- 22 Regulation of Calcium Homeostasis 165**
Line Vautour and David Goltzman
- 23 Magnesium Homeostasis 173**
Aliya Aziz Khan, Asiya Sbayi, and Karl Peter Schlingmann
- 24 Fetal Calcium Metabolism 179**
Christopher S. Kovacs
- 25 FGF23 and the Regulation of Phosphorus Metabolism 187**
Kenneth E. White and Michael J. Econs
- 26 Gonadal Steroids 194**
Stavros C. Manolagas and Maria Schuller Almeida
- 27 Parathyroid Hormone 205**
Thomas J. Gardella, Robert A. Nissenson, and Harald Jüppner
- 28 Parathyroid Hormone-Related Protein 212**
John J. Wysolmerski and T. John Martin
- 29 Calcium-Sensing Receptor 221**
Geoffrey N. Hendy
- 30 Vitamin D: Production, Metabolism, Action, and Clinical Requirements 230**
Daniel D. Bikle, John S. Adams, and Sylvia Christakos
- Section IV: Investigation of Metabolic Bone Diseases 241**
Section Editors: Douglas C. Bauer and Klaus Engelke
- 31 Techniques of Bone Mass Measurement in Children with Risk Factors for Osteoporosis 243**
Nicola J. Crabtree and Leanne M. Ward
- 32 Standard Techniques of Bone Mass Measurement in Adults 252**
E. Michael Lewiecki, Paul D. Miller, and Nelson B. Watts
- 33 Advanced Techniques of Bone Mass Measurements and Strength in Adults 260**
Kyle K. Nishiyama, Enrico Dall'Ara, and Klaus Engelke
- 34 Magnetic Resonance Imaging of Bone 272**
Sharmila Majumdar
- 35 Trabecular Bone Score 277**
Barbara C. Silva and William D. Leslie
- 36 Reference Point Indentation 287**
Adolfo Diez-Perez and Joshua N. Farr
- 37 Biochemical Markers of Bone Turnover in Osteoporosis 293**
Pawel Szulc, Douglas C. Bauer, and Richard Eastell
- 38 Scintigraphy and PET in Metabolic Bone Disease 302**
Lorenzo Nardo, Paola A. Erba, and Benjamin L. Franc
- 39 Bone Histomorphometry in Clinical Practice 310**
Robert R. Recker and Carolina Aguiar Moreira
- 40 Diagnosis and Classification of Vertebral Fracture 319**
James F. Griffith and Harry K. Genant
- 41 FRAX: Assessment of Fracture Risk 331**
John A. Kanis, Eugene V. McCloskey, Nicholas C. Harvey, and William D. Leslie

Section V: Genetics of Bone 341*Section Editor: Rajesh V. Thakker*

- 42 Introduction to Genetics 343**
Paul J. Newey, Michael P. Whyte, and Rajesh V. Thakker
- 43 Animal Models: Genetic Manipulation 351**
Karen Lyons
- 44 Animal Models: Allelic Determinants for Bone Mineral Density 359**
J. H. Duncan Bassett, Graham R. Williams, and Robert D. Blank
- 45 Transcriptional Profiling for Genetic Assessment 367**
Aimy Sebastian and Gabriela G. Loots
- 46 Approaches to Genetic Testing 373**
Christina Jacobsen, Yiping Shen, and Ingrid A. Holm
- 47 Human Genome-Wide Association Studies 378**
Douglas P. Kiel, Emma L. Duncan, and Fernando Rivadeneira
- 48 Translational Genetics of Osteoporosis: From Population Association to Individualized Assessment 385**
Bich Tran, Jacqueline R. Center, and Tuan V. Nguyen
- Section VI: Osteoporosis 393**
Section Editors: Paul D. Miller, Socrates E. Papapoulos, and Michael R. McClung
- 49 Osteoporosis: An Overview 395**
Michael R. McClung, Paul D. Miller, and Socrates E. Papapoulos
- 50 The Epidemiology of Osteoporotic Fractures 398**
Nicholas C. Harvey, Elizabeth M. Curtis, Elaine M. Dennison, and Cyrus Cooper
- 51 Fracture Liaison Service 405**
Piet Geusens, John A. Eisman, Andrea Singer, and Joop van den Bergh
- 52 Sex Steroids and the Pathogenesis of Osteoporosis 412**
Matthew T. Drake and Sundeep Khosla
- 53 Juvenile Osteoporosis 419**
Francis H. Glorieux and Craig Munns
- 54 Transplantation Osteoporosis 424**
Peter R. Ebeling
- 55 Premenopausal Osteoporosis 436**
Adi Cohen and Elizabeth Shane
- 56 Osteoporosis in Men 443**
Eric S. Orwoll and Robert A. Adler
- 57 Bone Stress Injuries 450**
Stuart J. Warden and David B. Burr
- 58 Inflammation-Induced Bone Loss in the Rheumatic Diseases 459**
Ellen M. Gravallese and Steven R. Goldring
- 59 Glucocorticoid-Induced Osteoporosis 467**
Kenneth Saag and Robert A. Adler
- 60 Human Immunodeficiency Virus and Bone 474**
Michael T. Yin and Todd T. Brown
- 61 Effects on the Skeleton from Medications Used to Treat Nonskeletal Disorders 482**
Nelson B. Watts
- 62 Diabetes and Fracture Risk 487**
Serge Ferrari, Nicola Napoli, and Ann Schwartz
- 63 Obesity and Skeletal Health 492**
Juliet Compston
- 64 Sarcopenia and Osteoporosis 498**
Gustavo Duque and Neil Binkley
- 65 Management of Osteoporosis in Patients with Chronic Kidney Disease 505**
Paul D. Miller
- 66 Other Secondary Causes of Osteoporosis 510**
Neveen A. T. Hamdy and Natasha M. Appelman-Dijkstra
- 67 Exercise for Osteoporotic Fracture Prevention and Management 517**
Robin M. Daly and Lora Giangregorio

- 68** Prevention of Falls **526**
Heike A. Bischoff-Ferrari
- 69** Nutritional Support for Osteoporosis **534**
Connie M. Weaver, Bess Dawson-Hughes, Rene Rizzoli, and Robert P. Heaney
- 70** Estrogens, Selective Estrogen Receptor Modulators, and Tissue-Selective Estrogen Complex **541**
Tobias J. de Villiers
- 71** Bisphosphonates for Postmenopausal Osteoporosis **545**
Andrea Giusti and Socrates E. Papapoulos
- 72** Denosumab **553**
Aline Granja Costa, E. Michael Lewiecki, and John P. Bilezikian
- 73** Parathyroid Hormone and Abaloparatide Treatment for Osteoporosis **559**
Felicia Cosman and Susan L. Greenspan
- 74** Combination Anabolic and Antiresorptive Therapy for Osteoporosis **567**
Joy N. Tsai and Benjamin Z. Leder
- 75** Strontium Ranelate and Calcitonin **573**
Leonardo Bandeira and E. Michael Lewiecki
- 76** Adverse Effects of Drugs for Osteoporosis **579**
Bo Abrahamsen and Daniel Prieto-Alhambra
- 77** Orthopedic Principles of Fracture Management **588**
Manoj Ramachandran and David G. Little
- 78** Adherence to Osteoporosis Therapies **593**
Stuart L. Silverman and Deborah T. Gold
- 79** Cost-Effectiveness of Osteoporosis Treatment **597**
Anna N.A. Tosteson
- 80** Future Therapies **603**
Michael R. McClung
- Section VII: Metabolic Bone Diseases 611**
Section Editors: Suzanne M. Jan de Beur and Peter R. Ebeling
- 81** Approach to Parathyroid Disorders **613**
John P. Bilezikian
- 82** Primary Hyperparathyroidism **619**
Shonni J. Silverberg, Francisco Bandeira, Jianmin Liu, Claudio Marcocci, and Marcella D. Walker
- 83** Familial States of Primary Hyperparathyroidism **629**
Andrew Arnold, Sunita K. Agarwal, and Rajesh V. Thakker
- 84** Non-Parathyroid Hypercalcemia **639**
Mara J. Horwitz
- 85** Hypocalcemia: Definition, Etiology, Pathogenesis, Diagnosis, and Management **646**
Anne L. Schafer and Dolores M. Shoback
- 86** Hypoparathyroidism **654**
Tamara Vokes, Mishaela R. Rubin, Karen K. Winer, Michael Mannstadt, Natalie E. Cusano, Harald Jüppner, and John P. Bilezikian
- 87** Pseudohypoparathyroidism **661**
Agnès Linglart, Michael A. Levine, and Harald Jüppner
- 88** Disorders of Phosphate Homeostasis **674**
Mary D. Ruppe and Suzanne M. Jan de Beur
- 89** Rickets and Osteomalacia **684**
Michaël R. Laurent, Nathalie Bravenboer, Natasja M. Van Schoor, Roger Bouillon, John M. Pettifor, and Paul Lips
- 90** Pathophysiology and Treatment of Chronic Kidney Disease—Mineral and Bone Disorder **695**
Mark R. Hanudel, Sharon M. Moe, and Isidro B. Salusky
- 91** Disorders of Mineral Metabolism in Childhood **705**
Thomas O. Carpenter and Nina S. Ma
- 92** Paget Disease of Bone **713**
Julia F. Charles, Ethel S. Siris, and G. David Roodman
- 93** Epidemiology, Diagnosis, Evaluation, and Treatment of Nephrolithiasis **721**
Murray J. Favus and David A. Bushinsky
- 94** Immobilization and Burns: Other Conditions Associated with Osteoporosis **730**
William A. Bauman, Christopher Cardozo, and Gordon L. Klein

Section VIII: Cancer and Bone 737*Section Editors: Theresa Guise and G. David Roodman*

- 95** Mechanisms of Osteolytic and Osteoblastic Skeletal Lesions **739**
G. David Roodman and Theresa Guise
- 96** Clinical and Preclinical Imaging in Osseous Metastatic Disease **743**
Siyang Leng and Suzanne Lentzsch
- 97** Metastatic Tumors and Bone **752**
Julie A. Sterling and Rachelle W. Johnson
- 98** Myeloma Bone Disease and Other Hematological Malignancies **760**
Claire M. Edwards and Rebecca Silbermann
- 99** Osteogenic Osteosarcoma **768**
Yangjin Bae, Huan-Chang Zeng, Linchao Lu, Lisa L. Wang, and Brendan Lee
- 100** Skeletal Complications of Breast and Prostate Cancer Therapies **775**
Catherine Van Poznak and Pamela Taxel
- 101** Bone Cancer and Pain **781**
Denis Clohisy and Lauren M. MacCormick
- 102** Radiotherapy-Induced Osteoporosis **788**
Laura E. Wright
- 103** Skeletal Complications of Childhood Cancer **793**
Manasa Mantravadi and Linda A. DiMeglio
- 104** Medical Prevention and Treatment of Bone Metastases **799**
Catherine Handforth, Stella D'Oronzo, and Janet Brown
- 105** Radiotherapy of Skeletal Metastases **809**
Srinivas Raman, K. Liang Zeng, Oliver Sartor, Edward Chow, and Øyvind S. Bruland
- 106** Concepts and Surgical Treatment of Metastatic Bone Disease **816**
Kristy Weber and Scott L. Kominsky
- Section IX: Sclerosing and Dysplastic Bone Diseases 823**
Section Editor: Michael P. Whyte
- 107** Sclerosing Bone Disorders **825**
Michael P. Whyte
- 108** Fibrous Dysplasia **839**
Michael T. Collins, Alison M. Boyce, and Mara Riminucci
- 109** The Osteochondrodysplasias **848**
Fabiana Csukasi and Deborah Krakow
- 110** Ischemic and Infiltrative Disorders of Bone **853**
Michael P. Whyte
- 111** Tumoral Calcinosis – Dermatomyositis **861**
Nicholas J. Shaw
- 112** Genetic Disorders of Heterotopic Ossification: Fibrodysplasia Ossificans Progressiva and Progressive Osseous Heteroplasia **865**
Frederick S. Kaplan, Robert J. Pignolo, Mona Al Mukaddam, and Eileen M. Shore
- 113** Osteogenesis Imperfecta **871**
Joan C. Marini
- 114** Fibrillinopathies: Skeletal Manifestations of Marfan Syndrome and Marfan-Related Conditions **878**
Gary S. Gottesman and Michael P. Whyte
- 115** Hypophosphatasia and Other Enzyme Deficiencies Affecting the Skeleton **886**
Michael P. Whyte
- Section X: Oral and Maxillofacial Biology and Pathology 891**
Section Editor: Laurie McCauley
- 116** Craniofacial Morphogenesis **893**
Erin Ealba Bumann and Vesa Kaartinen
- 117** Development and Structure of Teeth and Periodontal Teeth **901**
Petros Papagerakis and Thimios Mitsiadis
- 118** Genetic Craniofacial Disorders Affecting the Dentition **911**
Yong-Hee Patricia Chun, Paul H. Krebsbach, and James P. Simmer
- 119** Pathology of the Hard Tissues of the Jaws **918**
Paul C. Edwards
- 120** Osteonecrosis of the Jaw **927**
Sotirios Tetradis, Laurie McCauley, and Tara Aghaloo

- 121 Alveolar Bone Homeostasis in Health and Disease 933**
Chad M. Novince and Keith L. Kirkwood
- 122 Oral Manifestations of Metabolic Bone Diseases 941**
Erica L. Scheller, Charles Hildebolt, and Roberto Civitelli
- 123 Dental Implants and Osseous Healing in the Oral Cavity 949**
Takashi Matsuura and Junro Yamashita
- Section XI: Integrative Physiology of the Skeleton 957**
Section Editors: Mone Zaidi and Clifford J. Rosen
- 124 Integrative Physiology of the Skeleton 959**
Clifford J. Rosen and Mone Zaidi
- 125 The Hematopoietic Niche and Bone 966**
Stavroula Kousteni, Benjamin J. Frisch, Marta Galan-Diez, and Laura M. Calvi
- 126 Adipocytes and Bone 974**
Clarissa S. Craft, Natalie K. Wee, and Erica L. Scheller
- 127 The Vasculature and Bone 983**
Marie H el ene Lafage-Proust and Bernard Roche
- 128 Immunobiology and Bone 992**
Roberto Pacifici and M. Neale Weitzmann
- 129 Cellular Bioenergetics of Bone 1004**
Wen-Chih Lee and Fanxin Long
- 130 Endocrine Bioenergetics of Bone 1012**
Patricia F. Ducey and Gerard Karsenty
- 131 Central Neuronal Control of Bone Remodeling 1020**
Hiroki Ochi, Paul Baldock, and Shu Takeda
- 132 Peripheral Neuronal Control of Bone Remodeling 1028**
Katherine J. Motyl and Mary F. Barbe
- 133 The Pituitary–Bone Axis in Health and Disease 1037**
Mone Zaidi, Tony Yuen, Wahid Abu-Amer, Peng Liu, Terry F. Davies, Maria I. New, Harry C. Blair, Alberta Zallone, Clifford J. Rosen, and Li Sun
- 134 Neuropsychiatric Disorders and the Skeleton 1047**
Madhusmita Misra and Anne Klibanski
- 135 Interactions Between Muscle and Bone 1055**
Marco Brotto
- Index 1063**