Studies of twins have shown that osteoporosis may be genetically determined – up to 50% – and many genes are involved. Peak bone mass is therefore to some extent genetically programmed, and the subsequent degree of loss of bone density applies especially to trabecular (cancellous) bone. It has also been demonstrated that genes may have different effects on bones at different skeletal sites and play a part in overall bone development as well as in degree of osteoporosis at these sites. Recently the connection between the genes for vitamin D receptors and bone density has been of particular interest and subjects of research, though the results of such studies have been somewhat contradictory. Clinically, osteogenesis imperfecta is the most important of the hereditary osteoporoses. Other congenital syndromes with an osteoporotic component are Turner, Klinefelter, Ehlers-Danlos, Marfan and Werner. Studies of the congenital premature ageing syndrome dyskeratosis congenita have identified mutations in the genes that encode the telomerase complex. Cells of these patients have very short telomeres, and they age prematurely. The patients suffer from early greying of the hair, dental loss, osteoporosis and malignancies.

Recently it has been shown that bone may be influenced by the GH-IGF-1 axis in intrauterine (genetically determined) and in postnatal life. This effect may continue into adulthood suggesting a role for the GH-IGF-1 axis in the programming of bone mass in women. Results for men are awaiting publication. With successful enzyme replacement therapy in Gaucher’s disease, the infiltration decreases, but the osteoporosis increases and should be treated prophylactically after measurement of bone mineral density. Congenital syndromes with involvement of the muscles are also prone to lead to disturbances of bone remodelling and osteoporosis. It is also of interest that a polymorphism of the growth hormone receptor gene (exon-3 deletion, d3GHR) increases the response to recombinant human growth hormone (rhGH) in children, while in adults with growth hormone deficiency, it contributes to the differences in efficacy of short-term rhGH therapy only.

Numerous studies have now accumulated on genetics and disorders of bones and joints, on congenital syndromes, on genes involved in pathways of development and differentiation, on osseous phenotypes on genes associated with onset of osteoporosis and with various types of fractures and on genes associated with skeletal metabolism and race, ethnicity and age in population studies, investigations of which SNPs may be involved in differences of response to treatment as well as their association with bones and muscles in the metabolic syndrome. All these and more have made it clear that osteoporosis is related to multiple genes and many environmental factors. Some relevant studies are listed in the references.