



NTP Nonneoplastic Lesion Atlas

Bone, Joint – Degeneration

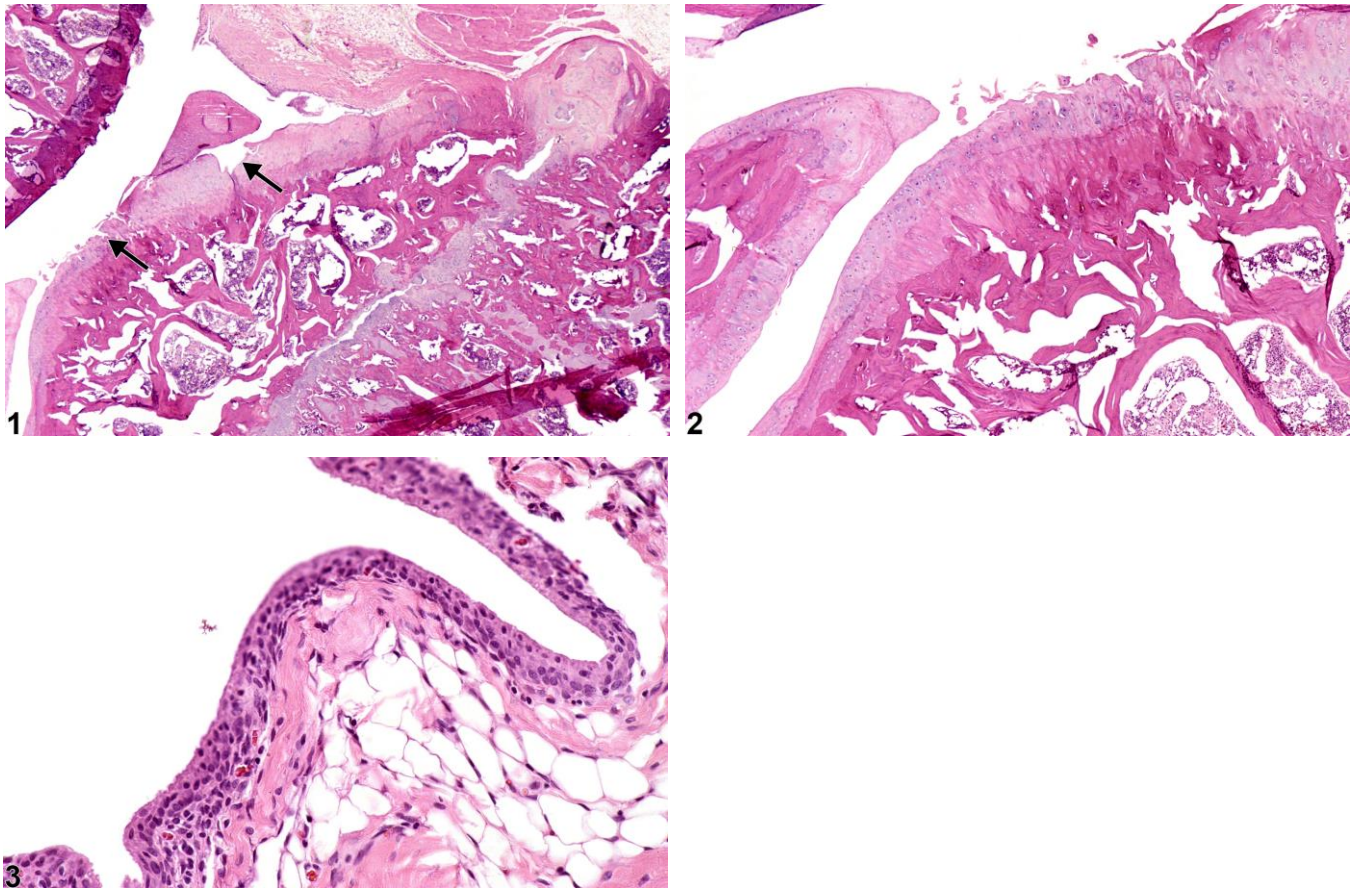
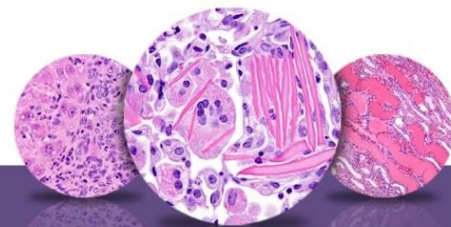


Figure Legend: **Figure 1** Bone, Joint - Degeneration in a female F344/N rat from a chronic study. The articular surface of the femorotibial joint is roughened and contains clefts (arrow). **Figure 2** Bone, Joint - Degeneration in a female F344/N rat from a chronic study (higher magnification of Figure 1). There is roughening and cleft formation of the articular surface and thickening of the subchondral bone. **Figure 3** Bone, Joint - Degeneration in a male B6C3F1/N mouse from a chronic study. The synovial lining of the femorotibial joint is hyperplastic.

Comment: Degeneration of the joint (osteoarthritis arthrosis, osteoarthrosis, osteoarthropathy, degenerative joint disease) is a noninflammatory, progressive disease of cartilage characterized by loss of articular cartilage, subchondral bone thickening (Figure 1) and cyst formation, and formation of osteophytes within the affected joint space. Early lesions of osteoarthritis consist of tinctorial alterations of the cartilage characterized by loss of basophilia and fibrillar consistency (resulting from loss of



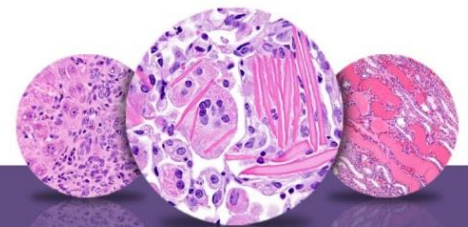
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mucopolysaccharides) of the cartilaginous matrix, fissure formation, and hypertrophy and hyperplasia of cartilage, evidenced by irregularly arranged clusters of enlarged chondrocytes. Severe lesions may be associated with cartilaginous clefts (Figure 2), leading to erosion and loss, thickening of the joint capsule and synovium (Figure 3), and osteophytosis and subchondral bone cyst formation. Synovial tissue may become thickened, with villous projections emanating from the synovium and protruding into the joint space. With chronicity, the synovium may undergo cartilaginous or bony metaplasia. In severe cases, ankylosis (fusion) of the joint may occur. Ultrastructurally, degenerative changes are characterized by abnormal Golgi, increased intracellular microfilaments, decreased numbers of proteoglycan granules, and disruption of collagen within the cartilaginous matrix.

Degenerative joint disease occurs in nearly all strains of rats and mice as a component of the aging process. In the B6C3F1 mouse, the disease occurs more commonly in males than females and has an incidence in the stifle joint of up to 2% for males and 4% for females. The disease is known to preferentially affect the stifle and elbow joints in the mouse but also occurs in the distal thoracic vertebrae and joints of the sternum. In the F344 rat, spontaneous lesions have been reported as early as 13 months. Although a normal age-related change, the disease is multifactorial and influenced by diet, strain, sex hormones, and weight, in addition to exposure to various toxicants, which can cause alterations in the cartilaginous matrix. Chondromucinous/cystic degeneration (aseptic necrosis) of articular cartilage or growth plates in the rat should not be confused with degenerative joint disease. This is a common spontaneous lesion in aged rats that may lead to spontaneous fractures of bony trabeculae of the physis and epiphysis but does not cause degenerative lesions of the articular cartilage.

Recommendation: Degenerative joint disease/osteoarthritis should be diagnosed as “Bone, Joint – Degeneration” and given a severity grade. It is not necessary to record all of the individual components, but they should be described in the narrative if the disease appears correlated with chemical exposure. In the narrative, the terms “degenerative joint disease” or “osteoarthritis” may be used to connote the disease associated with the morphology, if appropriate.

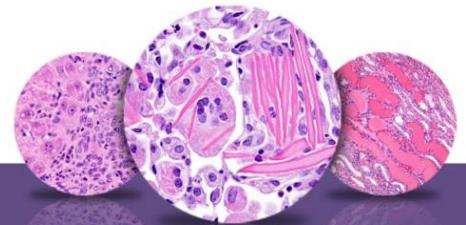


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Authors:

Mark J. Hoenerhoff, DVM, PhD, DACVP
Associate Professor
In Vivo Animal Core, Unit for Laboratory Animal Medicine
University of Michigan Medical School
Ann Arbor, MI

Amy Brix, DVM, PhD, DACVP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC