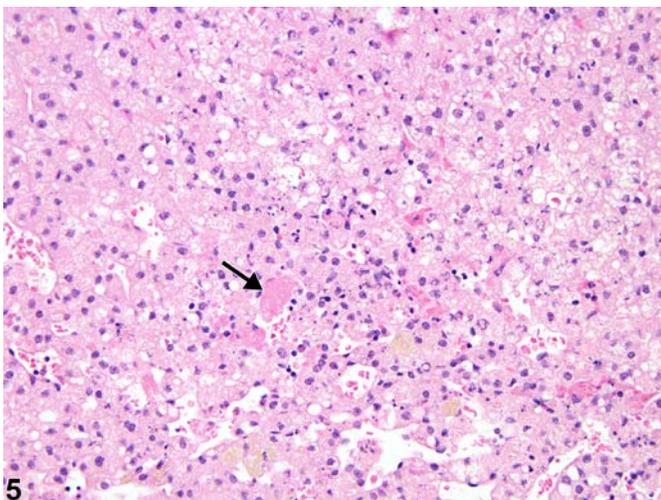
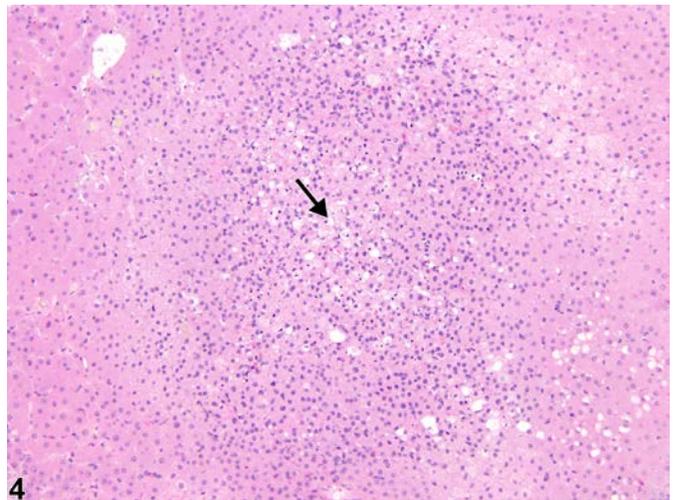
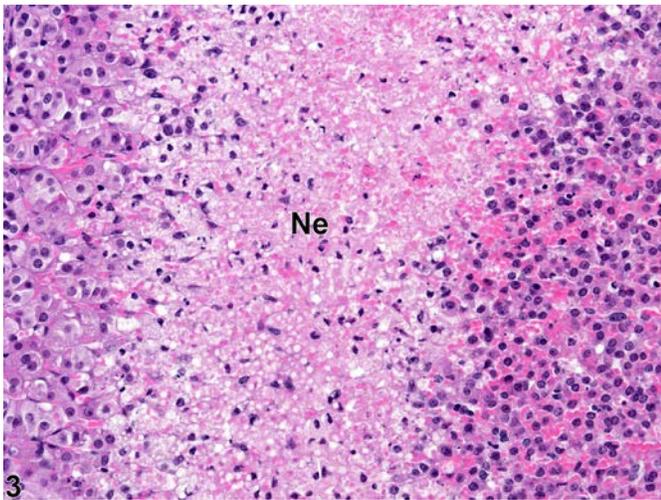
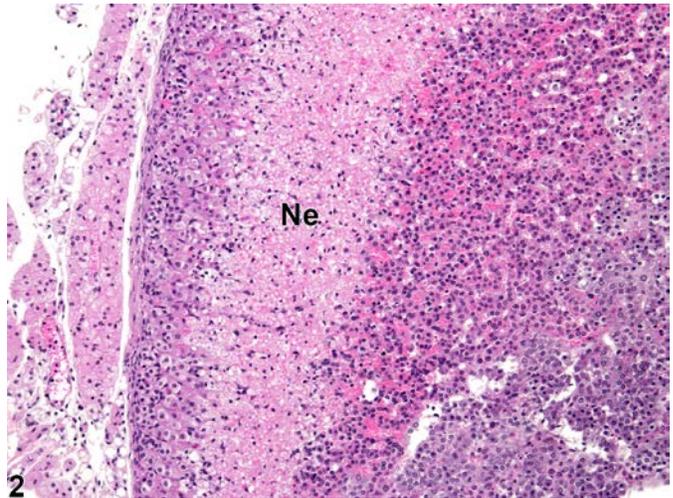
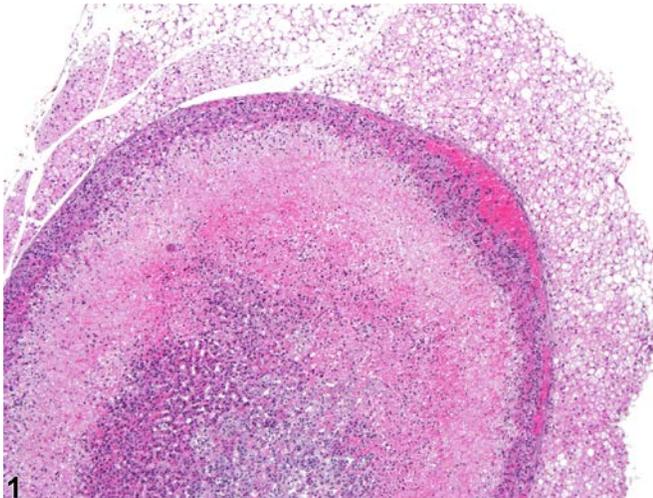


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Figure Legend: **Figure 1** Adrenal gland, Cortex - Necrosis in a female B6C3F1 mouse from a subchronic study. Diffuse cortical necrosis involves primarily the zona fasciculata. **Figure 2** Adrenal gland, Cortex - Necrosis in a female B6C3F1 mouse from a subchronic study (higher magnification of Figure 1). The zona fasciculata is collapsed due to necrosis of cortical cells (Ne). **Figure 3** Adrenal gland, Cortex - Necrosis in a female B6C3F1 mouse from a subchronic study (higher magnification of Figure 1). There is loss of cellular detail, fragmented cortical cells, and amorphous debris in the zona fasciculata (Ne). **Figure 4** Adrenal gland, Cortex - Necrosis in a female Sprague-Dawley rat from a chronic study. There is focal cortical necrosis in the zona fasciculata (arrow). **Figure 5** Adrenal gland, Cortex - Necrosis in a female Sprague-Dawley rat from a chronic study (higher magnification of Figure 4). There is a focal area in the zona fasciculata in which the normal architecture is disrupted and replaced by necrotic cells (arrow) and amorphous debris.

Comment: Adrenal gland necrosis (Figure 1, Figure 2, Figure 3, Figure 4, and Figure 5) can occur in any region of the adrenal gland, though the cortex (especially the zonae fasciculata and reticularis) is more frequently affected than the medulla. Necrosis can be focal or diffuse. Necrosis is characterized by disruption or obliteration of normal architecture, with fragmentation, hypereosinophilia, pyknosis, karyorrhexis, and/or karyolysis of the constituent cells (Figure 2 and Figure 5). Associated hemorrhage and/or inflammatory cell infiltrates may also be present.

Adrenal gland necrosis (especially cortical) is usually secondary to other pathologic processes, such as stress, ischemia, hemorrhage, inflammation, and systemic neoplasia (e.g., mononuclear cell leukemia in rats). However, adrenal cortical necrosis can also be induced by experimental administration of various agents, such as bacterial toxins or certain exogenous chemicals. Adrenal medullary necrosis, though less common, can also be induced by certain exogenous chemicals.

Recommendation: Adrenal gland necrosis should be diagnosed and assigned a severity grade and site modifier (i.e., cortex or medulla). If it is present in both the cortex and medulla, the site modifier may be omitted and the location described in the pathology narrative. When necrosis is secondary to another process (e.g., inflammation, degeneration, or neoplasia), it should not be diagnosed separately unless warranted by severity. Lesions that are secondary to necrosis (e.g., inflammation,



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mineralization) should not be diagnosed separately, unless warranted by severity, but should be described in the pathology narrative.

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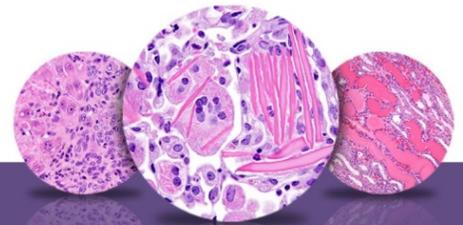
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