# What You Can See In the Eye of a Minipig

## (The ophthalmic examination in the Ellegaard Göttingen Minipig)

Helmut Ehall, Named Veterinary Surgeon, Department of Veterinary Services

*Huntingdon Life Sciences*

### 1. Introduction:

The minipig is today a commonly used non-rodent species in the safety assessment of new therapeutic drugs and other chemicals. Sometimes the endogenous or exogenous exposure to the test compounds will lead to structural and functional alterations within the visual system potentially affecting the ability to see. In many instances, ocular changes are the first and sometimes only clinical sign of toxicity. The ophthalmic examination is therefore an important integral part of most safety toxicology studies.

However, the majority of ocular lesions in animals are breed-specific or have at least a hereditary component to their pathogenesis. The examiner has to be able to recognise such lesions and differentiate them from a potential toxicological effect induced by the test material. It is therefore essential that the most common congenital and hereditary ocular lesions are known for each laboratory species. In comparison to other laboratory species, ocular lesions are relatively uncommon in minipigs, but incidental background findings will still be detected during routine examinations.

There are many ways to assess visual function in animals; however, in toxicology the routine ophthalmic examination will be limited to the use of a binocular indirect ophthalmoscope. By using a handheld converging lens as a magnifying lens (Panretinal 2.2) it is possible to view the anterior segments in appropriate detail and by using the same lens as a condensing lens a wide field of the posterior segments of the eye (i.e.: vitreal body, fundus) can be viewed. Some examiners may prefer to also use a slit lamp biomicroscope to examine the anterior segments of the eye in more detail. This may be of particular benefit if lesions are expected in the cornea or the lens.

To perform the examination, Tropicamide 1% (e.g.Mydriacyl®) is applied to the eyes prior to the examination. This will usually provide satisfactory dilatation of the pupils within 20 minutes after application. Mydriasis will be maintained for approximately an hour.

Minipigs up to an age of 6 months are best held in the arms of an assistant, when examined. Animals above 6 months of age are usually too heavy to be held by a person and are better restrained either in a sling or sat between the legs of the assistant with the pig's front legs lifted off the ground.

As with any observation of clinical signs, it is necessary to develop a routine for the ophthalmic examination. This will allow the examiner to carry it out quickly and to identify any relevant abnormalities.

Both eyes should be first examined from a distance, assessing the orbital and periocular conformation and the size and position of the globe. As the eyes are positioned in a quite lateral position within the skull in the pig, any asymmetrical abnormalities are best detected by looking at the orbitae and globes from the front and the top of the head.

By using the viewing lens s a magnifying lens, the eyelids and the conjunctiva should be examined. Due to the deep seated eyes and tight eyelids in the minipig, the examination will mainly involve the assessment of the lid margin and the marginally visible conjunctiva. The cornea should be assessed for irregularities and opacities, pigmentations and vascularisation. The limited area of cornea visible in the minipig may be increased by moving the head up and down, to the left and the right and by encouraging the minipig to look in different directions. The examination should continue with the anterior chamber, noting its depth and any abnormal haziness. Despite the induced mydriasis before examination, the iris should be included in the examination together with the pupil margin. The examination of the lens usually requires some experience. By moving the lens back and forwards all planes of the lens can be carefully searched for opacities/cataracts. The posterior suture line and the origin of the hyaloid remnant are useful landmarks to identify the focus on the posterior aspect and the anterior suture line and iris on the anterior aspect of the lens.

The ophthalmic examination will usually be concluded by the fundoscopy. This should include the assessment of the vitreous for any opacities or abnormal contents and the retina, optic nerve head and retinal blood vessels for any abnormalities.

### 2. Globe / Periorbita

Figure 1: reddish brown mucoid and crusty discharge.

A reddish brown and crusty discharge is commonly observed in older minipigs. The discharge occurs usually bilateral and is neither associated with conjunctivitis nor seems the drainage of the tears through the nasolacrimal system compromised. The aetiology of the condition is not known, but as the first signs of discharge usually appear when the animals become sexually mature and due to its prevalence in boars, it may be considered a courtship signal. Bacteriological examinations are from personal experience usually negative. The discharge is best left in situ as the animals do not seem to be affected by it and removal and cleaning of the crusts may only lead to irritation of the underlying skin.

## 3.Eyelids

***a. Entropion***

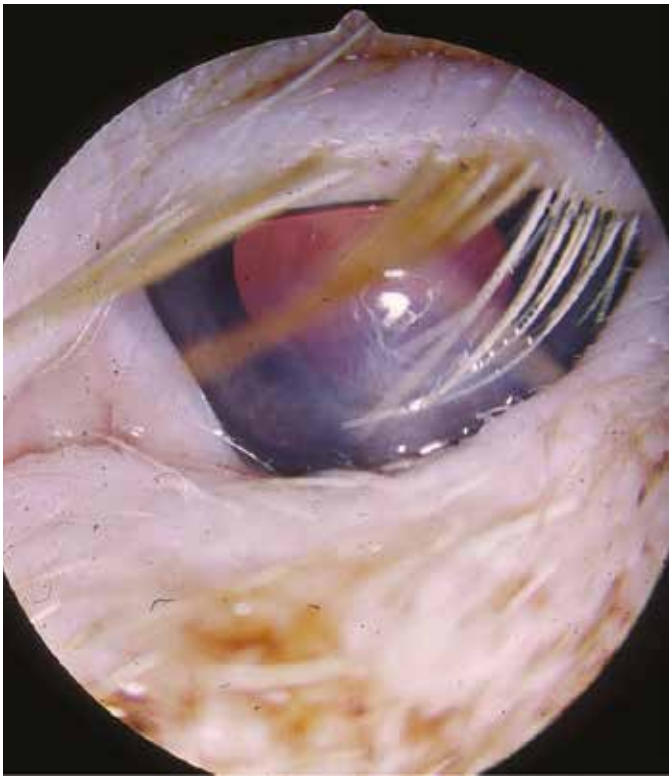


Figure 2: Entropion of the lower eyelid.

An entropion occurs when all or part of an eyelid is rotated towards the oculus, so that its hair-bearing margin touches the corneal surface causing permanent or intermittent corneal irritation. In regards to its treatment it is important to differentiate between primary entropions, which are due to poor conformation between eyelid and globe and secondary entropion, which is due to spasms of the orbicularis and /or malaris muscle or due to scar formation. It may also be induced by severe ocular pain and the associated endophthalmos. Most primary entropions will also be exacerbated by a secondary spastic component due to the corneal irritation [(1)]. It will be important to consider this when preforming a surgical repair. In the minipig, a large amount of subcutaneous fat in the periocular region and a disposition to entropion as part of its heritage from the Vietnamese pot-bellied pig may contribute to the occasional observation of entropion. Entropions are best repaired by a modified Hotz-Celsus procedure [(2)]. It has also been suggested that post-operative control of the animal's weight is beneficial for long-term success of the procedure.

## 4. Conjunctiva

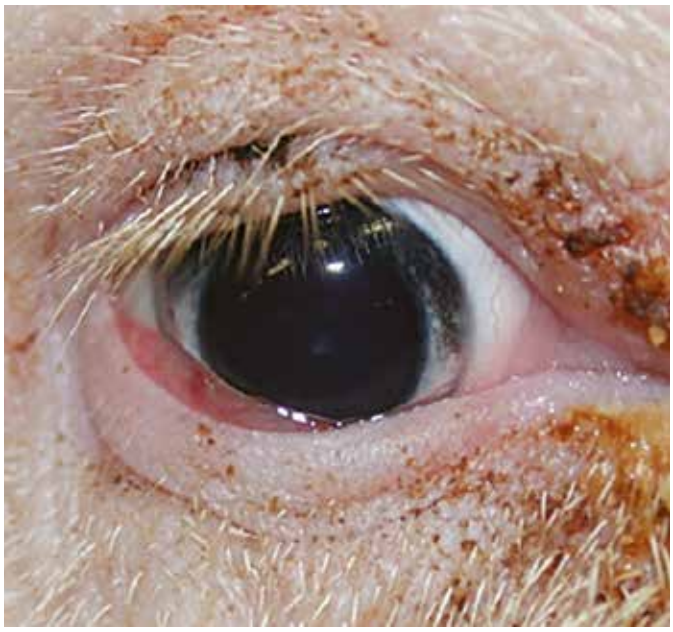


Figure 3: conjunctiva visible in the lateral half of the lower eyelid

In some minipigs, part of the conjunctiva is exposed in the area of the lateral part of the lower eyelid. It does not appear to be associated with conjunctivitis as hyperaemia is only very slight if present at all. Usually it is observed bilaterally and must not be mistaken as chemosis or conjunctival oedema. The conjunctiva may be mechanically exposed by a large amount of periorbital fat.

## 5. Cornea

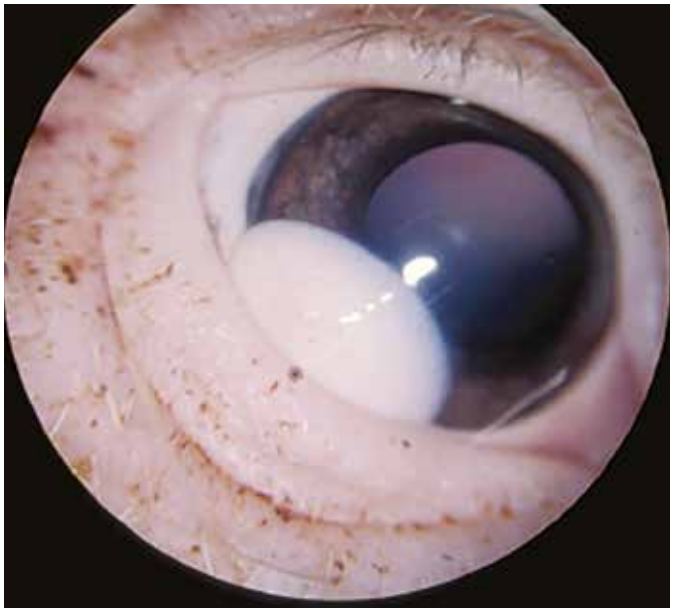


Figure 4: Dermoid on the tempero-ventral aspect of the cornea.

A Dermoid is a choristoma, which is a benign tissue element found on an abnormal location. An ocular dermoid is typically a skin-like, congenital mass of tissue, which can be found on

various ocular structures. It usually consists of keratinised epithelium, hair, blood vessels, connective tissue and smooth muscle, nerves, fat and glands [3]. They are frequently observed on the anterior surface of the globe near the temporo-ventral limbus [4]. In pigs, dermoids have only been described once as an approximately 7.5cm long tubular mass consisting of unorganised tissue derived form multiple embryonic germ layers, including bone and cartilage [3].

Metaplasia of the corneal epithelium is considered to be the most likely cause of dermoids, because it is the underlying mesodermal tissue, which determines whether surface ectoderm forms a non-keratinised stratified squamous epithelium and a Bowman's membrane as present in the cornea or keratinised epidermal adnexa as found in haired skin [4]. So dermoids are believed to either result form a primary aberration of invading corneogenic mesoderm or from abnormal inductive influences from underlying vestiges of the embryonic eye or from sequestration of dermal tissues destined to form keratinised skin.

Small dermoids may be left alone, in particular if they are unlikely to be irritant due to a lack of hair follicles. Larger dermoids or those, which are irritant to the eye, require surgical removal. On the cornea, the procedure of choice is a superficial keratectomy.

## 6.Iris

### *a. Heterochromia of the iris*

Figure 5: Heterochromia iridis.

Figure 6: Heterochromia iridum

Both, Heterochromia irides, a different colouring of the two irides of an animal and Heterochromia iridum, a multicoloured iris, are very commonly seen in the Goettingen minipig. While both may also be acquired, usually as a result of previous inflammation, in the Goettingen minipig they are congenital and are most certainly remains of the pigmented Vietnamese pot bellied pig which forms part of its ancestry. While the introduction of the Large White Landrace into the breeding programme successfully eliminated the occurrence of skin pigmentation, it seemed to only have partially lead to colour dilution in the eye. Apart from the variation in appearance, heterochromia of the iris is of no clinical significance.

### *b. Iris coloboma:*

Figure 7: Iris coloboma at a typical position at 6 o'clock.

Ocular colobomas are embryological maldevelopments leading to fissure-like lesions of any ocular tissue formed by the optic cup. In their typical form, these appear at a 6 o'clock position and are considered a failed fusion or closure of the embryonic ventral fissure of the optic stalk or cup [5]. A coloboma appearing at any other location than the 6 o'clock position is a so-called atypical coloboma and are caused by primary abnormalities in the outer layer of the optic cup [6].

## 7.Lens

### *a. Microphakia:*

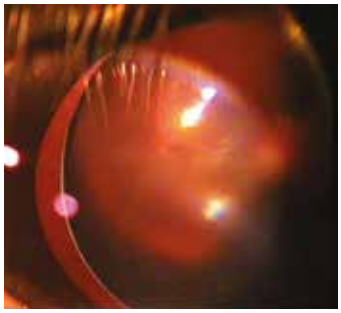


Figure 8 & 9: Microphakia

Congential microphakia is an abnormally small lens, which was observed on a breeding sow and one of its off-spring. A hereditary component can therefore not be excluded in the minipig. The area of contact between the optic vesicle and the surface ectoderm during embryological development will determine the ultimate size of the lens. Congenitally displaced lenses have also been described to be small and sphaerophakic, possibly due to an abnormal embryonic lens-zonule relationship [6,7]. Microphakia may also occur as a consequence of acquired lens zonular discorder and manifests in humans when the ciliary processes cause insufficient tractional forces on the lens [8].

***b. Cataracts:***

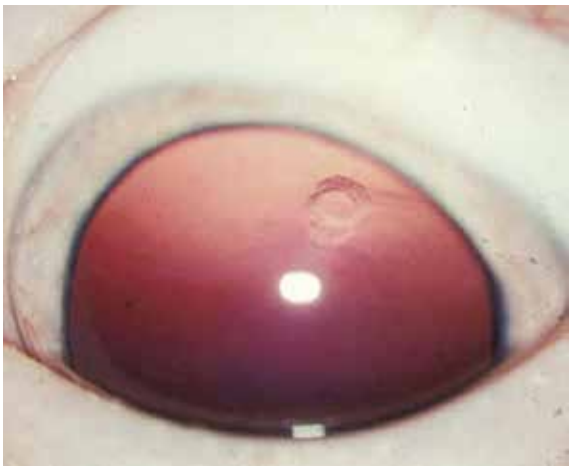


Figure 10: Anterior subcapsular opacity with peripheral extension.

Figure 11: Posterior polar subcapsular cataract

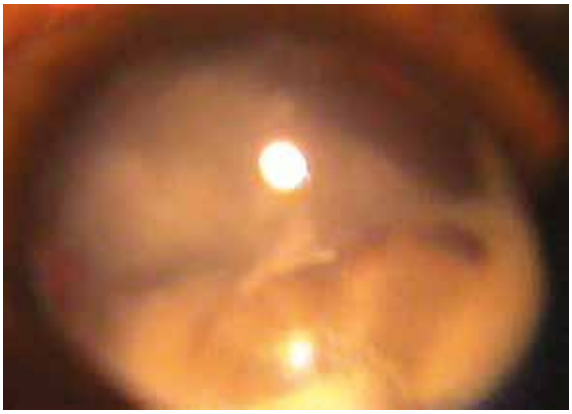


Figure 12: Total cataract

The lens is a refractive structure within the globe with the prime function to focus sharp images on the retina for accurate vision. Transperancy is therefore an essential property for the lens to fulfil its task. Due to the rather simple design, the lens depends on correct functioning of its biochemical processes. If disturbed, the lenticular fibres will react in a similar simplistic way and will loose transparency. Cataracts are therefore one of the most common test compound related ocular change in toxicology.
In contrast to other laboratory animals, congenital cataracts (which may only become apparent at a later age), are relatively rare in the minipig and a total cataract has so far only been observed once by the author. On occasions and appearing to be restricted to offspring from animals of one barrier, a faint to slight posterior subcapsular cataract can be observed. These seem to be similar to the cataracts described in Golden and Labrador Retriever breeds in dogs. The opacity appears at the confluence of the posterior suture line and in typically triangular, pyramidal or of an inverted Y shape *(Picture 11).* These are also, as observed in the minipig, non progressive and do not interfere with vision.

## 8. Vitreous

***a. Hyaloid remnant:***

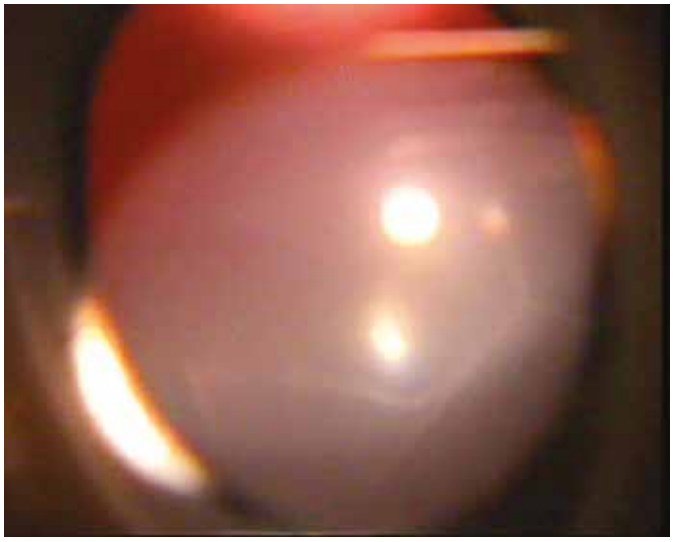


Figure 13: Hyaloid remnant

Figure 14: Hyperplastic hyaloid remnant

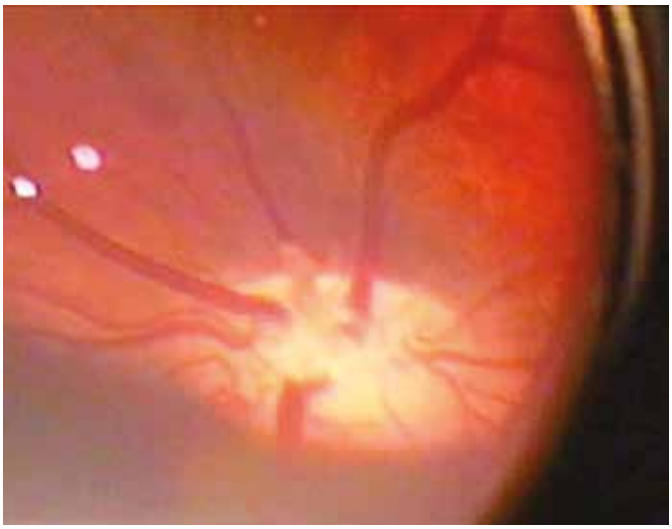
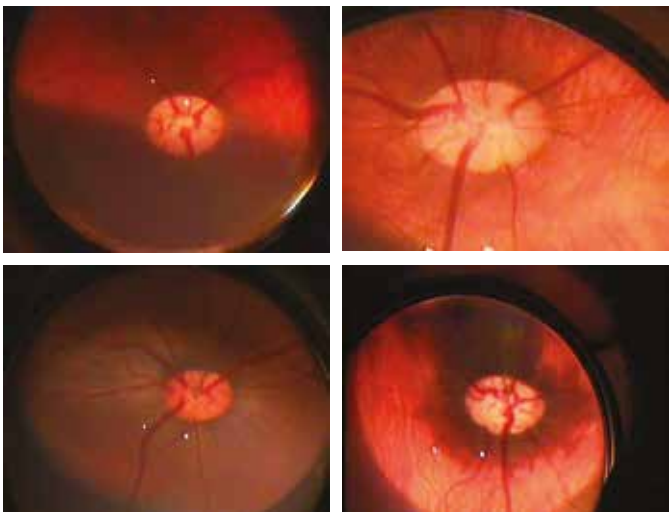


Figure 15: persistent hyaloid artery (white arrow)

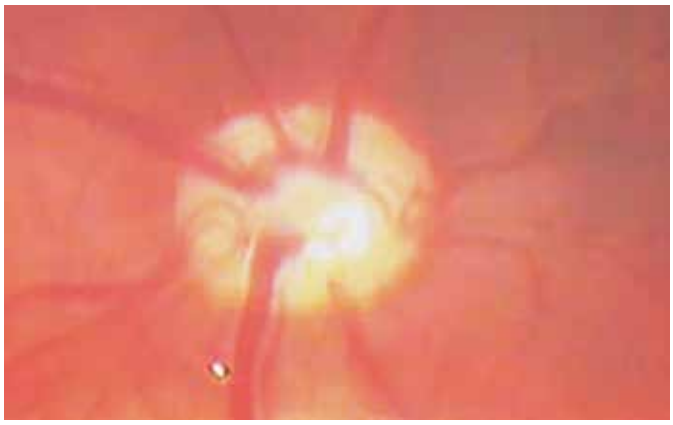
The hyaloid artery is the termination of the primitive ophthalmic artery and branches around the posterior lens capsule and continues anteriorly to anastomose with the network of vessels in the papillary membrane forming part of the tunica vasculosa lentis. The hyaloid artery and its associated vascular network provide the necessary nutrition to the developing lens in the foetus. Once aqueous humour is produced by the ciliary body and takes over nourishing the lens, the hyaloid system is no longer required and regresses. In most animals a remnant originating at the polar posterior lens capsule will continue to be evident. A small area of fibrosis on the posterior lens capsule, which represents the attachment of the hyaloids artery has been described as the Mittendorf's dot. In contrast to the dog, where it is seen as a small round opaque dot, in the minipig it features as a narrow line running along one of the Y-shaped posterior suture lines *(Picture 13 - arrow)*.

## 9. Fundus

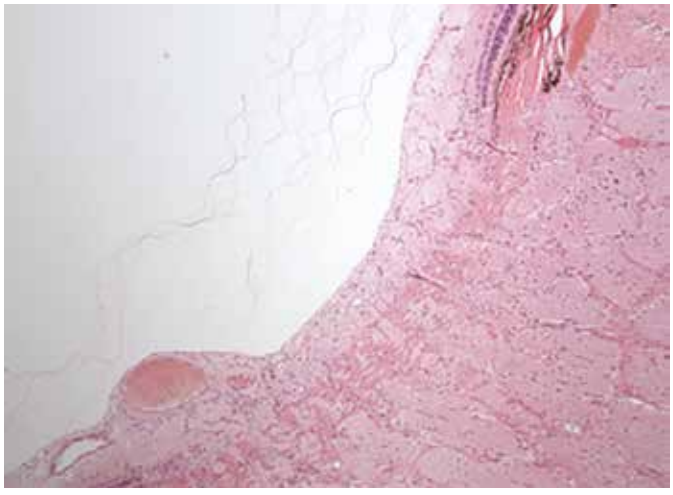


Picture 16 – 19: Normal variations in pigmentations of the retina

The fundus of the pig lacks a tapetum as seen in most other species and also does not have a visible macula like Primates. As mentioned with the iris, the retina has also got variable pigmentation due to the minipig's pigmented ancestors. The optic disc is horizontally shaped and sharply demarcated against the surrounding retina. The minipig possesses a holangiotic retina with direct blood supply to the inner neurosensory retina. Up to 10 arterioles branch dichotomously from the optic disc into the periphery, of which three to four are more prominent. Characteristic for the minipig is the commonly observed deep cup of the central part of the optic nerve head *(Picture 20 & 21)*. The deep cup of the optic disc can be a normal feature in the minipig and seems not to be associated with a compromise of vision or other ocular abnormalities. It must not be mistaken for cupping of the optic disc as is often observed in animals with glaucoma. In glaucoma, the raised intraocular pressure on the relatively weak lamina cribrosa will lead to optic nerve fibres exiting the globe and allowing the optic nerve head to bow outwards.

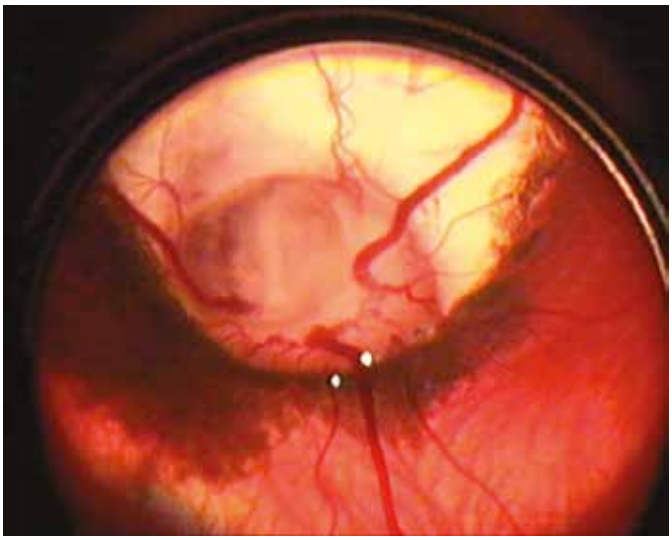


Picture 20: optic disc showing the deep cup often observed in the minipig



Picture 21: cross section disc showing the deep cup of the optic disc

Picture 22: Optic disc coloboma



Picture 23: Retinal coloboma involving the optic disc at a typical 6 o'clock position.

As mentioned earlier, ocular colobomas occur when the embryonic ventral fissure of the optic stalk and cup fails to fuse. If the most proximal portion of the optic stalk fails to close, this will lead to a coloboma of the optic disc. Optic disc or retinal colobomas have also been described in miniature swine [9] and the Yucatan micropig [10].

## References


1. Moore C.P., Whitley R.D.: Ophthalmic diseases of small domestic ruminants. Vet.Clin.North Am. Large Anim.Pract. 6,641-665, 1984
2. Linton L.L., Collins B.K.: Entropion repair in a Vietnamese pot bellied pig. J. Small Anim. Exotic Anim. Med. 2, 124-127, 1993
3. Brightman A.H., Everitt J., Bevier G.: Epibulbar solid dermoid choristoma in a pig. Vet. Pathol. 22,292-294, 1984.
4. Barkyomb S.D., Leipold H.W.: Nature and cause of bilateral ocular dermoids in Hereford cattle. Vet. Pathol. 21,316-324, 1984.
5. Barnett K.C., Knight G.C.: Persistent pupillary membrane and associated defects in the basenji. Vet.Rec. 85,242-249,1969.
6. Cook C.S.: Embryogenesis of congenital eye malformations. Vet.Comp.Ophthalmol. 5,109-123,1995.
7. Martin C.L., Leipold H.: Aphakia and multiple ocular defects in Saint Bernard puppies. Vet.Med.Sm.Anim.Clin. 69,448-453, 1974.
8. Eagle R., Spencer W.: Lens. In: Spencer W, ed. Ophthalmic Pathology, 4th ed. Philadelphia, WB Saunders. 372-427, 1996
9. Rubin L.F.: Atlas of Veterinary Ophthalmoscopy. Philadelphia: Lea & Febiger,1974.
10. Saint-Macary G., Berthoux C.: Ophthalmic observations in the young Yucatan micropig. Lab.Anim.Sci. 44,334-337,1994.