Figure Legend: Figure 1 Kidney, Renal tubule - Vacuolation, Cytoplasmic in a treated male B6C3F1 mouse from a chronic study. Numerous clear vacuoles are present in the cytoplasm of renal tubule epithelial cells. Figure 2 Kidney, Renal tubule - Vacuolation, Cytoplasmic in a treated male B6C3F1 mouse from a chronic study (higher magnification of Figure 1). There are variably sized, mostly large vacuoles in the renal tubule epithelial cells.

Comment: Cytoplasmic vacuolation is characterized by the presence of clear vacuoles in renal tubule epithelium in the absence of any morphologic changes associated with degeneration (Figure 1). Cytoplasmic vacuoles are normally present in the outer cortical tubules of male mice in certain strains, but are not typically present in female mice or rats. Abnormal, or pathologic, vacuolation may be seen anywhere along the various tubule segments and collecting ducts. It is more commonly observed in the proximal convoluted tubule epithelium. Vacuolation may be associated with single, larger vesicles (macrovesicular) or may be associated with several smaller vesicles (microvesicular). Osmotically active compounds such as some sugars often result in “osmotic nephrosis,” which appears as cytoplasmic vacuolation. Cytoplasmic vacuolation of renal tubule epithelium may also be seen with phospholipidosis-inducing chemicals, cyclodextrins, and other chemicals that induce vacuolation through phagolysosomes. Cytoplasmic vacuolation, in most cases, is reversible. Artifactual vacuolation, related to autolysis or poor fixation, is frequently observed in animals either dying on test or sacrificed in a moribund state. Often it becomes problematic to separate tubule toxicity from artifact.
**Recommendation:** Normally, male mice have variable cortical tubule cytoplasmic vacuolation and do not have to be diagnosed (see Kidney, Renal Tubule - Cytoplasmic Alteration). In male mice, cytoplasmic vacuolation should be diagnosed only when the number and/or size of vacuoles is greater than that of the concurrent controls. Cytoplasmic vacuolation in female mice and male and female rats should be diagnosed whenever present. This diagnosis should be reserved for those cases where the vacuoles are present in the absence of other morphologic features of degeneration. The tubule location and portion of the kidney affected should be described in the pathology narrative. Whenever it is diagnosed, cytoplasmic vacuolation should be graded. Artifactual vacuolation should not be diagnosed.

**References:**


Abstract: [https://www.jstage.jst.go.jp/article/tox/21/1/21_1_9/_article](https://www.jstage.jst.go.jp/article/tox/21/1/21_1_9/_article)
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