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Incomplete aniridia in a young rabbit belonging to the "Dutch" breed.

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Partial or complete aniridia of the colored part of the eye is a rare congenital defect in rabbits. It causes eye discomfort in presence of light and can lead to corneal opacity, juvenile cataract or juvenile glaucoma.

Aniridia is a complex congenital defect that is characterized by the incomplete development of the colored part of the eye (Figure 1). The impairment varies in severity, with a partial or total absence of the iris. The term "total absence" is actually

Figure 1: Young rabbit belong to the Dutch breed that shows a rare congenital malformation : a partial aniridia.

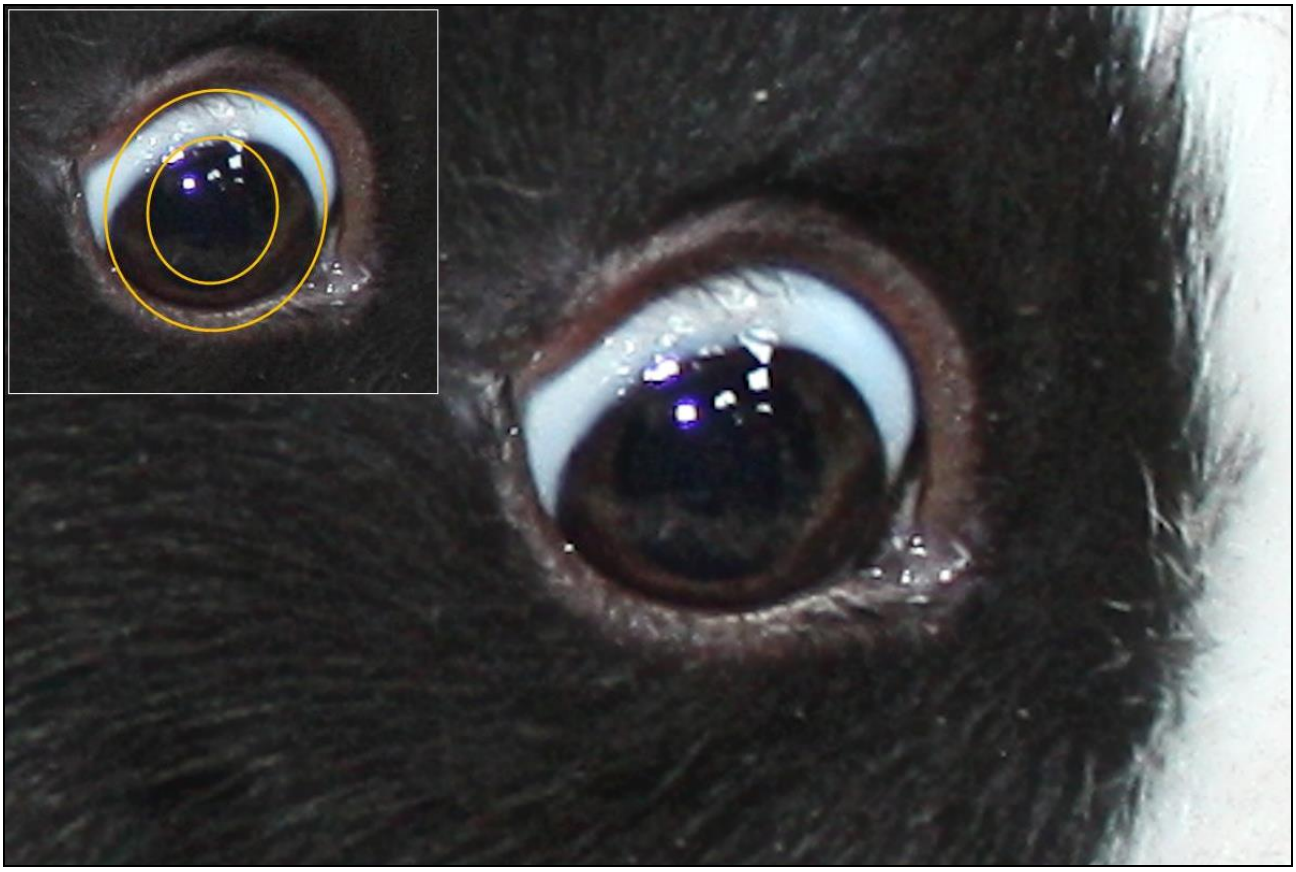

Figure 2: The iris is incomplete on its top and the pupil is dilated and unresponsive to differences in brightness. The animal tries to avoid bright lights by looking aside and strongly reacts to a flashlight.

a misnomer as a rudimentary and non-functional residue of iris tissue is present even in the case of a complete absence of the iris. It forms a very thin circle around the pupil that is barely visible.

Aniridia is usually bilateral. The degree of impairment may, nevertheless, be different between one eye and the other.

Aniridia is very rare. It has been observed in vertebrates: rodents, sheep, cow, horse, and man. No case of aniridia seems to have been reported in rabbits to this day (Figures 1, 2).

Effect on vision

The complete or partial absence of the iris makes it unable to filter the light properly. The pupil is often dilated and its size does not vary with changes of light brightness. In some cases, the pupil is so dilated so that it is possible to distinguish the equator of the lens and ciliary body to which the lens is attached. Thus, an individual with aniridia will suffer from photophobia and fear light. When photophobia is severe, the animal will try to avoid looking at the source of light and look aside. It also reacts strongly to a flash of light.

Visual acuity may be affected. It varies from excellent to very poor according to the degree of defect of the iris and of other eye structures.

Frequency of aniridia

This anomaly is seen in one individual in 50,000 to 100,000 in man. The frequency of

appearance of this anomaly is unknown in rabbits, but it is very rare.

Genetics of aniridia

Aniridia is a genetic defect in vertebrates and man. It can also occur spontaneously or be caused by a penetrating trauma.

A familial heredity has been observed. Penetrance of this eye disorder is variable. Transmission is usually on an autosomal dominant mode. Thus, if one parent is affected, there will be one chance on two that descendants will also be affected. Rarely, transmission occurs on an autosomal recessive mode. These individuals frequently suffer from balance problem and uncoordinated movements (ataxia) in addition to aniridia. Sometimes parents do not carry the aniridia gene. A spontaneous mutation may occur that leads to the loss or insertion of one or more nucleotides, causing this anomaly in a descendant.

In humans, the PAX6 gene is associated to aniridia. This gene is expressed in the early stages of embryogenesis and plays the leading role of "conductor" in the morphogenesis of the eye and the central nervous system (brain and spinal cord). It encodes for the PAX6 protein, a transcription factor. The Pax6 protein initiates and regulates downstream target gene clusters by attaching itself onto specific DNA regions. This system allows the regulation of the activity of certain genes, promoting the expression of genetic diversity in the offspring.

During the development of the embryo, the protein PAX6 control, among others:

- In the brain: differentiation of embryonic cells into brains cells and the regionalization of the brain, e.g. cells of the olfactory bulb or the infundibulum, as well as the establishment of a dorso-ventral polarity in the spinal cord.
- In the eye: genesis and early formation of the different structures of the eye such as the iris or the lens. It also prevents the formation of scar tissue in the eye during embryogenesis and after birth. PAX6 role in the formation of the eye has also been studied in other vertebrates such as rats or rabbits.
- In the pancreas: regulator of pancreatic islet transcription genes that secrete hormones.

The PAX6 protein also regulates various genes involved in the "maintenance" of the various ocular structures after birth. This prevents their degradation after their development in the embryo and throughout the life of an individual.

Panocular anomaly and effects on the eye

A mutation of the PAX6 gene leads either to a decreased synthesis of this molecule, the production of a non-functional molecule, or no production at all. This results in progressive panocular anomalies, including aniridia. The latter is potentially accompanied by ocular complications, as observed in man. They will have an impact on visual acuity. The more they are severe, the more vision will be affected.

Pupil

An enlargement and/or deformation of the pupil are a visible complication. Indeed, the iris contains muscles that control the size of the pupil in order to regulate the passage of light into the eye.

Cornea

The cornea may have structural defects such as a thickening (pannus) or abnormal vascularity which renders the cornea tissue opaque.

The conjunctiva sometimes covers the cornea. This is due to a reduced number of limbal stem cells, which are localized at the

periphery of the cornea and conjunctiva, in the limbus. This results in an inability to repair the cornea after an injury. Scarring or vascularization of the translucent portion of the cornea will lead to more or less important losses of vision.

Abnormality of the retina

Hypoplasia of the fovea - area of the retina where vision of details is most accurate, and of the optic nerve is observed.

Ocular lens and early cataract

Aniridia may be accompanied by abnormalities of the crystalline structure (ocular lens). These abnormalities can cause a full dislocation of the lens from its normal location or early opacification of the lens, with a gradual loss of vision (Figure 3).

Glaucoma

Abnormal or rudimentary structures in the corner of the eyes cause a drainage deficit of lachrymal fluids. An increase of pressure within the eye may contribute to the development of juvenile glaucoma (Figure 4).

Involuntary movement of the eye

The hindrance caused by light may be accompanied by an involuntary movement of the eyes (nystagmus).

Other anomalies

Individuals suffering from aniridia may also be affected by an inability to perceive odors.

A mutation in a gene that is expressed in the early stages of embryogenesis and is involved in early initiation and terminal differentiation of the eye and the central nervous system, thus, has a major impact on the formation of these organs. The expression of the mutation is different according to the vertebrate species: microphthalmia in rats, aniridia in sheep, cows and horses as well as in man. Knowledge obtained in animals and

Figure 3: Young Harlequin rabbit with a juvenile cataract.

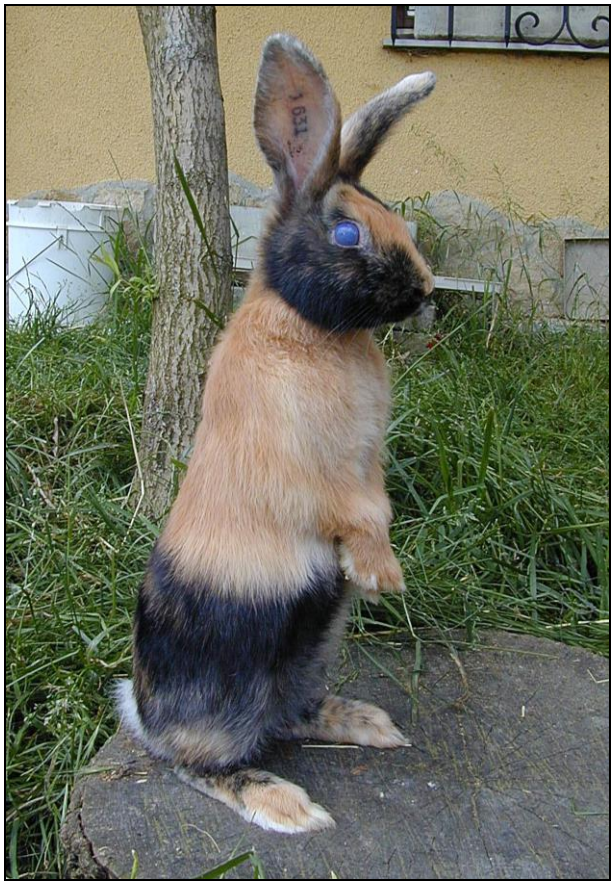

Figure 4: Young Harlequin rabbit with bilateral glaucoma.

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Thank you

observations in man may hopefully lead to new therapeutic strategies.

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