Structural changes of collagen fibrils in skeletal dysplasias

Ultrastructural findings in the iliac crest*

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Summary. The skeletal dysplasias are constitutional, generalized or localized disorders of the skeletal system involving a disturbance of growth and/or bone density; their genetic transmission varies. Pathomorphologically, a combined functional-structural disturbance of the cartilaginous and/or bone tissue is present. Clinically, the result is varying degrees of dwarfism.

Within the framework of a systematic examination of skeletal dysplasias, a total of 84 iliac crest specimens/biopsies obtained from stillborn infants and patients varying in age from a few days to 40 years, were investigated in the electron microscope. The sections prepared extended from the perichondrium through the proximal resting zone to the primary mineralization zone. The structure of the collagen fibrils was studied in diastrophic dysplasia, pseudoachondroplasia, the WOLCOTT-RALLISON syndrome, osteogenesis imperfecta, and idiopathic juvenile osteoporosis.

In diastrophic dysplasia, pseudoachondroplasia and idiopathic osteoporosis, the cartilaginous ground substance contains collagen fibrils that can vary considerably in length, structure, and diameter. In one case of WOLCOTT-RALLISON syndrome, the lacunae of the chondrocytes are found to contain very wide amianthoid-like and inadequately aggregated collagen fibrils. In numerous cases, osteogenesis imperfecta reveals very fine and also irregularly structured collagen fibrils with scarcely discernible cross-striation in the region of the osteoid, which is of varying width. In some of the cases, catechin has a favourable effect on the formation of collagen fibrils, resulting in broader and more densely packed fibrils. In addition, the conditions are associated with considerable intracellular changes in the rough endoplasmic reticulum, the Golgi apparatus and the mitochondria.

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The varying collagen fibril findings in the cartilage and bone tissue also represent a morphological marker of the combined functional-structural disorder of chondrocytes and/or osteoblasts, and an expression of the differing aetiopathogenesis.

**Key words:** Skeletal dysplasia – Diastrophic dysplasia – Pseudoachondroplasia – Osteogenesis imperfecta – WOLCOTT-RALLISON Syndrome

**Introduction**

The skeletal dysplasias are constitutional, generalized or localized diseases of the skeletal system with a disturbance of growth and/or bone density. These diseases are usually genetically determined with a variable mode of inheritance, predominantly autosomal dominant or autosomal recessive. To date, they have been classified exclusively on the basis of clinical and radiological findings, with no account being taken of their pathogenesis. In accordance with the “Paris Nomenclature” revised in 1983 by the European Society for Paediatric Radiology, these entities are subdivided into six main groups containing numerous sub-groups (Table 1). The leading clinical feature is disproportionate dwarfism of varying degree, accompanied by deformation of the vertebral column and the extremities, which can manifest within the uterus or after birth. Pathomorphologically, a combined functional-structural disturbance of cartilage and/or bone tissue is found (Stöß et al. 1982), which can be either intracellular or extracellular in origin.

So far, more attention has been directed towards the intracellular disorders of the chondrocytes and osteoblasts (Rimoin 1975; Stanescu et al. 1977; Sillence et al. 1979) than towards the extracellular changes in the cartilaginous and bony ground substances. In this article, our attention has been focussed on the collagen fibrils, as an ordered component of the ground substance, taking diastrophic dysplasia, pseudoachondroplasia, the WOLCOTT-RALLISON syndrome, osteogenesis imperfecta and idiopathic juvenile osteoporosis as examples.

**Material and methods**

A total of 84 iliac crest specimens or biopsies were obtained from stillborn infants and patients varying in age from several days to 40 years, with diastrophic dysplasia, pseudoachondroplasia, WOLCOTT-RALLISON syndrome, osteogenesis imperfecta, or idiopathic juvenile osteoporosis. After fixation in buffered, 1% glutaraldehyde/4% formaldehyde solution (Trump and Jones 1978), the non-decalcified iliac crest specimens were cut into consecutive slices ranging, in accordance with the growth zone, from the perichondrium via the proximal resting zone to the distal zone of primary mineralization, and investigated zone by zone. After post-fixation in 1% osmic acid, the specimens were dehydrated in increasing concentrations of acetone, block-contrasted with phosphotungstic acid and uranyl acetate, and then embedded in low-viscosity epoxy resin (Spurr 1969), using a technique modified by Schulz (1977). The blocks of resin were then cut with the aid of a Dupont diamond knife to provide ultra-thin sections, post-contrasted with uranyl acetate and lead citrate, and investigated in an Elmiskop 101 electron microscope.