Contents

1 Epidemiology of Osteoporosis ............ 1
   1.1 Osteoporosis: A Silent Thief! ........ 1
   1.2 Osteoporosis: The Global Scope of the Problem ............ 2

2 Biology of Bone .......................... 7
   2.1 Bone: An Architectural Masterpiece 7
   2.2 Bone: A Permanent Building and Rebuilding Site ........... 10
   2.3 Remodelling Units .................... 15
   2.4 Some Biological Perspectives on the Mechanisms Involved in the Control and Regulation of Bone Remodelling 17
   2.5 Minimodelling ......................... 18
   2.6 Stimuli, Triggers and Mechanisms of Activation of Bone Remodelling ......... 19
   2.7 Control of Bone Remodelling: A Network of Complex Mechanisms 20
   2.8 Osteoimmunology: A Representative of Systems Biology .................. 23
   2.9 The RANK/RANKL/Osteoprotegerin System .................. 23
   2.10 Leptin: Role of the Central Nervous System in Regulation of Bone ...... 25
   2.11 Growth of the Embryo in the Uterus ... 26
   2.12 Peak Bone Mass: An Investment for a Healthier Life ........... 27

3 Pathogenesis of Osteoporosis ............ 29
   3.1 Factors in the Development of Osteoporosis .................. 29
   3.2 Definition of Osteoporosis ............ 30
   3.3 Osteoporosis – Which Bones are Vulnerable? .................... 31
   3.4 Osteoporosis – Also a Question of Quality! .................... 32
   3.5 Definition of “Fracture” .................. 34
   3.6 Vertebral (Spinal) Fractures ........... 34
   3.7 Hip Fractures .......................... 36
   3.8 Wrist Fractures ......................... 37
   3.9 Other Fractures ........................ 37

4 Subgroups of Osteoporosis ............ 39
   4.1 According to Spread .................... 39
   4.2 According to Age and Sex ............ 40
   4.3 According to Extent .................... 42
   4.4 According to Histology ................ 43

5 Risk Factors for Fractures ............ 45
   5.1 Risk Factors Which Cannot (Yet) be Influenced .................. 46
   5.2 Risk Factors Which Can be Influenced .................. 48

6 Clinical Evaluation of Osteoporosis .... 55
   6.1 Indicative Symptoms .................... 55
   6.2 Osteoporosis and Teeth, Skin and Hair – What are the Connections? ....... 57
   6.3 Role of Conventional X-Rays in Osteoporosis .................. 57
   6.4 Other Useful Imaging Techniques .... 60

7 Bone Density in Osteoporosis ............ 63
   7.1 Why Measure Bone Mineral Density? .................. 63
   7.2 Which Instruments to Use? ................ 63
   7.3 Which Bones to Measure? ............ 70
   7.4 Who is Due or Overdue for a BMD Test? .................. 70
7.5 Bone Densitometry in Children
   – Now Readily Available! .............. 72
7.6 BMD Measurement – Not a Scary Procedure, Nothing to be Afraid of? 73

8 Laboratory Evaluation of Osteoporosis .... 75
8.1 Recommended Tests .................. 75
8.2 Significance of Markers of Bone Turnover .................. 75
8.3 Recommendations for Practical Use of Bone Markers .................. 79
8.4 Potential of Bone Biopsy in Clinical Practice .......................... 79
8.5 When is a Bone Biopsy Indicated? .... 80
8.6 Up-to-Date Methods .................. 81

9 Prevention of Osteoporosis .......... 83
9.1 Step 1: First of all a Calcium-Rich Diet! .......................... 83
9.2 Step 2: Ensure an Adequate Supply of Vitamins! ......................... 85
9.3 Step 3: Protect the Spine in Everyday Life! .......................... 86
9.4 Step 4: Regular Physical Activity – for the Preservation of Strong Bones! .......................... 87
9.5 Step 5: No Smoking, Please! ............. 90
9.6 Step 6: Reduce Nutritional “Bone Robbers”! .......................... 90
9.7 Step 7: Strive for an Ideal Body Weight! .......................... 91
9.8 Step 8: Identify Drugs that Cause Osteoporosis and Take Appropriate Steps to Counteract Them When Possible and Necessary! .......................... 92
9.9 Step 9: Recognize Diseases Which Damage Bones! .......................... 92
9.10 Step 10: Management of Patients Who Have Already Sustained a Fracture .......................... 93

10 Physical Activity and Exercise Programs .................................. 95
10.1 Strong Muscles Make and Maintain Strong Bones! .......................... 95
10.2 The Muscle–Bone Unit and Sarcopenia .......................... 96
10.3 Exercise Programs – Preventive and Restorative .......................... 97
10.4 Implementation of a Training Program .......................... 97

11 Treatment Strategies in Osteoporosis .... 99
11.1 Evidence-Based Strategies for the Therapy of Osteoporosis .... 99
11.2 Comprehensive Approach to the Therapy of Osteoporosis .... 103
11.3 Indication for Treatment – Combining BMD with Clinical Factors .......................... 104

12 Management of Pain in Osteoporosis ......................................... 107
12.1 Start with the Patient, not the Disease! .......................... 107
12.2 Acute Phase .......................... 107
12.3 Chronic Phase – Short Term .... 108
12.4 Chronic Phase – Long Term .... 109
12.5 Electric Potentials in Bone .......................... 109

13 Calcium and Vitamin D .................. 111
13.1 Calcium: A Lifelong Companion .... 111
13.2 The Concept of Vitamin D in the 21th Century .......................... 113
13.3 Vitamin D: Don’t Relly on Sunshine, Take Supplements .... 114
13.4 Rickets .......................... 115
13.5 Other Vitamins Involved in Skeletal Health .......................... 117

14 Hormones for Replacement Therapy ........................................ 119
14.1 Hormone Replacement Therapy for Women – Now Recommended for Symptoms Only! .......................... 119
14.2 Which Oestrogens and Progestins, and How to Take Them? .... 120
14.3 Which Women to Treat? .... 121
14.4 How Long to Treat? .... 121
14.5 How to Monitor HRT? .... 121
14.6 What are the Risks and Adverse Events of HRT? .......................... 122
14.7 What are the Main Contraindications? .......................... 122
14.8 Natural Oestrogens – How Effective are They? .......................... 122
14.9 Dehydroepiandrosterone (DHEA) – Is it Useful for the Prevention of Bone Loss? .......................... 124
14.10 Testosterone – Good for Bones and Well-Being in Men! .......................... 124
14.11 Anabolic Steroids – Strong Muscles for Healthy Bones! .......................... 124
## 15 Bisphosphonates

15.1 A Brief Survey of Bisphosphonates .................................. 128
15.2 Pharmacokinetics ................................................. 131
15.3 Toxicity and Contraindications ..... 132
15.4 Osteomyelitis/Osteonecrosis of the Jaw (ONJ) ................... 133
15.5 Contraindications ................................................. 135
15.6 Oral Bisphosphonates Currently Used in Osteoporosis .............. 135
15.7 Alendronate ......................................................... 135
15.8 Risedronate ......................................................... 136
15.9 Etidronate ......................................................... 137
15.10 Ibandronate ....................................................... 137
15.11 Intravenous Bisphosphonates for the Treatment of Osteoporosis .... 138
15.12 Ibandronate ....................................................... 138
15.13 Zoledronate ....................................................... 138
15.14 Clodronate and Pamidronate ..... 139
15.15 Recommendations for Intravenous Therapy ................................ 139
15.16 Duration of Therapy with Bisphosphonates and Long-Term Studies ................................................. 139
15.17 A Summary of Results Achieved to Date ................................. 140
15.18 Meta-analyses of Antiresorptive Substances ............................... 142

## 16 Selective Oestrogen-Receptor Modulators

16.1 A Brief Overview of SERMs – New Selective Antiresorptive Agents ..... 145
16.2Raloxifene – Utilization of Physiological Effects on Bone .............. 145

## 17 Peptides of the Parathyroid Hormone Family

17.1 Osteoanabolic Action of PTH – Paradoxical Effects Depend on Type of Administration ........................................ 149

## 18 Strontium Ranelate ............................................. 153

## 19 Calcitonin and Fluoride ............................................. 155

## 20 Combination and Sequential Therapies ............................... 157

## 21 Future Directions ...................................................... 159

## 22 Adherence and Monitoring of Osteoporosis Therapy .................. 161

22.1 Adherence to Treatment ...................................... 161
22.2 Monitoring Treatment ...................................... 161
23.3 Monitoring Antiresorptive Therapy .................................. 163
24.4 Monitoring Osteo-anabolic Therapy .................................. 164

## 23 Osteoporotic Fractures ............................................. 165

23.1 Frailty Fractures ................................................. 165
23.2 Fractures and the Healing Process .................................. 166
23.3 Effects of Drugs and Lifestyle on Fracture Healing ................. 167
23.4 Risk Factors for Osteoporotic Fractures ................................ 168
23.5 Management of Osteoporotic Fractures ................................ 171
23.6 Prevention of Further Fragility Fractures with Specific Drugs ..... 171
23.7 Fracture Sites and Their Clinical Significance .......................... 171

## 24 Pregnancy and Lactation ........................................... 179

## 25 Osteoporosis in Men ................................................ 183

25.1 Clinical Evaluation of Osteoporosis in Men .......................... 183
25.2 Special Features in Men ............................................. 186
25.3 Prevention and Treatment in Men .................................. 186
25.4 Therapy of Osteoporosis in Men .................................. 187

## 26 Osteoporosis in Children ........................................... 189

26.1 First Clarification – Hereditary or Acquired? ............................ 189
26.2 Idiopathic Juvenile Osteoporosis, Idiopathic Juvenile Arthritis, and Other Conditions ........................................ 194
26.3 Osteogenesis Imperfecta Must Not Be Overlooked! ................. 195
26.4 Turner Syndrome and Charge Syndrome ................................ 197
26.5 X-Linked Hypophosphatemic Rickets ................................ 197
26.6 Gaucher’s Disease ................................................. 197

## 27 Immobilization Osteoporosis ...................................... 199

27.1 Examples of Bone Loss ........................................... 199
27.2 Space Travel and the Force of Gravity ................................ 200
27.3 Therapy of Immobilization Osteoporosis ............................... 200