Ocular, Orbital and Periorbital Neoplastic Conditions of the Horse.

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Primary neoplasia of the eyelids is common in horses even though the range of disorders is relatively narrow. There are published case reports on neoplastic disorders for almost every ocular structure even though there are relatively few specific tumour types. For example squamous cell carcinoma can affect the eyelids (palpebral carcinoma), the conjunctiva (conjunctival carcinoma), and the cornea (in situ carcinoma). Likewise, melanoma can occur in the eyelids (Rebhun, 1998), the iris (uveal melanoma) and in the retina. Whilst then commonest periorbital tumour of all is undoubtedly then sarcoid (in its various forms) this condition is not considered in this paper.

When faced with a suspected neoplastic disorder the clinician needs to appreciate the range of diagnostic possibilities and a logical approach to the case will usually provide enough information to give the owner sensible evidence based information upon which to make decisions. Abnormal tissues should be submitted for histopathology as the clinical appearance, although helpful, is not necessarily diagnostic. Many of the tumours that occur in and around the eye have distinctive histopathology but some are more complicated. The availability of specific immunohistochemical pathology techniques have enabled a much greater accuracy of diagnosis for all rumour types. For example the case series of orbital paraganglioma cases described by Meisner et.al, (2009) and the malignant neuroectodermal tumour (retinoblastoma) described by Knottenbelt, Roberts and Hetzel (2007) relied heavily for diagnoses on meticulous use of immunohistochemical staining.

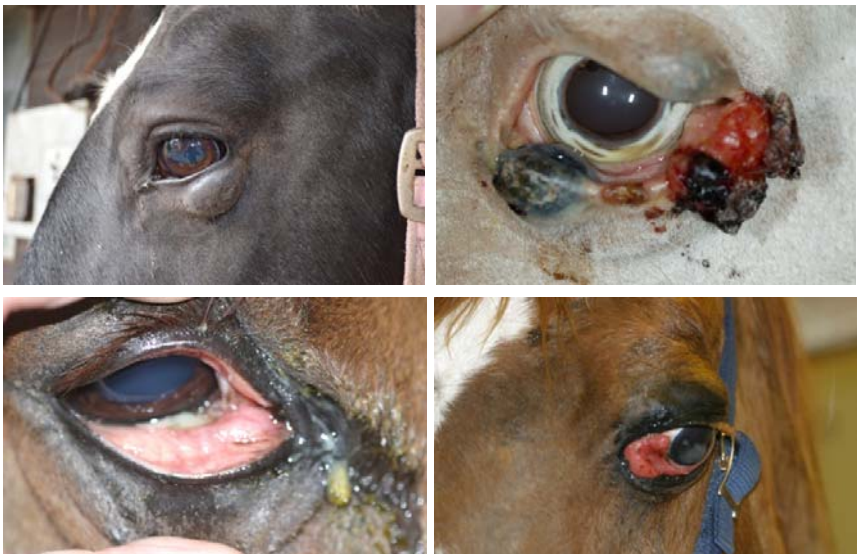


Figure 1: Top left: Palpebral mast cell tumour. Top right: Multiple tumours including melanoma, sarcoid and carcinoma (horse was not called "Lucky"!) Bottom Left: Orbital and conjunctival carcinoma Bottom Right: Extra-adrenal paraganglioma causing exophthalmos and resulting in carcinoma of the chronically exposed conjunctiva.

Less commonly, secondary neoplasia, usually lymphoma, may infiltrate the eyelids or the orbit – secondary tumours in the eye itself are extremely rare. These cases should be differentiated from other causes of swollen eyelids or altered glob position. Whilst primary neoplasia of the eyelids is usually unilateral, secondary neoplasia is probably more likely to be bilateral.

Many of the tumour conditions are easily mistaken for other physical or infectious conditions (see Figure 2) and it is matter of regret that delays in diagnosis are often enough to reduce the prognosis significantly. There are also plentiful tumour like conditions that affect the eyelid and eyelid, the orbit and the eye itself. These include viral papilloma of the eyelid, foreign body and conjunctival infections,, trauma and some cystic conditions of the glands of the eyelids. Additionally, treatment and prognosis for the various tumours varies widely and so it is important to firstly establish the diagnosis.

Figure 2: The initial presentation for ocular or periocular / orbital neoplastic disease can be misleading. Eyelid swelling, conjunctival edema / exophthalmos and haemolacrimation (top 3 pictures from left to right respectively) can commonly be mistaken for trauma. The characteristic discharge associated with conjunctival squamous cell carcinoma (bottom middle) can be easily (and commonly is) mistaken for "infection". Top left: Mast cell tumour involving the orbit. Top middle: Malignant lacrimal gland carcinoma. Right: Undifferentiated conjunctival carcinoma with orbital bone destruction. Bottom left: Mastocytoma of the conjunctiva of the upper lid causing firm, non-edematous swelling. Bottom right: Conjunctival squamous cell carcinoma - note the 'characteristic ocular discharge.

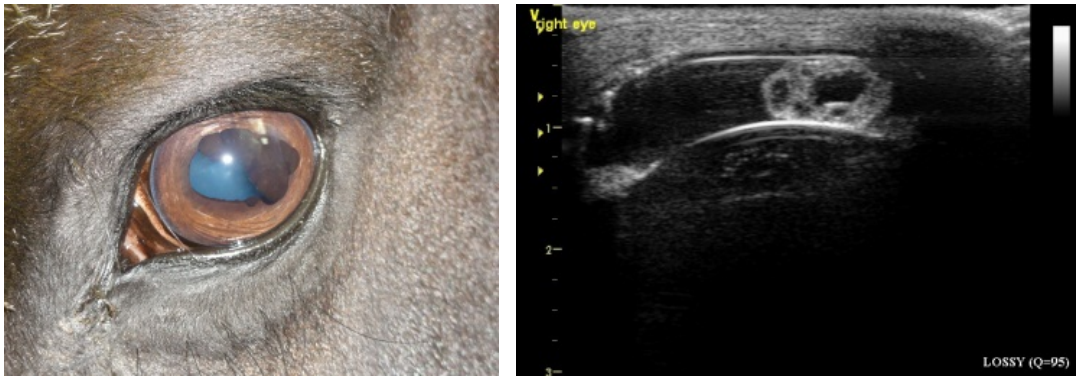


Figure 3: Cystic granulae iridica can be mistaken for melanoma but ultrasound is an effective diagnostic aid.

Orbital tumours:
Tumours in the orbit itself are a serious diagnostic and therapeutic challenge. Diagnosis is constrained by the lack of effective simple imaging methods and therapy is a challenge because of the inaccessibility of the retrobulbar structures. The advent of better quality ultrasound facility and in particular MRI and CT diagnostics has improved the imaging of the orbital structures enormously and we are getting better at identifying the various neoplastic and non-neoplastic space occupying masses in the equine orbit. The commonest presenting sign would (as might reasonably be expected) usually be exophthalmos. A wide variety of tumours have been identified in the orbit of horses (Lavach and Severin, 1977) including neuroendocrine tumours (Basher et al., 1997; Bistner et al., 1983); Goodhead et al., 1997; Meisner et al., 2009) , lymphoma (Rhebun and Bertone, 1984), osteoma (Richardson and Acland, 1983) and melanoma (Sweeney and Beech, 1983).

The clinical evidence of retrobulbar masses is usually restricted to an insidious onset of progressive unilateral exophthalmos. Distension of the supraorbital fossa may be present but this is not always the case. Vision may be normal but in some cases there are visual compromises and this may be due to stretching of the optic nerve or to direct involvement of the nerve. Attempts to retropulse the globe are usually met with resistance and the nictitans may not protrude when this is attempted, this giving the impression of a nictitans problem. In the authors experience this is a common initial clinical finding – even before obvious exophthalmos is present. Once the eye is markedly exophthalmic chemosis, exposure conjunctivitis and keratitis and possibly even carcinoma development (see Figure 1) can occur. Concurrent pressure induced damage to the orbital bone can extend to the point of bony destruction and sinus involvement. In a few cases in the authors experience, the frontal lobes of the cerebral cortex can be involved.

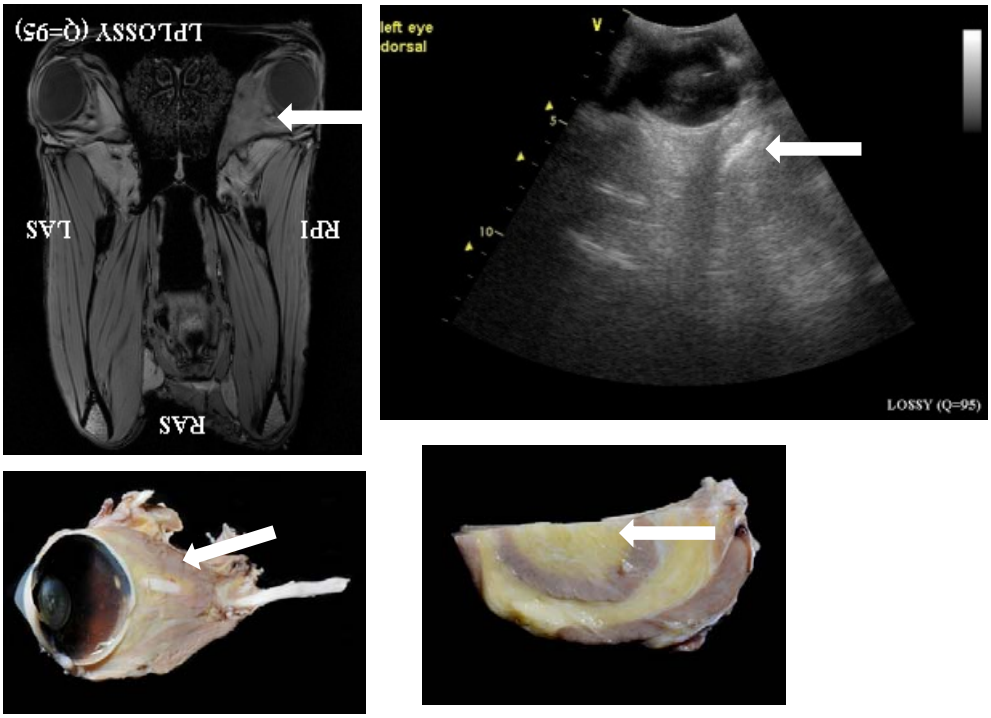


Figure 4: This 14 year old mare had a previous history of removal of the nictitans for a 'localised' carcinoma. The histology report noted tumour extension into the lymphatics at the excisional margin. !4 months later the horse was presented with a widely dilated pupil, blindness, retinal vascular attenuation and disc atrophy with a normal intraocular pressure. MRI (left) CT and ultrasound (right) identified a dense mass in the retrobulbar region

(ARROWS) that was later identified as carcinoma. It is clear that excision of the nictitans is not always a "trivial" surgery.

Orbital extensions of ocular or adnexal carcinoma or hemangiosarcoma can occur and can result in at least some of the signs associated with orbital primary neoplasia (Bolton et al 1990).(Figure 2).

All carry a guarded prognosis. Since most of the tumours in this region are presented in mature or older horses and since most are presented late the justification for surgical intervention is bound to be constrained. There are major hazard in dealing with retrobulbar tumours of any sort but many of course are likely to be irresolvable anyway. Since most of these cases have a visual eye and are pain free, unless early diagnoses and specialist surgical facilities and expertise are available, a benign neglect approach can probably be justified.

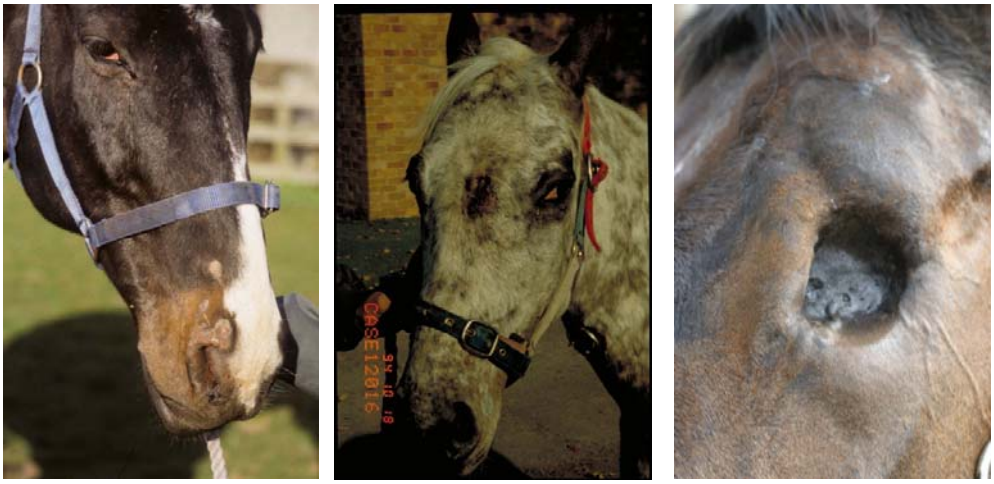


Figure 5: LEFT: A horse presented with headshaking signs and facial neuralgia that had a lacrimal gland carcinoma which had invaded into the caudal maxillary sinus. Middle: A sinus carcinoma invaded the orbit and caused prominent exopthamlmos. A lacrimal gland carcinoma was removed via exenteration surgery 5 years previously but there was gradual expansion of residual tumour over the previous 4 years. Histology confirmed the same tumour type. Metastatic tumours were present in te guttural pouch and lungs.

Protrusion of globe and supraorbital fossae can be caused by:

- Lacrimal gland carcinoma: This is a rare tumour but carries a poor long term prognosis in te authors experience. Diagnosis is usually made only following exenteration since biopsy is extremely problematic even with sophisticated imaging guidance. The recurrences within the orbit are only part of the problem since secondary metastatic spread to the local retropharyngeal lymph nodes and lungs seems to be the inevitable outcome. However, the rate of tumour expansion (both in the primary tumour(s) and the post-surgical recurrence is very slow so the short term outlook appears rather better than the long term one. This suggests that it may be in fact better to leave the s alone (assuming a diagnosis can be made!) or to subject the tumour to external beam radiation. There are no literature reports of this tumour type
    - Melanoma: Retrobulbar melanoma is possibly one of the commoner neoplastic causes of exophthalmos but is still very rare (Sweeney et al, 1983).
    - Extra-adrenal paraganglioma (Meisner et al, 2009)
    - Sinus carcinoma / adenocarcinoma (extension from the caudal or frontal maxillary sinus)
    - Ethmoid haematoma (extension from the nasal cavity)

- Fibroma (Colitz et al., 2000)

Non-neoplastic conditions that result in exophthalmos and which need to be considered as part of the differential diagnosis of orbital neoplasia include, retrobulbar abscess, orbital and sinus granuloma and hydatid cyst and jugular thrombosis.

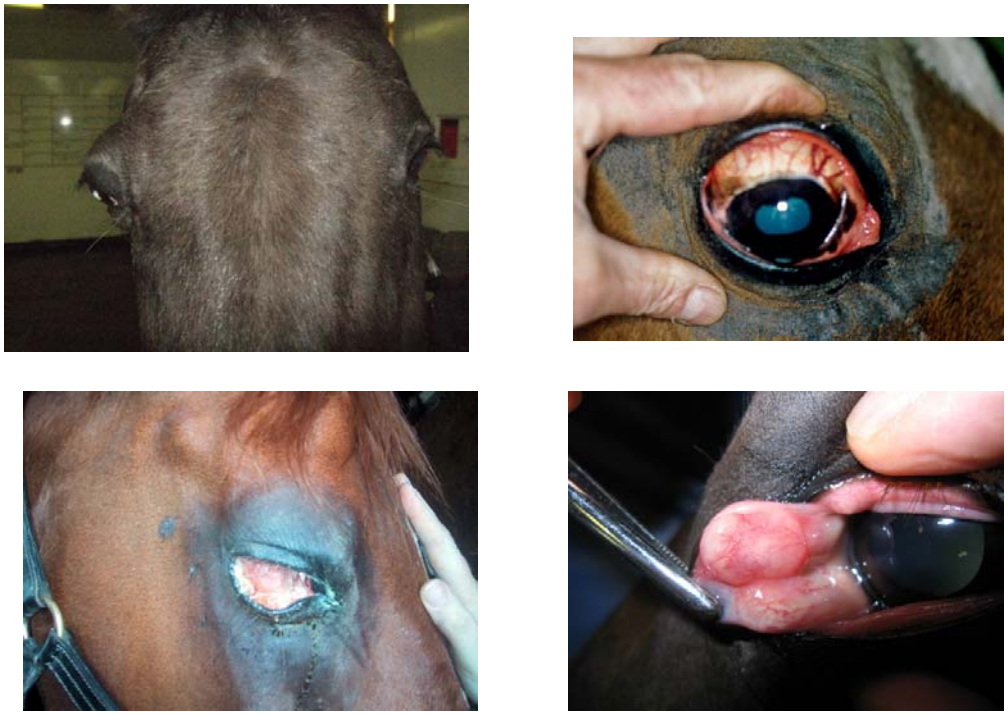


Figure 6: Top left and right: Exophthalmos is a prominent sugn of retrobulbar masses and whilst a few cases ahave visual deciits as resul, many are fully visual. Overt visible neoplasia makes diagnisis easy but often by the time it is seen the extent of the changes in the orbit are severe (bottom left). Th ebotom right picture shows an example of co9ncjunctival lymphoma. This case showed only very subtle changes in the position of the nictitansnoticed by a very astute owner. There were 8 similar sall localised tumours within the orbit. All were removed and no recurrence was enocountered over 9 years. However 3 similar tumours were reoved from the contraltareka eye sme 4 years later.

Investigative procedures for orbital retrobulbar neoplasms should include ultrasonography, radiography CT and MRI where available) and of course a careful assessment of the horse itself and the eye. Although scintigraphy has been suggested as an effective diagnostic tool, in the authors experience its lack of specificity does not compensate for its sensitivity! There is strong tendency in practice to ignore the horse and concentrate on the immediate and most obvious sign! For example a fetid nasal odour and a sero-purrulent unilateral nasal discharge may be present and unless this is noticed valuable diagnostic information lost. Similarly examination of the chest ad endoscopy of the upper airways may help a great deal in establishing the totality of the symptoms that might relate to the primary presenting problem of exophthalmos. Careful endoscopic and radiographic examination of the nasal cavity (and the ethmoid region in particular) and the paranasal sinuses is indicated. The proximity of the ethmoid region and the caudal maxillary sinus means that tumours in these sites will almost inevitably involve the orbit and result in significant exophthalmos. The major draining lymph nodes of the orbital structures are not palpable externally but are visible within the guttural pouches and so they should be examined endoscopically. MRI and CT imaging is becoming more routinely available for the head of horses at least! The imaging value of these is incredible and every horse

with a retrobulbar “problem” should probably be subjected to the se immediately since this will usually identify the extent and location of the problem and in many cases even the likely nature of the mass. Additional diagnostic aids include fine needle aspiration or hollow needle biopsy under ultrasonographic guidance.

Neoplastic masses that can be found in the orbit include primary tumours of the lacrimal glands (lacrimal gland adenocarcinoma) or lymphatic tissue (lymphoma or lymphosarcoma), extra-adrenal paraganglioma (Miesner et al., 2009), hemangiosarcoma, melanoma and orbital extension of tumours from the eye, eyelids or conjunctiva (usually either carcinoma or lymphoma) and extensions from tumours of the nasal cavity or paranasal sinuses (adenocarcinoma, squamous cell carcinoma or progressive ethmoid haematoma). The major presenting sign is usually exophthalmos without any significant buphthalmos or any effect on the sight of the eye. Later in the development there may however be a strabismus and some progressive deterioration in the vision arising from optic nerve involvement and atrophy. The diagnosis of retrobulbar tumours is difficult. Distortion of the local anatomy, chemosis (edema of the conjunctiva) and haemorrhage from the conjunctiva are easily seen by owners and so these may be the first presenting complaints.

Treatment of tumours in the orbit should be viewed with some trepidation and, unless the horse is painful or is otherwise clinically hampered by the condition, it is probably wise to practice benign neglect until there is no alternative to surgery. Enucleation is invariably required. Access to the retrobulbar tissues is extremely difficult. Consideration of the tumour type involved will dictate the likely “best” approach to treatment. In general however, it might be better to leave an exophthalmic non-painful, visual eye until there is evidence of some compromise. However, taking a contrary view, typically of neoplastic disease, it is usually better to treat a tumour early. This aspect was highlighted by Miesner et al. (2009) in their series of extra-adrenal paraganglioma cases where the outlook appeared to be good for cases that were not advanced and where no local destruction had taken place. In this series the prognosis for such cases was excellent whilst in more advanced cases the outlook was poor. The author has only encountered 4 of these cases and all have had significant orbital destruction on presentation and have proven to be an impossible diagnostic challenge due to the extreme and uncontrollable haemorrhage. Although extensions from conjunctival carcinoma are rare they can be a serious cause of orbital distortion.

Payne et al., 2009 reported no significant complications and no extension of carcinoma following nictitans removal for conjunctival carcinoma but the author has encountered several cases of orbital carcinoma following prior nictitans removal. However, it is clear that direct extension to the orbit can occur (see Figure 2) and this has also been reported by *****.

Eyelid / Conjunctival tumours:

The most common eyelid tumours of adult horses include:

- [Papilloma]
- [Periocular sarcoid]
- Squamous cell carcinoma (SCC)
- Melanoma.
- Lymphoma

Less common tumours reported include:

- Adenoma / Adenocarcinoma,
- Angioma / Angiosarcoma /Haemangiosarcoma
- Basal cell carcinoma,
- Fibroma /Fibrosarcoma,
- Mast cell tumour
- Undifferentiated myxoma / carcinoma

Squamous cell carcinoma: the squamous cell carcinoma is the second most common adnexal tumour (after sarcoid). It is far more prevalent in eyelids that lack pigmentation (see figure 6). The

condition is also more prevalent in Appaloosa and Rocky Mountain spotted horses as well as Shire and Clydesdale breeds. Exposure to high levels of UV light is suggested as being a significant carcinogen.

SCC can be mistaken for several other conditions – in the case series of 24 animals with a presumptive clinical diagnosis of nictitans carcinoma by Payne et al, (2009) 16 of these 21 cases were diagnosed with carcinoma and three cases were diagnosed histologically as lymphoid hyperplasia, one as a mast cell tumour and one as a sebaceous gland adenocarcinoma.

Dugan et al, (1991) found, in series of 147 cases of adnexal and ocular squamous cell carcinoma in USA, that 28% involved the nictitans and / or the medial canthus / caruncle, and 28% involved the lateral limbal conjunctiva. They also reported that the location was a significant prognostic factor in so far as those tumours that involved then eyelid and the orbit carried the worst prognosis. Payne et al., 2009, reported that there was no recurrence of carcinoma following third eyelid resection in a series of 24 cases in UK, this implying that the outlook was excellent. However Dugan et al (1991) and Rebhun, 1998) have suggested otherwise in other cases. Most ophthalmic surgeons are wary of carcinoma at best and it is clear that timely aggressive treatment following early diagnosis is by far the best approach.

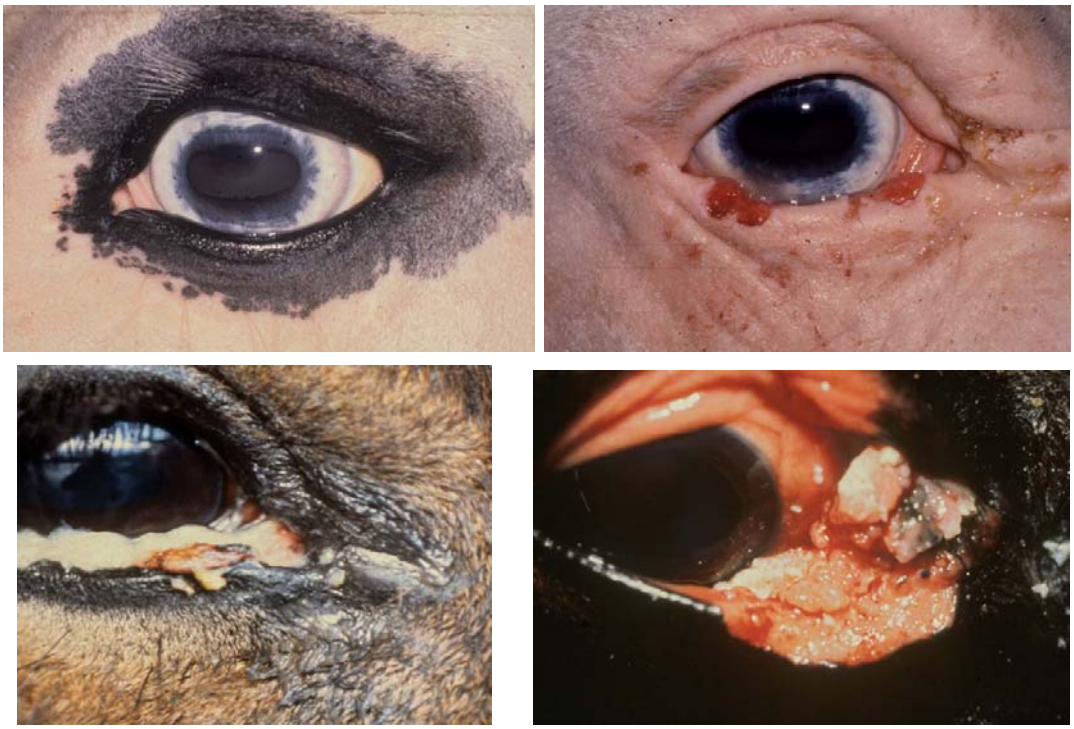


Figure 7: Palpebral AND conjunctival carcinoma is commonest in non -pigmented eyelids and conjunctiva (particularly in those affecting the lateral limbal conjunctiva and the third eyelid). The top two pictures (*courtesy Shelia Crispin*) show the two eyes of the same horse. Carcinoma is limited to the non-pigmented eyelid and the lower lid is typically more often affected). However pigmented eyelids can be affected – the bottom left picture shows a squamous papilloma that was in an early carcinoma transforming state and the destructive carcinoma shown in the right bottom picture also occurred in densely pigmented eyelid.

Whilst surgical removal, cryosurgery, local chemotherapy in combinations can be effective, radiation is clearly the gold standard treatment modality with over 80% of eyelid and conjunctival carcinoma

being resolved in a series described by Theon, (1998). Surgical resection or cryonecrosis are sometimes feasible although the need to remove a safe margin an result in significant tissue deficits that have to be reconstructed. Concurrent chemotherapy with intralesional cisplatin, topical and / or intralesional 5 fluorouracil or mitomycin C will usually result in a good outcome. Radiation is by far the best approach however; this by can by interstitial brachytherapy, plesiotherapy or by external beam teletherapy. The options for treatment will vary widely according to facilities but usually a strategy can be constructed that will have reasonable chance of success.

Perhaps the most challenging type of squamous cell carcinoma is the intraepithelial *(in situ*) corneal carcinoma. This can develop in several ways. Probably the commonest form is that which extends directly from limbal (usually lateral) conjunctival carcinoma. Invasion of the cornea can take place early or it can be a later development. The cardinal features of this form are the high differentiation of the tumour with prominent keratin pearl formation. Oftentimes there is an accumulation of keratin under ten carcinomatous epithelium giving the surface of the eye a raised outline and a yellow, pale appearance. Many cases have deeper ('basement membrane') penetrations so that removal by surgical superficial keratectomy is much more difficult and more prone to recurrence. There is invariably prominent vascularisation. (see Figure 7).

Figure 8: Conjunctival carcinoma affecting the nictitans and ventral palpebral conjunctiva (top left), the lateral limbal conjunctiva (top right), the cornea (well differentiated in situ carcinoma) (bottom left) and a seeded corneal in situ carcinoma that probably developed from the small but highly malignant carcinoma affecting the free margin of the nictitans)

Carcinoma can also develop directly on the corneal epithelium without any primary limbal / conjunctival tumour. This type is much thinner usually and the cells are less differentiated. However, they are usually very slow growing and the presenting clinical sign is usually a highly vascularised plaque of grey tissue lying on a variable area of the cornea. This type usually remains intraepithelial making surgical removal more practical. Adjunctive plesiotherapy using strontium pencil / wand or topical 1% 5 fluorouracil or 0.2 % mitomycin C will significantly improve the prognosis. Mitomycin C has significant advantages in reducing the amount of fibrosis following resection and therefore seems to improve corneal clarity.

Direct seeding of the cornea can also take place as result of corneal contact with an eyelid carcinoma. (see figure 7). This is rare but it is important that the clinician examine the whole eye (and indeed the other eye!!) to check for any possible site of carcinoma involvement. Failure to make a diagnosis and treat the tumour in timely and aggressive fashion can be catastrophic. Whilst most palpebral, conjunctival and corneal carcinoma cases give the clinician adequate time to consider the options many do ultimately become severe (see figure 7).

Melanoma

Melanomas are common in grey horses and rare in other colours of horse. They usually present as nodules in the eyelid and often involve the eyelid margin (Figure 8). They rarely ulcerate and are most often of a benign slow growing nature.

The vast majority of these (including those that occur within the globe) are benign and their effects are limited to their space occupying properties. Most pathologists view the “normal” melanoma as an aggregation of normal melanocytic cells without any truly neoplastic properties”. Any non-pigmented (pink or grey) appearance within the tumour mass should however be viewed with considerable suspicion, as a few are highly malignant (Moore et al., 2000).

Melanomas are commonly found as nodules in the eyelids and can involve orbital tissues as well. In the former case they are obvious to visual inspection but in the latter a non-buphthalmic exophthalmos may be suggestive in grey horses. Both of these forms are exceedingly rare in colours other than grey. Matthews and Crispin (1987) noted that melanoma was the commonest intraocular tumour of the horse but in any case they are still rare at this site.

The pathological definition of melanomas has been the source of considerable debate for many years. Many intraocular melanomas are primary lesions (Barnett and Platt, 1990). Although these may be potentially malignant it seems from literature reports that this is unlikely and that other lesions occurring on a horse might merely be co-incidental. The pathological appearance of the melanomas occurring in the eye are consistently different from those elsewhere. Their low mitotic index and slow expansive growth patterns are not suggestive of a high tendency to malignancy. The growth pattern also tends to be by expansion rather than infiltration. The accumulation of melanin in the cells is irregular and this may explain the slightly bluish colour that is typical of some of these. The condition tends to be regarded as a totally benign condition that affects almost every grey horse. While the physical size of melanomas can be limiting of function (such as in the parotid region or perineum) by far the majority certainly appear to have little or no tendency to malignancy. Nevertheless an occasional lesion will become very aggressive and so it is unwise to assume that everyone will a) be benign and b) responsive to surgical removal with no secondary effects.

Palpebral melanoma is relatively common in grey horses. Most are rather benign in nature, at least at first and it is certainly true that melanomas in non-grey horses and those that develop in horses under 12 years of age have a more aggressive pathological behaviour. It is also true to say, in my

experience at least, that almost all start out benign and almost all finish as malignant tumours at some stage – it's just the time scale that varies. The clinician needs to be able to answer a client's query as to why treatment is being avoided / postponed.

Single reports of intraocular involvement have been reported sporadically over many years. Barnett and Platt (1990) reviewed the reported clinical features of cases of intraocular melanoma. All those with a colour record occurred in predominately grey horses. The six "new" cases of iris melanoma reported by Barnett and Platt (1990) all occurred in mature horses. Four out of the six were grey and two others were roan and Palomino. It is therefore reasonable to assume that the condition is extremely unlikely in a bay or darkly coloured horse. No reported cases suggest that the slowly expanding intraocular lesions are painful and furthermore they do not appear to cause any secondary effects such as glaucoma or uveitis. Several reports describe intraocular melanomas as being of a grey-blue colour and most are encountered in the nasal quadrants of the iris and ciliary body. Malignant eyelid melanomas are however invariably secondary and so may not be of serious concern when compared to the involvement of other organs.

A few melanomas occur in the eye itself. They are most often located in the nasal quadrants at the base of the iris – often they have a blue-black appearance rather than pure black (this may distinguish them from iris cysts and granulae irridica (see Figure 3) that characteristically have a very black or dark brown appearance). They may be bilateral (Matthews and Barry, 1987) (Figure 10).

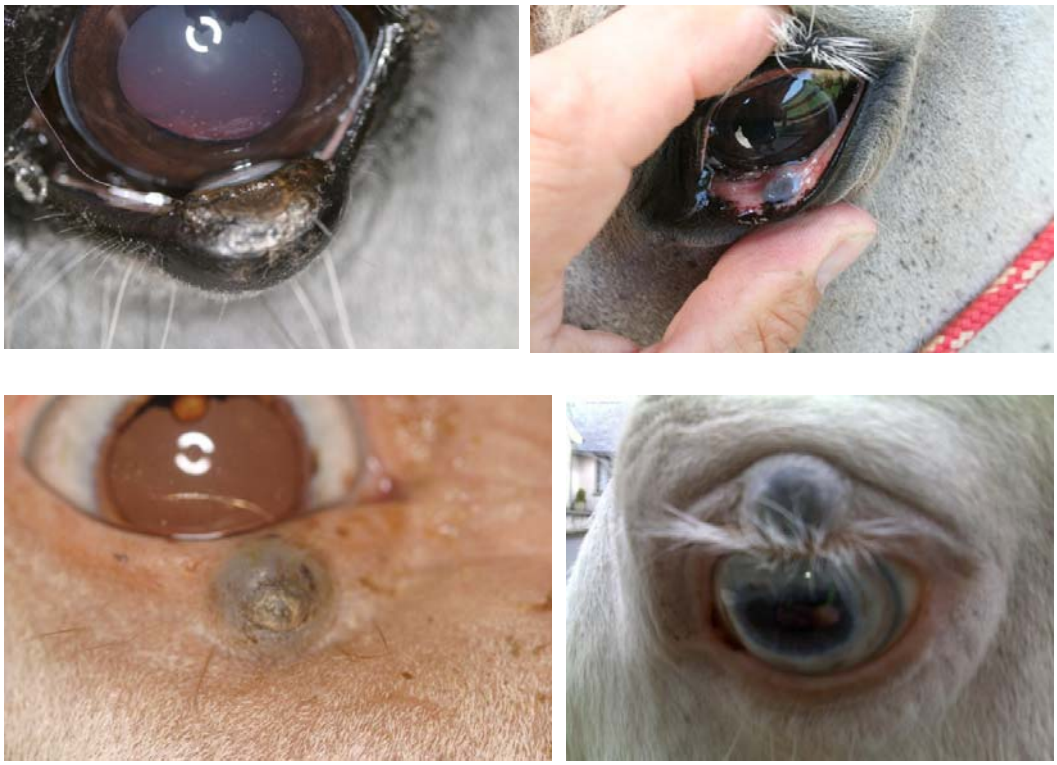


Figure 9: Palpebral melanoma is common in grey horses - most cause obvious eyelid swelling / nodules (top left) but some are more difficult to spot (top right)! Upper eyelid tumours are always more problematic from a surgical perspective of course. Melanomas in non-grey horses have a higher tendency to malignancy and so should be removed as soon as they are noticed. Both of these cases presented significant surgical challenges and both were of a highly malignant form.

Within the eye iris cysts and uveal stromal cysts are commonly mistakenly diagnosed as melanomas and hyperplastic granula iridica can also give the impression of being a melanomatous mass. Uveal and iris cysts, which are commonest in dark brown or bay horses, may be diagnosed as melanomas. Iris stromal cysts commonly occur in pale blue and heterochromic irises but the clinical features of these should preclude confusion with melanomas. Individual horses may have very prominent granula iridica and it should be remembered that they might normally appear on both the inferior and superior pupillary margins. There is no reported case of a melanoma developing from hyperplastic granula iridica even though the latter can become very large (often enough to limit vision when miosis is strong). There is a strong age related prevalence of melanoma in the horse but eye lesions appear to be somewhat more likely in the younger mature horse. Most reported lesions involve horses around 6 – 10 years. Nevertheless older horses have a relatively high incidence of palpebral melanoma.

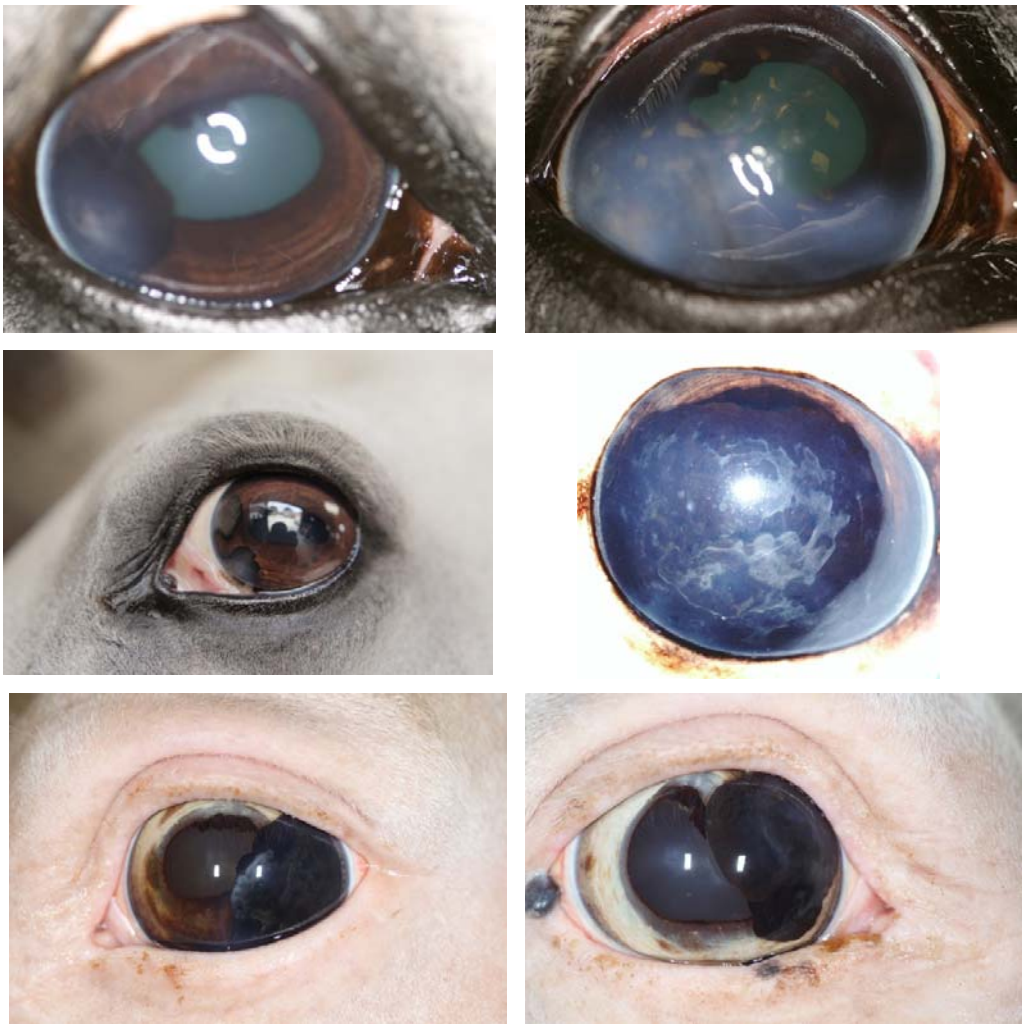


Figure 10: Iridal melanoma occurs with some frequency. They are usually slow growing and benign. They do not have the characteristics of metastatic tumours and do not seem to become malignant. However, they do progress. The pictures top left and right show the same eye 9 months apart. On the second occasion scanning of the eye showed that the tumour had expanded into the posterior segment and the horse was visually compromised. The middle left picture shows small very static melanomas that have remained visually and ultrasonographically the same for 7 years. The question to answer is "Is this a nevus or a

melanoma?" – we will only know that at some point in the future but meantime we monitor carefully! The picture middle right shows an advanced melanoma that caused blindness by its space occupying nature. The tumour involved the majority of the posterior segment but somewhat remarkably this was the only tumour we could identify on this horse. The bottom pictures show the two eyes of a cremello pony gelding. Bilateral tumours (and incidentally, concurrent palpebral melanomas) do occur on cream or colour diluted horses.

Most cases involving the eyelid can justifiably be left alone – they may not alter significantly for many years but must be professionally checked at regular intervals. Checking such cases should involve careful assessment of the parotid salivary gland and parotid and retropharyngeal lymph nodes (often best checked by endoscopic examination of the guttural pouches). However, on the premise that "they are only going to get bigger, more difficult and more dangerous", it is probably wider to remove any palpebral melanoma as soon as it is obvious.

Surgical excision is a realistic proposition provided that the tumour can be removed without significant skin damage, eyelid functional compromise or scarring. This usually involves removal of a small portion of the eyelid margin and scrupulous reconstructive surgery to preclude the complications arising from poor eyelid function. Cryonecrosis of melanoma lesions is a fast but rarely effective method of treatment. Lesions that are ulcerated and which bleed significantly can be managed by careful cryosurgery. On the eyelids however, this is probably not advisable.

Oral cimetidine therapy has been reported to be successful in some cases of melanoma but its value in palpebral and ocular melanoma is not reported independently. Cimetidine acts through its effects on T Killer cells and so may be expected to have some effect. However, the results are very variable with some reports finding no benefit but as it is relatively simple it is at least an option. Cimetidine is administered by mouth at 3.5 mg/kg (q 12h) or 7.5 mg / kg (q 24h). Treatment is continued for up top 6 weeks but if no change is detected by 3 weeks there is probably little point in continuing. If however, there is a response then the treatment should continue until 3 weeks after there is no further improvement. The value of long-term treatment is uncertain but we have found that pulse treatments applied for 4 weeks every 8 weeks is capable of maintaining the improvement. The results of this protocol are almost impossible to assess without a more detailed trial that badly needs to be done! The author has not yet encountered any significant improvement although it is fair to say that a few owners have felt that at least the tumours have become static during the treatment period.

The value of cisplatin is also uncertain but we have had considerable success with treatment of melanomas at other sites using a cisplatin / almond oil emulsion containing 1 mg cisplatin per ml. The material can be infiltrated into the lesion at fortnightly intervals. We have no specific experience of its use on eyelid melanoma but it would seem likely to be worth a try. The emulsion appears to have no harmful or painful effects on the eye (when we have used it for other palpebral tumours).

Recent developments in the management of human malignant melanoma using X-irradiated autogenous melanoma cells suggest that there may be some expectation of an immunological method of treatment. The reports of the use of this method in horses are preliminary at present (Jeglum 1997) but there does appear to be some value in the process.

Radiation treatment has a surprisingly poor effect on melanoma tumours. High doses of gamma radiation delivered via a linear iridium ^{192} source had no material effect on one case treated at Liverpool University. Similarly beta radiation also had no effect when applied to two individual lesions on the lower lids of a horse.

Mastocytoma / Mast Cell Tumour

Mast cell tumours occur rarely in the eyelids and conjunctiva where they are often confused with eosinophilic granulomas and even conjunctival habronemiasis. The cardinal features of the palpebral

and conjunctival mastocytoma include a slow growth rate, an ill-defined outline and localised tissue invasion. Careful direct examination may confirm the presence of “yellow kunkers” – these are hard, gritty, yellow/beige granules that comprise mast cells and eosinophils and other inflammatory debris. The main problem with mast cell tumours is that they are very difficult to diagnose histologically since the mast cells attract eosinophils and vice versa. There is considerable debate about te true nature of equine cutaneous and conjunctival mastocytosis / mast cell tumours.

A tumourous immune mediated response to migrating onchocerca or locally invading habronema larvae have been proposed as causative factors. Skilled pathological examination of biopsy samples is required.

Figure 11: Equine periocular and conjunctival mast cell tumours. Top left: A typical mast cell tumour in the lower eyelid. It is easily mistaken for several other tumour types! Tope right: A conjunctival mast cell tumour showing te prominent “kunkers”. This lesion was removed surgically and confirmed as mast cell tumour by several different pathologists upon repeated reviews. Bottom: A 14 year old Fell pony mare was presented with a non-responsive superficial corneal ulcer. Examination under the upper lid revealed an extensive mast cell tumour – note the hard yellow kunkers within the conjunctiva. This proved to be a really big therapeutic challenge!

Mast cell tumours respond reasonably well to intralesional injection of diluted corticosteroid. However, since they often invade locally recurrence is common and a combination of surgical excision and steroid possibly with other chemotherapeutics might be advisable. There arre very few reports and even fewer case series relating to mast cell tumour s in horses and none of these refer to the eye region specifically. The author has however encountered 28 cases of such tumours and none has proven to be malignant nor has any tumour recurred following surgical resection and concurrent chemotherapy – usually restricted to distilled water and corticosteroid.

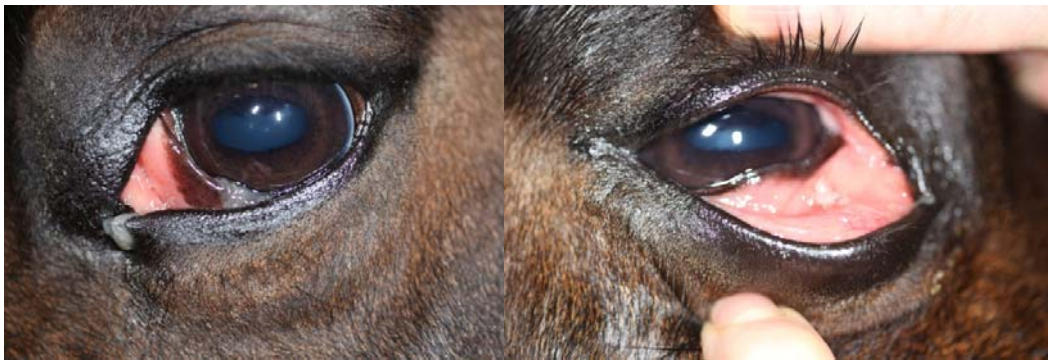
Adnexal Lymphoma / lymphosarcoma

Although the large majority of ocular lymphoma and lymphosarcoma lesions are secondary to others elsewhere (Murphy et al, 1989) it has been described as am primary site. (Glaze et al. 1990). The majority of reported cases (including those reported by Rebhun and Bertone, 1984) had other signs attributable to the systemic effects of lymphosarcoma and so the relatively benign eye lesions might be regarded as an incidental.

A biopsy is indicated early in the development of the disease but it is equally important to establish whether the lesion is primary (and therefore possibly treatable) or secondary (and therefore probably not relevant). This can be very difficult especially if the primary lesions are internal. The systemic effects may be detectable but usually there are few overt clinical features of lymphosarcoma that will confirm the diagnosis. Recurrent undulating fever and periodic or persistently elevated serum calcium, sometimes with a low globulin concentration can help with the diagnosis. Where the lesion can be demonstrated to be primary (such as the case described by Glaze et al. 1990) the affected tissue can be widely excised. This may only be practicable in certain anatomical locations such as the nictitans.

Prolapse of the orbital fat is the commonest mistaken diagnosis for this condition. There are clearly major problems in this event since one condition is totally benign and the other can be extremely dangerous if left.

Figure 12: Periocular lymphoma occurs in several different forms and can be unilateral or bilateral. The conjunctival nodular form is shown in Figure 5. They are usually presented with some displacement of the nictitans with a firm nodular conjunctival or sub-conjunctival lesion (top left) and occasionally with more generalised concurrent conjunctival inflammation. There is a focal eyelid form that presents with a single or a series of well defined nodules in ten lower lid in particular (top right). The bottom two pictures show the two eyes of the same horse which had extensive orbital lymphoma. Firm nodular swellings involved the conjunctiva of both eyes and extended deeply into the orbit on both sides. Notice the difference in pupil diameter – the left eye had little menace response but a positive direct and consensual reflex. Following a surgical removal of the tumours the eyes settled extremely well but over the following 12 weeks the case deteriorated systemically with all the signs of disseminated lymphoma and tumour cells were found predominately in the hear muscles.



<u>Conjunctival / Corneal hemangiosarcoma</u>:
Hemangiosarcoma occurs occasionally in the conjunctiva (both palpebral and bulbar / nictitans (Bolton et al, 1990). The tumours can be isolated and small or can be aggressive and malignant. The author has encountered 2 cases of metastatic hemangiosarcoma (presumed) in the orbit and cornea, The large majority however appear to be spontaneous and localised in the conjunctiva. although they can take on an aggressive and invasive pathologic behaviour.

The diagnosis is achieved by biopsy; it is important to recognise that a purely clinical impression of a red/ purple highly vascularised mass in the conjunctiva may in fact not be a hemangiosarcoma. Squamous cell carcinoma and focal lymphoma as well as some non-neoplastic masses may be very similar in appearance.

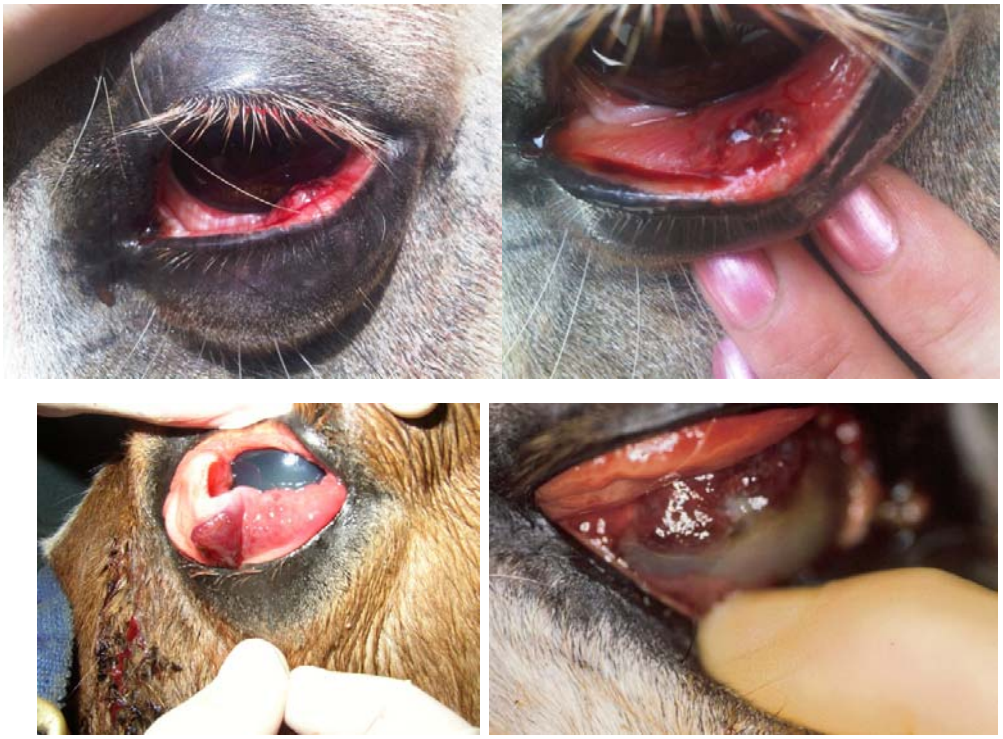


Figure 13: Hemangiosarcoma tends to affect hte conjunctiva particularly and is a cause of hemolacrimation. The bottom tight picture shows an aggressive hemangiosarcoma that invaded the cornea and anterior segment of the eye.

INTRAOCULAR TUMOURS:

The large majority of intraocular tumours are detected incidentally – some can cause obvious signs such as corneal opacity (e.g. intraocular melanoma) and some are [possibly] responsible for behavioural or visual compromises. Evidence of intraocular tumours may therefore be attributed to other more easily diagnosed conditions such as glaucoma, uveitis (corneal edema / endothelial opacity). The value of ultrasonography cannot be overstated. High frequency ultrasound

Intraocular lymphosarcoma is almost impossible to diagnose clinically – the signs are almost identical to uveal inflammation. The tumour can be bilateral or unilateral. (Rebhun and del Piero , 1998) case s that fail to respond to normal treatment for uveitis might justifiably be examined in greater detail in case the ophthalmic signs are associated with a generalised lymphoma. In reality the eye lesions may be a prominent early sign but they will not be the biggest problem the horse has!
instruments can provide really significant information both on the size, the location and the type of tumour.

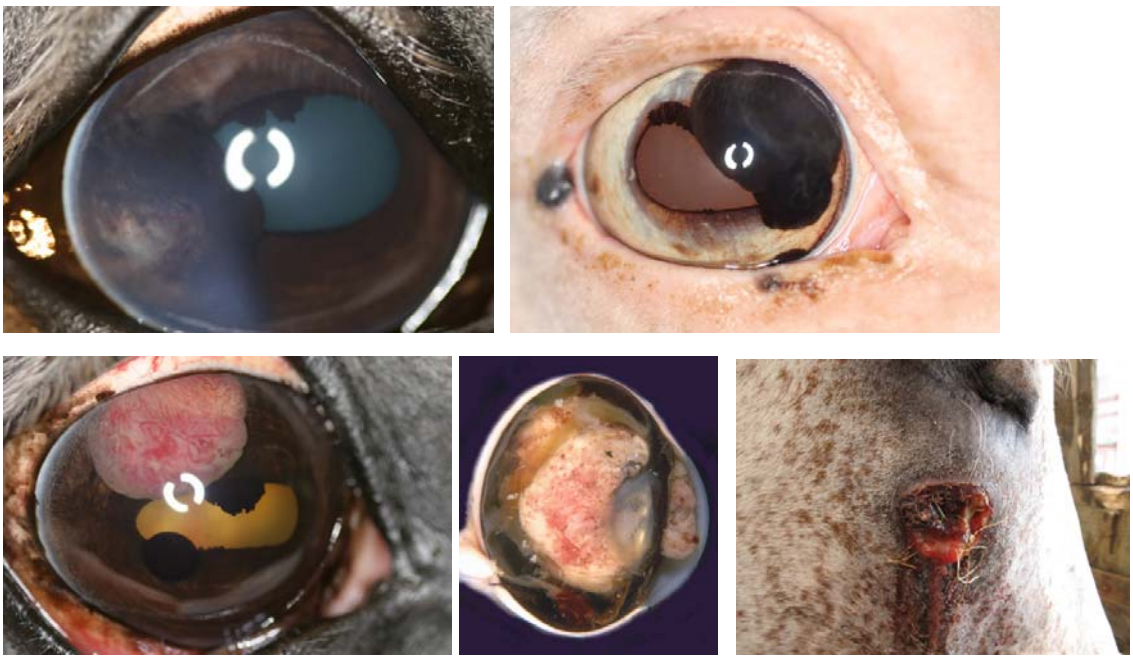


Figure 14: The melanoma (top left and right) are by far the commonest intraocular tumour type in horses. Meduloepithelioma / Retinoblastoma occurs rarely and has a distinctive appearance. Bottom: This retinoblastoma was diagnosed definitely by use of extensive immunohistochemical staining. Although no evidence of extension was detected in the surgical tissues removed during exenteration, some 6 months later the tumour erupted from te orbit and at necropsy was found to extend into the maxillary sinus and the ethmoidal region of the nasal cavity. Tumours were identified on the tricuspid valve leaflets but no others were found.

Other posterior segment tumours:

Retinal and posterior segment tumours are rare.

There some putatively neoplastic conditions affecting te retina and optic nerve head including neurofibrioma, glioma and retinal / choroidal melanoma.

Astrocytoma and proliferative optic neuropathy are encountered with some frequency (Saunders et al, 1972)). Little is known about them either in terms of their pathological behaviour or indeed their pathological nature. The few facts that are recognised include:

a) Slow growth
b) Benign pathologic behaviour
c) Little visual effect unless they involve the papilla d the optic nerve

Probably the biggest difficulty with the se is knowing what to advise at pre-purchase examination.

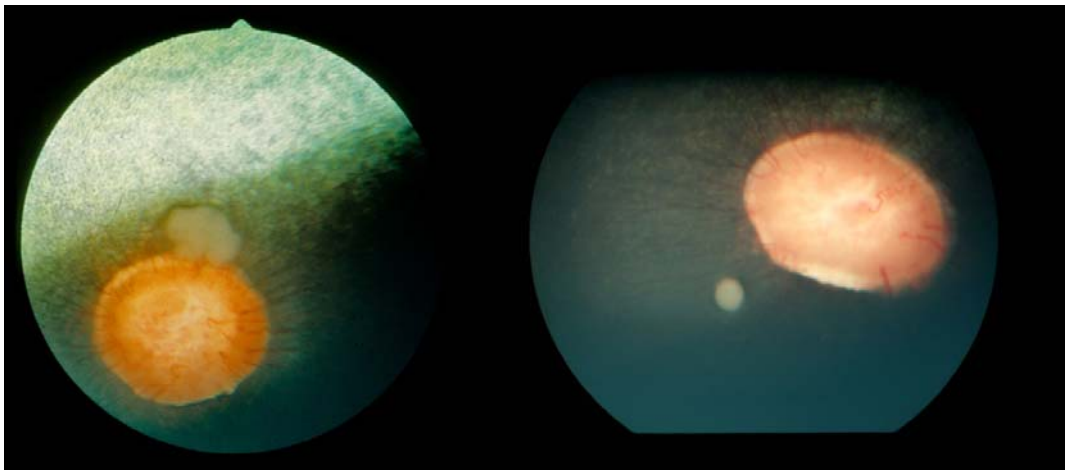


Figure 15: There are some difficult "neoplastic" lesions that occur within the eye of the horse. In the posterior segment there are some poorly understood tumours and tumour like conditions such as proliferative optic neuropathy (bottom left) and astrocytoma (bottom right)

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