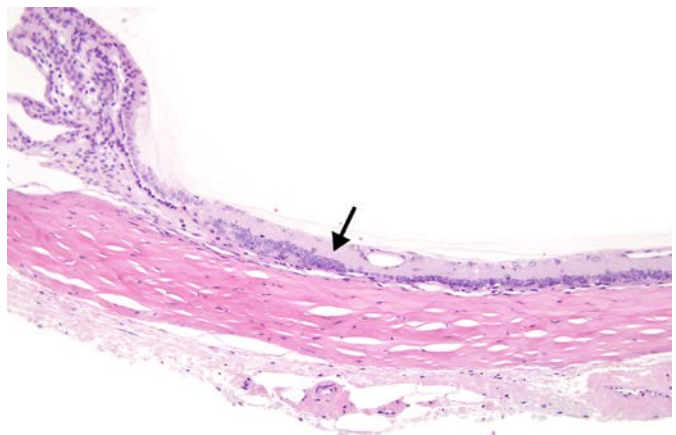
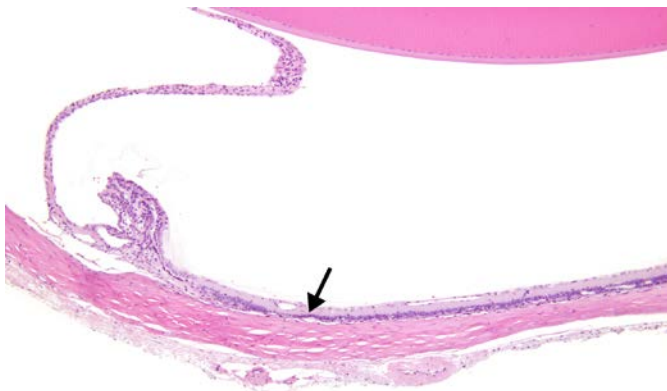
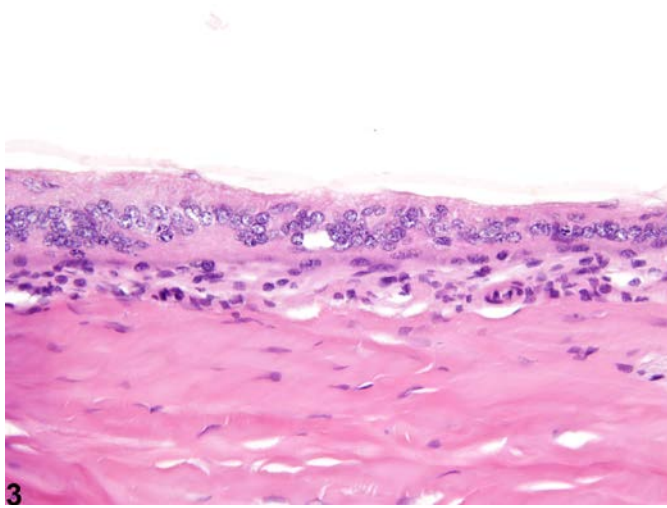
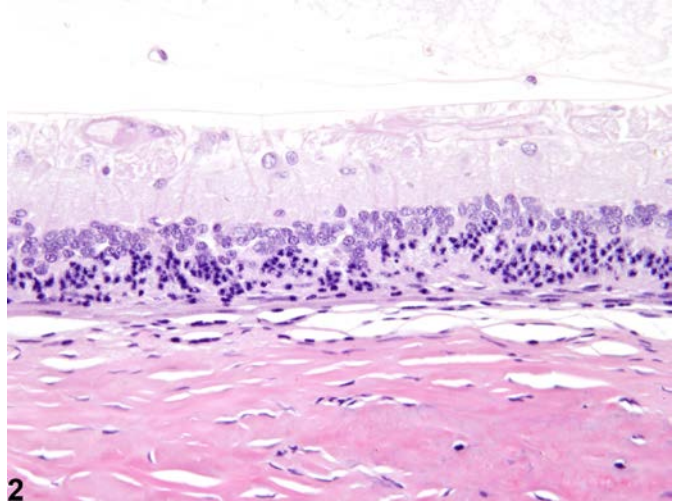
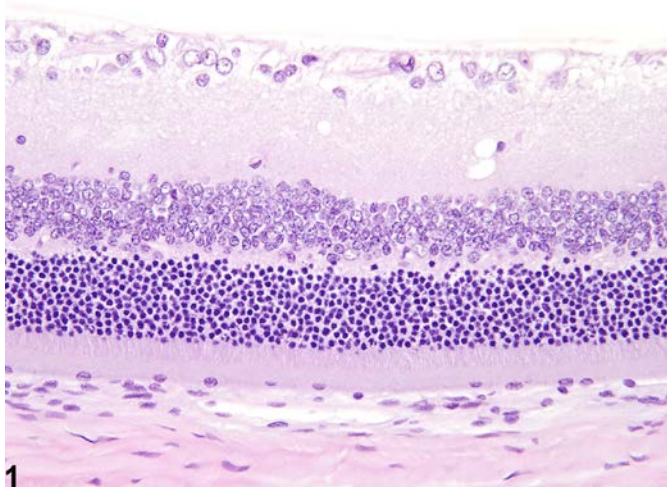




NTP Nonneoplastic Lesion Atlas

Eye, Retina – Degeneration



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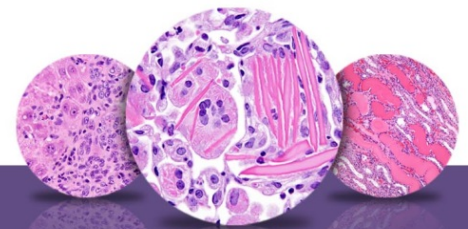
NTP Nonneoplastic Lesion Atlas

Eye, Retina – Degeneration

Figure Legend: **Figure 1** Eye, Retina - Normal in a male F344/N rat from a chronic study. Normal retina for comparison to Figures 2 and 3. **Figure 2** Eye, Retina - Degeneration in a male F344/N rat from a chronic study. Mild retinal degeneration, featuring loss of rod and cone photoreceptor processes, single-cell necrosis of outer nuclear layer photoreceptor cells, hypocellularity and disorganization of the inner and outer nuclear layers, and narrowing or absence of the plexiform layers. **Figure 3** Eye, Retina - Degeneration in a male F344/N rat from a chronic study. Marked retinal degeneration, featuring overall thinning, architectural disruption, loss of almost all cellular elements, and complete absence of the rod and cone photoreceptors and the plexiform layers. **Figure 4** Eye, Retina - Normal in a female F344/N rat from a chronic study. Normal peripheral retina (arrow) for comparison to Figures 5 and 6. **Figure 5** Eye, Retina - Degeneration in a female F344/N rat from a chronic study. There is marked thinning of the peripheral retina (arrow). **Figure 6** Eye, Retina - Degeneration in a female F344/N rat from a chronic study (higher magnification of Figure 5). The marked thinning of the peripheral retina (arrow) is due to hypocellularity or absence of retinal layers.

Comment: Retinal degeneration in rats and mice can occur as an aging change or secondary to various insults, such as physical trauma, retinal detachment, inflammation, infectious agents (e.g., viruses), vascular derangements (e.g., infarction), increased intraocular pressure, and nutritional deficiencies. Numerous heritable retinal degenerations have also been documented in various strains of laboratory mice and rats. So-called light-induced retinal degeneration can occur when rats and mice (especially albino strains) are exposed to overly intense ambient light. Retinal degeneration can also be a direct toxic effect of systemically or topically administered chemical agents. Spontaneously occurring retinal degeneration of uncertain etiology has also been reported in laboratory rats and mice. In many types of retinal degeneration, the most commonly affected retinal neurons are the rod and cone photoreceptors and/or the ganglion cells. Depending on the cause, degenerative changes may be localized (or more extensive) in particular retinal topographic regions (i.e., superior vs. inferior, central vs. peripheral).

Mild retinal degeneration (Figure 2, compare to Figure 1) typically consists of loss of the rod and cone photoreceptor processes, apoptosis of outer nuclear layer photoreceptor cells, hypocellularity and disorganization of the inner and outer nuclear layers, and narrowing or absence of the plexiform layers. More pronounced retinal degeneration (Figure 3, compare to Figure 1) is typically characterized by



NTP Nonneoplastic Lesion Atlas

Eye, Retina – Degeneration

overall thinning, architectural disruption, and loss of cellular elements, as well as complete absence of the rod and cone photoreceptors and the plexiform layers. Degenerate retinas may also exhibit other morphologic features, such as diffuse or nodular proliferation of retinal glial cells (e.g., Müller cells and astrocytes), fixed fold and rosette-like formations, and intraretinal cavitations or cysts (“microcystoid” formation and retinoschisis), as well as concurrent proliferation and/or intraretinal migration of the adjacent retinal pigment epithelium.

Rats and mice can also exhibit an incidental aging change known as peripheral retinal degeneration (Figure 5 and Figure 6, compare to Figure 4), which is characterized by marked thinning of the peripheral retina due to hypocellularity or absence of retinal layers. Although not illustrated, cystic cavitations (“microcystoid” change) are also common features of this peripheral age-related degeneration.

Recommendation: Retinal degeneration should be diagnosed and graded whenever present. The location (peripheral or central) and extent of the lesion within the retina, as well as the retinal layers affected, should be described in the pathology narrative. The pathologist’s opinion as to whether it is the peripheral, age related, background form of the lesion (or an exacerbation thereof) or a primary treatment-related lesion should be included in the pathology narrative. The various morphologic features of retinal degeneration (hypocellularity of specific layers, rod and cone photoreceptor process loss, etc.) should not be diagnosed separately but should be described in the narrative. The presence of retinal degeneration should prompt careful examination of the optic nerve for concurrent lesions.

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Eye, Retina – Degeneration

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