## NTP Nonneoplastic Lesion Atlas

## Esophagus - Hyperkeratosis



Figure Legend: Figure 1 Esophagus - Hyperkeratosis in a female F344/N rat from a chronic study. There are excess, anuclear keratin layers on the surface of the epithelium. Figure 2 Esophagus Hyperkeratosis in a female F344/N rat from a chronic study (higher magnification of Figure 1). There are excess, anuclear keratin layers on the surface of the epithelium.

Comment: Hyperkeratosis is a common alteration of the esophagus. Hyperkeratosis (thickening of the stratum corneum) occurs in two forms: orthokeratotic or parakeratotic hyperkeratosis. In orthokeratotic hyperkeratosis (sometimes referred to as orthokeratosis squamous epithelial cells are anuclear, whereas in parakeratotic hyperkeratosis (sometimes referred to as parakeratosis) the squamous epithelial cells have retained pyknotic nuclei. Hyperkeratosis frequently accompanies hyperplasia. Dietary composition affects keratinization, with low-fiber, low-protein, or liquid diets resulting in increased thickness of the keratinized epithelial layer. Also, animals that are not eating will often have hyperkeratosis of the esophagus without associated hyperplasia.

Hyperkeratosis in the absence of hyperplasia has interpretative implications different from those of hyperkeratosis occurring as part of the process of enhanced epithelial proliferation. In the anorectic rodent, the excess keratin is presumably the result of reduced mechanical removal by the passage of food. In cases of hyperkeratosis in the esophagus associated with anorexia, hyperkeratosis is usually also present in the forestomach. In these situations, there will be no evidence of an increased proliferative response in the basal layer. Alternatively, vitamin imbalance and zinc deficiency can cause parakeratotic hyperkeratosis and associated squamous cell hyperplasia.

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Recommendation: Hyperkeratosis is often seen when hyperplasia of the mucosa is present and is usually not diagnosed as a separate entity, although it may be mentioned in the description of hyperplasia in the narrative. When hyperkeratosis is present in the absence of hyperplasia or when hyperkeratosis is extreme, then it should be documented and graded. The severity grade is based on the degree of thickness of the keratin and the area of the esophagus affected. Hyperkeratosis is not divided into orthokeratosis and parakeratosis in the diagnosis, but this should be well described in the narrative.

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