

# Case Report

## A review of five cases of parotid melanoma in the horse

C. FINTL AND P. M. DIXON

*Department of Veterinary Clinical Studies, Easter Bush Veterinary Centre, Roslin, Midlothian EH25 9RG, UK.*

### Introduction

Equine melanocytic growths have been recognised for more than 2 centuries, particularly in mature grey horses (Rooney and Robertson 1996). Neoplasms have been estimated to affect 1–3% of all horses (Cotchin 1977) and melanomas are reported to comprise 3–15% of all equine tumours (Sundberg *et al.* 1977; Pascoe and Summers 1981). However, the true incidence of equine melanomas is probably much higher, as these characteristic growths are readily recognised clinically and, even if surgically removed, are seldom submitted for histology. One survey indicated that more than 80% of grey horses over 15 years old were affected with such growths (Stannard 1972). Yager *et al.* (1993) suggested that all grey horses would eventually develop such lesions if they lived long enough. However, these tumours may less commonly develop in any age or colour of horse (Theilen and Madewell 1987). Goetz and Long (1993) suggested that the incidence of equine melanocytic tumours in North America is on the increase as is the case with human melanomas, with a 17-fold increase in the latter reported over the previous 65 years, possibly due to increased ultraviolet (UV) radiation exposure (Balch *et al.* 1989). All equine melanotic growths may not be true neoplasms and, in this paper, the term melanoma is used to include all melanocytic growths, whether truly neoplastic or not. **This paper reviews 5 cases of melanomas involving the parotid region in horses examined at the Large Animal Hospital of the Royal (Dick) School of Veterinary Studies between 1985 and 1996.** All 5 cases were referred for investigation of parotid growths. During this period, many additional horses (data not presented) referred for various other disorders were noted to have asymptomatic and usually smaller melanocytic swellings of the parotid regions (Fig 1).

### Materials and methods

#### Case histories

##### Case 1

A nine-year-old grey Welsh section B pony gelding had a left parotid area swelling *circa* 5 cm diameter at purchase, 2 years prior to referral. At that time, it was believed that the swelling was fibrous tissue, possibly caused by a ruptured parotid lymph node abscess. The parotid swelling remained unchanged for 20 months, but then grew rapidly

and spread caudally over the proximal aspect of the left jugular vein. Latterly, the pony began to lose weight. At the time of presentation, an 8–10 cm diameter hard swelling protruded over the rostral aspect of the left jugular area and the separate, original parotid swelling was now of a similar size.

Under general anaesthesia, surgical exploration of the mass overlying the left jugular vein revealed friable, black to grey, homogenous tissue that had deeply infiltrated adjacent normal tissues, including the jugular vein. It was clear that this mass could not be fully removed surgically. Histopathology of the excised growth showed it to be a malignant melanoma. The pony was subsequently subjected to euthanasia and *postmortem* examination showed a 10 cm diameter malignant melanoma within the left parotid salivary gland, with two additional 2 or 3 cm diameter black, neoplastic nodules situated dorsally and medially to the gland. There was early metastatic infiltration of the retropharyngeal lymph nodes. The left jugular vein was occluded and adjacent tissues were deeply invaded by tumour. No other organs were grossly involved.

##### Case 2

A 12-year-old grey Thoroughbred cross gelding pleasure horse was first noticed to have multiple, focal, 2 or 3 cm diameter swellings of both parotid regions 3 or 4 months



**Fig 1: This grey pony has had very large, irregular, hard swellings over both parotid regions for many years. As the animal had always been asymptomatic, the owner did not want any further investigation. The great size of these melanomas indicates that their growth was in a lateral rather than a medial direction, therefore avoiding compression of pharyngeal and laryngeal structures.**



**Fig 2:** This 12-year-old Thoroughbred cross gelding (Case 2) has a firm, 8 cm long melanotic swelling over the left parotid region.



**Fig 4:** This 14-year-old Irish Draught cross gelding (Case 4) had a 6 cm diameter melanoma excised from the right thorax. A melanotic swelling of the right parotid region is also evident.



**Fig 3:** Case 2 also has a slightly smaller melanotic swelling (circa 10 cm long) over the right parotid region.



**Fig 5:** Close up view of the parotid melanomas of Case 4 (Fig 4) showing a large, irregular right parotid swelling with a smaller focal lesion present beneath it.

prior to presentation. These had subsequently tripled in size and over the previous 2 months had spread below the parotid salivary glands. Additionally, the horse was now becoming dyspnoeic during exercise. Latterly, dysphagia and weight loss had also occurred. At admission, the horse had bilateral parotid swellings (circa 18 cm diameter over the left and 10 cm diameter over the right) (Figs 2 and 3). Multiple 2 or 3 cm diameter melanomas were also present in the perineal region. The horse was now unable to swallow any type of feed without much of it appearing at the nostrils. Endoscopy showed marked bilateral nasopharyngeal roof collapse due to medial expansion of the parotid lesions, with invasion into the guttural pouches, which was causing dyspnoea and pharyngeal dysphagia. The animal was subsequently subjected to euthanasia but *postmortem* examination was not permitted.

### Case 3

An 8-year-old grey Highland pony gelding had been in the owner's possession for 7 years. Eighteen months prior to

referral, a 3 or 4 cm diameter swelling was noticed over the dorsal aspect of the left parotid region, with a slightly smaller growth also present on the ventral aspect of the tail base. The parotid swelling remained unchanged for 10 months but then enlarged, doubling in size over the following 6 months. At the time of referral, a firm diffuse mass appeared to be widespread throughout the left parotid area. Endoscopy showed the lateral wall of the lateral compartment of the left guttural pouch to be infiltrated with darkly pigmented tissue. Due to the extent and diffuse nature of the melanoma and because the pony was asymptomatic, surgery was not performed. The melanomas continued to grow slowly over the following 6 months, but the horse remained asymptomatic. Follow-up enquiries 8 years later found that the parotid growths had remained unchanged in size and the pony was still asymptomatic and working normally.

### Case 4

A 14-year-old grey Irish Draught cross hunter gelding had



**Fig 6:** This frontal view of Case 4 shows large melanotic swellings protruding bilaterally from the dorsal aspect of the parotid areas.

bilateral, small submandibular and parotid swellings when purchased 5 years previously. These swellings had grown steadily and were up to 9 cm in diameter at the time of presentation. More recently, a 6 cm diameter, firm mass had developed over the right thorax and was now interfering with the girth. Under general anaesthesia, the thoracic growth was excised with wide margins (Figs 4 and 5) and the lesion was shown to be a melanoma.

The horse was re-examined 23 months later because of further growth of the parotid masses (Fig 6) and because new growths *circa* 10 cm diameter had since appeared bilaterally on the crest of the neck. The horse was now making abnormal respiratory sounds during exercise and appeared to have reduced exercise tolerance. In addition, the horse was now salivating excessively at rest. Endoscopy revealed partial, bilateral occlusion of the nasopharyngeal lumen by medial growth of the parotid melanomas that compressed the lateral nasopharyngeal walls and also partially occluded the lateral compartment of the left guttural pouch (Fig 7). Additionally, rectal examination revealed a firm, 3 x 4 cm swelling at the bifurcation of the aorta. Surgical removal of the parotid melanomas was not considered feasible due to the multicentric and infiltrative nature of the lesions that lay among multiple vital structures.

A 2 month course of cimetidine (2.5 mg/kg bwt t.i.d. *per os*) was then administered. This was initially reported to have resulted in clinical improvement, with the horse being able to perform fast, prolonged work without distress, and with less drooling of saliva at rest. The horse was re-examined 12 weeks later, with no change in the size

of the melanomas detected clinically or endoscopically. A further 4 week course of cimetidine was administered, but the dyspnoea worsened greatly during this period and the horse was subjected to euthanasia. *Postmortem* examination was not permitted by the owner.

### Case 5

A 16-year-old grey, general purpose Thoroughbred mare had been in the owners' possession for 11 years. A firm swelling was noticed over the left parotid region 8 months prior to presentation to our hospital and this had doubled in size (to approximately 13 x 8 cm) in the month prior to presentation. A 3 cm diameter growth was also present ventral to the tail base, but the horse was otherwise asymptomatic. At presentation, an additional smaller mass was palpable deep in the right parotid salivary gland. Additionally, endoscopy showed the lateral compartment of the left guttural pouch to contain a discreet melanoma, *circa* 0.5 cm diameter (Fig 8).

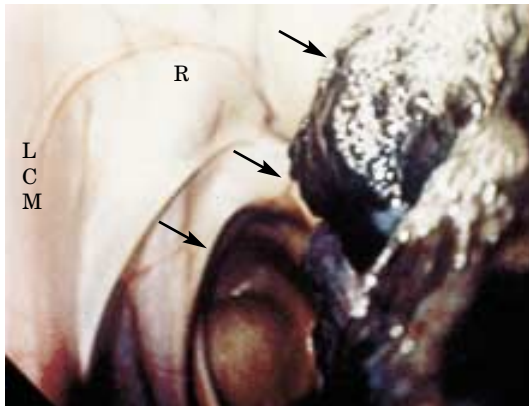
No treatment was given at this time and the mare was re-examined 4 times over the following 8 months, during which time the left parotid mass continued to enlarge. Abnormal respiratory noises now became apparent at exercise and, latterly, even at rest when the horse became excited. Endoscopy now showed a 5 cm diameter mass on the medial floor of the left guttural pouch (Fig 9) which was causing ventral deviation of the left dorsal nasopharyngeal wall and also ventrally compressing the left arytenoid cartilage (Fig 10). Some weeks later, the stridor worsened and increased nasopharyngeal compression was now observed (Fig 11). Left-sided ptosis and mild left-sided facial paresis also developed at this time. The mare was eventually subjected to euthanasia following an episode of acute respiratory distress accompanied by permanent dorsal displacement of the soft palate.

*Postmortem* examination revealed a malignant melanoma of the left parotid salivary gland and adjacent tissues, including the guttural pouch. The submandibular, retropharyngeal and prescapular lymph nodes were all enlarged and contained melanomas. Both lungs had dark, nodular, 1 cm diameter lesions throughout the diaphragmatic lobes (Fig 12). Similar lesions were present in the spleen and liver. Histopathology of the main parotid mass and secondary tumours showed a mixture of melanocytes with heavy infiltration of fibrous stromal cells and large pigment-filled macrophages.

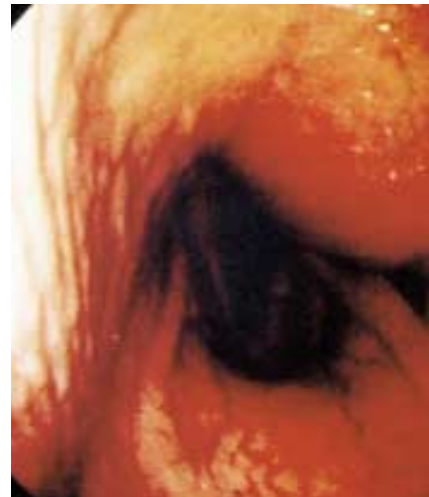
### Discussion

Melanocytes arise embryonically in the neural crest and, by the time the fetus is a few weeks old, the precursors of these cells will have arrived at their final destinations, i.e. primarily the epidermal-dermal junction, the eye and meninges (Scott 1988; Jones *et al.* 1997). It has been suggested that the ability of these cells to migrate so easily through tissues may have biological implications for the spread of melanocyte tumours later in life (Balch *et al.* 1989).

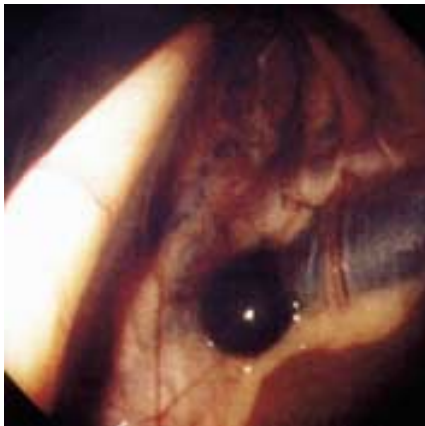
Yager *et al.* (1993) considered equine melanomas to be



**Fig 7:** Endoscopic view of the medial compartment of the left guttural pouch of Case 4 showing extensive melanoma growth in the lateral compartment, whose lumen is completely obliterated by this growth. LCM = longus capitus muscle, R = roof of medial compartment. Arrows indicate the melanoma protruding in a medial direction from the lateral compartment of the guttural pouch.



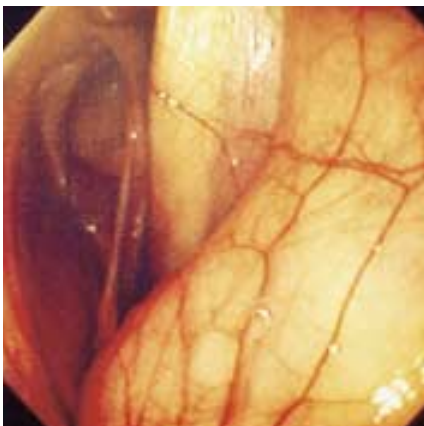
**Fig 10:** Nasopharyngeal endoscopy of Case 5 showing medial collapse of the left nasopharyngeal wall and left arytenoid - with subsequent partial occlusion of the left dorsolateral aspect of the larynx.



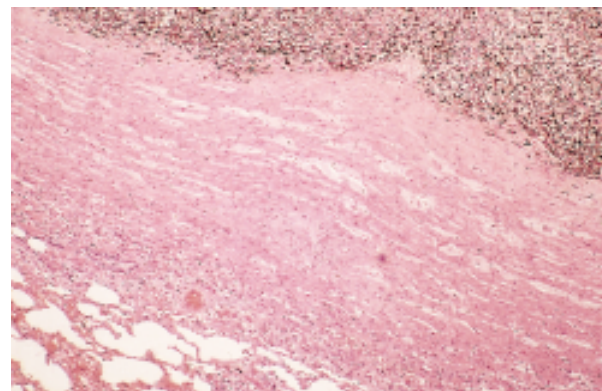
**Fig 8:** Endoscopic view of the left lateral compartment of Case 5 showing a small (5 mm diameter) discrete melanoma overlying the external maxillary vein.



**Fig 11:** Endoscopy of Case 5 some weeks later (shortly before euthanasia). The nasopharyngeal collapse now also involves the right side of the nasopharynx and is causing very extensive obstruction of the nasopharyngeal and laryngeal lumina.



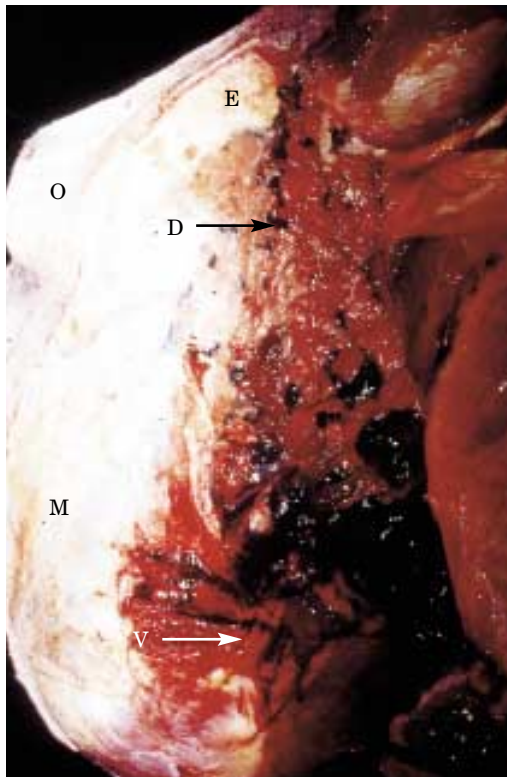
**Fig 9:** Endoscopic appearance of the left guttural pouch of Case 5, some months following the endoscopy shown in Figure 8. This now shows extensive distortion of the floor of the medial compartment due to further submucosal extension of melanoma.



**Fig 12:** Histology of lung section from Case 5 showing the margin of a metastatic melanoma lesion.



**Fig 13: Endoscopic image of the guttural pouch of an asymptomatic grey horse showing focal areas of melanosis submucosally.** This is not an uncommon finding in grey horses and is believed to have little significance.



**Fig 14: Caudolateral view of the left parotid region of an asymptomatic grey horse at postmortem examination** (E = ear, O = orbit, M = masseter muscles, D = dorsal aspect of parotid salivary gland, V = ventral aspect of parotid salivary gland). The partly dissected left parotid salivary gland displays extensive infiltration with melanosis. There are some smaller focal areas of melanosis dorsally (arrows), at the possible sites of the parotid lymph nodes. However, the most extensive melanosis are focally on its ventral aspect, areas which do not normally contain significant lymphatic tissue.

of 2 types, both benign, with the most common type being a biologically unique form of dermal melanocytosis that may not be truly neoplastic. Inexplicably, these authors also described some equine melanomas that reached several kg in weight and that appeared to metastasise. It has also been suggested that some melanocytic lesions in older horses may be a type of storage disease (Hargis 1995). In contrast, other authors (as reviewed by Rooney and Robertson 1996) believe that approximately 30% of melanomas are malignant and metastasise. Although usually occurring in adult horses, there have been some reports of congenital melanomas (Hamilton and Byerly 1974) and of melanomas in young horses (Foley *et al.* 1991), which appear to show more variation in location and also in coat colour of affected animals, than do melanomas of adult horses (Foley *et al.* 1991).

As observed in the above 5 cases, the gross appearance of melanomas can vary considerably. They may present as a single mass but are more likely, especially in older horses, to occur as multilobular or multiple individual growths. Some lesions are located subcutaneously, while others are firmly attached to deeper tissues. Melanomas may become ulcerated and infected, especially if located in areas that interfere with tack and also if they are large or rapidly growing tumours.

In addition to the main predilection sites at the ventro-proximal aspect of the tail, perineal and perianal areas, other predilection sites include the pinnae, periocular areas and male genitalia. (Scott 1988). It is unclear how common it is for the parotid area to be involved in equine melanomatosis. Pascoe and Summers (1981) found the parotid region to be the second most common site, involving 6 of 33 cases, while Valentine (1995) recorded parotid melanomas in 3 of 51 cases. In contrast, Runnels and Benbrook (1941) and Foley *et al.* (1991) found no parotid involvement in 16 and 18 equine cases of melanoma, respectively.

Concerning melanomas of the parotid region, Rooney and Robertson (1996) and Johnson (1998) both state that melanocytes preferentially accumulate within the parotid lymph nodes. However, in the 5 current cases, it was not always clear if the initial site was the parotid salivary gland or the parotid lymph nodes. In horses, the presence of parotid lymph nodes is variable. If present, they often lie medial to or within the dorsal aspect of the parotid salivary gland. More consistently, lymph nodes lie medial to the parotid area, along the course of the external carotid artery (Sisson and Grossman 1953). Grey horses of all ages, (including those without detectable melanomas) often have focal superficial areas of melanosis (circa 2–5 mm in diameter) on the lateral walls of the guttural pouch (Fig 13), and multiple focal areas of melanosis are also frequently incidentally encountered in the perilaryngeal fascia of grey horses of all ages during prosthetic laryngoplasty (P. M. Dixon, unpublished data). At *postmortem* examination of 2 of the present cases, the extent of the parotid region melanomas made determination of their exact site of origin impossible, but both cases had diffuse melanotic infiltration of the parotid salivary glands, including of areas ventral to the usual site of parotid lymph nodes. A similar distribution was

found at *postmortem* of an additional case (data not presented) (**Fig 14**).

Melanomas are typically dark brown to black, or grey in colour, and are occasionally nonpigmented (Theilen and Madewell 1987). The latter type can only be identified accurately by histopathology (Johnson 1998) with great pleomorphism and variation in pigmentation being hallmarks of malignant melanomas (Jones *et al.* 1997). If anaplastic, immunohistochemistry may also be required for diagnosis (Hellquist 1989). It is interesting that melanocytic melanomas in horses may be preceded by vitiligo as also observed in man and in pigs (Scott 1988). This is thought to result possibly from destruction of normal melanocytes through auto-immune mechanisms (Yu 1997). Rooney and Robertson (1996) noted that melanocytes and melanin preferentially accumulate in the perineal subcutaneous tissues and parotid lymph nodes of grey horses and termed these melanotic areas as melanosis, without any prediction of their future biological behaviour. These authors also stated that the perineal melanocytes are the origin of the majority of equine malignant melanomas, while the parotid lymph nodes are rarely the origin of such malignancies.

There have been conflicting reports concerning the relationship of gender and the incidence of melanocytic tumours in the horse (Sundberg *et al.* 1977; Foley *et al.* 1991), but no clear gender predilection has been demonstrated (Johnson 1998). Some of the disagreement concerning age, breed and colour predisposition to this tumour may be due to variations in the nomenclature and classification used for this tumour. Valentine (1995) suggested the following system. (1) Melanocytic nevi (melanocytoma): these tumours are characterised by being located in the superficial dermis or at the dermo-epidermal junction. Epithelial involvement is common. Melanocytic nevi are usually benign, although invasive behaviour occasionally occurs. The cellular appearance of the tumour includes distinct nests of relatively large, frequently pleomorphic, epithelioid to spindle-shaped tumour cells with euchromatic nuclei, occasional binucleate cells and mitotic figures, and variable cytoplasmic pigmentation. Melanocytic nevi have histological features commonly associated with malignancy (epithelial involvement, cellular pleomorphism, variable pigmentation, mitotic activity), necessitating careful distinction from clearly malignant tumours (e.g. anaplastic malignant melanoma). Further differentiation may be aided by signalment; anaplastic melanomas are more likely to affect aged horses, whereas melanocytic nevi are most commonly seen in younger horses. (2) Dermal melanoma and dermal melanomatosis: these tumours are located deep in the dermis and are histologically characterised by small, homogenous, indistinct, round or dendritic cells with condensed chromatin and dense cytoplasmic pigmentation. Mitotic figures are not observed. The term dermal melanoma should be used if only 1 or 2 discrete tumours are present and the term dermal melanomatosis is recommended if multiple confluent dermal melanomas are present. Dermal melanoma and dermal melanomatosis are histologically similar. Dermal melanomatosis arises in the

typical locations already mentioned and tends to affect horses over age 10 years (median age 18 years). Complete surgical excision is usually impractical, with regrowth commonly occurring at the surgical site. (3) Anaplastic malignant melanoma: these tumours are composed of extremely pleomorphic epithelioid cells, with single cell epithelial invasions, poor or absent pigmentation and numerous mitotic figures. Affected horses are usually age >20 years and are not always grey in colour. Although rare, these tumours are aggressively metastatic and usually lead to widespread dissemination within months of diagnosis.

While the above system helps classify this tumour, a range of histological changes may occur within an individual melanoma. This occurred in *Case 1*, where the presence of epithelial/spindle cell types would classify this lesion somewhere between dermal melanomatosis and anaplastic malignant melanoma. It was unclear if this particular tumour was truly anaplastic, because it was still possible to identify melanocytic cells. Grossly, however, there was no doubt of the malignancy of the tumour in this particular case, with large secondary lesions present in the submandibular and retropharyngeal lymph nodes and aggressive invasion of the jugular vein and adjacent deep cervical tissues present.

Similar histopathological findings were noted at the *postmortem* examination of *Case 5*, where an extensive parotid mass and guttural pouch mass compressed the pharynx and larynx. Histopathology of the main parotid mass and the secondary tumours showed a mixture of melanocytes with heavy infiltration of fibrous stromal cells and of large pigment-filled macrophages.

Apart from metastases in some cases, melanomas may cause problems by expansion at their primary location. For example, parotid melanomas can physically compress the nasopharynx and the arytenoid cartilages causing respiratory obstruction and dysphagia, which were the presenting signs in 2 of the current cases. Endoscopy showed pharyngeal compression caused by the enlarged parotid glands, but also by swellings at the sites of the retropharyngeal lymph nodes (on the floor of the guttural pouches). A further case (*Case 4*) had exercise-related dyspnoea due to ventral compression of the nasopharyngeal roof onto the arytenoids. Involvement of the facial nerve (probably compression against the caudal aspect of the mandible) caused facial paralysis in *Case 5*.

The behaviour of equine melanomas has been typically described as following one of 3 patterns. Firstly, they may be malignant with rapid, invasive growth from the outset. More commonly, they show slow growth for many years, followed by sudden rapid growth (Scott 1988), which was the pattern seen in 4 of these cases. Finally, there may be prolonged slow growth (up to 20 years) without invasive behaviour or metastasis (Scott 1988), as occurred in one horse here (*Case 3*).

As with many other tumours, ulcerated melanomas appear to be more biologically aggressive lesions since they invade directly through rather than displace tissues. The presence of ulceration in human cutaneous melanoma has a marked adverse prognostic effect (Balch *et al.* 1989). Similarly, lesions that metastasise also carry a poor

prognosis, especially if more than 2 lymph nodes are affected (Balch *et al.* 1989). Although rare, familial melanoma has been reported in man. Genetic factors that control the immune response to melanoma are believed to be important predisposing factors in these patients (Balch *et al.* 1989). Although there are undoubted differences between human and equine melanomas, it is interesting to speculate whether similar genetic factors play a role in the incidence of melanomas of grey horses.

Various treatments have been used for equine melanomas, including surgical removal, cryotherapy, chemotherapy, immunotherapy or combinations of these treatments, with limited success reported for all to date. Surgical excision was performed in 2 of the current cases. In *Case 1*, the deeply infiltrative nature of the tumour, in an area that contains multiple vital structures, became apparent during surgery and, following confirmation of the malignant nature of the tumour by histopathology, the horse was subjected to euthanasia. *Case 4* had a reasonably well defined mass removed from the lateral thoracic wall, with some of the underlying muscle mass also removed to ensure complete excision. This growth did not recur but, as noted, the horse re-presented 22 months later due to progression of melanomas at multiple other sites. Subsequent cimetidine therapy was unsuccessful. One horse (*Case 2*) was subjected to euthanasia immediately due to cachexia and widespread melanomas, while the other 2 (*Cases 3* and *5*) were not treated, with the latter monitored endoscopically until eventually subjected to euthanasia due to upper respiratory tract obstruction.

Surgical excision has been advocated in cases where the tumour mass seems to be well differentiated from the adjacent tissues. Melanocytic nevi are readily treated in this manner as they are frequently well defined and solitary (Foley *et al.* 1991). However, if wide margins of excision cannot be achieved there is a very high incidence of recurrence (Johnson 1998). In human patients with melanoma, surgical removal is usually only considered in the presence of 1 to 3 lesions, with dissection of the local drainage lymph nodes usually concurrently performed. In human medicine, it is now considered that the depth of the resection may be more important than the width of the lateral margins (Balch *et al.* 1989). In the equine parotid area, the presence of multiple adjacent vital structures precludes the radical resection of melanomas, unless they are small and are surrounded by apparently normal parotid salivary gland.

Cryotherapy has been used either alone or in combination with other treatment options. Prior surgical debulking of larger melanomas is beneficial by improving the precision of cryoprobe application (Hanson 1997). Repeated treatment is often necessary and tumour regrowth may be more aggressive (Johnson 1998). The presence of adjacent vital structures in the equine parotid region limits the use of cryotherapy in this area.

It is proposed that some horses with melanotic tumours have a limited immune response to the tumour due to excessive suppressor T cell activity mediated by histamine via H2 receptors (Brown *et al.* 1982; Goetz *et al.* 1989). Cimetidine may indirectly enhance immunity by blocking

activation of suppressor T cell activity through its H2 receptor blocking mechanism (Goetz and Long 1993). Although cimetidine therapy was unsuccessful in the single current case, Goetz and Long (1993) reported partial response to cimetidine therapy, with up to 50% reduction of size and a decrease in lesion numbers, with the best response in actively growing lesions. In addition to its questionable efficacy, the high cost and necessity for frequent administration are further disadvantages of this therapy. However, it may be of use in selected cases, to reduce tumour size prior to surgery. It has been recommended that if tumours do not decrease in size within 3 months of administration, cimetidine therapy should be discontinued (Goetz *et al.* 1989).

Other treatments utilised in horses include intralesional chemotherapy, most commonly with cisplatin (cis-diamminedichloroplatinum), a heavy metal compound that directly binds to and inhibits DNA synthesis, leading to death of actively dividing cells (Théon *et al.* 1993; Théon 1997). This treatment is best used in smaller growths or in larger lesions that have been surgically debulked. It involves injecting 1 mg/ml cisplatin per ml of tumour into the target area. The cisplatin is mixed with a carrier such as sesame oil to allow its slow release and create a high tumour:plasma drug concentration and also to limit potential systemic toxic side-effects (Théon 1997). One standard protocol includes 4 intralesional injections at 2 week intervals (Goetz and Long 1993). This course can be repeated after a 4 week rest period. In human patients, intralesional chemotherapy, such as the injection of methanol or benzene derivatives, has also been successful with small localised lesions. In man, the treatment of limb lesions by isolated limb perfusion with cytotoxic agents has been successful, as has regional chemotherapy using an intra-arterial infusion of cisplatin or decarbazine (Balch *et al.* 1989). It is unlikely that such therapy is currently applicable to the horse.

A less common therapy is intralesional immunotherapy using injection of bacille Calmette-Guerin (BCG). This agent is believed to induce a cell-mediated immunological reaction against melanoma antigens, leading to its regression. Multiple BCG injections are administered in order to stimulate an anamnestic cell-mediated immune response, with the aim of causing tumour rejection. The response of equine melanocytic tumours to this drug is variable (Johnson 1998). A very wide range of systemic chemotherapy agents, in particular decarbazine or combinations of this and other cytotoxic agents, have been utilised to treat human melanomas, especially disseminated lesions. However, the National Cancer Institute reported that only 2 out of 30 tested drugs gave satisfactory responses in more than 10% of patients, with complete responses uncommon (Balch *et al.* 1989). Tumour vaccines have long been utilised for human melanomas with limited success (as is the case with most tumour vaccines), possibly due to the weak immunogenicity of tumour antigens, the heterogeneity of antigen expression in tumours and the ability of tumours to escape the immune response.

The rapid evolution of molecular biology has allowed

the development of agents, including antimelanoma monoclonal antibodies and cytokines, such as interferons and interleukin-2, that are known to influence melanoma growth (Flodgren *et al.* 1985). Such agents have been utilised extensively (Kirkwood *et al.* 1996) but so far unsuccessfully in treating human melanomas. Other strategies, such as conjugating radioisotope to monoclonal antimelanoma antibodies, are also being evaluated (Balch *et al.* 1989).

## Acknowledgements

We thank Drs Rod Else, Susan Rhind and Alan Rowland for pathological examinations of the current cases. Constanze Fintl is a Home of Rest for Horses Senior Clinical Scholar in Equine Studies.

## References

- Balch, C.M., Houghton, A. and Peters, L. (1989) Cutaneous melanoma in cancer. In: *Principles and Practice of Oncology*, Eds: V. DeVita Jr, S. Hellman and S.A. Rosenberg, J.B. Lippincott Co., Philadelphia. pp 1499-1542.
- Brown, A.E., Badger, A.M. and Poste, G. (1982) The effect of cimetidine on immune cell function and host response to tumours. In: *Current Concepts in Human Immunology and Cancer Immunomodulation*, Elsevier, Amsterdam. pp 513-519.
- Cotchin, E. (1977) A general survey of tumours in the horse. *Equine vet. J.* **9**, 16-21.
- Flodgren, P., Malmstrom, P., Axelsson, B., Boketoft, A., Borgstrom, S. and Sjogren, H.O. (1985) Immune functions in melanoma patients during treatment with interferon (HuIFN-(Le)) alone or in combination with cimetidine. *Anticancer Res.* **5**, 197-204.
- Foley, G.L., Valentine, B.A. and Kincaid, A.L. (1991) Congenital and acquired melanocytomas (benign melanomas) in eighteen young horses. *Vet. Path.* **28**, 363-369.
- Goetz, T.E. and Long, M.T. (1993) Treatment of melanomas of horses. *Comp. cont. Educ. pract. Vet.* **4**, 608-610.
- Goetz, T.E., Boulton, C.H. and Ogilive, G.K. (1989) Clinical management of progressive multifocal benign and malignant melanomas of horses with oral cimetidine. *Proc. Am. Ass. equine Practnrs.* **35**, 431-438.
- Goetz, T.E., Ogilive, G.K., Keegan, K.G. and Johnson, P.J. (1990) Cimetidine in treatment of melanomas in three horses. *J. Am. vet. med. Ass.* **196**, 449-452.
- Hamilton, D.P. and Byerly, C.S. (1974) Congenital malignant melanoma in a foal. *J. Am. vet. med. Ass.* **164**, 150-152.
- Hanson, R.R. (1997) Cryotherapy for equine skin conditions. In: *Current Therapy in Equine Medicine*, Eds: N.E. Robinson and M.A. Williams, W.B. Saunders Co., Philadelphia. pp 370-372.
- Hargis, A.M. (1995) Integumentary system. In: *Thomson's Special Veterinary Pathology*, Eds: W.W. Carlton and M.D. McGavin, Mosby-Year Book, Inc., St. Louis, Missouri. pp 461-504.
- Hellquist, H.B. (1989) Malignant melanoma and metastatic neoplasms. In: *Pathology of the Nose and Paranasal Sinuses*, London, Butterworth. pp 143-148.
- Jones, T.C., Hunt, R.D. and King, N.W. (1997) The skin and its appendages. In: *Veterinary Pathology*, 6th edn., Eds: T.C. Jones, R.D. Hunt and N.W. King, Williams and Wilkins, Baltimore. pp 856-858.
- Johnson, P.J. (1998) Dermatologic tumours (excluding sarcoids). *Vet. Clin. N. Am.: Equine Pract.* **14**, 625-658.
- Kirkwood, J.M., Strawderman, M.H., Ernstoff, M.S., Smith, T.J., Borden, E.C. and Blum, R.H. (1996) Interferon alfa-2 $\beta$  adjuvant therapy of high risk resected cutaneous melanoma: the Eastern Cooperative Oncology Group Trial EST 1684. *J. Clin. Oncol.* **14**, 7-17.
- Pascoe, R.R. and Summers, P.M. (1981) Clinical survey of tumours and tumour-like lesions in horses in south east Queensland. *Equine vet. J.* **13**, 235-239.
- Rooney, R.R. and Robertson, J.L. (1996) Integument. In: *Equine Pathology*, Eds: R.R. Rooney and J.L. Robertson, Iowa State University Press, Ames, Iowa. pp 287-307.
- Runnels, R.A. and Benbrook, V.M.D. (1941) Malignant melanomas of horses and mules. *Am. J. vet. Res.* **2**, 340-344.
- Scott, D.W. (1988) Structure and function of the skin. In: *Large Animal Dermatology*, W.B. Saunders Co., Philadelphia. pp 4-5.
- Sisson, S. and Grossmann, J.D. (1953) The lymphatic system. In: *The Anatomy of the Domestic Animals*, Eds: S. Sisson, and J.D. Grossman, W.B. Saunders Co., Philadelphia. p 712.
- Stannard, A.A. (1972) The skin. In: *Equine Medicine and Surgery*, 2nd edn., Eds: E.J. Catcott and J.F. Smithcors, American Veterinary Publications, Wheaton, Illinois. pp 395-396.
- Sundberg, J.P., Burnstein, T., Page, E.H., Kirkham, W.W. and Robinson, F.R. (1977) Neoplasms of equidae. *J. Am. vet. med. Ass.* **170**, 150-152.
- Theilen, G.H. and Madewell, B.R. (1987) Tumours of the skin and subcutaneous tissues. In: *Veterinary Cancer Medicine*, 2nd edn., Eds: G.H. Theilen and B.R. Madewell, Lea and Febiger, Philadelphia. pp 315-325.
- Théon, A.P. (1997) Cisplatin therapy. In: *Current Therapy in Equine Medicine*, Eds: N.E. Robinson and M.A. Williams, W.B. Saunders Co., Philadelphia. pp 372-377.
- Théon, A.P., Pascoe, J.R., Carlson, G.P. and Krag, D.N. (1993) Intratumoral chemotherapy with cisplatin in oily emulsion in horses. *J. Am. vet. med. Ass.* **202**, 261-267.
- Valentine, B. (1995) Equine melanocytic tumors: a retrospective study of 53 horses (1988 to 1991). *J. vet. int. Med.* **9**, 291-297.
- Yager, J.A., Scott, D.W. and Wilcock, B.P. (1993) The skin and appendages. In: *Pathology of Domestic Animals*, Eds: K.V.F. Jubb, P.C. Kennedy and N. Palmer, Academic Press, Inc., San Diego. pp 719-721.
- Yu, A.A. (1997) Dermatologic conditions associated with abnormal pigmentation. In: *Current Therapy in Equine Medicine*, Eds: N.E. Robinson and M.A. Williams, W.B. Saunders Co., Philadelphia. pp 391-393.