Osteoporosis has traditionally been categorized as primary or secondary. Primary osteoporosis occurs together with and as a result of the major physiological condition known as ageing (senescence) and its causes and consequences. Secondary osteoporosis develops as a consequence of the major physio-pathological effects on the bones of the skeleton of numerous disorders and diseases of other organs and tissues in the body.

The mechanisms involved in both categories have been extensively investigated and obviously depend on specific conditions and occurrences, such as for example the decrease in levels of ovarian and testicular hormones in primary, involutional osteoporoses. With respect to secondary osteoporoses, it is equally clear that these are correlated with the disorders with which they are associated, and possibly also with the mechanisms and corresponding pathways responsible for these disorders. These aspects are already being taken into consideration today when considering the treatment of osteoporosis required by patients with, for example, co-morbidities such as diabetes, AIDS or a cardiovascular disorder, all of which also affect the bones.

4.1 According to Spread

Osteoporosis may be localized to one or more skeletal regions, i.e. focal or regional osteoporosis, as distinct from the classic generalized osteoporosis (systemic, global). The most important causative factors responsible for bone loss are:

- Inactivity (immobilization osteoporosis): The classic example of this is regional osteoporosis which occurs when an extremity is immobilized either because of a fracture or a motor-neuron injury. The lack of use and movement results in increased osteoclastic resorption which, if sufficiently extensive, is also accompanied by hypercalciuria and hyperphosphaturia. On cessation of immobilization and resumption of activity the process can be reversed and the bones normalized, especially those in children and young people.

- Complex regional pain syndrome (CRPS, Sudeck’s disease, algodystrophy, sympathetic reflex dystrophy): This affects mainly the hands, knees and ankles and is characterized by swelling, pain, hyperaesthesias and vasomotor reactions.

- Transient (transitory) osteoporosis: Transient osteoporosis is a regional process first described in the pelvic bones in pregnant women. Since then, it has also been observed in knee and ankle joints in both young men and young women. The pain appears to start spontaneously without apparent prior trauma. The diagnosis is established by means of magnetic resonance imaging (MRI), which shows extensive oedema of the bone marrow around the painful joint. Clinically, the process is self-limiting with
complete restitution within 1 year. Together with CRPS this disorder is now summarized under the heading of “bone marrow oedema syndrome” and can be treated effectively with intravenous bisphosphonates (complete remission in about 80% of cases) (see Chap. 31).

- **Gorham-Stout syndrome** (“vanishing bone disease”): The cause of this rare bone disease has not yet been elucidated, although a vascular and lymphatic connection has been suggested, mainly by way of activated endothelium. It begins with completely uncoupled osteoclastic resorption of a bone and spreads to adjoining bones. Progression is variable. Severe or life-threatening complications may occur when bones of the thorax or the vertebrae are involved. To date, the only effective therapy is administration of bisphosphonates as early as possible to prevent extensive loss of bone (see Chap. 31).

- **Other osteolytic syndromes**: These may be due to a variety of causes, including infections, tumours, trauma as well as metabolic, vascular, congenital and genetic aberrations.

- **Generalized (systemic) osteoporosis**: This is far more frequent than localized osteoporosis. In spite of its name, generalized osteoporosis is rarely manifested in the whole skeleton, but it does have a symmetrical distribution. Juvenile and postmenopausal osteoporoses generally affect the axial skeleton, while the age-related form also attacks the tubular bones, especially in men. Consequently, the presence of normal bone density in bones of the extremities does not rule out (possibly even severe) osteoporosis of the axial skeleton. This is important to bear in mind in the evaluation of local measurements of bone mineral density (BMD), which only represent the bone measured and cannot be extrapolated to the rest of the bones in the skeleton.

### 4.2 According to Age and Sex

- **Idiopathic juvenile osteoporosis**: This is a rare self-limiting disease in prepubertal children, usually occurring between 8 and 14 years of age. It generally manifests as compression fractures of the vertebrae accompanied by severe back pain. The differential diagnosis includes osteogenesis imperfecta, Cush-

- **Idiopathic osteoporosis in young adults**: This primarily affects men between the ages of 30 and 50 years and is also characterized by fractures of the vertebral bodies. Biochemical parameters and bone biopsy findings show increased resorption of bone. Frequently the patients are heavy smokers, smoking having been implicated as a possible contributory factor. A mild form of osteogenesis imperfecta, not previously diagnosed, must be excluded in these patients.

- **Postmenopausal (type I) osteoporosis** (Fig. 4.1): This is the most common form of osteoporosis and occurs in women between 51 and 75 years of age as a consequence of cessation of ovarian function. The loss of bone actually starts years beforehand and increases at the time of the menopause (perimenopausal). About 30% of all women develop osteoporosis after the menopause. Cessation of oestrogen secretion leads to a decrease in IL-6 and other cytokines, which in turn leads to increased recruitment and activation of osteoclasts. In addition, bone becomes more sensitive to the resorption stimulating action of parathyroid hormones. As a consequence there is increased resorption of cancellous bone in the vertebrae and in the hip bones with a corresponding increase in fracture risk. Obviously this postmenopausal form of osteoporosis occurs only in women, but men are also subject to increased bone resorption as a consequence of testosterone deficiency, although at a later stage in life, from 50 to 60 years onwards. Intestinal absorption of calcium in some postmenopausal women has been associated with hypercalciuria and linked to bone loss in idiopathic osteoporosis as well as in calcium nephrolithiasis. The hypothesis was put forward that these might be two subtypes of the response to hypercalciuria of intestinal origin.

- **Involutional (age-related, type II) osteoporosis** (Fig. 4.1): In women, postmenopausal and in men postandropausal osteoporosis merges imperceptibly into the involutional, age-related type which represents part of the aging process and which can lead to frailty. This is characterized by many factors common to osteoporosis including sarcopenia, falls, decreased physical activity, cognitive decline, changes in many hormones, vitamins and cytokines.
