

NTP Nonneoplastic Lesion Atlas

Bone – Physeal Dysplasia

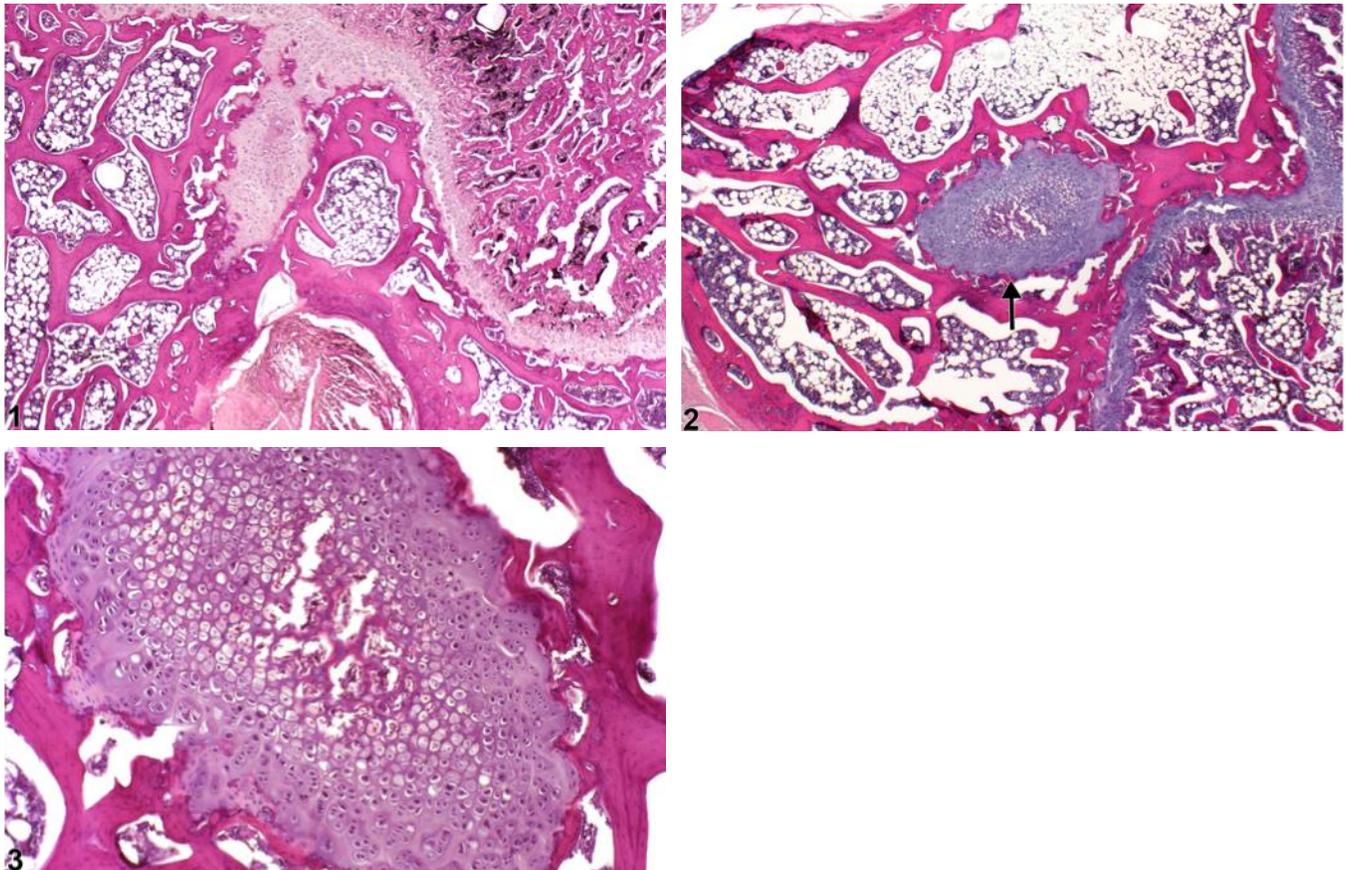


Figure Legend: **Figure 1** Bone - Physeal dysplasia in a male F344/N rat from a subchronic study. The cartilaginous growth plate is thickened and disorganized. **Figure 2** Bone - Physeal dysplasia in a male F344/N rat from a subchronic study. The growth plate is irregular and disorganized, and there is a focal area of chondrocyte hypertrophy and hyperplasia (arrow). **Figure 3** Bone - Physeal dysplasia in a male F344/N rat from a subchronic study (higher magnification of Figure 2). There is focal area of chondrocyte hyperplasia, hypertrophy, and disorganization.

Comment: Dysplasia of physeal cartilage (Figure 1 and Figure 2) results from defective mineralization and decreased cartilage resorption. Pharmaceutical agents that inhibit vascular penetration of the physis can lead to physeal thickening and dysplasia (Figure 1); this is an example of decreased cartilage resorption. This leads to a persistence of enlarged chondrocytes (Figure 2) and an enlarged zone of hypertrophy, resulting in a growth plate that is markedly widened centrally and tapered at the



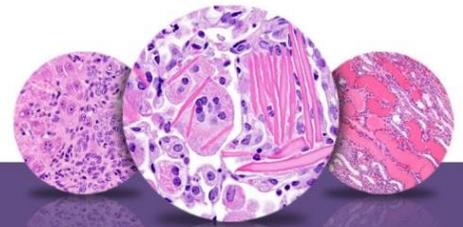
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peripheral margins. In advanced lesions in the rat, the physes become irregular, with enlarged extensions of unmineralized cartilage extending deep within the metaphysis. Lesions are most prevalent in the fastest-growing bones, including the radius, tibia, metatarsals, and metacarpals. Increased amounts of unmineralized osteoid (hyperosteoidosis) may be a component of advanced lesions when a systemic defect in mineralization is present. In rats, the formation of a “rachitic rosary,” or markedly enlarged costochondral junctions, may occur along the lateral margins of the ribs.

Physeal dysplasia may occur as a result of disturbances in mineralization secondary to nutritional deficiencies, metabolic disease, or chemical exposure. When these lesions occur as a result of a nutritional disturbance (deficiency in vitamin D, calcium, or phosphorus) in mineralization, particularly at the growth plate, they are referred to as rickets. Often, the term “osteomalacia” has been used to describe defective mineralization of epiphyseal cartilage; however, this is not the preferred nomenclature, since “osteomalacia” (see Bone - Increased Osteoid) is used to describe increased amounts of unmineralized bone matrix (osteoid) causing generalized thickening of bony trabeculae, and an overall decrease in bone density, rather than delayed or impaired mineralization of physeal or epiphyseal cartilage, as seen in physeal dysplasia. Furthermore, the term “osteomalacia” denotes a gross morphologic change and should be considered inappropriate for histologic characterization. Compounds interfering with calcium, phosphorus, or vitamin D metabolism may result in disturbances in mineralization. Dysplasia of cartilage may also result from defective mineralization induced by chemical exposure or metabolic disturbances.

Recommendation: Physeal dysplasia should be recorded and given a severity grade. An attempt to associate these lesions with nutritional (rickets), metabolic, or compound-related etiologies can be made in the narrative.



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