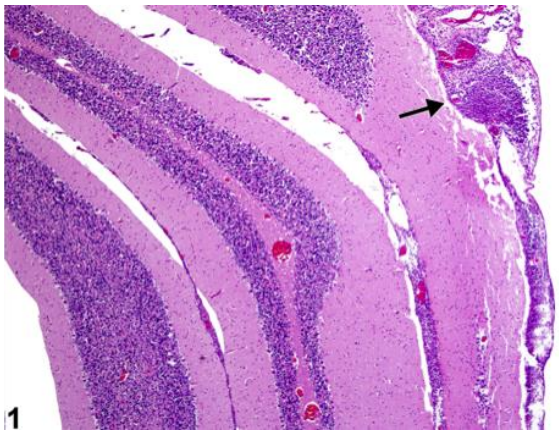
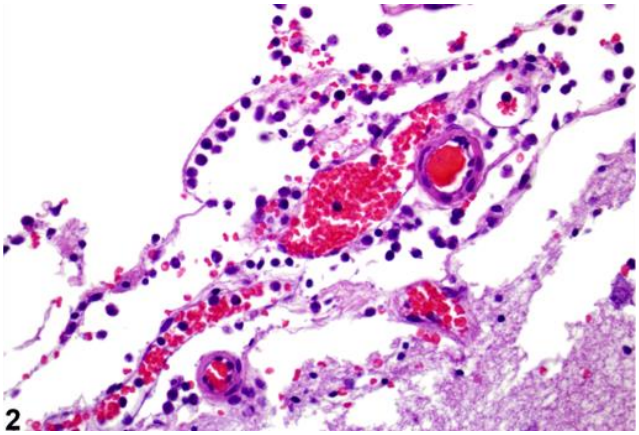
Brain – Inflammation





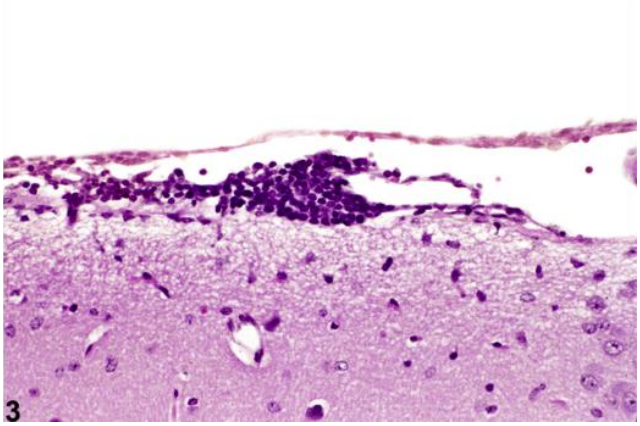


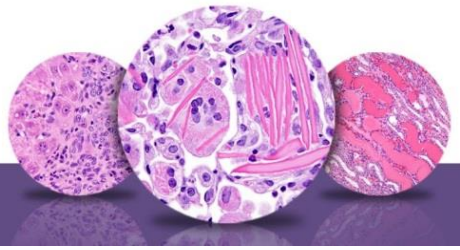
Figure Legend: Figure 1 Brain, cerebellum, leptomeninges–accumulation of acute inflammatory cells (arrow) in the leptomeninges of the cerebellum, subsequent to septicemia, resulting in acute suppurative meningitis, in a female B6C3F1 mouse. **Figure 2** Brain, cerebellum, leptomeninges–inflammation in a female B6C3F1 mouse (higher magnification of Figure 1). **Figure 3** Leptomeninges–focal aggregation of lymphocytes in the leptomeninges in a female B6C3F1 mouse from a chronic study. In this case, it was an incidental finding.

Comment: Acute bacterial or other infectious disease is occasionally seen in experimental studies, and the inflammatory processes that such infections produce need to be recognized and diagnosed since they may reflect compound effects on the immune status of the animal. Figure 1 depicts the accumulation of acute inflammatory cells (arrows) in the leptomeninges of the cerebellum at low magnification. Figure 2 is the magnified appearance of acute inflammatory cells in the leptomeninges in Figure 1. A mixture of lymphocytes and neutrophils is apparent in

this exudate. Figure 3 shows the focal aggregation of lymphocytes in the leptomeninges of a mouse. In this case, it was an incidental finding. The occurrence of such a lesion may, however, indicate a response to a recent viral infection in the nervous system. Occasionally, a small, apparently inert cluster of mononuclear cells without any other reactive responses in the vicinity may be referred to as inflammatory infiltrate. However, the presence of neutrophils should alert the pathologist to conduct a diligent evaluation for other complementary signs of inflammation.

In NTP studies, there are five standard categories of inflammation: acute, suppurative, chronic, chronic-active, and granulomatous. In *acute inflammation*, the predominant infiltrating cell is the neutrophil, though fewer macrophages and lymphocytes may also be present. There may also be evidence of edema or hyperemia. The neutrophil is also the predominant infiltrating cell type in *suppurative inflammation*, but they are aggregated, and many of them are degenerate (suppurative exudate). Cell debris from both the resident cell populations and infiltrating leukocytes, proteinaceous fluid containing fibrin, fewer macrophages, occasional lymphocytes or plasma cells, and, possibly, an infectious agent may also be present within the exudate. Grossly, these lesions would be characterized by the presence of pus. In the tissue surrounding the exudate, there may be fibroblasts, fibrous connective tissue, and mixed inflammatory cells, depending on the chronicity of the lesion. Lymphocytes predominate in *chronic inflammation*. Lymphocytes also predominate in *chronic-active inflammation*, but there are also a significant number of neutrophils. Both lesions may contain macrophages. *Granulomatous inflammation* is another form of chronic inflammation, but this diagnosis requires the presence of a significant number of aggregated, large, activated macrophages, epithelioid macrophages, or multinucleated giant cells.

Recommendation: When inflammation is diagnosed, the narrative should include a description of the cell types present. The recognition of rare examples of neural suppurative or nonsuppurative infiltrates should be diagnosed with a severity grading and their anatomic subsite location. If not considered treatment related, they are discounted in the final study assessment.



Brain – Inflammation

If the study pathologist prefers a nonstandard category of inflammation (as described above), then the narrative should include a description of the predominant cell types present along with prominent features of the inflammation.

In the presence of concurrent lesions, lesions with the most severity are typically diagnosed. Other concurrent lesions may be diagnosed separately, if warranted by the severity.

Authors:

Peter Little, DVM, MS, PhD, DACVP
Neuropathology Consultant
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC

Deepa B. Rao, BVSc, MS, PhD, DABT, DACVP
NTP Pathologist (Contractor)
Integrated Laboratory Systems, Inc.
Research Triangle Park, NC