



NTP Nonneoplastic Lesion Atlas

Lung, Epithelium – Degeneration

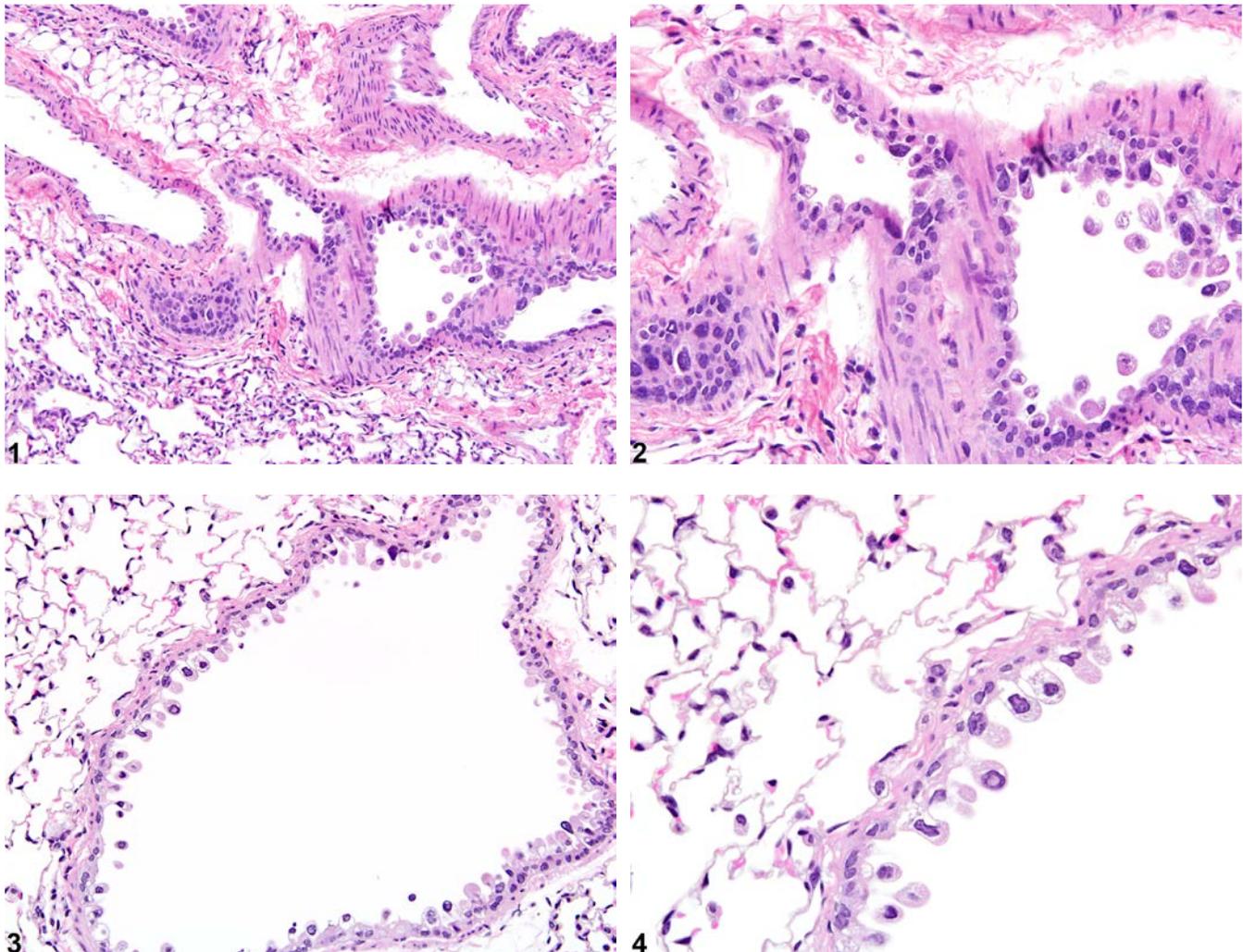


Figure Legend: **Figure 1** Lung, Epithelium, Bronchiole - Degeneration in a male B6C3F1/N mouse from a subchronic study. The epithelial cells in this bronchiole are sloughing into the lumen, but there is little inflammation. **Figure 2** Lung, Epithelium, Bronchiole - Degeneration in a male B6C3F1/N mouse from a subchronic study (higher magnification of Figure 1). The epithelial cells are vacuolated and sloughing and have lost their cilia, but there is little necrotic debris or inflammation. **Figure 3** Lung, Epithelium, Bronchiole - Degeneration in a male B6C3F1/N mouse from a subchronic study. The epithelial cells are sloughing into the lumen, and there are occasional pyknotic nuclei, but there is little necrotic debris or inflammation. **Figure 4** Lung, Epithelium, Bronchiole - Degeneration in a male



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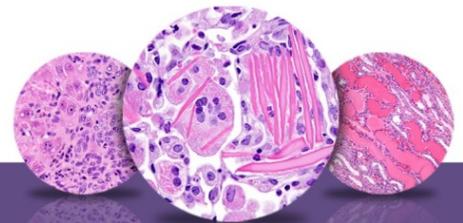
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B6C3F1/N mouse from a subchronic study (higher magnification of Figure 3). The epithelial cells are vacuolated and sloughing, but there is little necrotic debris or inflammation.

Comment: Degeneration (Figure 1, Figure 2, Figure 3, and Figure 4) and necrosis are considered to be parts of the continuum of cell damage, with degeneration representing reversible cell damage and necrosis representing irreversible cell damage. The light microscopic hallmarks of reversible cell damage (degeneration) include cellular swelling, cytoplasmic vacuolation, perinuclear clear spaces, formation of cytoplasmic blebs, loss of normal apical blebs from Clara cells, and loss of cilia. In some cases, detachment of viable cells from the epithelial surface and nuclear condensation (pyknosis) and cellular shrinkage of scattered cells within the epithelium, suggestive of imminent death of individual cells, may be interpreted as epithelial degeneration because it may be consistent with reversible damage to an epithelial surface and evidence of outright necrosis may be lacking. The light microscopic features of necrosis include nuclear pyknosis, karyorrhexis, or karyolysis, cell swelling, loss of cellular detail, cell fragmentation, and cytoplasmic hypereosinophilia (in which the cytoplasm often has a homogeneous appearance). Necrosis of the epithelial cells lining the airways as a result of toxic injury is often characterized by sloughing of necrotic cells or cellular debris into the lumen. Other lesions often accompany necrosis and degeneration, such as inflammation and hemorrhage.

The anatomic location of degenerative lesions may vary due to the physicochemical properties of the test agent or the susceptibility of a particular cell type to the test agent. The epithelium of the terminal bronchioles and alveolar ducts (i.e., the centriacinar region) and alveoli are particularly susceptible to injury due to the large surface area and fragility of the alveolar type I cells, the metabolic activity of P450 enzymes in Clara cells, and the generally thinner mucous layer.

Recommendation: Lung, Epithelium - Degeneration should be diagnosed and graded whenever present. A site modifier should be included in the diagnosis to indicate the location of the lesion within the lung (e.g., alveolus, bronchiole) since toxic insults can preferentially target specific sites. There is significant overlap, morphologically, between degeneration and necrosis, so the pathologist will need to use his or her best judgment when diagnosing these lesions. If the degeneration is secondary to another process, such as severe inflammation, it is preferable to diagnose the major process and to describe the degeneration in the narrative. If degeneration and a concurrent, related lesion (e.g.,



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inflammation) are both prominent, the pathologist may choose to record both lesions and grade them separately. Again, the pathologist will need to use his or her judgment in deciding whether or not to diagnose the degeneration separately.

References:

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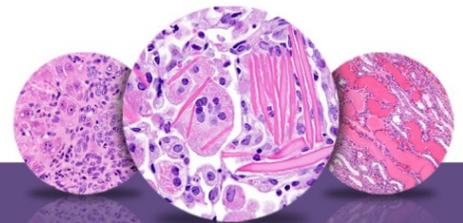
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