The Principles of Surgical Oncology

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ABSTRACT

Oncology is a field in veterinary medicine which is demanding more attention from both veterinarians and their clients. An understanding of the principles of oncology and its treatment is essential for a successful outcome. The role of the veterinary surgeon in treating cancers in companion animals is reviewed. (**Liptak, J.M.** (1997). *Aust. Vet. Practit.* **27**:114)

INTRODUCTION

Cancer is one of the major causes of death in cats and dogs (Ogilvie, 1995; Withrow, 1996a). Successful cancer treatment requires a positive and dedicated attitude by both the owner and veterinarian but this approach should also be realistic. The treatment of cancer requires knowledge of tumour behaviour, surgical techniques, and adjunctive therapies such as chemotherapy and radiotherapy.

The role of surgery in oncology is multifactorial and includes diagnosis with various biopsy techniques, curative with complete excision of the tumour, palliative when the type or severity of tumour prevents curative surgery, adjunctive or cytoreductive surgery to facilitate the effectiveness of other therapies such as cryosurgery, chemotherapy and radiotherapy, and the resection of metastatic disease.

DIAGNOSIS

Many cancer patients are old and hence it is important to assess their health (Soderstrom & Gilson, 1995). The following tests should be considered on an individual basis: haematology, biochemistry, electrocardiogram, radiography, computed tomography scans, nuclear medicine, and magnetic resonance imaging (Straw, 1995).

Radiography always requires a minimum of two views for proper assessment of the size and extent of the tumour. Thoracic radiographs require four views to ensure the best opportunity of detecting metastatic disease. These projections are right and left laterals, dorsoventral and ventrodorsal (Straw, 1995). Secondary nodules are usually identifiable if their diameter is greater than 10mm or if their cross-sectional diameter is less than that of a major pulmonary vessel (Straw, 1995). The two lateral views are required as atelectasis and increased perfusion occurs in the dependant lung fields which results in poorer definition of metastatic nodules (Straw, 1995). The non-dependant lung fields have increased ventilation and, combined with the greater lesion-to-film magnification, make diagnosis of metastatic pulmonary nodules easier (Straw, 1995). Metastasis may still exist despite the failure to detect pulmonary nodules.

Paraneoplastic Syndromes

Cancer can alter the metabolism and function of all body parts at the primary tumour site, metastatic disease site or distant to the actual tumour (Ruslander & Page, 1995). These are called paraneoplastic syndromes. They are not related to tumour size, metastasis or tissue of origin (Ruslander & Page, 1995). The cause of paraneoplastic syndromes is unknown but hypothesised to result from tumour cell production of biochemicals including polypeptides, hormones, hormone-like substances and toxins (Gilson & Stone, 1990b; Gorman, 1990; Ruslander & Page, 1995). The incidence of paraneoplastic syndromes is unknown but affects 15% to 20% of human patients, not including cachexia, and up to 75% of patients with untreatable cancers (Gilson & Stone, 1990b). Paraneoplastic syndromes occur most frequently with endocrine and haematological tumours (Gorman, 1990). Paraneoplastic syndromes have been reviewed in the veterinary literature (Dyer, 1992; Forrester & Fallin, 1992; Forrester & Relford, 1992; Rogers, 1992; Ruslander & Page, 1995; Ogilvie, 1996).

INTRODUCTION TO SURGERY

The surgical removal of localised tumours cures more human and animal cancers than any other mode of therapy but it is only part of a multidisciplinary approach involving tumour biology, chemotherapy, radiotherapy

and other treatment modalities (Gilson & Stone, 1990a; Birchard, 1995; Soderstrom & Gilson, 1995) A knowledge of these principles should be acquired by all oncologists and oncological surgeons. The goal of therapy is to maximise the benefits of treatment and cure rates while minimising the side-effects (Gilson & Stone, 1990a). The advantages of surgery are that it is non-carcinogenic and less immunosuppressive compared to chemotherapy and radiotherapy (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995). The disadvantages include the morbidity and mortality associated with procedure, decreased function and disfigurement (Gilson & Stone, 1990a). Important questions to be asked prior to planning oncological surgery are (Withrow, 1996c):

1. What am I treating?
2. Do the biopsy results fit the clinical situation?
3. What is the known biological behaviour of the cancer?
4. Is a cure possible?
5. What is the proper surgical approach (intralesional, marginal, wide or radical)?
6. What are my alternatives to treatment?
7. What are the expectations and attitude of the owner and are these reasonable?

There are five different surgical goals with cancer: prevention, diagnosis, cure, palliation, and combination therapy (Withrow, 1996c).

Pre-operative Assessment

The pre-operative management of the oncological surgical patient should include an assessment of intercurrent disease which may be related (e.g., vomiting and dehydration with a gastro-intestinal tumour) or unrelated (e.g., renal or hepatic disease) to the neoplastic process (Gilson & Stone, 1990b). Intercurrent disease increases the morbidity and mortality associated with surgery, can limit the extent of surgery and alter post-operative management but it should not be a contraindication to surgical therapy as its recognition and management will reduce physiological stresses (Gilson & Stone, 1990b; Soderstrom & Gilson, 1995). The risk of haemorrhage is a serious complication with both biopsy and surgery, and hence blood coagulation tests and correction of any haemostatic abnormalities should be performed prior to surgical intervention (Straw, 1995). Chemotherapy, radiotherapy and/or surgery can be altered, incorporated or eliminated on the basis of intercurrent disease (Gilson & Stone, 1990b). For example, nephrotoxic chemotherapeutic agents such as cisplatin should not be used in animals with renal failure and limb amputation should not be performed if other joints are affected by degenerative joint disease. Paraneoplastic syndromes should be treated or controlled prior to surgery to minimise surgical morbidity and mortality.

Cancer Cachexia & Nutritional Support

Cancer cachexia, a form of malnutrition due to competition between the host and the tumour for nutrients, results in a number of nutritional imbalances, can cause immune system failure, inhibit wound healing, and increase morbidity associated with surgery and other treatment alternatives (McCaw, 1989; Gilson & Stone, 1990b; Ogilvie, 1993; Ogilvie &Vail, 1996). The most significant nutritional imbalances include disturbances in carbohydrate, protein and lipid metabolism.

The tumour metabolises glucose for energy by anaerobic glycolysis which forms lactate as an end product. The host uses energy to convert lactate to glucose through the Cori cycle resulting in a net energy gain for the tumour and loss for the host (Holyroyde & Reichard, 1981). This is exacerbated by diets high in simple carbohydrates and intravenous fluids containing either glucose or lactate, such as lactated Ringer's solution, as these increase blood lactate concentrations (Ogilvie, 1993).

Cancer causes decreased body muscle mass and skeletal protein synthesis, negative nitrogen balance, and a concurrent increase in skeletal protein breakdown, liver protein synthesis, and whole-body protein synthesis (Langstein, 1991). Tumours preferentially use amino acids via gluconeogenesis at the expense of the host (Kurzer & Meguid, 1986). Amino acids are also important in the treatment of tumours. Arginine stimulates lymphocyte blastogenesis and decreases tumour growth and metastatic rate in some rodents (Tachibana *et al.*, 1985). Glycine reduces cisplatin-induced nephrotoxicity (Heyman *et al.*, 1991).

Fat loss accounts for the majority of weight loss in animals with cancer cachexia. Abnormalities in lipid metabolism include decreased lipogenesis and increased lipolysis (Ogilvie, 1993). Some tumour cells have difficulty in utilising lipids as an energy source hence enabling the host to continue oxidising fats for energy (Ogilvie, 1993). Research has demonstrated that high amounts of specific types of fat, such as omega-3 fatty acid, can improve nitrogen intake and balance, in vitro lymphocyte mitogenesis, and wound healing time (Tisdale *et al.*, 1991).

The most effective method of treating cancer cachexia is through the elimination of the primary tumour, although the alterations in carbohydrate, protein and lipid metabolism can continue after the animal is tumour free, but it can be managed with enteral or parenteral nutrition such as nasogastric, pharyngostomy, oesophagostomy, gastrotomy or jejunostomy feeding tubes (Gilson & Stone, 1990b). Nutritional support should be considered when anorexia is present for greater than five days, there is greater than a 10% acute loss of body weight, the existence of a disease or tumour which interferes with oral feeding for greater than three days, and laboratory results indicating hypoalbuminaemia, lymphopaenia and/or anaemia (Gilson & Stone, 1990b). Total parenteral nutrition is effective but technically demanding and expensive (Gilson & Stone, 1990b).

Peri-operative Treatment

Prophylactic antibiotics should be used with cancer surgery as infection is likely due to immunosuppression resulting from anaesthesia, surgery, chemotherapy, radiotherapy, neoplastic disease, malnutrition, splenectomy, and/or intercurrent disease (Gilson & Stone, 1990b).

Blood or blood based products are often requried to treat the anaemia of chronic disease present with tumours,

chemotherapy and radiotherapy, malnutrition, and blood loss or myelophthisis (Gilson & Stone, 1990b). Blood transfusions can cause marked immunosuppression through prostaglandin E-mediated suppression of macrophage and lymphocyte function and increased T suppressor cell activity (Gilson & Stone, 1990b). Blood transfusions decrease five year survival rates by 26% in human cancer surgery but are still indicated when required (Gilson & Stone, 1990b).

Tumour-associated pain is present in 15% of non-metastatic tumours, 33% of early metastatic tumours and 60% to 90% of advanced metastatic tumours (Gilson & Stone, 1990b). Sixty two percent to 78% of pain is tumour-related due either to mechanical or chemical stimulation of nociceptors (Gilson & Stone, 1990b). Nineteen percent to 25% of pain is due to the treatment regimes (Gilson & Stone, 1990b). Pain can be controlled through the administration of narcotic agents, non-steroidal anti-inflammatories, and local anaesthesia.

PREVENTATIVE SURGERY

Forms of preventative surgery include early ovariohysterectomy, to reduce the incidence of cancers of the ovary, uterus and mammary glands; and castration to prevent sertoli cell tumours in cryptorchid dogs and perianal adenomas (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995).

DIAGNOSTIC SURGERY — BIOPSY

The ideal biopsy technique should safely and simply provide an adequate sample of tissue that will consistently provide an accurate diagnosis (Soderstrom & Gilson, 1995). There are several methods to obtain a biopsy, including fine needle aspirate, needle biopsy, surface-biting instrument, incisional biopsy, and excisional biopsy (Withrow, 1996b). Improper use or the use of faulty biopsy instruments may damage the biopsy sample and hence should be avoided. Forceps, suction and other handling methods may also damage the biopsy sample (Withrow, 1996b).

All biopsies should be submitted for histopathological examination by a trained veterinary pathologist (Withrow, 1996b). Medicolegal concerns dictate that all biopsy samples be submitted for pathology and, if the owner does not want to submit the biopsy, then at least it should be stored in formalin (Straw, 1995). The histological type and grade of tumour are important for assessing surgical technique, hence most biopsies should be performed prior to surgery (Withrow, 1996b). Biopsy results should be discussed with the pathologist as they should fit the clinical findings (Straw, 1995). If the results do not fit the clinical findings, then request resectioning, special stains for possible tumour types (such as toluidine blue for mast cells, or a second opinion from another pathologist (Straw, 1995). A pre-operative biopsy is recommended if the tumour type will affect the treatment, the extent of treatment, or the owner's willingness to proceed with treatment (Powers *et al.*, 1995; Withrow, 1996b).

Fine Needle Aspiration

Fine needle aspiration (FNA) is an inaccurate biopsy method but should differentiate between benign and malignant tumours (Clinkenbeard & Cowell, 1994). It is an acceptable method for the diagnosis of round cell tumours such as mast cell tumour, lymphoma and histiocytoma (Clinkenbeard & Cowell, 1994). All skin tumours should have FNA performed as one study showed that 74% of skin tumours were diagnosed correctly with FNA cytology (Clinkenbeard & Cowell, 1994). Other collection methods for cytological evaluation include transtracheal washes and bronchoalveolar lavage. Histopathological confirmation following excision is still required.

Needle Biopsy

Needle biopsies are atraumatic, easy to use, relatively inexpensive, versatile, and long-lasting (Withrow, 1996b). Tumours are poorly innervated and hence local anaesthesia is not required but the overlying skin will need to be anaesthetised and a small stab incision made for the insertion of the biopsy needle (Withrow, 1996b). Multiple specimens should be obtained to ensure a representative sample for histopathological examination (Withrow, 1996b). Care must be taken when handling the tissue and removing it from the needle. Remove the sample with a scalpel blade, hypodermic needle or fine toothed forceps (Withrow, 1996b). Needle biopsies are more accurate than FNAs but not as reliably accurate as incisional or excisional biopsies (Clinkenbeard & Cowell, 1994). Complications are rare but include fistula formation, haemorrhage, spread of infection, and tumour seeding (Withrow, 1995).

Incisional Biopsy

Incisional biopsy is recommended in preference to needle biopsy for soft or friable tumours, peripheral lymph nodes, and highly inflammed and necrotic tumours (Withrow, 1996b). Incisional biopsy is performed using a scalpel blade to obtain a wedge of tissue. The biopsy should include a junction between normal and abnormal tissue. However, some surgeons believe that this may disrupt and extend the tumour margins as the peripheral tumour is where greatest cellular activity occurs (Gilson & Stone, 1990a; Birchard, 1994; Withrow, 1995; Withrow, 1996b). Normal tissue should not be included if that tissue will be involved in subsequent reconstructive procedures following definitive treatment (Withrow, 1996b). Electrocautery and other tissue damaging techniques should be avoided as they will disrupt tumour architecture (Withrow, 1996b). Incisional biopsy should not be performed in areas of ulceration, necrosis, or inflammation (Withrow, 1996b). Multiple samples are preferred as a single sample may not be representative (Withrow, 1996b). Careful haemostasis and asepsis is required while performing incisional biopsies, dead space should be reduced, and the use of drains avoided (Withrow, 1996b). The incisional biopsy should be performed by the surgeon so definitive surgery can be planned to remove the biopsy tract with the tumour as the biopsy procedure can seed normal tissue and be a source of local tumour recurrence (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995; Straw, 1995; Withrow, 1996b). For adequate fixation, the biopsy should be less than one centimetre thick and placed in 10% buffered formalin at one part tissue to 10 parts fixative (Gilson & Stone, 1990a; Powers, 1996; Withrow, 1996b).

Excisional Biopsy

The role of excisional biopsy is controversial. Some oncologists believe that excisional biopsy is more frequently performed than is indicated but some authors regard it as the preferred method of biopsy as the biopsy procedure may be curative as well as diagnostic (Gilson & Stone, 1990a; Withrow, 1996b). A complete pre-operative work-up, including either FNA or needle biopsy, will provide knowledge of the likely tumour and better planning for curative surgery. For example, a mast cell tumour can be diagnosed by FNA, but if an excisional biopsy is performed without this knowledge then the tumour will be incompletely excised resulting in an unnecessary risk to the patient and the need for further and more extensive surgery. The first surgery is the best chance for cure and this should not be compromised by inadequate planning (Mann & Pace, 1993; Soderstrom & Gilson, 1995; Straw, 1995). Excisional biopsy should be performed when the treatment would not be altered by knowledge of the tumour type such as splenectomy for splenic masses (Withrow, 1996b).

STAGING OF TUMOURS

The location and extent of tumours can be classified according to the World Health Organisation clinical staging system for tumours in domestic animals (Table 1). The classfication involves local (T), regional (N) and distant (M) disease (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995). Staging is an aid to the planning of treatment, establishing a prognosis, evaluating results, investigating tumours and assisting in the exchange of information between veterinarians (Powers *et al.*, 1995). Tumour staging should be done in a standardised and reproducable manner. The minimum staging required prior to surgery should include preoperative biopsy, thoracic radiography and FNAs of the regional lymph nodes (Soderstrom & Gilson, 1995). Other methods of staging tumours include laboratory tests, ultrasound, computed tomography, magnetic resonance imaging, and nuclear scintigraphy (Powers *et al.*, 1995; Soderstrom & Gilson, 1995).

	PRIMARY TUMOUR
T0	No evidence of neoplasia
T1	Tumour < 1cm in diameter and not invasive
T2	Tumour 1-3cm in diameter or locally invasive
T3	Tumour > 3cm in diameter or evidence of ulceration or locally invasive
	NODE
N0	No evidence of nodal involvement
N1	Node firm and enlarged
N2	Node firm, enlarged and fixed to surrounding tissue
N3	Nodal involvement beyond regional lymph nodes
	METASTASIS
M0	No evidence of metastasis
M1	Metastasis to one organ system
M2	Metastasis to more than one organ system

TABLE 1: World Health Organisation's TNM classification of tumours in domestic animals. World Health Organisation, Geneva, 1980.

CURATIVE SURGERY

Curative surgery involves complete excision of the tumour. The first surgery is the best chance for a cure. Benign and malignant tumours will recur if excision is incomplete. Tumours recurring after intial surgery are often more locally invasive due to altered vascularity and local immune responses and the destruction of normal tissue planes in the initial surgery will make subsequent surgeries more difficult (Soderstrom & Gilson, 1995). Surgical planning depends on knowledge of tumour type, grade, stage, and expected behaviour (Gilson, & Stone, 1990a). If mass biopsy or staging has not been completed then surgery should be planned with all possible considerations including intraoperative cytology or frozen section histopathology (Gilson & Stone, 1990a; Rogers *et al.*, 1996).

Preparation

General anaesthesia is usually required although neoplasms in appropriate locations can be amenable to regional blocks or epidurals. Local anesthesia should be avoided as it can distort tumour architecture, increase the difficulty of microscopic interpretation, and potentiate metastasis (Soderstrom & Gilson, 1995). The patient should be prepared with a widely clipped area to allow for an extension of incisions if required (Gilson & Stone, 1990a). Aseptic preparation is especially important as cancer patients are immunosuppressed and hence more susceptible to infections. Gentle skin preparation is required as vigorous scrubbing can result in tumour cell exfoliation (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995).

Surgical Technique

Following skin and subcutaneous skin incisions, protective drapes should be placed on skin edges to prevent tumour seeding (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995). Normal tissue must be protected from tumour cells, hence determination of tumour stage and margins before surgery minimises the amount of normal tissue exposed and the disruption of tumour margins (Soderstrom & Gilson, 1995). If an exploratory abdominal or thoracic surgery is being performed, then the entire cavity should be examined to determine the extent of the tumour (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995).

Tumours are considered an infective nidus and hence careful handling is required to prevent exfoliation of tumour cells and local recurrence (Gilson & Stone, 1990a; Birchard, 1995; Soderstrom & Gilson, 1995; Withrow, 1996c). Five-year survival rate in humans with colonic cancer improved 100% with careful intra-operative handling (Gilson & Stone, 1990a). The tumour is isolated with a laparotomy sponge and, if required, manipulated with stay sutures. These can also act as markers to orientate the pathologist (Mann & Pace, 1993; Birchard, 1995). All vascular and lymphatic vessels should be ligated as early as possible to prevent the release of tumour emboli into the ciruclation (Gilson & Stone, 1990a; Straw, 1995; Soderstrom & Gilson, 1995; Withrow, 1996c). This is especially important for

tumours with good arterial and venous supply such as splenic tumours, retained testicles and lung tumours (Straw, 1995). If a malignant tumour is opened during resection, then it is no better than a large biopsy. If tumour margins are disrupted, then electrocoagulate or fulgurate the exposed surface and change gloves, instruments and drapes (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995).

Tumour dissection should have at least one tissue plane between the mass and the excision (Withrow, 1996c). Tumour and adhesions should be removed *en bloc* as adhesions may be related to local tumour invasion (Soderstrom & Gilson, 1995). Lavage should not be performed in cavities as it is difficult to recover but lavage of wound surfaces is acceptable as it washes exfoliated cells away but the effect of dilution is unknown (Gilson & Stone, 1990a; Birchard, 1995; Straw, 1995; Withrow, 1996c). Lavage should not replace the need for gentle tissue handling (Straw, 1995).

Scalpel blades should be used as they are theoretically the smoothest and least traumatic of all the cutting instruments especially on skin and hollow organs (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995). The proper use of the scalpel will reduce tissue trauma and preserve vascular supply but scissors are useful to separate fascial planes and for the use in body cavities where scalpels may be either impractical or hazardous (Soderstrom & Gilson, 1995). Electrosurgery is good for oral and vascular neoplasms with good haemostasis and decreased risk of tumour seeding but thermal necrosis can result in delayed healing, decreased resistance to infection, and distortion and damage of biopsy samples due to polarisation of mitotic figures (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995; Powers, 1996; Withrow, 1996b). Other techniques include laser surgery and cryosurgery (Withrow, 1996b).

Gloves, drapes and instruments should be changed after excision of the tumour (Gilson & Stone, 1990a; Birchard, 1995). If radiation is planned, then drains, tissue flaps, and grafts should be placed to minimise the field of radiation (Straw, 1995). If chemotherapy is planned, then the use of non-absorbable suture materials should be considered due to delayed healing especially if an intestinal anastomosis has been performed.

Margins for Tumour Excision

The aggressiveness of surgery is categorised as intracapsular, marginal, wide and radical (Soderstrom & Gilson, 1995; Straw, 1995; Withrow, 1996c). The most common mistake in oncological surgery is to use too low a level of aggressvieness in surgery. Intracapsular surgery is defined as debulking with macroscopic tumour remaining and is only indicated for benign disease such as draining of an abscess (Soderstrom & Gilson, 1995). Marginal surgery is the excision of the tumour outside the pseudocapsule with microscopic tumour remaining (Soderstrom & Gilson, 1995; Withrow, 1996c). Marginal excisions are indicated for benign tumours such as lipomas. Wide surgery is complete excision with margins free of tumour cells (Soderstrom & Gilson, 1995; Withrow, 1996c). Radical surgery is complete excision involving the removal of a body part such as limb amputation or mastectomy (Soderstrom & Gilson, 1995; Withrow, 1996c).

The margins of excision should be determined on the basis of tumour type, aggressiveness (especially mast cell tumours and soft tissue sarcomas), anatomic location, and the barrier provided by surrounding tissue (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995; Straw, 1995). Margins are three dimensional and hence are lateral, medial and deep (Birchard, 1995; Withrow, 1996c). Cartilage, tendons, ligaments, fascia, and other collagen-dense, vascular-poor tissue are resistant to neoplastic invasion (Straw, 1995). Fat, subcutaenous tissue, muscle, and parenchymal tissue are not resistant (Straw, 1995). Muscle fascia should be removed with the tumour. The margins of excision should be greater if the tumour is invasive, recurrent, or inflamed (Straw, 1995). Tumours should never be shelled out as malignant tumours are often surrounded by a pseudocapsule of compressed, viable neoplastic cells and not healthy, reactive host cells (Soderstrom & Gilson, 1995; Straw, 1995; Withrow, 1996c).

The excised mass should always be submitted for pathology to evaluate the tumour and margins. The pathology report should include margin evaluation, mitotic index, vascular or lymphatic invasion, and the grade of tumour (Soderstrom & Gilson, 1995). Marking the tumour margins with sutures or a dye is recommended to assist in orientating the pathologist or the margins can be submitted separately (Mann & Pace, 1993; Birchard, 1994; Seitz *et al.*, 1995; Withrow, 1996b). A recent study identified alcian blue as the preferred dye but Indian Ink in acetone and commercially available marking kits were acceptable (Seitz *et al.*, 1995). Ink should not be used when hormone receptor assays are anticipated as false results are common (Mann & Pace, 1993). Pathologists do not often examine all the margins and hence clean margins should not always be interpreted as complete removal (Mann & Pace, 1993). Further surgery is required if the neoplastic cells extend to the margins of excised tissue as the excision in incomplete.

Closure

Primary wound closure is preferred if possible but, as Straw (1995) quotes Withrow saying, "It is better to leave a wound partly open with no cancer than to close the wound with residual cancer". The aggressiveness of surgery should not be compromised by the ease of wound closure (Withrow, 1996c). Wounds can be closed with simple reconstructive techniques, skin grafts or secondary intention healing. The most useful reconstructive surgery techniques are the advancement flap, transposition flap, and axial pattern flaps such as the caudal superficial epigastric and the thoracodorsal flaps. A knowledge of these techniques prior to major reconstructive surgery will reduce patient morbidity and decrease the risk of compromising the margins of excision (Soderstrom & Gilson, 1995).

The Lymph Nodes

The regional lymph node is vital to the host's immune response but studies have not been conducted to determine the effects of lymph node resection (Gilson & Stone, 1990a). The current recommendations are to

resect the regional lymph node if firm, fixed, nodular or if there is histological evidence of tumour cells (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995; Straw, 1995; Withrow, 1996c). Firm lymph nodes may indicate hyperplasia secondary to tumour antigen stimulation, haemorrhage, or infection within the tumour (Straw, 1995). Most reactive nodes are enlarged but soft and non-painful while neoplastic nodes are enlarged, firm and painful. FNA of regional lymph nodes should be performed prior to surgery (Straw, 1995; Rogers *et al.*, 1996; Withrow, 1996c). Epithelial tumours (carcinomas) are more likely to metastasise to regional lymph nodes than sarcomas (Straw, 1995; Rogers *et al.*, 1996; Withrow, 1996c). Enlarged lymph nodes in critical areas (hilar, retropharyngeal and mesenteric) should not be removed but biopsied as removal will be complicated and further adjuvant therapy can be considered on the basis of the biopsy results (Straw, 1995; Withrow, 1996c).

PALLIATIVE SURGERY

Palliative surgery is designed to improve the quality of life where the type or extent of disease prevents curative surgery (Soderstrom & Gilson, 1995; Straw, 1995). Examples of palliative surgery include removal of ulcerated mammary adenocarcinoma in a patient with asymptomatic pulmonary metastasis, splenectomy for haemangiosarcoma, limb amputation for osteosarcoma, and gastrojejunostomy for duodenal obstruction. The patient gain should always outweigh the potential risk of surgery (Gilson & Stone, 1990a; Soderstrom & Gilson, 1995; Straw, 1995; Withrow, 1996c). Heroic surgery may not be indicated and the question we have to ask ourselves is when do we give up?

CYTOREDUCTIVE SURGERY

Cytoreductive surgery is the incomplete removal of a tumour which is rarely an acceptable or indicated form of sole therapy as tumours that are incompletely excised will usually recur in a short period of time (Straw, 1995; Withrow, 1996c). It is a practical consideration prior to cryosurgery and may increase the efficacy of chemotherapy or radiotherapy (Straw, 1995; Withrow, 1996c).

Combination therapy involves decreasing the tumour load with cytoreductive surgery and using adjuvant therapies such as chemotherapy, radiotherapy, hyperthermia, or immunotherapy (Withrow, 1996c). Cytoreductive surgery removes drug and radiation resistant tumour cells, circulating immune complexes, and tumour associated immunosuppressants (Withrow, 1996c). Expermentally, surgery induces cell division but this is a short-lived phenomenon (Straw, 1995). The residual cells are sensitive to chemotherapy, radiotherapy, and immunotherapy (Withrow, 1996c). The principles and indications for hyperthermia (Page, 1993), radiation therapy (Adams, 1991; Gillette & Gillette, 1995; McEntee, 1995; Thrall & Ibbott, 1995; LaRue & Gillette, 1996) and chemotherapy (Helfand, 1990; Squires & Gorman, 1990; Read, 1992; McEntee, 1995) are described elsewhere.

The timing of adjunctive therapies is an important consideration when planning curative or cytoreductive surgery. Neoadjuvant therapy, which is administered prior to surgery, has some potential benefits (Tables II and III) but their disadvantages depend on the agent being used and its adverse effects such as bone marrow suppression (McEntee, 1995). For example, vincristine has no adverse effects on wound healing (Cohen *et al.*, 1975) but wound breaking strength was decreased for up to 30 days when doxorubicin was administered to rats prior to, during and after surgery (Lawrence *et al.*, 1986.

Radiation therapy is indicated prior to surgery as the vascular supply of the tumour is not disturbed and hence tumour cells are better oxygenated and more radiosensitive. The risk of dissemination of tumour cells at surgery is reduced and tumour size may be decreased (Adams, 1991). Radiotherapy should be administered three weeks prior to surgery to allow the acute side effects of radiation to subside and to minimise the delay in wound healing (Adams, 1991; McEntee, 1995). If the

NEOADJUVANT
Advantages
Reduction in tumour size to facilitate surgical resection
Treatment of metastatic disease
Determines tumour sensitivity to chemotherapy for post-operative treatment
Disadvantages
Risk of further tumour growth making complete surgical resection difficult
Possible delayed wound healing
INTRAOPERATIVE
Advantages
Direct administration of chemotherapy to tumour bed (intralesional therapy)
Increased tumour drug levels without increased systemic toxicity
Treatment of microscopic metastatic disease
Disadvantages
Decreased wound healing
ADJUVANT
Advantages
Chemotherapy more effective when microscopic disease present and cell turnover rate is higher at both primary and metastatic sites
Wound healing is not delayed
Definitive surgery is not delayed
Disadvantages
Efficacy of chemotherapy difficult to determine when only microscopic disease is present
Decreased blood supply to tumour with fibrous tissue formation

TABLE 2: The advantages and disadvantages of chemotherapy administered either as a neoadjuvant (or prior to surgery), intra-operatively or adjunctively (following surgery). [McEntee, 1995]

PRE-OPERATIVE
Advantages
Blood supply to tumour is maintained, which decreases the risk of radio-resistant hypoxic tumour cells
Smaller radiation field so less normal surrounding tissue is irradiated
Decreased risk of disseminating tumour cells during surgery
Reduction in tumour size facilitates surgical resection
Disadvantages
Delayed wound healing
INTRA-OPERATIVE
Advantages
Visualisation of tumour bed and accurate delivery of radiation dose
Decreased exposure of surrounding normal tissue to irradiation
Ability to deliver larger total radiation dose to tumour
Disadvantages
Special facilities required
Complications of larger total dose includes fibrosis and stricture of hollow viscera
Delayed wound healing
Potential increased risk of late radiation effects and tumour induction
POST-OPERATIVE
Advantages
Definitive surgery is not delayed
Wound healing is not delayed
Staging of disease more complete
Disadvantages
Larger radiation field required
Increased risk of disseminating tumour cells during surgery
Altered blood supply to tumour with increased radio-resistant hypoxic tumour cells
Repopulation of tumour after surgery and before radiotherapy

TABLE 3: The advantages and disadvantages of radiotherapy administered either pre-operatively , intra-operatively or post-operatively (McEntee, 1995).

lag period between radiotherapy and surgery is greater than three weeks then there is an increased risk of tissue fibrosis and compromised regional vasculature which may also affect wound healing (McEntee, 1995).

Adjunctive treatment is more commonly employed with chemotherapeutic agents. These should be administered after the animal has recovered from surgery and wound healing has advanced to the remodelling stage. Chemotherapy can be started when the animal is recovering from anaesthesia as neoplastic and metastatic cells are more susceptible to the effects of chemotherapeutic agents immediately after surgery (McEntee, 1995). Post-operative radiotherapy is not recommended (McEntee, 1995).

POST-OPERATIVE MANAGEMENT

Post-operative management should include assessment of the wound healing process, a return to normal physiologic function, and checking for tumour recurrence and metastasis (Gilson & Stone, 1990b). This may be performed with any of the diagnostic tests previously mentioned. Re-evaluations should be individually assessed according to the tumour type, grade, and stage (Gilson & Stone, 1990b).

OTHER INDICATIONS FOR SURGERY IN VETERINARY ONCOLOGY

The five-year survival rate for surgical resection of metastatic disease is 25% to 65% in humans (Gilson & Stone, 1990a). The criteria for surgery includes absolute control of the primary tumour, long tumour doubling time (greater than 40 days), late onset of metastatic disease (greater than one year), the location of metastasis, and, to a lesser extent, the tumour type, number of metastatic nodules, and effectiveness of adjuvant treatment (Gilson & Stone, 1990a; O'Brien *et al.,* 1993; Straw, 1995). The aim of metastectomy is to provide a cure and hence requires careful patient selection and thorough preoperative staging to determine the extent and behaviour of the tumour (Soderstrom & Gilson, 1995). Palliative surgery of metastatic disease is possible but treatment should not be worse than no treatment. The role of surgery in the treatment of radiation injury has been described elsewhere (Dernell & Wheaton, 1995a; Dernell & Wheaton, 1995b).

COMPLICATIONS

The major complication of oncology is tumour recurrence (Gilson & Stone, 1990a; Kisseberth & MacEwen, 1996). This can occur due to inadequate tumour removal, microscopic infiltration of tumour cells outside the surgical margins, or tumour cell exfoliation into the surgery site or circulation. Recurrence can be minimised by reducing tumour cell exfoliation through gentle tissue handling and wide exposure to prevent tumour manipulation (Soderstrom & Gilson, 1995).

Metastasis is a major cause of mortality in human and animal cancers (Kisseberth & MacEwen, 1996). Microscopic or macroscopic metastases may be present at the time of surgery. The risk of metastasis can be predicted from the clinical stage and histological grade of the tumour and its location (Kisseberth & MacEwen, 1996).

Delayed wound healing can result from chemotherapy, radiotherapy, cachexia, and tumour type (McCaw, 1989). Wound healing is delayed with chemotherapy and radiotherapy due to damaged macrophages, capillary endothelial cells, and collagen producing fibroblasts (McCaw, 1989; Gilson & Stone, 1990b). This can be exacerbated by malnutrition and intercurrent disease (McCaw, 1989; Gilson & Stone, 1990b). Some of these complications are nevertheless unavoidable due to tumour behaviour, host defences, and physiological status.

CONCLUSION

Surgery is a primary tool in the diagnosis and treatment of cancer but is only a part of a multidisciplinary approach which also includes chemotherapy, radiotherapy and immunotherapy. The surgeon should have a thorough knowledge of tumour type and behaviour prior to definitive surgery. A FNA or biopsy should be performed by the surgeon and examined by a qualified veterinary pathologist prior to surgery. The surgery should be planned so that adequate margins are achieved in three dimensions, especially deep to the tumour. Other roles of surgery in oncology include prevention, palliation, cytoreduction, and metastectomy.

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