Lung, Epithelium – Necrosis

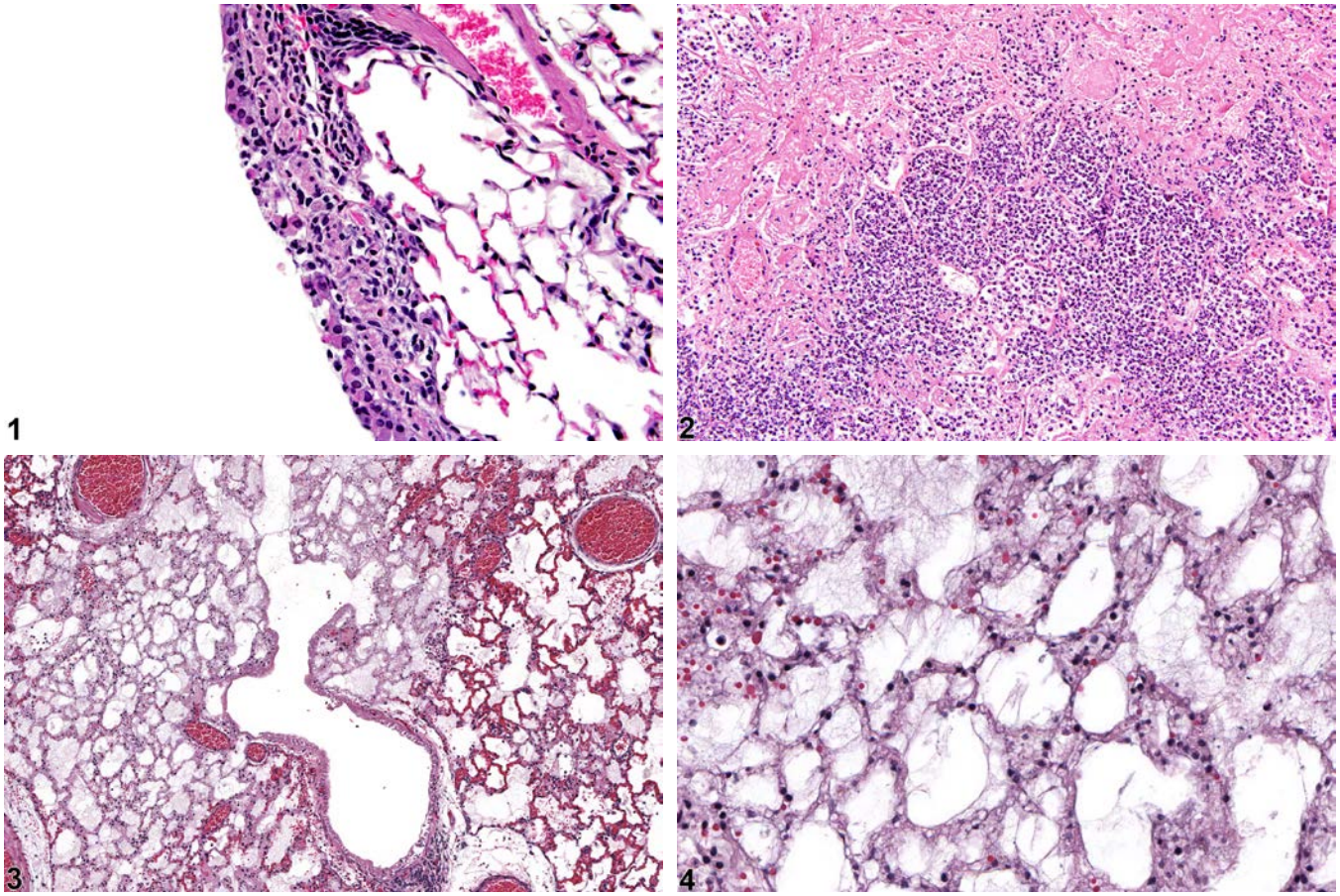
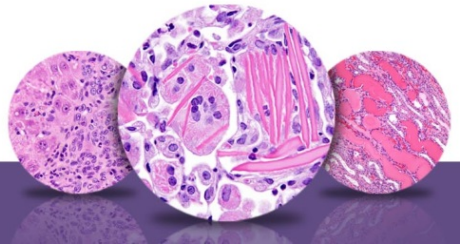


Figure Legend: **Figure 1** Lung, Bronchiole, Epithelium, Bronchiole - Necrosis in a female B6C3F1/N mouse from a subchronic study. The epithelial cells are fragmented, with pyknotic and karyorrhectic nuclei. **Figure 2** Lung, Epithelium - Necrosis in a male Wistar Han rat from a chronic study. There is a large area of coagulative necrosis surrounded by suppurative inflammation. **Figure 3** Lung, Epithelium, Alveolus - Necrosis in a female F344/N rat from a subchronic study. There is loss of epithelial cells, and many of the interstitial cells have pyknotic nuclei. **Figure 4** Lung, Epithelium, Alveolus - Necrosis in a female F344/N rat from a subchronic study. In this focal lesion, there is loss of epithelial and interstitial cells.

Comment: Necrosis (Figure 1, Figure 2, Figure 3, and Figure 4) and degeneration are considered to be parts of the continuum of cell damage, with necrosis representing irreversible cell damage and



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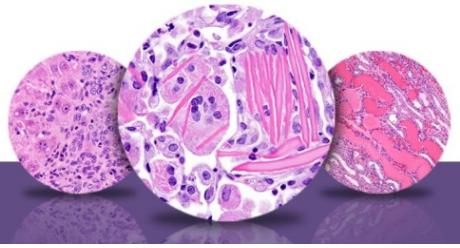
degeneration representing reversible cell damage. The light microscopic features of necrosis include nuclear pyknosis, karyorrhexis, or karyolysis, cell swelling, loss of cellular detail, cell fragmentation, and cytoplasmic hypereosinophilia (in which the cytoplasm often has a homogeneous appearance). Large areas of necrosis (Figure 2, Figure 3, and Figure 4) may also have disrupted tissue architecture, large areas of necrotic debris, loss of staining intensity, and inflammatory cells. 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. The light microscopic hallmarks of reversible cell damage 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. Other lesions often accompany necrosis and degeneration, such as inflammation and hemorrhage.

The anatomic location of necrotic 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 - Necrosis 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. If more than one site is affected, the site modifier may be omitted and the locations described in the pathology narrative. 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 necrosis is secondary to another process, such as severe inflammation, it is preferable to diagnose the major process and to describe the necrosis in the narrative. If the necrosis and a concurrent, related lesion (e.g., inflammation) are both prominent, the pathologist may choose to record both lesions and grade them



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separately. Again, the pathologist will need to use his or her judgment in deciding whether or not to diagnose the necrosis or degeneration separately. If the necrotic cells have detached, exposing the underlying tissue, the term “ulcer” or “erosion” should be used (see Lung - Ulceration). However, if the necrotic cells are still present and covering the basement membrane, necrosis is the preferred diagnosis.

References:

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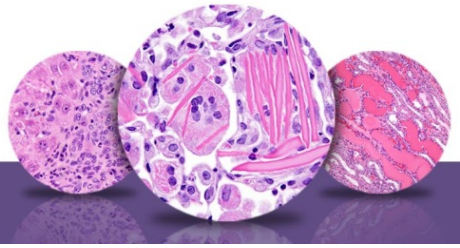

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