14

Future Therapies and Clinical Trials

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Second to being right in this world is being totally wrong.

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14.1. Introduction

The diagnosis and treatment of osteoporosis is still a relatively young science. Although Albright first described osteoporosis in 1947, it is only since the late 1980s and early 1990s that we have had the instruments available for the diagnosis and then treatment of this disease. As for any medical area in its infancy, we can, therefore, expect a significant number of changes in the coming years, as a result of more comprehensive understanding of bone physiology and elucidation of the genetic factors leading to increased risk factors.

14.2. Future Therapies

When the first edition of this book was written, it was stated that “In the immediate future the therapeutic regimens that will be available to the prescribing physician will increase to include several different formulations of hormone replacement therapy (HRT), with several different modes of delivery, three bisphosphonates available in Europe (two in the USA), nasal calcitonin, and selective estrogen receptor modulators or SERMs.” In the 4 years since the book was written, the therapeutic landscape has changed dramatically. HRT, which was once the first-line therapy for osteoporosis, is no longer used, because it was shown in the Women’s Health Initiative study (2002) that women taking this drug had an increased risk of developing breast cancer. In 2002, the first recombinant parathyroid hormone (PTH) drug was introduced onto the market [PTH(1–34); Forteo® (Eli Lilly and Company, Indianapolis, USA)]. A second PTH [PTH(1–64); Preos® (NPS Pharmaceuticals, Parsipany, NJ, USA)] is approved in the European Union (EU) and under review by the US Food
and Drug Administration (FDA). Several more versions of PTH are currently in various stages of development, including forms using different methods of delivery, not just subcutaneous injection. There have been some safety issues, which on the whole have been resolved (i.e. osteosarcoma was reported in rats). It is also worth noting that, after a number of years of prescribing, this issue has not been reported in humans.

Modern medicine and treatment of disease is, generally, based on treating each disease specifically and separately. However, several new therapies (including SERMs) have provided the opportunity for prevention and/or treatment of more than one disease at a time. At the time of writing the first edition of this book, one SERM was on the market (raloxifene) and a second drug in this class was in phase III development. This latter compound, lasofoxifene, was rejected by the FDA for the indication of prevention of osteoporosis in 2005.

A novel area that has shown some major promise is the receptor for activation of NF-KB (RANK) ligand inhibitor denosumab. Phase II study results have demonstrated that twice-yearly subcutaneous injections of the compound demonstrated an increase in bone mineral density (BMD) at the lumbar spine of 5.1% after 24 months.3

The other major development is the bisphosphonate zoledronic acid, which has been show to increased BMD over a 12 month period following a single annual injection.4 Although bisphosphonates have been well characterized, and are the leading treatment for osteoporosis, this finding will be an interesting development and could potentially be the first therapy, in any field (except for vaccines), for which a single annual injection provides treatment for 1 year.

14.3. Osteoporosis-Related Diseases

Other bone diseases will also appear on the “radar screen”, developing the range of uses for these treatments. Already, we have seen male osteoporosis become a treatable disease, with alendronate (Fosamax®, Merck & Co. Inc., Whitehouse Station, NJ, USA). It was only a few years ago that the general opinion was that osteoporosis was a female disease. This is no longer the case. We are starting to see development in other therapeutic areas. Bone diseases in children have been an area of minimal concern, but with the FDA now promoting studies in children, we can expect to see diseases such as osteogenesis imperfecta being treated with the bisphosphonates. In later adolescence, amenorrhoea caused either by anorexia nervosa and related diseases or by extreme physical activity, for example Olympic female gymnasts, can result in decreased bone accretion in the formative years. If the level of bone deposition in these juveniles can be improved with the use of some of the new therapeutic agents, the incidence of fracture throughout an individual’s life span can be reduced.

There are a number of other conditions that have a secondary effect of excessive bone loss that are currently untreated or undertreated. The use of steroids and bone loss is well documented, but not everyone is treated. Women taking luteinizing