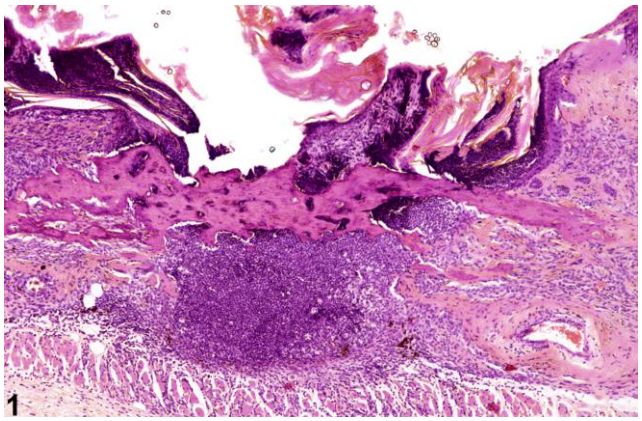
National Toxicology Program
U.S. Department of Health and Human Services

NTP Nonneoplastic Lesion Atlas

Skin – Inflammation, [Acute, Suppurative, Chronic, Chronic Active, Granulomatous]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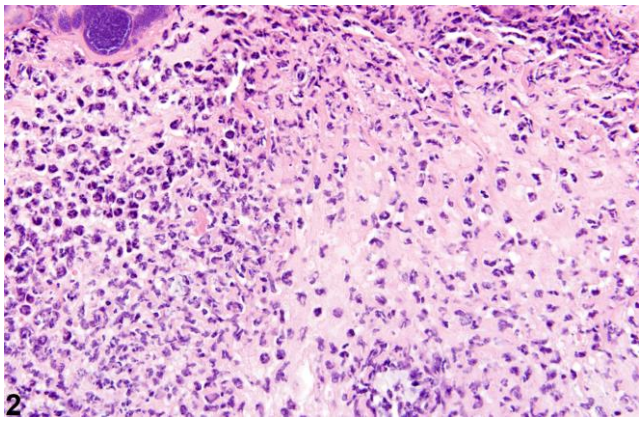
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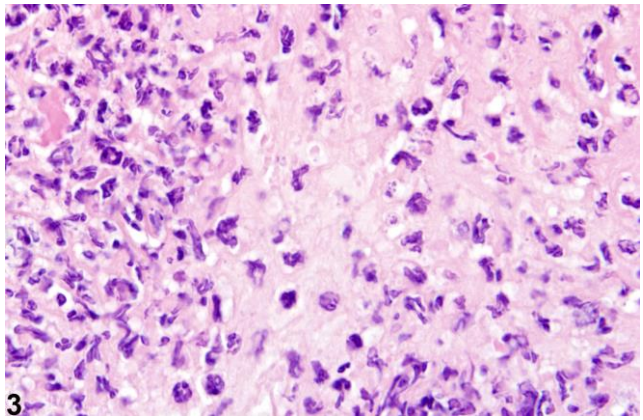
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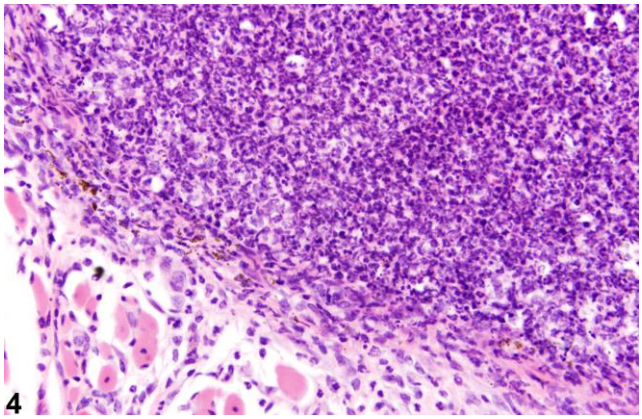
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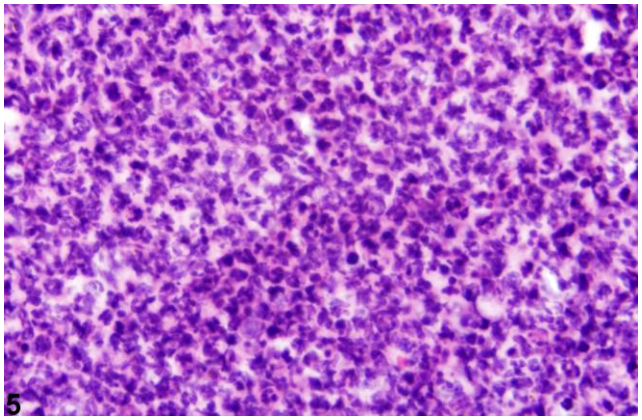
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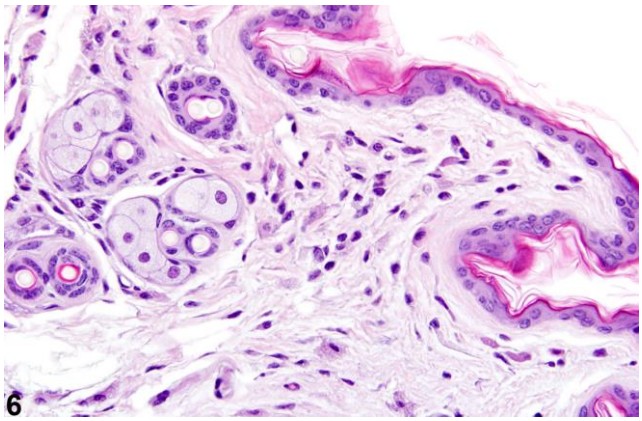
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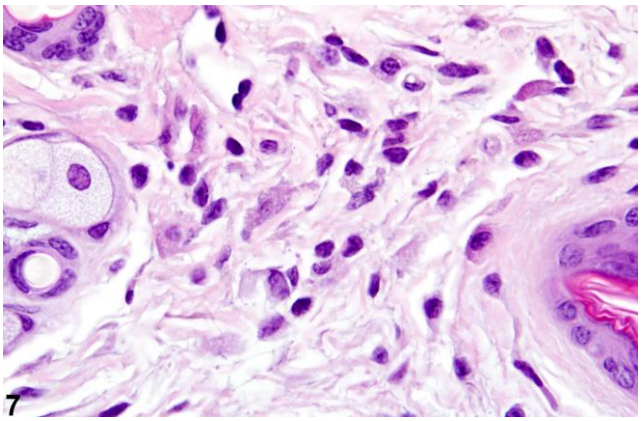
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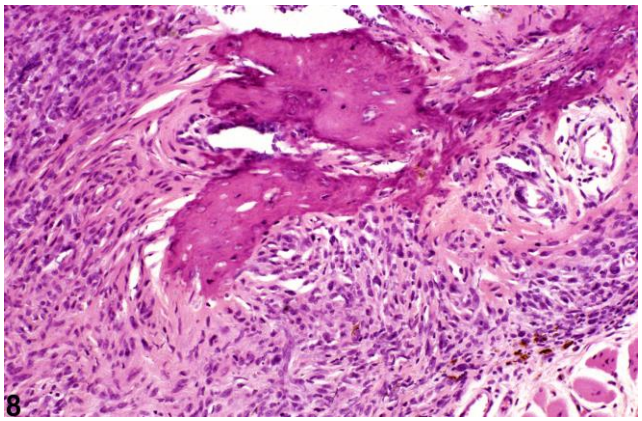
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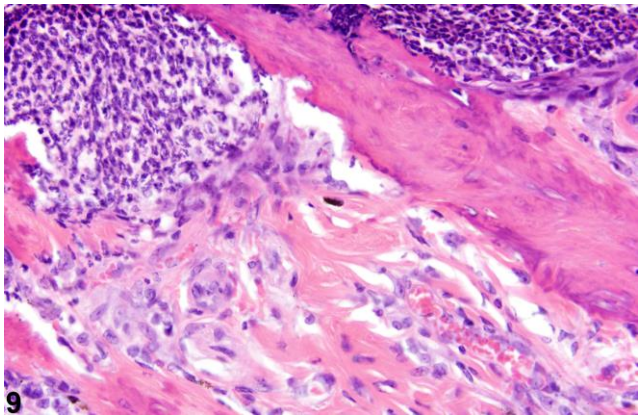
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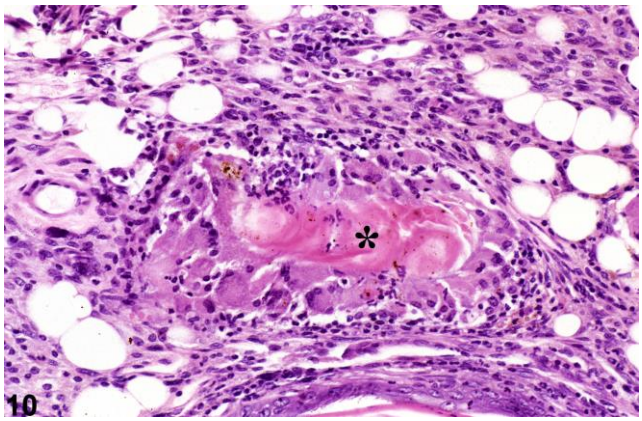
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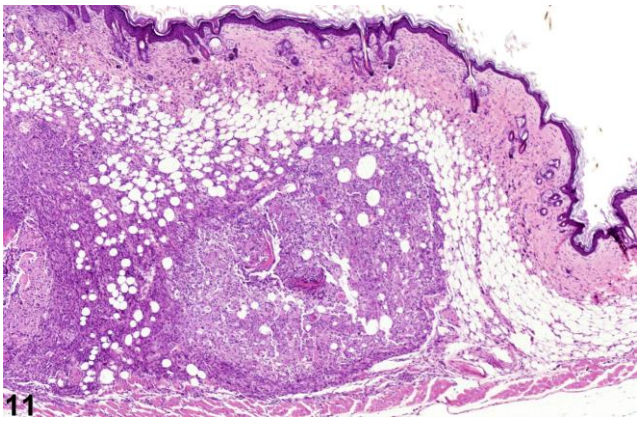
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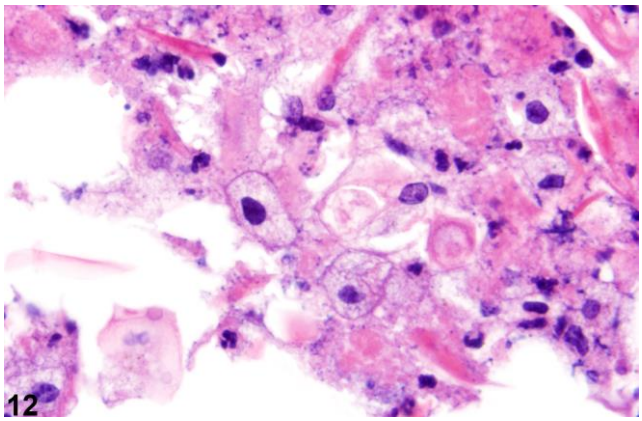
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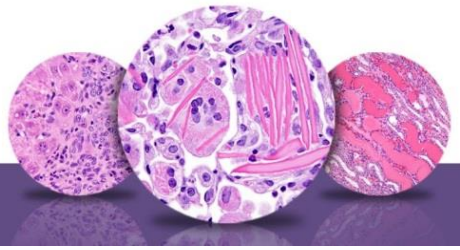

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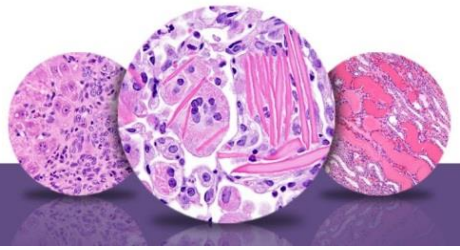
Figure Legend: Figure 1 Acute inflammation–dense infiltrations of neutrophils and osseous metaplasia in a male B6C3F1 mouse from a chronic study. **Figure 2** Acute inflammation–infiltrations of neutrophils in a male B6C3F1 mouse from a chronic study. **Figure 3** Acute inflammation–infiltrations of neutrophils in a male B6C3F1 mouse from a chronic study. **Figure 4** Suppurative inflammation–degenerate neutrophils and cellular debris in an untreated male B6C3F1 mouse from a chronic study. **Figure 5** Suppurative inflammation–degenerate neutrophils and cellular debris in an untreated male B6C3F1 mouse from a chronic study. **Figure 6** Chronic inflammation–mononuclear cells and fibrosis in a female B6C3F1 mouse from a chronic study. **Figure 7** Chronic inflammation–mononuclear cells and fibrosis in a female B6C3F1 mouse from a chronic study. **Figure 8** Chronic active inflammation–mononuclear inflammation, neutrophilic inflammation, fibrosis, and osseous metaplasia in a male B6C3F1 mouse from a chronic study. **Figure 9** Chronic active inflammation–mononuclear inflammation, neutrophilic inflammation, fibrosis, and osseous metaplasia in a male B6C3F1 mouse from a chronic study. **Figure 10** Granulomatous inflammation–multinucleated giant cells surrounding central necrosis (asterisk) in a male B6C3F1 mouse from a chronic study. **Figure 11** Granulomatous inflammation–large accumulation of macrophages within the subcutis in a male B6C3F1 mouse from a chronic study. **Figure 12** Granulomatous inflammation–macrophages with cellular debris in a male B6C3F1 mouse from a chronic study.

Comment: In dermal application toxicity/carcinogenicity studies, inflammation is one of the most common responses to chemicals. Inflammation may be nonspecific or related to trauma from self-mutilation (scratching), contact with edges of equipment, arthropod parasitism, or wounds from fighting. Secondary inflammation can also be associated with cutaneous neoplasms.

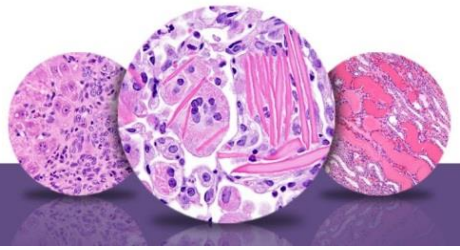
Acute inflammation (Figure 1, Figure 2, and Figure 3) in the skin is characterized by infiltration of neutrophils, which may be accompanied by eosinophils and macrophages as well as occasional mast cells, lymphocytes, and plasma cells. *Suppurative inflammation* is characterized by discrete pockets of degenerate neutrophils and cellular debris (Figure 4 and Figure 5). Evidence of chronicity, such as fibrosis and lymphoplasmacytic infiltrates, may also surround these pockets. *Chronic inflammation* (Figure 6 and Figure 7) is characterized by the



presence of mononuclear cells (lymphocytes, macrophages, and plasma cells) and may be accompanied by fibrosis or the accumulation of melanin within cells in the dermis. *Chronic active inflammation* (Figure 8 and Figure 9) is characterized by the coexistence of elements of chronic inflammation (lymphocytes, macrophages, and fibrosis) and superimposed acute inflammation (neutrophilic and/or eosinophilic). *Granulomatous inflammation* (Figure 10, Figure 11, and Figure 12) is characterized by an accumulation of macrophages and multinucleated giant cells, with variable numbers of lymphocytes, plasma cells, or neutrophils. A typical form of granuloma is one in which natural products of the skin (e.g., keratin, hair shaft, adnexal secretions) are introduced into the connective tissues, usually by trauma. These skin products act as foreign bodies, inciting a “foreign body granuloma,” a characteristic feature of which are multinucleated giant cells and/or epithelioid macrophages.

All forms of inflammation may be accompanied by associated lesions, including edema (though this is more commonly associated with acute inflammation), epithelial hyperplasia, hyperkeratosis, neovascularization, or hemorrhage with or without hemosiderin-containing macrophages.

Recommendation: Whenever present, the specific type of inflammation should be recorded and assigned a severity grade. When present as a secondary finding associated with neoplasia, fat necrosis or epithelial necrosis, or epithelial or other types of cysts, inflammation need not be diagnosed separately but should be described in the pathology narrative. When secondary findings such as edema, hemorrhage, or osseous metaplasia are present, they need not be diagnosed but should be described in the narrative. If the inflammation is accompanied by epithelial hyperplasia, hyperkeratosis, or excessive fibrosis, such findings should be diagnosed and graded independently of chronic inflammation. When granulomatous inflammation is accompanied by foreign material, both diagnoses should be documented separately, but the diagnosis of foreign material should not be graded.



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