interaction of genetic, environmental, endocrinological, and mechanical factors regulating bone metabolism. Each of these factors influences the structure, the degree of mineralization, and the turnover of bone tissue (Figure 1).4-6

Genetic syndromes and diseases may affect bone structure and quality directly or indirectly, with the involvement of systems regulating bone metabolism from conception (Table 1). This has a negative impact on the attainment of PBM and predisposes patients to develop more or less severe forms of osteoporosis, with a consequent deterioration in quality of life.

Unfortunately for many of these patients, there are still few studies with regard to bone metabolism in the short and long term. One of the reasons for this is that it is difficult to obtain meaningful data from the small number of patients available.

The study of bone tissue in individuals with genetic syndromes is very complex because, in addition to the limits presented by various diagnostic techniques, there are also obstacles related to the correct interpretation of the data, such as the short stature or pubertal problems that are frequently present in these patients.3,7,8 Moreover, information on bone age at the time of bone status evaluation are often missing as delayed bone age can confound the results on bone mineral density measurements. Thereafter, in some genetic syndromes the special morphology of the bone or tissue composition may affect data collection. However, the lack of specific reference for height or bone quality and mass values for specific syndromes may be false positives or false negatives because the reference values are matched to the normal population.7,8 The presence of mental retardation is also frequent and can make it difficult to use some techniques that require good compliance.3

For these reasons, there are currently no commonly accepted protocols or guidelines regarding the appropriate use of various techniques for assessing bone mass. Meanwhile, it is also very difficult to identify the specific alteration of the metabolic defect in the context of rare and extremely complex syndromes, which also complicates the preventive and therapeutic approach.

The eventual identification of a defect in bone metabolism at an early stage of life makes it possible to employ specific diagnostics, treatment, and follow-up to improve the quality of life of patients and to prevent further disability.

This review provides an updated overview of bone pathophysiology and characteristics in patients with Down, Turner, Klinefelter, Marfan, Williams, Prader-Willi, Noonan, and 22q11 deletions syndrome. Additionally, some options for the treatment of bone impairment will be briefly discussed.

### DOWN SYNDROME

Down syndrome (DS; OMIM #190685) is a frequent genetic disorder that exhibits a prevalence of 1 in 700 live births and results from an extra 21 chromosome or a duplication of a critical portion of it.9 DS patients show cognitive impairment, low muscle