Lymph Node – Infiltration, Cellular, Histiocyte

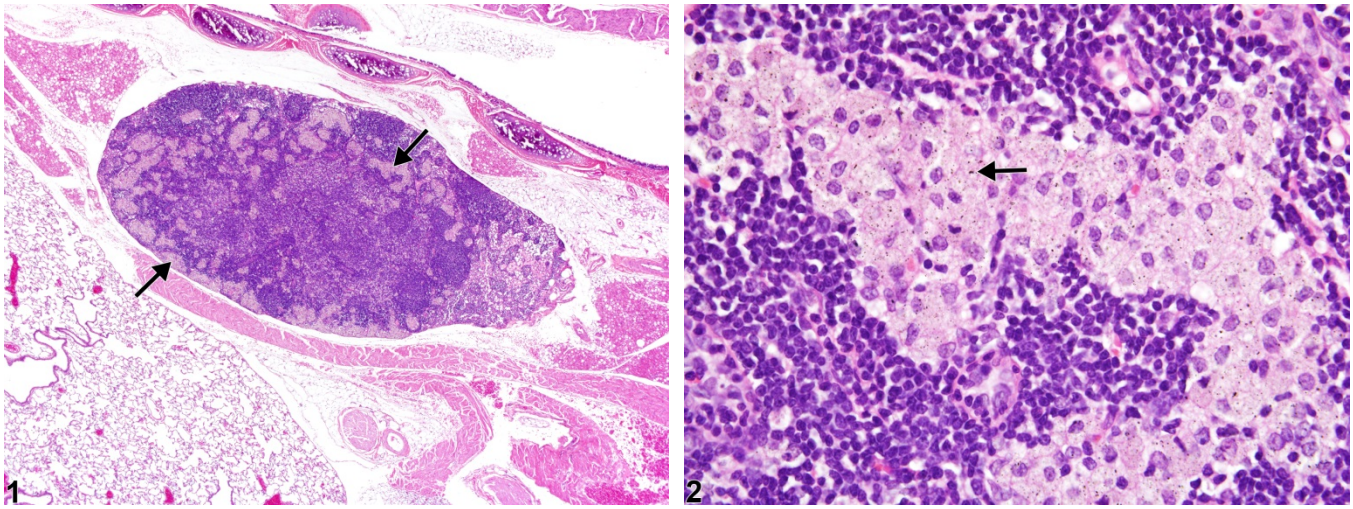
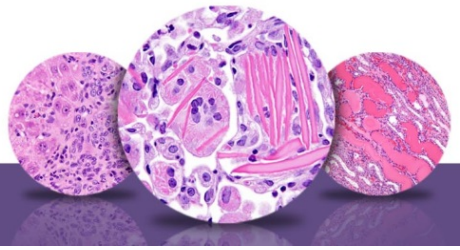


Figure Legend: Figure 1 Lymph node - Infiltrate, Cellular, Histiocyte in a male Harlan Sprague Dawley rat from a subchronic study. Increased numbers of histiocytes are present within the paracortical and subcapsular sinuses (arrows). **Figure 2** Lymph node - Infiltrate, Cellular, Histiocyte in a male Harlan Sprague Dawley rat from a subchronic study (higher magnification of Figure 1). Histiocytes contain intracytoplasmic insoluble particulate matter (arrow).

Comment: Histiocytes may be increased in the lymph nodes of rats and mice. This lesion can occur spontaneously (e.g., dietary antigenic stimulation of mesenteric lymph nodes) or secondary to treatment. Increases may reflect proliferation of resident sinusoidal histiocytes or an increased influx of histiocytes via the afferent lymphatics. This lesion may be within subcapsular, paracortical, or medullary sinuses (Figure 1, arrows). If this lesion occurs in the same lymph node for a particular dose group (e.g., bronchial lymph node in an inhalation study), it may suggest a treatment-related effect. Histiocytes in affected lymph nodes may contain intracytoplasmic insoluble particulate matter, such as phagocytized test article or vehicle material (Figure 2, arrow) or pigment (hemosiderin, etc.). Histiocyte increases in lymph nodes under constant spontaneous antigenic or foreign material stimulation (e.g., mesenteric lymph nodes) must be differentiated from increases due to treatment. Previous terms for histiocytes in lymph nodes are “histiocyte hyperplasia” and “histiocyte infiltrate.”

Recommendation: Whenever present, histiocyte increases in the lymph nodes of rats and mice should be diagnosed and given a severity grade. This lesion should always be diagnosed in the context



of the test article, treatment group, route of administration, and lymph node involved (compare with concurrent controls).

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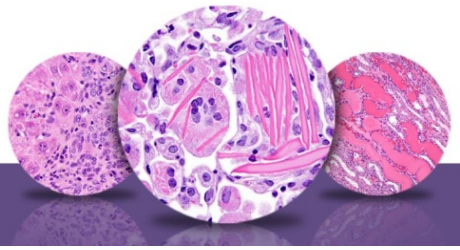

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