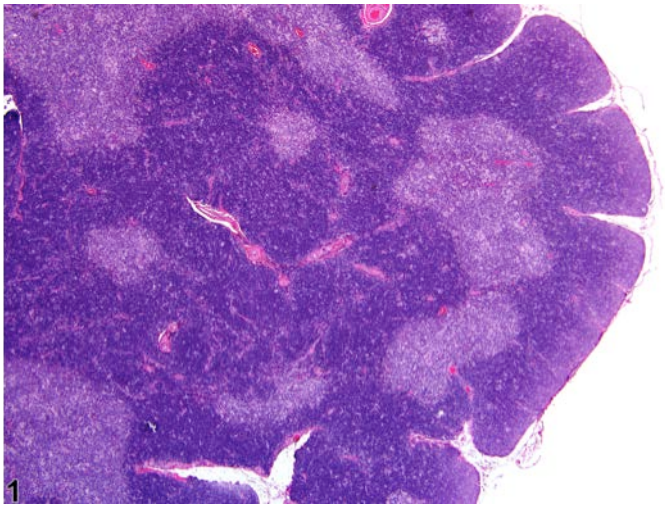
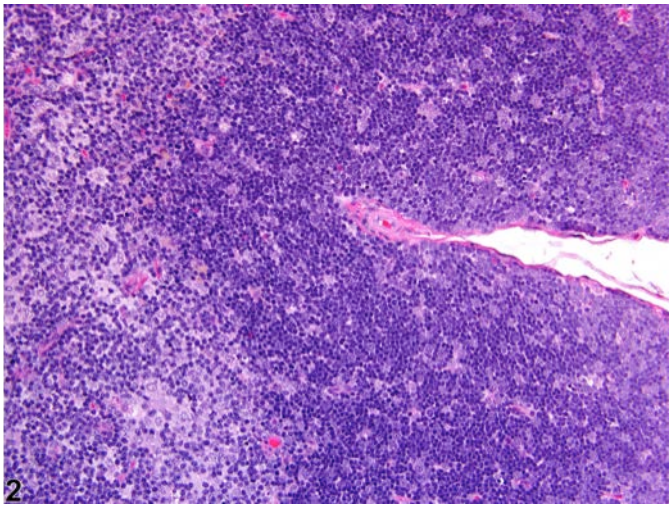
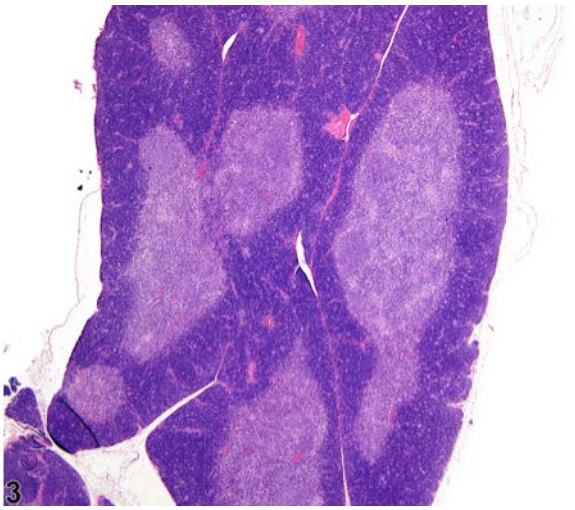
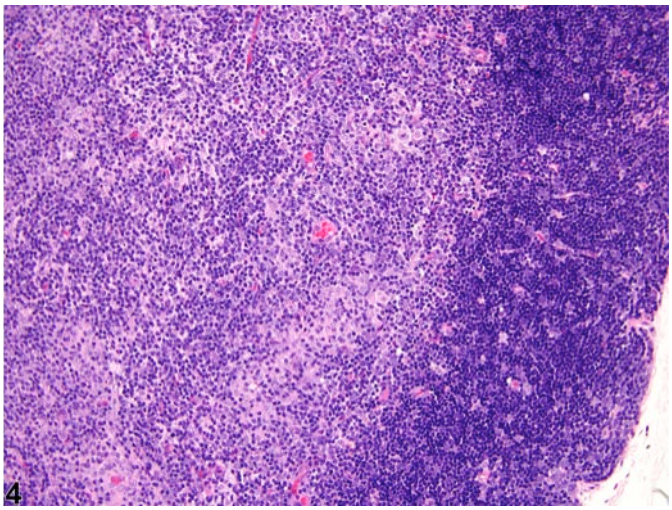
NTP Nonneoplastic Lesion Atlas

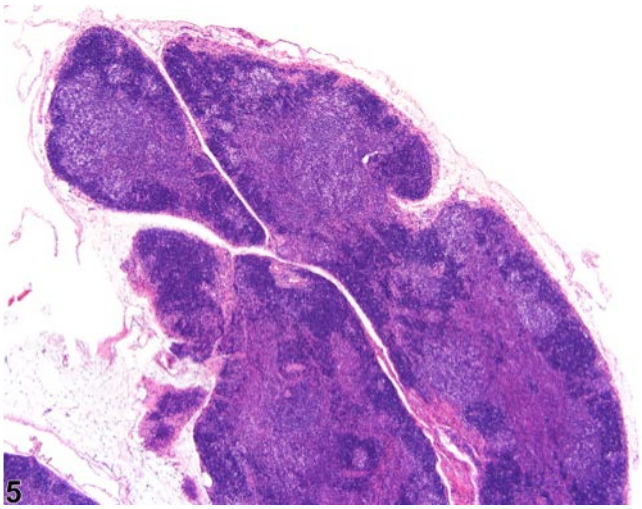
Thymus – Atrophy

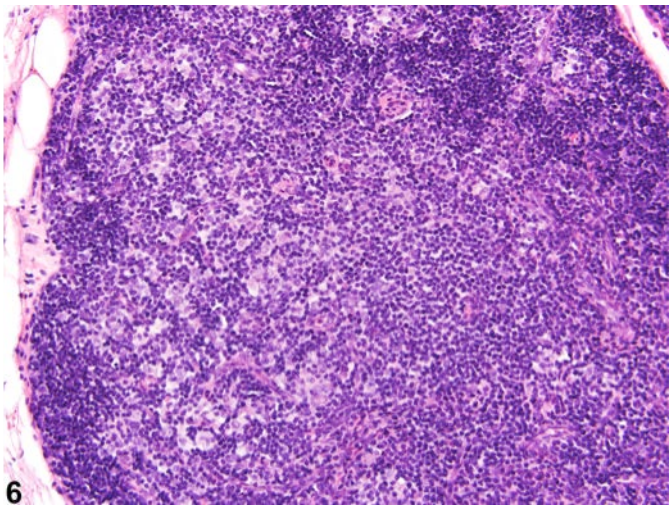












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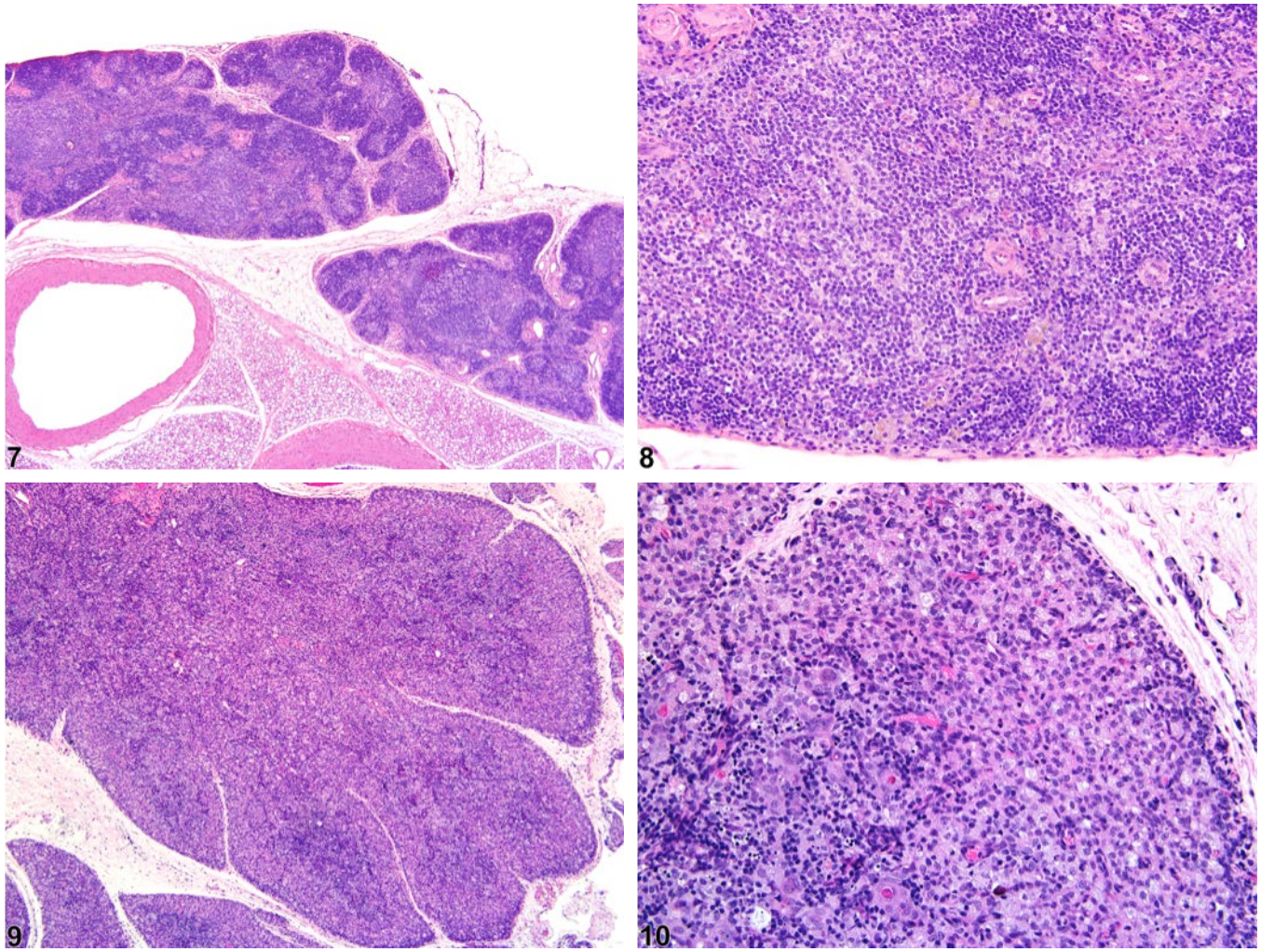
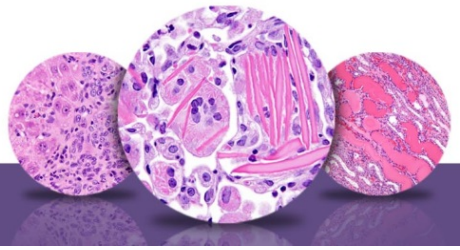
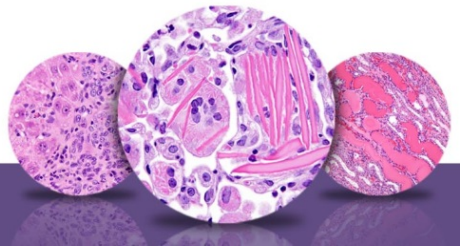


Figure Legend: **Figure 1** Thymus - Normal in a male Harlan Sprague-Dawley rat from a subchronic study. The ratio of cortex to medulla is approximately 2:1 (1:1:1, two cortices to medulla). **Figure 2** Thymus - Normal in a male Harlan Sprague-Dawley rat from a subchronic study (higher magnification of Figure 1). The lymphocytes are more numerous in the cortex than in the medulla. **Figure 3** Thymus - Atrophy in a treated female F344/NTac rat from a subchronic study. The cortex, showing minimal atrophy, is thinner and more irregular compared with normal (Figure 1). **Figure 4** Thymus - Atrophy in a treated female F344/NTac rat from a subchronic study (higher magnification of Figure 3). The cortex, showing minimal atrophy, is thinner and more irregular compared with normal (Figure 2). **Figure 5** Thymus - Atrophy in a treated female Harlan Sprague-Dawley rat from a chronic study. With mild



atrophy, the cortex becomes progressively thinner and the cortical-medullary junction becomes less distinct. **Figure 6** Thymus - Atrophy in a treated female Harlan Sprague-Dawley rat from a chronic study (higher magnification of Figure 5). The cortex is thinner, and the cortical-medullary junction is less distinct compared with Figure 4. **Figure 7** Thymus - Atrophy in a treated female Harlan Sprague Dawley from a chronic study. With moderate atrophy, delineation of the cortex and medulla is multifocally indistinct. **Figure 8** Thymus - Atrophy in a treated female Harlan Sprague Dawley from a chronic study (higher magnification of Figure 7). With moderate atrophy, delineation of the cortex and medulla is multifocally indistinct. **Figure 9** Thymus - Atrophy in a treated female Harlan Sprague-Dawley from a chronic study. With marked atrophy, the lack of distinction between the cortex and medulla due to lymphocyte depletion gives the thymus a more uniform appearance. **Figure 10** Thymus - Atrophy in a treated female Harlan Sprague-Dawley from a chronic study (higher magnification of Figure 9). With marked atrophy, the distinction between the thymic cortex and medulla is no longer visible due to lymphocyte depletion.

Comment: Atrophy is characterized by reduced thymus size and weight secondary to thymic lymphocyte depletion. A normal thymus typically has similarly sized lobules, a closely apposed capsule, a densely cellular cortex compared with the medulla, a distinct corticomedullary (CM) junction, and a cortex to medulla ratio of ~1:1:1 (two cortices to the medulla) (Figure 1 and Figure 2). With minimal atrophy (Figure 3 and Figure 4), the cortex may become thinner and irregular, with progressive loss of the CM demarcation as the lesion becomes mild (Figure 5, Figure 6) and moderate (Figure 7 and Figure 8). As the lesion becomes marked (Figure 9 and Figure 10), cellularity of the cortex and medulla is decreased, and the CM junction may no longer be apparent. The medulla may appear larger than the cortex, and the cellular appearance of thymic compartments may appear reversed, with a pale eosinophilic cortex due to reduced cellularity and a darkly basophilic medulla due to increased cellularity. Thymic atrophy may be influenced by nutrition, adrenocortical hyperactivity, and changes in hormone levels (e.g., sex or growth hormones). Thymic atrophy must be differentiated from thymic involution. Age-related involution is a gradual, nonreversible change, likely associated with sex steroid circulation. In addition to decreased cortical cellularity, normal involution may include blurring of the CM junction, adipocyte infiltration of the capsule and parenchyma, increased prominence and/or hyperplasia of medullary epithelial cells, and formation of follicular-like B-cell aggregates in the medulla.



Thymus – Atrophy

Atrophy that is unrelated to age is generally caused by toxic insult and is potentially reversible with removal of the inciting agent.

Recommendation: When present, atrophy of the thymus should be diagnosed and graded. If atrophy involves only one lobe or is localized, this should be discussed in the pathology narrative. Induced atrophy must be differentiated from normal involution of the thymus. An animal with potential treatment-related thymic atrophy should be compared with age- and sex-matched concurrent controls. Age of the animal and a clear dose-response relationship will help differentiate between thymic atrophy and normal involution.

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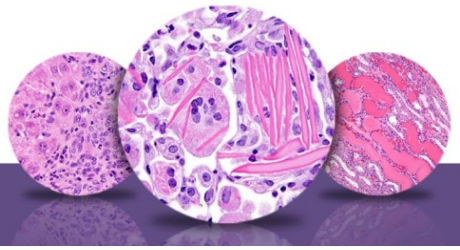

Thymus – Atrophy

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