Introduction

Neoplastic diseases are a major cause of morbidity and mortality among domestic animals, just as they are in man. In the horse, the skin is the organ most commonly affected by neoplasia and the sarcoid is the most common neoplasm occurring at this site (Sundberg et al. 1977; Goodrich et al. 1998). However, other neoplasms affecting all parts of the body can and do occur, albeit at a lower frequency than tumours of the skin. With some exceptions, neoplasms tend to be associated with ageing. Ageing per se is not generally considered a direct factor in the induction of tumours, but presumably allows increased opportunity to develop neoplasia, including cumulative exposure to environmental carcinogens (Cockerall and Cooper 2002). This is probably one reason why neoplasms are seen more commonly in dogs and cats than in other domestic animals, because these species are allowed to live out their natural life span. As geriatric populations of equids increase, it is likely that more cases of neoplasia will be encountered in the horse population (Savage 1998a). However, not all cases of neoplasia occur in older horses, and some specific tumours are commonly seen in young animals, including lymphoma (lymphosarcoma) (Rebhun and Bertone 1984; Mair et al. 1985; Mair and Hillyer 1992) and hepatocellular carcinoma (Roby et al. 1990; East and Savage 1998).

Pathogenesis, cancer biology and clinical staging

Over the past 40 to 50 years there has been significant progress in the basic understanding of the pathogenesis of neoplasia (also known as oncogenesis or carcinogenesis). Although details of the pathogenesis of neoplasia are beyond the scope of this article, it is likely that future advances in the diagnosis, prognosis, and treatment of neoplasia in the horse and other species will be closely tied to advancements in the understanding of the pathogenesis and biology of neoplasia. It is common to refer to a neoplastic cell as a transformed cell and the associated event as transformation. At this time, there is no single, unified concept of the biological mechanisms that underlie transformation and the development of neoplastic disease, and the reader is referred to more detailed texts that describe the major theories about pathogenesis of neoplasia (Ross 1998; Cockerell and Cooper 2002; Kelsey et al. 2002). It is generally believed that most neoplasms are monoclonal in origin, i.e. they arise from genetic mutations within a single affected cell, although in certain tumours in some species (e.g. equine sarcoid and feline sarcoma) a polyclonal mechanism may be involved. Over subsequent cell divisions in the neoplasm, heterogeneity can develop through the accumulation of further abnormalities (Kelsey et al. 2002). The genes most commonly affected are those controlling cell cycle check points, DNA repair and DNA damage recognition, apoptosis, differentiation and growth signalling. Proliferation may continue at the expense of differentiation, which together with the failure of apoptosis (apoptosis is also known as ‘programmed cell death’) leads to tumour formation with the accumulation of abnormal cells (Rudin and Thompson 1997). In general, benign tumours grow slowly, and malignant tumours grow rapidly. The growth rate of an individual neoplasm is determined by such factors as the length of the mitotic cycle, proportion of cells in mitosis and rate of cell loss, amongst others.

The spread of neoplastic cells by metastasis is the most serious consequence of malignancy. More cancer treatment failures and deaths in man result from the effects of metastasis than of the primary tumour (Fidler 2000; Cockerell and Cooper 2002). In many cases, metastatic dissemination of a malignant neoplasm will have occurred before it can be detected clinically. Microscopic spread, especially via blood vessels and lymphatics, is the reason why surgical removal of a primary malignant neoplasm is likely to fail to be curative in approximately 50% of patients.

Grading and staging of neoplasms are commonly used in many human cancers as a means of quantifying the behaviour of the neoplasm in an individual patient. Grading represents an attempt to quantify the degree of malignancy at the...
microscopic level. Staging represents an attempt to classify the neoplasm according to its progression or extent, with the size of the primary lesion, the presence of lymph node involvement, and the presence of metastasis being taken into account (Cockerell and Cooper 2002). Such grading and staging systems are helpful not only in predicting outcome, but also for guiding treatment. For example, clinical staging of canine lymphoma correlates with prognosis, and can be used to define the most effective chemotherapeutic regimen (Madewell 1999). In canine lymphoma, staging is based upon the results of a standard set of tests, including a physical examination, complete blood count, biochemical profile, urinalysis, thoracic and abdominal radiographs, abdominal ultrasound, lymph node and bone marrow aspiration cytology, and lymph node biopsy (Rosenthal 2001).

Unfortunately such systems have not been described or evaluated in the horse, mainly due to size of the patients, small numbers and difficulties in obtaining follow-up. The sheer size of the equine patient makes clinical staging difficult to perform. The identification of abdominal tumours or metastases in the horse can be especially difficult, and often the neoplasia will have reached an advanced stage by the time clinical signs occur and a diagnosis is achievable (East and Savage 1998). Similarly, mediastinal tumours (primarily lymphoma) may be present for a considerable length of time before clinical signs become apparent, and their identification can be difficult using standard techniques of ultrasonography and radiography because of anatomical factors (Mair et al. 1985).

Despite these problems, attempts to implement staging systems should be encouraged in the most common equine neoplasms, and would probably aid in the development of chemotherapeutic and other approaches to treatment. For example, clinical staging of squamous cell carcinoma of the penis and prepuce of male horses has been suggested as being potentially valuable in defining prognosis and aiding treatment choices (Madewell 1999).

**Principles of chemotherapy**

A variety of different treatment modalities are used for treating neoplasia. Surgery (including traditional ‘sharp’ surgery, laser therapy and cryosurgery) remains the most effective form of treatment for most solid tumours of skin, soft tissues and bone, but early treatment and aggressive resection are necessary in cases of malignant disease. The use of chemotherapy following surgical management of a primary mass is frequently used in the treatment of cancer in man and small animals, the use of cytotoxic drugs in horses has found only limited application. This is partly because of the high costs involved with treating horses with such drugs, but also because of perceived problems with adverse drug effects (see below). Local chemotherapy, including topical and intratumoral chemotherapy, has been used in cutaneous neoplasms as a way of maximising the exposure of the tumour to the drug, while avoiding systemic toxicity. The high incidence of cutaneous neoplasia in the horse makes topical/local therapy a logical approach. The major indication for systemic use of cytotoxic drugs in the horse is in the treatment of lymphoproliferative diseases such as lymphoma. Despite the limitations of chemotherapy in horses, it is likely that as people become more knowledgeable about available treatments for cancer in man, they will demand more sophisticated treatment options for their animals, including horses. Provided they have an understanding of the treatment goals and costs, many owners are appreciative of honest attempts to control neoplastic disease (Chun 2001).

In general, chemotherapeutic agents damage DNA (and RNA) and result in cellular death, apoptosis or inability to undergo mitosis. Some may cause frank necrosis. For many of these drugs there is a fairly narrow therapeutic window between effective systemic treatment and toxicity to normal tissues (therapeutic index). The drugs are not cancer-specific, but act on neoplastic cells preferentially because of their increased cellular proliferation rates. However, the proliferation rate in neoplastic tissues is usually not that much greater than normal tissues, and toxic effects in normal tissues are therefore common in humans receiving systemic chemotherapy. For this reason, the dose and schedule of chemotherapy is limited by normal tissue tolerance, especially in those tissues that proliferate rapidly such as the bone marrow and gastrointestinal tract mucosa. Other tissues can also be affected depending on the individual tissue affinity of

<table>
<thead>
<tr>
<th>Category</th>
<th>Major mechanisms of action</th>
<th>Drug examples</th>
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<tbody>
<tr>
<td>Alkylating agents</td>
<td>Damage DNA and interfere with cell replication</td>
<td>Cyclophosphamide, Chlorambucil, Melphalan</td>
</tr>
<tr>
<td>Antitumour antibiotics</td>
<td>Damage DNA and interfere with nucleic acid synthesis</td>
<td>Doxorubicin, Mitoxantrone, Actinomycin D, Bleomycin</td>
</tr>
<tr>
<td>Plant alkaloids</td>
<td>Distract mitosis in the metaphase</td>
<td>Vincristine, Vinblastine</td>
</tr>
<tr>
<td>Hormones</td>
<td>Immunosuppression and anti-tumour effects</td>
<td>Prednisolone, Prednisone, Dexamethasone</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>Interfere with DNA and RNA synthesis by interaction with enzymes</td>
<td>L-asparaginase, Methotrexate, Cytosine arabinoside, S-fluorouracil</td>
</tr>
<tr>
<td>Taxanes</td>
<td>Interfere with cell division</td>
<td>Taxol</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Enzymatic destruction of amino acids</td>
<td>Asparaginase</td>
</tr>
</tbody>
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the particular chemotherapeutic agent. Although many of the chemotherapeutic agents used in veterinary medicine are the same as those used in human medicine, veterinary applications tend to use lower doses and less aggressive protocols, and so adverse effects are less of a problem. In veterinary patients quality of life is generally as important as (or perhaps, more important than) disease control (Chun 2001).

Many tumours will develop resistance to single-agent chemotherapy. For this reason, intermittent combination chemotherapy was developed. With such regimes, several drugs are combined together or sequentially, chosen on the basis of differing mechanisms of action and nonoverlapping toxicities (Kelsey et al. 2002). The drug combination is given over a period of a few days, followed by a rest period of a few weeks, during which time the normal tissues have the opportunity for regrowth. If the normal cells are more proficient at DNA repair than the cancer cells, then it may be possible to deplete the tumour while allowing restoration of normal tissues between chemotherapy cycles.

Chemotherapeutic drugs

Categories of commonly-used chemotherapeutic agents and examples of drugs are shown in Table 1. A number of the cytotoxic agents cause direct damage to DNA. Alkylating agents such as cyclophosphamide act by covalently linking alkyl groups and their major effect is to cross-link DNA strands, thereby interfering with DNA synthesis and causing strand breaks (Kelsey et al. 2002). These were among the earliest of the cytotoxic drugs developed for use in man, but they are still widely used in cancer treatment. Platinum compounds, including cisplatin, cause interstrand cross-links of DNA and are often regarded as non-classical alkylating agents. As with other heavy metal compounds, they can have toxic effects on the kidneys and peripheral nerves. The antimitabolites, such as 5-fluorouracil (5-FU), cytosine arabinoside and methotrexate, are structural analogues of naturally occurring metabolites; they interfere with the normal synthesis of nucleic acids by falsely substituting purines and pyrimidines in metabolic pathways. The most commonly used drug of this class in the horse, 5-FU, consists of a uracil molecule with a substituted thymidylate synthetase which is essential for pyrimidine synthesis.

The cytotoxic antibiotics, such as doxorubicin, act by intercalating adjoining nucleotide pairs on the same strand of DNA and by inhibiting DNA repair. The vinca alkaloids, including vincristine and vinblastine, act by binding to tubulin and inhibiting mirotubule formation (part of the cytoskeleton of the cell), thus disrupting mitosis. The taxanes also bind to tubulin and prevent their assembly into microtubules.

Topical chemotherapy for cutaneous neoplasms

Topical and intralosomal chemotherapy enable high concentrations of cytotoxic drugs to be maintained within cutaneous and other superficial neoplasms over a long period while sparing adjacent normal skin (Theon 1998), thus minimising toxicity. Immunotherapeutic agents can also be successfully used by these application routes.

Topical treatment with 5-FU has been used successfully for the treatment of squamous cell carcinoma of the external genitalia (Fortier and MacHarg 1994) and other skin sites (Paterson 1997). The treatment involves the repeated application of the drug to the tumour surface. In addition to having cytotoxic activity, 5-FU acts as a contact allergen and induces a delayed hypersensitivity reaction that causes the superficial cell layers to slough (Mansell et al. 1975). Although 5-FU destroys the superficial layers of the tumour, the precise depth of action is impossible to predict. Normal skin is less sensitive to the effects of the drug because of the lower proliferation rate of skin cells and the barrier effect of keratin that prevents the drug from penetrating to the deeper epithelial layers. Since the topically applied cream does not penetrate deeply, it is most useful for superficial tumours (including squamous cell carcinoma) less than 2 mm thick, but not for the treatment of nodular or deeply invasive tumours (Theon 1998). It can be used as an adjunct to surgery for the treatment of squamous cell carcinoma after surgical debulking leaving a tumour bed less than 3 mm thick. Treatment should be started as soon as possible after surgery since the drug does not affect wound healing and will not penetrate through a healed skin wound. Treatment is generally applied daily for 3-4 months, or longer, until complete tumour regression has occurred. Total regression of the lesion should be confirmed (preferably by biopsy) before treatment is discontinued, because accelerated regrowth can occur if the lesion is not completely eliminated (Theon 1998). The number of treatments required can be reduced if the area can be covered by a waterproof dressing. For the treatment of squamous cell carcinoma of the penis, the prepuce acts as a dressing and the treatments can be reduced to applications at two week intervals (Theon 1998).

Ocular (conjunctival and corneal) squamous cell carcinoma can also be treated using topical 5-FU, either alone or in combination with other treatments. Ophthalmic drops containing 5-FU have been used in man (Yeatts et al. 2000; Foy et al. 2002), but there is very limited information about the efficacy of this therapy in horses. This drug has also been used to treat equine sarcoids (Figs 1a and b), often in combination with other therapies such as surgical debulking. Sarcoids are common, locally invasive, non-metastatic, fibroblastic tumours that can affect any part of the body, but especially the ventral abdomen, limbs and head (Goodrich et al. 1998; Foy et al. 2002). To aid the penetration of the 5-FU through the superficial epidermis, the drug can be mixed with podophyllin, an irritant cathartic (McConaghy et al. 1994; Piscopo 1999). Topical 5-FU needs to be applied daily for 30–90 days. Alternatively, it can be applied less frequently under a bandage (Roberts 1970). It is most useful for single, small occult or verrucose sarcoids, or for larger areas of occult or verrucose sarcoids that are not amenable to any other form of treatment. The treated area can show a marked inflammatory reaction, but scarring is usually minimal (Pascoe and Knottenbelt 1999).

Heavy metal compounds, including inorganic arsenic, antimony and mercury salts, cause tissue necrosis, and can be used topically to treat sarcoids (Pascoe and Knottenbelt 1999). A topical ointment (AW-3-LUDES) containing a variety of
heavy metals with 5-FU and thiouracil has been used in the UK for the treatment of sarcoids for several years (Knottenbelt and Walker 1994; Knottenbelt and Kelly 2000; Newton 2000). The ointment is applied on successive or alternate days for 3–5 treatments, depending on the size, number and nature of the sarcoids, and the strength of the ointment used. An inflammatory reaction is usually seen after one or more treatments. In some cases, a painful and marked oedematous reaction occurs, necessitating anti-inflammatory treatment. A full response is usually seen in 5–10 weeks, characterised by necrosis and sloughing of the sarcoid tissue. A granulated wound bed usually remains once the sarcoid tissue sloughs. A resolution rate of over 80% has been reported in cases where sarcoids are being treated with topical AW-3-LUDES for the first time (Knottenbelt and Walker 1994) (Figs 2a, b and 3a, b).

The success rate decreases by 30–40% for each previous unsuccessful treatment. A topical paste (Xxterra) containing zinc chloride and plant alkaloids derived from the bloodroot plant has recently become available in the USA, and there is anecdotal evidence that it can be successful in eliminating small, localised sarcoids (Palmer 2002). A rapid response to the extract is usually seen, with inflammation followed by pus accumulation under the tumour base and sloughing of the lesion in 7–10 days; the surrounding healthy skin is left intact. The reaction appears to be similar to that seen in graft rejection. There is anecdotal evidence of effect on sarcoids remote from those being treated in some cases. Another bloodroot extract (Animex) containing Sanguinaria canadensis, puccoon, gromwell, distilled water and trace minerals has also recently been used to treat various skin lesions including sarcoids (Foy et al. 2002). The ointment is said to penetrate the lesion, killing the affected cells while leaving the surrounding healthy tissue intact. In the UK, a topical ointment of undisclosed composition is available commercially (Camrosa). There is anecdotal evidence of efficacy of this substance in the treatment of all types of sarcoid.

Unfortunately, the results of topical therapies using the above mentioned drugs are difficult to quantify. Although there are many anecdotal reports indicating good efficacy, there appear to be few published studies, and it is not possible to compare the short- and long-term results of these treatments with other therapies.

**Intralesional chemotherapy for cutaneous neoplasms**

Intralesional injection of cytotoxic drugs into the tumour and tumour bed allows higher intratumoral drug concentrations to be achieved and permits accurate placement of the drug within the tumour. The beneficial effects of this route of administration are enhanced if drug carriers that prolong the persistence of the drug in the tissue are used. Viscous fluid preparations such as sesame seed oil or almond oil are frequently used to achieve this effect (Theon et al. 1993). The viscosity of the drug mixture can be altered, and vasoactive agents included that will alter drug reabsorption, depending on the individual characteristics of the tumour being treated. Cisplatin is the drug most widely used in this manner, although carboplatin, 5-FU and bleomycin are also suitable for intralesional use.
Intralesional cisplatin therapy has been found to be effective in the treatment of a variety of solid tumours including squamous cell carcinoma (Fig 4), sarcoid, soft tissue sarcomas, lymphoma, plasmacytoma and hamartoma (Theon 1998). For melanomas, it has been suggested that more effective treatment is achieved when a vasoactive agent such as adrenaline is added to the formulation (Theon 1997). Intralesional cisplatin can be effective as the sole treatment for tumours measuring up to 3–5 cm in diameter; for larger tumours (>20 cm³), the treatment should usually be combined with surgery (Theon et al. 1994). Emulsions made up from 1 ml of an aqueous solution of 10 mg cisplatin/ml and 2 ml sesame oil are frequently used at a dose rate of 1 mg cisplatin/cm³ of tumour (Goodrich and Semevolos 2000). The emulsion is created by attaching 2 luer-lock syringes (one with the aqueous cisplatin solution and one with the sesame oil) to a 3-way valve; the valve is closed towards the exit (i.e. needle port) and the solution and oil are mixed by alternatively pushing the plunger of each syringe until a milky white suspension develops. The target volume of tissue to be injected should include all visible tumour plus a margin of normal tissue of 1–2 cm (Theon 1997). This formulation of cisplatin (3.3 mg of cisplatin/ml of emulsion) is relatively stable and will not separate into two phases over a 3 hour period (Theon et al. 1993). The target volume of tissue to be infiltrated is infiltrated with the emulsion through a 20–23-gauge needle attached to a luer-lock syringe; the last step is important, since the high viscosity of the emulsion frequently causes for the needle to get detached from the syringe (spilling its contents on the patient or the operator) if a luer-lock mechanism is not used. To administer the drug, the needle is inserted into the tissue to the desired depth and the drug is injected as the needle is withdrawn. The desired volume of emulsion is injected via multiple sites using a parallel-row technique or field-block technique. The rows of...
injections should be kept 0.6–0.8 cm apart (Theon 1997). Injection into multiple tissue planes may be required (Goodrich and Semevolos 2000). Repeated injections every 2 weeks are continued until all clinical evidence of neoplasia has disappeared. Local wound toxicity is minimal and perioperative cisplatin treatment does not appear to affect wound healing. Alternative formulations of cisplatin have been described. An emulsion of almond oil and cisplatin with a final concentration of 1 mg cisplatin/ml, injected every 5–7 days, resulted in complete resolution in 6 of 18 cases of periorbital sarcoid in one report, and improved but did not resolve a further 10 of 18 cases (Knottenbelt and Kelly 2000). A mixture of aqueous cisplatin (5 ml; 1 mg/ml) and 1 ml of epinephrine (adrenalin 1:1000) is described by Doyle (1998); the solution is administered weekly.

Intralesional cisplatin treatment generally has good cosmetic results, and can be used at sites such as the eyelid, pinna, muzzle, penis and base of tail (Theon 1998; Knottenbelt and Kelly 2000). A 2-year local control rate of approximately 90% has been reported for sarcoïds and 70–90% for squamous cell carcinoma (Theon et al. 1993, 1994; Goodrich and Semevolos 2000).

Intralesional 5-FU has been used most commonly in the treatment of squamous cell carcinoma. In one study 5-FU was found to be ineffective as a single intralesional agent for the treatment of squamous cell carcinoma (Orenberg et al. 1992), although it can be effective when combined with surgery or used as multiple treatments. A solution of 5-FU (500 mg in 10 ml) can be mixed with 3 ml of epinephrine (1 mg/ml) and administered intralesionally (50–60 mg/cm3) (Doyle 1998). It may also be injected together with cisplatin. At The Ohio State University we have used a 5-FU/sesame oil emulsion for intralesional injection of squamous cell carcinomas with a high degree of success. We typically mix 250 mg of 5-FU (i.e. 5 ml) with 3–5 ml sesame oil in a 12 ml luer-lock syringe and administer every 2 weeks for 3–5 treatments as described above. Adverse effects are minimal and over 75% of the tumors experience complete or partial remission.

A variety of other agents administered by intralesional injection have been used in the treatment of cutaneous neoplasms in horses. These include chemicals such as formalin, calcium chloride, zinc chloride and copper sulphate. Although there are anecdotal reports of their efficacy, no published studies exist to support the use of such substances.

Systemic chemotherapy

Systemic chemotherapy has been used and reported relatively infrequently in adult horses. There are, however, a limited number of reports of chemotherapeutic treatment of equine lymphoma (lymphosarcoma) (Fig 5). Lymphoma is the commonest of the lymphoproliferative diseases in horses. It is also the commonest malignant neoplasm seen in this species (Rebhun and Bertone 1984) and carries a grave prognosis. As the disease is most commonly multicentric or generalised, surgical resection of lymphomatous masses is unlikely to be beneficial. However, in cases of solitary lymphoma with no spread, local surgical resection or radiotherapy can be beneficial or curative (Coumbe 1994). Small intestinal and large colon resection have proved curative in a limited number of cases of solitary intestinal lymphoma masses (Dabareiner et al. 1996).

Chemotherapeutic protocols have been used in cases of generalised lymphoma with some limited success (Couto 1994; Savage 1998b; Johnson 1998). Most protocols have included combinations of vincristine, cyclophosphamide, cytosine arabinoside, chlorambucil, doxorubicin, dactinomycin and prednisolone. The dosages are generally extrapolated from small animal and human oncology, and are calculated on a square metre basis using the following formula (Couto 1994; Doyle 1998):

\[
\text{Body surface area (m}^2) = \frac{\text{weight} (\text{g}^{2/3}) \times 10.5}{10^4}
\]

An approximately 50% remission is usually achieved and is seen within 2–4 weeks (Figs 6a and b). Dosages for the commonly used antineoplastic agents are summarised in Table 2.

The Ohio State University currently uses the CAP protocol, a combination of cytosine arabinoside at an average dose of 1–1.2 g (total dose), subcut. or i.m., once every 1–2 weeks; cyclophosphamide at a dose of 1 g (total dose) i.v., every 2 weeks (alternating with cytosine arabinoside); and prednisolone at a dose of 1 mg/kg, per os, every other day. Vincristine (2.5 mg, i.v.) is added on the weeks when the cytosine arabinoside is administered if there is no response. These are starting doses; the total doses can be increased by 20–30% without expecting complications. With remission, the starting doses are maintained for 2–3 months and then

### Table 2: Dosages of chemotherapeutic agents used systemically in equine neoplasia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose rate</th>
<th>Route</th>
<th>Frequency</th>
<th>Typical doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone</td>
<td>1 mg/kg</td>
<td>per os</td>
<td>Every other day</td>
<td>2.5–3.0 mg/horse/dose</td>
</tr>
<tr>
<td>Vincristine</td>
<td>0.5 mg/m²</td>
<td>i.v.</td>
<td>Weekly</td>
<td>1–1.5 g/horse/dose</td>
</tr>
<tr>
<td>Cytosine arabinoside</td>
<td>200–300 mg/m²</td>
<td>subcut., i.m., i.v.</td>
<td>Every 1–2 weeks</td>
<td>1 g/horse/dose</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>200 mg/m²</td>
<td>i.v.</td>
<td>Every 1–2 weeks</td>
<td>2.5–3.0 mg/horse/dose</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>20–30 mg/m²</td>
<td>i.v.</td>
<td>Every 2–3 weeks</td>
<td>2.5–3.0 mg/horse/dose</td>
</tr>
<tr>
<td>Dactinomycin</td>
<td>0.5–0.75 mg/m²</td>
<td>i.v.</td>
<td>Every 3 weeks</td>
<td>2.5–3.0 mg/horse/dose</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>20 mg/m²</td>
<td>per os</td>
<td>Every 2 weeks</td>
<td>100 mg/horse/dose</td>
</tr>
<tr>
<td>L-asparaginase</td>
<td>10,000–40,000 i.u./m²</td>
<td>i.m.</td>
<td>Every 2–3 weeks</td>
<td>50,000–200,000 i.u./horse/dose</td>
</tr>
</tbody>
</table>
the horse is switched onto a maintenance protocol. The first cycle of maintenance therapy increases the treatment interval for each antineoplastic agent by one week (except prednisolone which is kept at the same frequency but with a reducing dose). If the horse is still in remission after 2–3 months of the first cycle, the second cycle is begun by adding a further week to the treatment intervals of each drug. Most horses in remission are treated for a total of 6–8 months (Schneider 1997). Approximately 50% of multicentric lymphoma patients can be brought into remission for several months to a year using this protocol. Recurrence is likely following withdrawal of the treatment. Horses receiving systemic chemotherapy should be monitored for signs of gastrointestinal, renal or neurological toxicity. Weekly haematological evaluations, as well as occasional serum biochemical profiles, are advised. Myelosuppression and gastrointestinal adverse effects are extremely rare in horses receiving systemic multi-agent chemotherapy (unpublished observations).

Other chemotherapy protocols have included single agent L-asparaginase i.m. once every 2–3 weeks, single agent cyclophosphamide i.v. once every 2–3 weeks and combinations of either cytosine arabinoside or cyclophosphamide with prednisolone (Schneider 1997). Corticosteroids, such as oral or parenteral dexamethasone, used alone have also proved helpful in reducing lymphoma masses and controlling some clinical signs temporarily (for up to 18 months) in some cases (Schneider 1997; McClure 2000; Carlson 2002; Gerber et al. 2002). Corticosteroids are also indicated to treat immune mediated anaemia and thrombocytopenia that may occur in association with lymphoma.

Chemotherapy safety

Cytotoxic drugs have a very narrow margin of safety, and use of proper personal protection equipment during preparation and chemotherapy administration is necessary to minimise exposure of personnel to the drugs (Lucroy 2002). Disposal of materials used should also follow the appropriate guidelines (Yodaiken and Bennett 1986). Drugs such as 5-FU are commonly dispensed to owners for topical treatment over a prolonged time course. As the drug is mutagenic and carcinogenic, safety guidelines for handling the drug and for disposal of contaminated dressings must be followed by the owners.

Acknowledgements

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Manufacturers’ addresses

1 D.C. Knottenbelt, University of Liverpool, Neston, South Wirral, UK.
2 Larson Labs Inc., Vet Line, Fort Collins, Colorado, USA.
3 NIES Inc., Las Vegas, Nevada, USA.
4 Camrosa Equestrian Ltd., Wadhurst, East Sussex, UK.

References


