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Newborn rabbit with a congenital upper eyelid agenesis and a cephalocele

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Agenesis of the upper eyelid is a palpebral anomaly with severe consequences as the eye is left without protection against environmental aggressions. It is very rarely observed in rabbits.

Eyelids are mobile folds of skin that move thanks to muscles. They protect the eyeball against attacks from the outside environment by shutting down over it:

- Drying by evaporation because the tear film and the lipid layer can no longer be

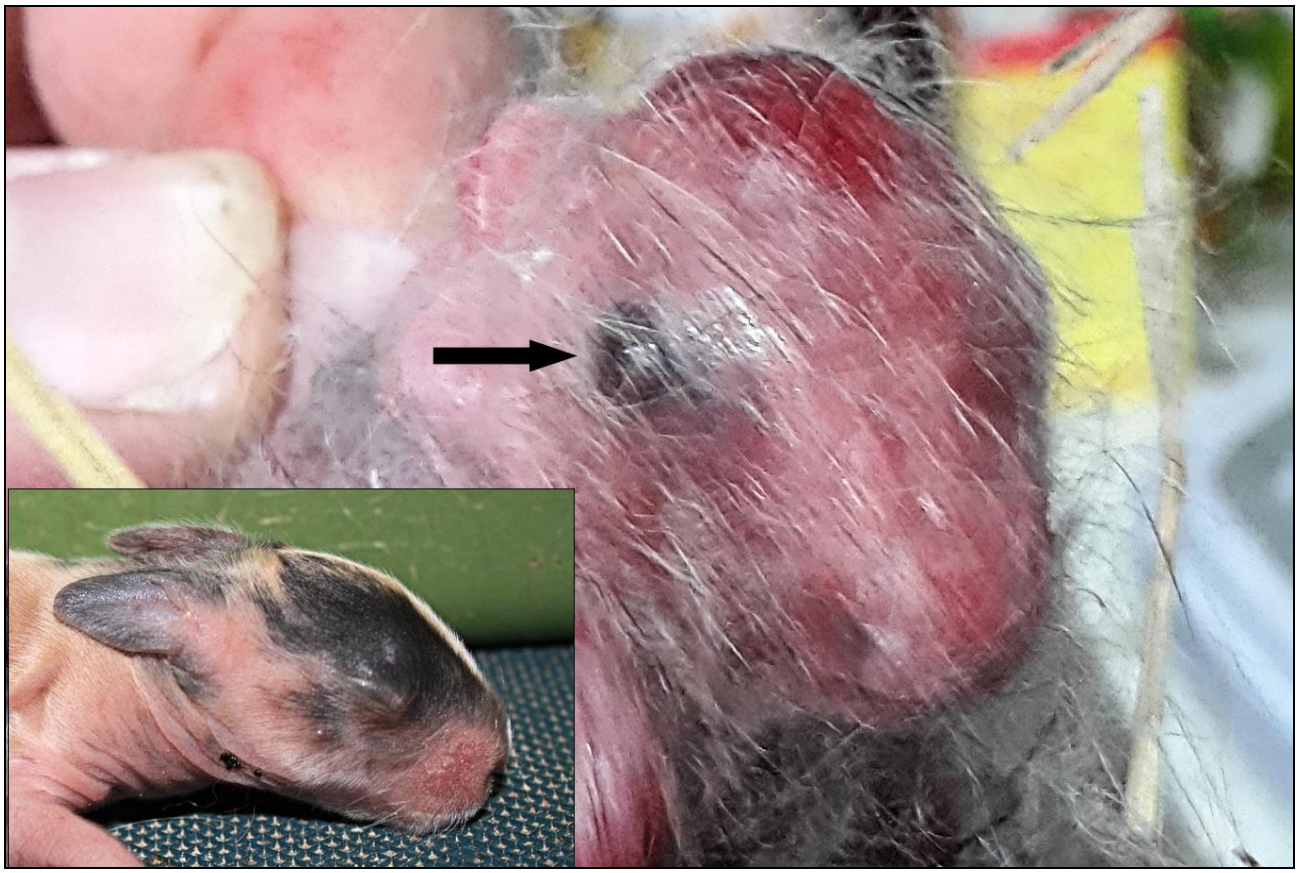


Figure 1: Newborn rabbit of harlequin breed with open eyes due to a bilateral agenesis of the upper eyelid (arrow). Here the right eye. Inset: Normal newborn with closed eyes.

spread on the surface of the cornea.

- Lack of feeding of the ocular surface by the tears and the Meibomian glands located at the edge of the eyelids.
- Light and UV, the lack of eyelid allows light to enter the eye and stimulate the optic nerve during sleep.
- Injury caused by dust, e.g. a strand of hay or straw.

A rabbit has three eyelids: an upper eyelid, a lower eyelid and a third eyelid or nictating membrane, which is barely visible. The upper eyelid is the most mobile. The third eyelid is located in the medial canthus of the eye. It is visible primarily when the eyeball retracts.

The tissue forming the upper eyelids can be divided into three regions:

Outer layer

It includes skin covered with fur and a glabrous edge as well as the subcutaneous fascia. The subcutaneous tissue is, furthermore, a fat-poor tissue.

Superficial muscular layer

It includes the *orbicularis oculi* muscle (closing), the levator muscle of the upper eyelid (opening) and deep retractor muscles. The movement of the third eyelid is possible thanks to two smooth muscles.

Fibrous layer

It includes a strong fibrous plate that renders the eyelid rigid and firm (tarsus) and the orbital septum.

Movement of the upper and lower eyelids is controlled by different branches of the trigeminal nerve, respectively the upper and lower branch of the oculomotor nerve. The nictitating membrane is innervated by two postganglionic neurons belonging to the sympathetic chain ganglia, which is located close to the path of the trigeminal nerve on part of its way in the skull.

The internal side of the upper and lower eyelids is lined with a mucous membrane, the palpebral conjunctiva. It is firmly attached to the tarsus. It consists of an epithelium with cylindrical cells. Its deep layer is composed of 3 layers of cuboidal cells on a basal membrane and a superficial layer consisting of tall columnar cells. The tissue is rich in blood and lymphatic vessels, glands and is well innervated.

The free edges of the eyelids are lined by a row of sebaceous glands: the Meibomian glands or tarsal glands. Their lipid secretions play an important role in the formation of the tear film, preventing dehydration of the eyeball.

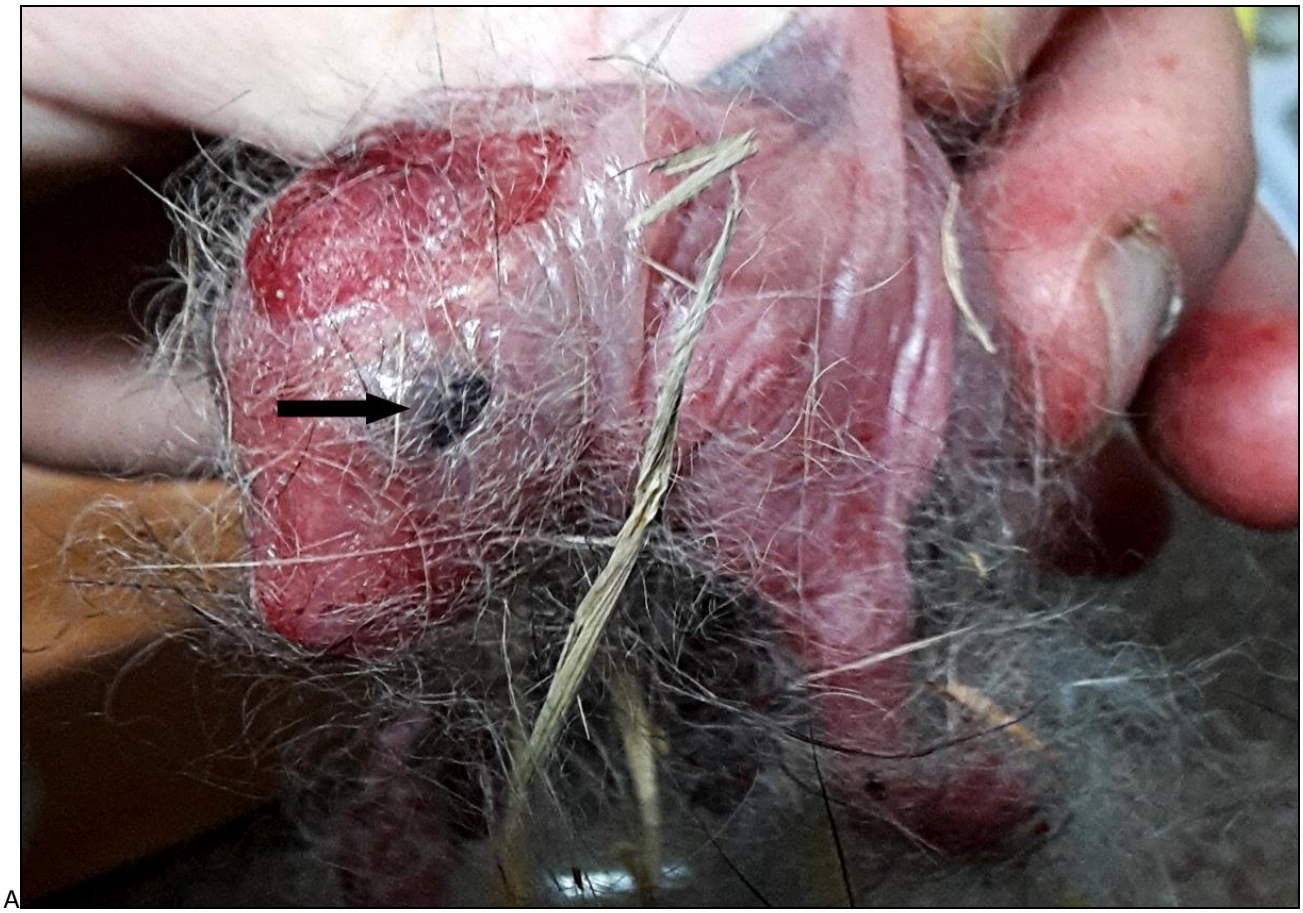
Finally, there are the lacrimal drainage openings located at the junction of the lower eyelid and the conjunctiva. These lachrymal puncta allow the secretion of lachrymal fluid onto the surface of the eye. The opening and closing movement of the eyelid creates pressure changes that will aspirate the tear fluid onto the surface of the eye after which it will be distributed on its surface.

Beside the fact that defects of the eyelids are an aesthetic disgrace, they can have serious consequences such as irritation of the conjunctiva membrane or the appearance of keratitis and corneal ulcers. As a result, corneal scarring will make the cornea opaque, leading to a loss of vision and even blindness.

1. Agenesis of the upper eyelid

The full (agenesis) or partial (coloboma) absence of the upper eyelid is a congenital palpebral anomaly, which is considered very rare in rabbits even when its true incidence in newborn maybe be considerably higher (Figures 1, 2, 3). Breeders who discover such cases may, indeed, be reluctant to

A



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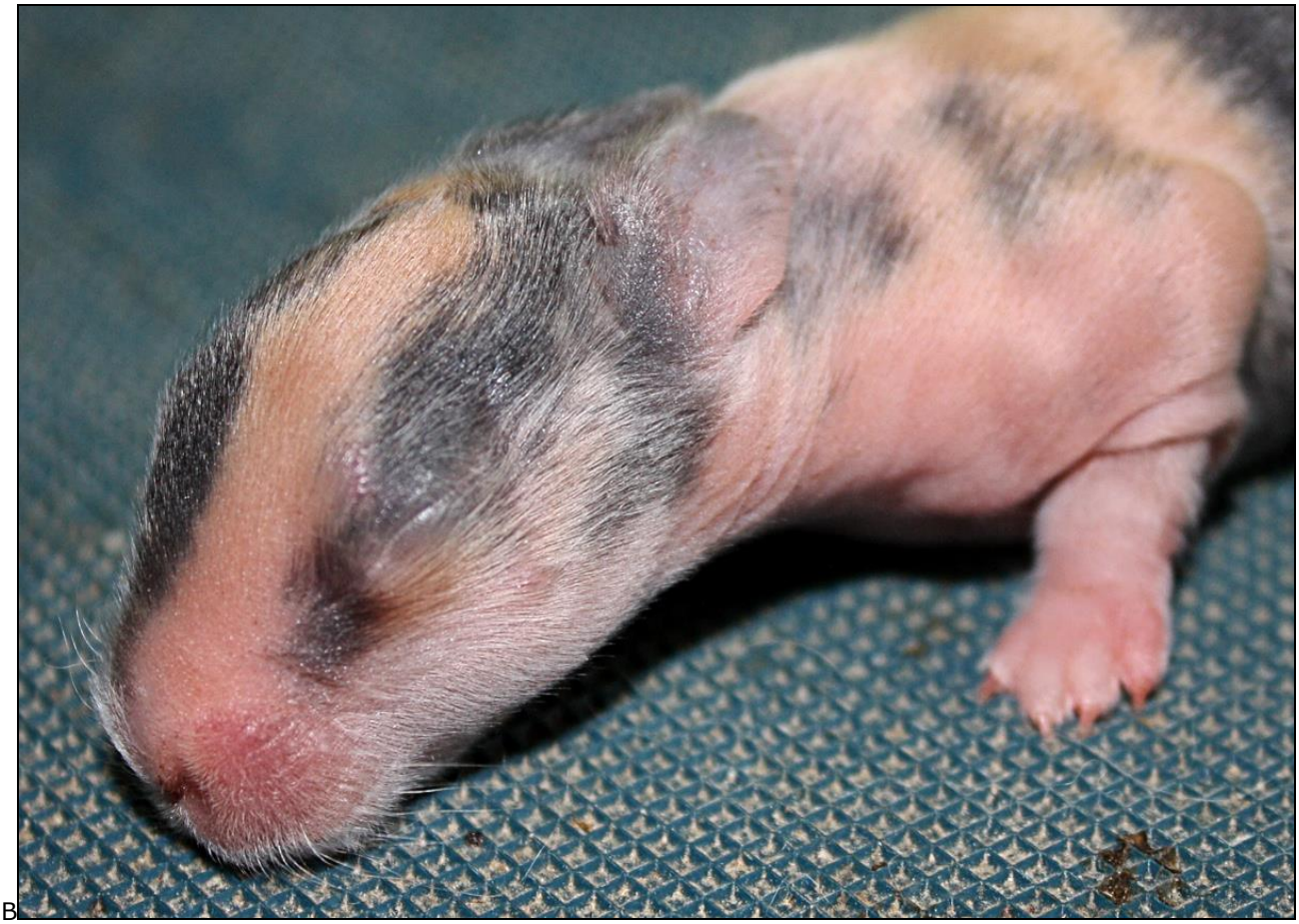

Figure 2: A: The left eye is also affected by the full absence of eyelid. B: Normal newborn of harlequin breed with intact and closed eyelids.

share these findings. In other animals upper eyelid agenesis is rare too, except in cats.

Agenesis of the upper eyelid is characterized by the absence of part or all components of the eyelid. The extent of the anomaly varies in severity, ranging from a single nick at the edge of the eyelid to the full absence of the eyelid. In man, it is generally observed at the junction of the internal third and the median third. Even though one or two eyes may be affected, agenesis of the eyelid is usually bilateral.

The development of agenesis or coloboma of the upper eyelid is usually an isolated occurrence. Sometimes, it is accompanied by other eye problems like:

- Persistence of residual embryonic vascular tissue in the eye (persistence of the pupillary membrane, in cats and dogs.
- Colobomateous syndrome in cats, with multiple eye anomalies like coloboma of the eyelid, the iris, a decolorized circular region of the retina (optical disk), of the choroid, one of the layers of the eye ball, or the optic nerve. They may be accompanied by dysplasia of the retina, microphtalmic eyes and cataract.

The absence of eyelid causes an irritation of the eye, which leads to exposure kerato-conjunctivitis accompanied by a vascularization of the retina due to the lack of a protecting lachrymal layer at the surface of the eyeball. It is sometimes accompanied by secondary trichiasis. The rubbing of hair on the surface will cause corneal ulcers that are both painful and difficult to treat or epithelial hypoplasia.

Etiology of eyelid agenesis

Different physio-pathologic theories have been proposed in order to try explaining the etiology of the upper eyelid agenesis, but none could be proved due to lack of information or sufficient cases. In cats and dogs, a genetic predisposition is suspected but not proven. Other suggested causes include a viral infection, ingestion of a teratogenic product or medication, or an influence of the environment.

2. *Cranium bifidum*

The newborn rabbit also suffers from a craniofacial anomaly with a protrusion in the frontal region of the skull typical of *cranium bifidum* (Figure 3). The part of the brain that is located in a pocket outside the skull is usually covered by skin or a very thin membrane. Most cephalocele are large (Figure 4), but some are small or barely visible (Figures 3, 5).

Morphogenesis of this anomaly is not only caused by the incorrect closure of the bones on the sagittal line of the skull, between the forehead and the nostril (*crania bifida*) with a secondary protrusion (hernia) of intracranial tissue (Figures 3, 4, 5). It starts with a closure defect of the neural tube during fetal growth. The neural tube is a fine structure that folds and closes in order to finalize the development of the central nervous system and the brain. The non-closure of the tube is caused by a focal failure of dehiscence of neural tube from the embryonic ectoderm. The development of the axial skeleton encasing the neural tube fails. As a consequence, a protrusion or hernia may appear along the median suture lines of the skull: an encephalocele (brain and meninges) or a meningocele (meninges and cerebrospinal fluid).

Etiology of cranial celes

The etiology of craniofacial cephaloceles is not well understood. They often appear spontaneously. Causes seem multifactorial, the result of a combination of factors. The

Figure 3: Lateral and frontal view of the newborn with complete agenesis of the uppereyelids. It is also affected by a cephalocele (arrow).

closure failure of skull bones may, however, be linked to a genetic predisposition in certain lineages or families. The autosomal recessive gene is expressed either as *spina bifida* of the spinal cord or as a cephalocele of the brain on the head as observed in pigs and Burmese cats.

It may also be the result of toxins or molecules with teratogenic effects like the antifungal griseofulvin, some corticosteroids, arsenic or trypan blue on the fetus. Viral or bacterial infections are also suspected.

Finally, a deficiency in vitamins and minerals and, especially folic acid in the doe during pregnancy increases the incidence of closure defect of the neural tube in the fetus.

Symptoms linked to a cephalocele

The presence of a cele may be accompanied by hydrocephaly or paroxismal convulsions in rabbits. Other symptoms observed in other affected animals include paralysis of limbs and a retardation of growth.

Acknowledgements

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Figure 4: Another one day old rabbit newborn belonging to the Belgian beard rabbit breed, with an encephalocele.

Figure 5: Other newborn presenting a closure defect of the crnial bones, causing a frontal cephalocele. Its mother had a 50% Fauve de Bourgogne inheritance while the was a purebreed belgian beard rabbit. Inbreeding can ths be exclused in this case.

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