**Figure Legend:**  
**Figure 1** Lung, Bronchiole - Vacuolization, Cytoplasmic in a female B6C3F1/N mouse from a chronic study. The bronchiolar epithelial cells have vacuolated cytoplasm. **Figure 2** Lung, Bronchiole - Vacuolization, Cytoplasmic in a female B6C3F1/N mouse from a chronic study (higher magnification of Figure 1). Most of the cells have also lost their cilia. **Figure 3** Lung, Bronchiole - Vacuolization, Cytoplasmic in a female B6C3F1/N mouse from a chronic study. The bronchiolar epithelial cells contain clear, intracytoplasmic vacuoles. **Figure 4** Lung, Bronchiole - Vacuolization, Cytoplasmic in a female B6C3F1/N mouse from a chronic study. The bronchiolar epithelial cells contain clear, intracytoplasmic vacuoles and have lost their cilia.
**Lung – Vacuolization, Cytoplasmic**

**Comment:** Cytoplasmic vacuolization in the lungs is most commonly seen in the airway epithelium of mice (Figure 1, Figure 2, Figure 3, and Figure 4) but may also be seen in other species and in other types of epithelial cells. Cytoplasmic vacuolization is generally thought to represent a reversible degenerative change. The vacuolization may represent distended and pinched off endoplasmic reticulum. Mitochondrial damage may lead to insufficient beta-oxidation and accumulation of triglycerides within the mitochondria or cytoplasm. Damage to cellular components involved in protein synthesis may lead to decreased levels of apolipoproteins, which lead to decreased lipid transport and the accumulation of lipid in the cytoplasm. The vacuoles may be large and distend the cytoplasm, but frequently the vacuoles are very small (i.e., visible only with electron microscopy) and numerous and give the cytoplasm a pale or bluish gray appearance. Since cytoplasmic vacuolization is thought to be a degenerative change, it is often accompanied by other changes associated with tissue damage, such as inflammation and necrosis.

**Recommendation:** Lung – Vacuolization, Cytoplasmic should be diagnosed and graded. The site (e.g., bronchus, bronchiole, alveolus) should be specified as part of the diagnosis. If the cytoplasmic vacuolization is a feature of a more severe degenerative or necrotic change, then degeneration or necrosis should be the recorded lesion (see Lung, Epithelium – Necrosis and Lung – Regeneration) and the vacuolization should be described in the narrative. Associated lesions, such as inflammation, should be diagnosed and graded separately.

**References:**


National Toxicology Program. 1991. NTP TOX 5. Toxicity Studies of Cobalt Sulfate Heptahydrate in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NIH Publication No. 91-3124. NTP, Research Triangle Park, NC.


National Toxicology Program. 2011. NTP TR 564. Toxicology and Carcinogenesis Studies of 1-Bromopropane (CAS No. 106-94-5) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NTP, Research Triangle Park, NC.

Lung – Vacuolization, Cytoplasmic

References:


Authors:

Mark F. Cesta, DVM, PhD, DACVP
Staff Scientist/NTP Pathologist
NTP Pathology Group
National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Darlene Dixon, DVM, PhD, DACVP
Group Leader
Molecular Pathogenesis Group
National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Ronald A. Herbert, DVM, PhD
Group Leader/NTP Pathologist
Pathology Support Group
National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Lauren M. Staska, DVM, PhD, DACVP
Senior Pathologist
WIL Research
Hillsborough, NC