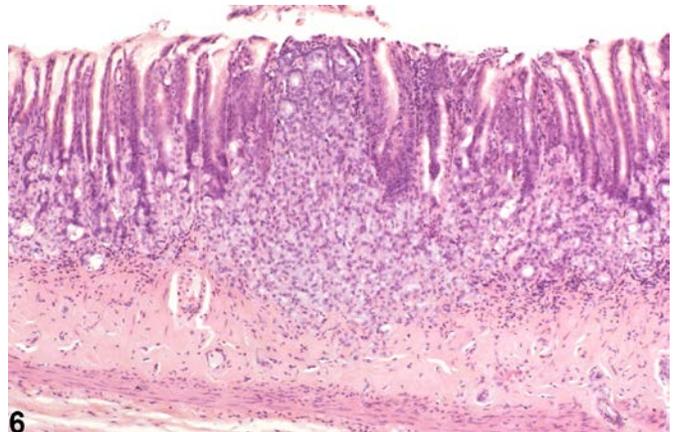
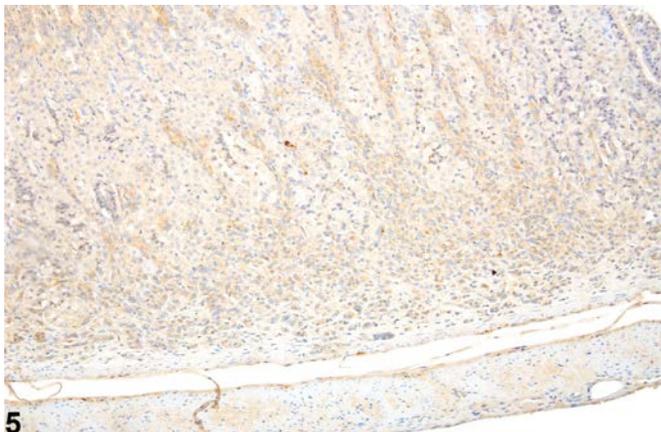
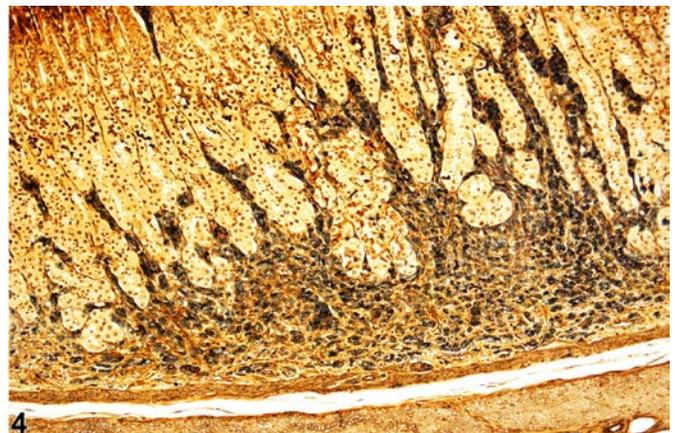
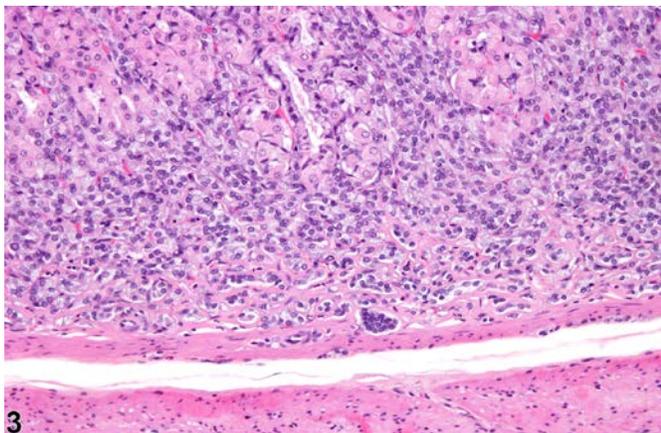
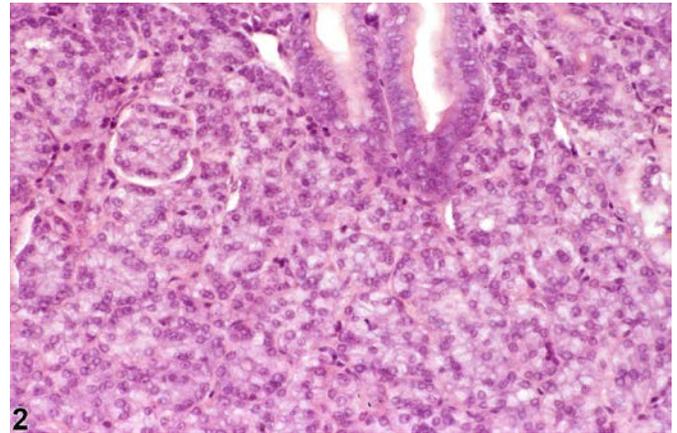
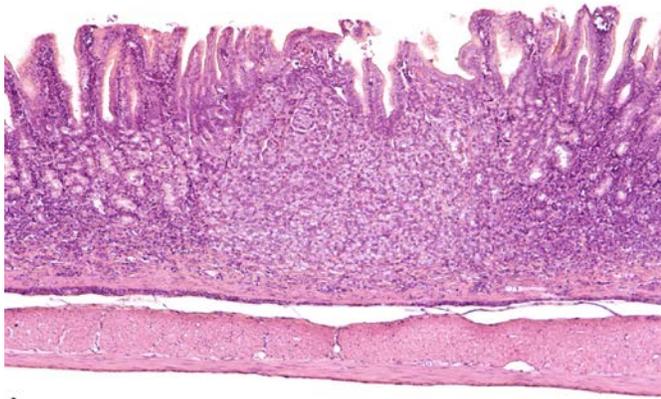


# NTP Nonneoplastic Lesion Atlas

## *Stomach, Glandular Stomach, Neuroendocrine Cell – Hyperplasia*



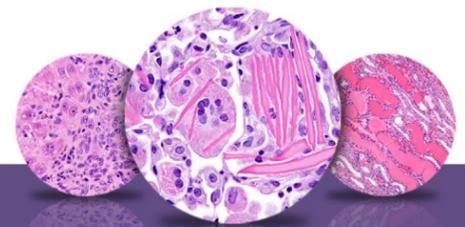


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**Figure Legend:** **Figure 1** Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study. The mucosa is expanded by a pale focus of cells. **Figure 2** Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study (higher magnification of Figure 1). The hyperplastic cells have small cytoplasmic vacuoles and are grouped in to small clusters separated by a fine vascular stroma. **Figure 3** Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study. The mucosal glands are separated by smaller cells with fine cytoplasmic vacuoles. **Figure 4** Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study (Sevier-Munger stain). The cells separating the glands stain positively with a silver stain. **Figure 5** Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study (Chromagranin A immunohistochemistry). The cells separating the glands are immunopositive for Chromagranin A). **Figure 6** Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study (Sevier-Munger stain). The gastric glands are separated by pale-staining cells.

**Comment:** Hyperplasia of the neuroendocrine cells consists of increased numbers of neuroendocrine cells in the mucosa. The neuroendocrine cells are attached to the mucosa basement membrane and are wedged between the mucous, parietal, and chief cells; some neuroendocrine cells have cytoplasmic extensions that reach the mucosa lumen. Because of their attachment to the basement membrane, hyperplasia will be noted primarily in the lower half of the mucosa. Neuroendocrine cells are difficult to recognize with H&E stains but are identifiable with special argyrophilic stains (Grimelius, Sevier-Munger), immunohistochemistry, or electron microscopy. Argyrophilic stains reveal small granules in the cytoplasm. Chromagranins are proteins that represent the predominant constituent of neurosecretory granules, so antibodies to Chromagranin A are used to identify neuroendocrine cells in tissue sections. Hyperplasia of the neuroendocrine cells of the glandular stomach can be induced with histamine 2 blockers or proton pump inhibitors and was seen in the NTP chronic methyleugenol gavage study. In addition, rats and mice in the methyleugenol study had an increase in neuroendocrine tumors of the glandular stomach. Hyperplasia of the neuroendocrine cells of the glandular stomach is not seen as a background lesion.



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**Recommendation:** Neuroendocrine hyperplasia should be diagnosed and graded whenever present. Grading should be based on the number of hyperplastic neuroendocrine cells present.

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