ated with an increased bone mass and in some cases protection against fracturing, are of relevance for osteoporosis. One of the major breakthroughs in the field of bone metabolism has been the role of canonical Wnt signaling in bone formation. The unraveling of several sclerosing bone dysplasias have been instrumental for this. Furthermore, in other conditions the regulation of this pathway turned out to be disturbed resulting in an increased bone formation rate. This is nicely exemplified in sclerosteosis and Van Buchem disease lacking sclerostin, a bone specific inhibitor of canonical Wnt signaling. Finally, the study of monogenic skeletal diseases not only contributed towards the understanding of mechanisms and regulation of bone homeostasis but also provided some novel targets for drug development for the treatment or prevention of osteoporosis. For example, monoclonal antibodies against sclerostin and cathepsin K are currently under development. This supports the idea that the study of rare monogenic conditions has important implications also for more common related conditions.

KEYWORDS: genetic skeletal disorders, Wnt signaling, sclerostin, cathepsin K.

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PRIMARY HYPERPARATHYROIDISM: CHALLENGES IN NORMOCALCEMIC AND MILD CASES

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The clinical presentation of primary hyperparathyroidism (PHPT) has changed dramatically in Western societies after increased accessibility to biochemical analyses. Thus, the diagnosis is today often made by change in patients without specific symptoms. Operative treatment is always an option and recommended in patient with markedly increased calcium levels or typical symptoms. However, the vast majority of patients in the modern Western clinic do not present organ related symptoms and their calcium levels are only slightly increased, or even within the upper limit of normal. Several consensus development conferences have discussed management of these patients with mild, borderline PHPT during the last twenty years. In developing countries in The Middle East, Asia and Latin America, patients still present with classical symptoms, severe hypercalcaemia, osteitis fibrosa and prevalent fractures. The female preponderance is much less pronounced in these areas and the presentation and severity of the disease related to vitamin D deficiency. With the recent change in socio-economic status in these areas, the clinical presentation of PHPT has drifted towards the more non-classical presentation with non-specific symptoms raising the same discussion on treatment indications. As disease severity in PHPT seems to be related to vitamin D deficiency and as the true calcium level might be masked by low levels, patients might be repleted with vitamin D during work-up and in preparation for surgical treatment. Only few studies have so far addressed this question, however based on recent randomized and controlled studies, pre-surgical Vitamin D treatment in PHPT seems to be safe and beneficial regarding PTH levels and BMD. Thus, in the modern clinic, most patients will present with few if any symptoms, high normal or slightly increased calcium levels with only slightly or moderately elevated PTH. Differential diagnoses must be ruled out and familiar or syndromic forms identified. Before decision for active treatment or observation is made, the patient should be handled to optimize vitamin D levels and ensure that no medical treatment is interfering with calcium levels.

KEYWORDS: primary hyperparathyroidism (PHPT), hypercalcaemia, vitamin D.

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GENETIC CAUSES OF HYPERPARATHYROIDISM

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Primary hyperparathyroidism (PHPT) is caused by autonomous hypersecretion of parathyroid hormone (PTH) by solitary parathyroid adenoma (~85%), parathyroid hyperplasia/multiple adenomas (~15%) or less frequently by parathyroid carcinoma (~1—5%). The majority of cases of PHPT are sporadic. Only 10—20% occur as a part of one of familial syndromes which include multiple endocrine neoplasia type 1, type 2A, type 4, hyperparathyroidism-jaw tumour syndrome, familial hypocalciuric hypercalcemia and familial isolated hyperparathyroidism, and has specific features in each of them. To date only two genes (tumor suppressor gene *MEN1* and oncogene *CCND1*) have been proven to play a role in tumorigenesis of sporadic parathyroid adenomas. Somatic *CDC73* mutations are frequently associated with parathyroid carcinomas. The role of somatic mutations in other genes in parathyroid tumorigenesis remains controversial.

KERWORDS: hyperparathyroidism, genetics, adenoma.

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SECONDARY HYPERPARATHYROIDISM DUE TO CHRONIC KIDNEY DISEASE. THE MANAGEMENT OF CALCIUM — PHOSPHOROUS DISTURBANCE

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Chronic kidney disease (CKD) is a widespread disease, which is characterized by progressive deterioration of kidney function. CKD is not only limited to negative effects on the kidney but is associated with a multifactorial dysregulation of bone and vascular calcification and is closely linked to increased cardiovascular disease and concomitant bone disease. These comorbidities are responsible for increased and premature mortality in CKD pa-