Liver – Necrosis
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**Figure Legend:** **Figure 1** Necrosis—sharply demarcated centrilobular necrosis in a male B6C3F1 mouse from a subchronic study. **Figure 2** Necrosis—sharply demarcated centrilobular necrosis in a male B6C3F1 mouse from a subchronic study. **Figure 3** Necrosis—patchy areas of coagulation necrosis in a female Swiss Webster mouse from a subchronic study. **Figure 4** Necrosis—patchy areas of coagulation necrosis in a female Swiss Webster mouse from a subchronic study (higher magnification of Figure 3). **Figure 5** Necrosis—hemorrhagic necrosis in a Swiss CD-1 mouse from a chronic study. **Figure 6** Necrosis—hemorrhagic necrosis in a Swiss CD-1 mouse from a chronic study. **Figure 7** Necrosis—focal necrosis with fatty change in a male B6C3F1 mouse from a chronic study. **Figure 8** Necrosis—focal necrosis with fatty change in a male B6C3F1 mouse from a chronic study (higher magnification of Figure 7). **Figure 9** Necrosis—hepatocyte necrosis accompanied by hepatocyte degeneration in a male B6C3F1...
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mouse from a subchronic study. **Figure 10** Necrosis–hepatocyte necrosis accompanied by hepatocyte degeneration in a male B6C3F1 mouse from a subchronic study (higher magnification of Figure 9).

**Comment:** The extent, pattern, and morphologic features of hepatocellular necrosis depend on the degree of metabolic activation of hepatotoxic xenobiotics, host response to the toxicant, dose and duration of xenobiotic exposure, and timing of liver sample evaluation after dosing. Classical coagulation necrosis is typically caused by ischemia or infarction, and tissue architecture is somewhat maintained because lysosomal enzymes responsible for proteolysis are denatured. Another form of necrosis, liquefaction necrosis, may result in cellular dissolution and loss of cytologic architecture. Changes that may accompany necrosis include hemorrhage, fatty change, cytoplasmic vacuolization, cytologic degeneration, and inflammatory cell infiltration.

Figure 1 and Figure 2 represent sharply demarcated centrilobular necrosis with loss of hepatocyte cytologic detail. Figure 3 and Figure 4 represent irregular patchy areas of coagulation necrosis with early infiltration of inflammatory cells. There is no distinctive lobular pattern to this necrosis. Figure 5 and Figure 6 represent an example of necrosis characterized by loss of hepatocytes and replacement with erythrocytes. This is an example of hemorrhagic necrosis. Figure 7 and Figure 8 represent focal necrosis associated with fatty change. The patches of necrosis (see Figure 8, bottom center) are hypereosinophilic, and the fatty change is centrilobular with extension well into midlobular areas.

Figure 9 and Figure 10 represent a diagnosis of hepatocyte necrosis accompanied by hepatocyte degeneration, microvesicular fatty change, nuclear pyknosis, and inflammation. “Degeneration” is a term often used to indicate reversible cell or tissue damage and is considered to be a precursor to necrosis. Because the presence of the inflammatory response is extensive, an additional diagnosis of inflammation (cellular infiltrate) to capture the ongoing process with more fidelity may be appropriate.
**Recommendation:** Necrosis should not be subclassified based on type, with the exception of single-cell necrosis. For a given xenobiotic, dose and animal variability in response can influence whether hepatocellular necrosis is panlobular or centrilobular and whether it is focal or occurs in extensive irregular patches. If the fundamental process is the same, the lesion(s) should be recorded simply as necrosis and assigned a severity grade. The pattern and other features of the hepatocellular necrosis should be described in the pathology narrative. Splitting out diagnoses too finely will result in complicated incidence tables and may compromise appropriate interpretation of any induced toxicity. When accompanying changes such as fatty change or inflammation are sufficiently extensive, separate diagnoses may be warranted with severity grading and discussion in the pathology narrative. Since degeneration is considered part of the continuum of changes involved in the necrotic process, it should not be diagnosed separately when present with necrosis. However, degeneration without necrosis may occur at exposure levels below doses that cause necrosis and thus may warrant a separate diagnosis. In some cases, hepatocellular necrosis can result in cavernous, blood-filled spaces within the hepatic parenchyma. These blood-filled spaces should not be diagnosed as hemorrhage because they are secondary to necrosis.

**References:**


Abstract: [http://www.cacheriverpress.com/books/pathmouse.htm](http://www.cacheriverpress.com/books/pathmouse.htm)
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References:


Author:

Robert R. Maronpot, DVM, MS, MPH, DACVP, DABT, FIATP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC