Bone – Fibrous Osteodystrophy

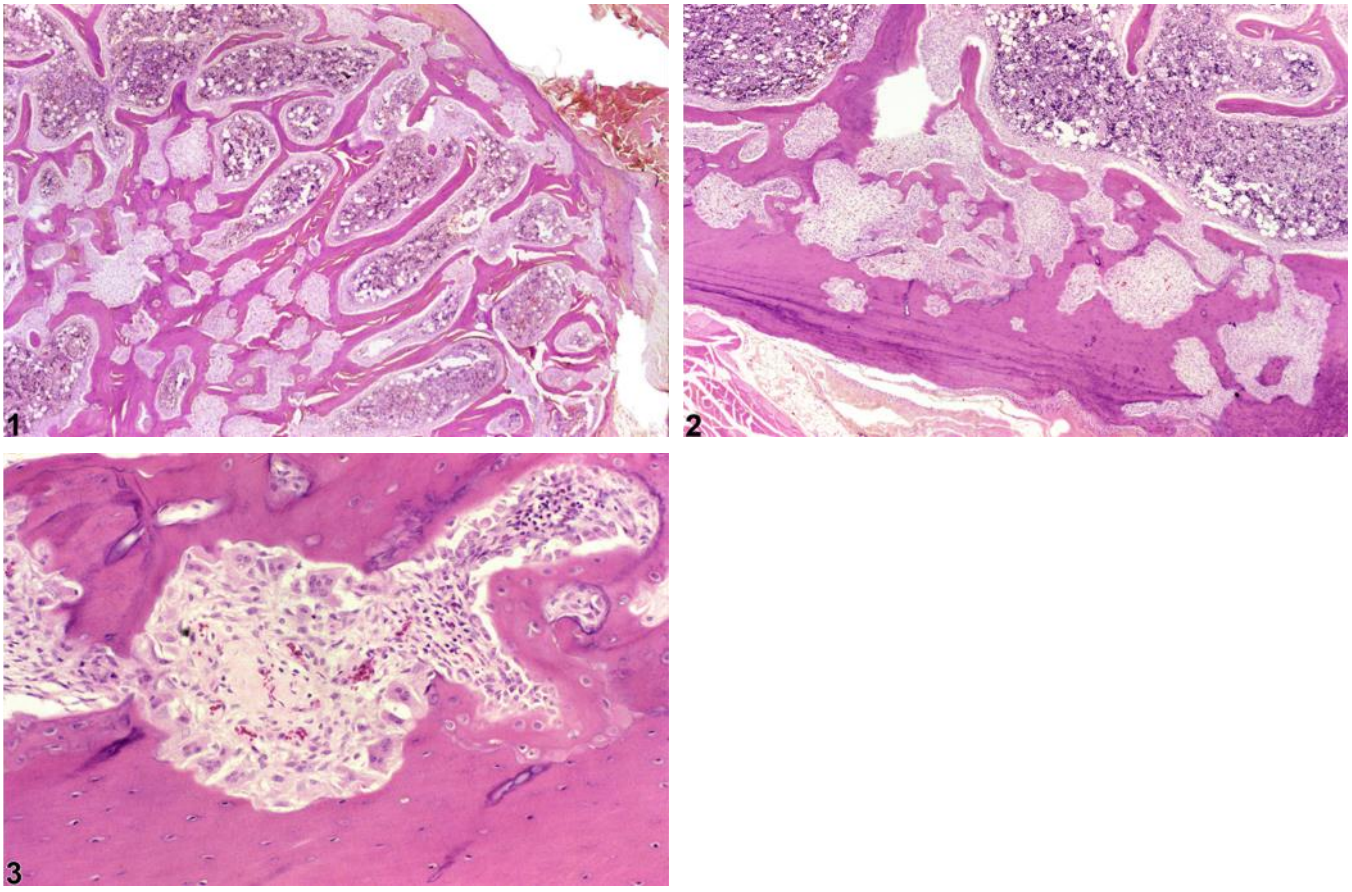
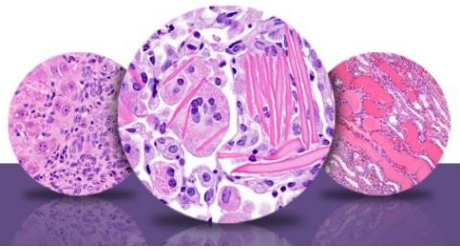


Figure Legend: Figure 1 Bone - Fibrous osteodystrophy in a male F344/N rat from a chronic study**.** There is replacement of bone by fibrous connective tissue. **Figure 2** Bone - Fibrous osteodystrophy in a male F344/N rat from a chronic study (same animal as in Figure 1)**.** There is replacement of cortical bone by fibrous connective tissue. **Figure 3** Bone - Fibrous osteodystrophy in a male F344/N rat from a chronic study (higher magnification of Figure 2)**.** The lesion is characterized by osteoclastic resorption of bone with replacement by fibrous connective tissue.

Comment: Fibrous osteodystrophy (FOD) (Figure 1, Figure 2, and Figure 3) (previously referred to as osteodysplasia, fibrous dysplasia, and osteofibrosis) is characterized by osteoclastic resorption of cancellous or cortical bone, with replacement by loose to mature fibrous connective tissue. This lesion is the result of a metabolic bone disease that occurs in conjunction with hyperparathyroidism, whether due to a functional parathyroid tumor (primary) or chronic renal disease (secondary). Primary chief cell



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tumors are very uncommon and usually nonfunctional in rodents, and most often, FOD occurs as a result of secondary hyperparathyroidism in conjunction with chronic progressive nephropathy. Exacerbation of chronic progressive nephropathy may result from treatment by various chemicals, leading to secondary hyperparathyroidism, FOD, and metastatic calcification of various organs, including the heart, aorta, and other soft tissues. Early FOD lesions are characterized by a moth-eaten appearance of the affected bone, with increased osteoclast numbers and "scalloping" of mature bone (Figure 3), eventually progressing to replacement by fibrous connective tissue and immature osteoid (Figure 1 and Figure 2).

The incidence of FOD is low in B6C3F1 mice (1% in females, 0% in males) due to the low incidence of chronic renal failure in this strain.

Recommendation: Several NTP compounds have been shown to induce parathyroid hyperplasia as a result of chronic progressive nephropathy in rats, and as such, FOD may be a compound-induced lesion. Therefore, although it can be a background lesion in aged rats with chronic progressive nephropathy, FOD should be reported and given a severity grade in studies in which there is a dose-related increase in incidence or severity. This lesion should be diagnosed as FOD rather than diagnosing the components of the lesion separately (e.g., decreased bone, fibrosis).

References:

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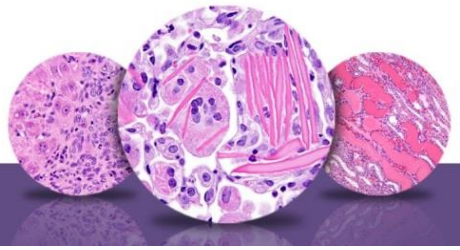

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