4-8-08

NEOPLASENE TREATMENT OF ABNORMAL TISSUE

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Abstract

Neoplasene attacks neoplasm by preferentially triggering apoptosis and sparing healthy tissue. Squamous cell, mast cell, spindle cell, sarcoid, transitional cell, melanoma, osteosarcoma, nerve sheath and many more classifications of neoplasm have been treated with Neoplasene and NeoplaseneX. Treatment protocols have been generally the same with variations specific to the situation presented. Treatment has been largely successful with less than satisfactory outcome associated most often with noncompliance to protocol and situations where the neoplasm is greater in size and more aggressive than can be handled by even the most aggressive treatment efforts. Many case histories are presented including squamous cell, osteosarcoma, mast cell, sarcoma, spindle cell, neurofibroma, and transitional cell carcinoma of the bladder.

Neoplasene

Neoplasene is not bloodroot, black salve or an escharotic. It is made up, in part, of plant alkaloids extracted from the botanical known as bloodroot and other plant species. These alkaloids are a small constituent of Neoplasene. The action of Neoplasene is apoptotic not escharotic and ointments called black salves vary widely and may, or may not, be escharotic, apoptotic or both. The menstruum used to extract the active chemicals from the plant material is a collection of halogen species. The isoquinoline alkaloids sanguinarine, sanguidimerine, chelerythrine, protopine and others are, in addition to being extracted, also chemically modified and this contributes to the efficacy of Neoplasene.

Neoplasene is administered topically, orally, by intralesion injection and also infused into the bladder, prostate, udder, nares, etc. The notable side effect is that systemically Neoplasene is an emetic. Antiinflammatories of any kind inhibit the action of Neoplasene and are to be avoided during its use.

Theory

Neoplasm is widely viewed as a visible and palpable mass with structural organization and defined boundaries (i.e. a tumor) and there are but two conditions, namely a tumor is benign, therefore great relief is felt, or it is malignant and the death knell is sounded. Widespread occurrence of the disease is attributed to metastasis, a spreading of the disease from the tumor by the circulatory system to distant locations. This model is in general incomplete. Neoplasm may present as a tumor, a field of diseased cells or small sets or even isolated cells that escape notice, more often, all of these present simultaneously.

In fact there is a continuous process by which healthy normal tissue is invaded with diseased cells that escape notice. This neoplastic tissue may progress to become more and more diseased, aggressive and noticeable. Thus there are an infinite number of states of diseased neoplastic tissue. A benign tumor is diseased but just not as diseased and hostile as it may, and often does, become. Metastasis while a part of the progression of the disease is secondary to the independent development of neoplasm at many anatomical locations as a result of the ongoing debilitation of the normal apoptotic process.

Assume there are about 40 billion cells per pound of flesh each of which will divide by mitosis about fifty times before it dies itself, creating daughter cells numbering about 1,100 million, million cells. Without an ongoing process of cell suicide by genetically controlled apoptosis, all creatures would if enough food and space were available become behemoth. The rapid process of apoptosis rids the individual of cells that are not a needed part of the individual's bodily systems (i.e. growth and replacement). Slowly, usually with advancing age, hormonal changes, exposure to external carcinogens, exposure to radiation, etc., widespread degeneration occurs in a small percentage of cells that modifies or in the limit eliminates the apoptotic gene giving rise to the build up of tissue that does not self destruct as it should. It may self destruct after a fashion or it may not, or it may exhibit a spectrum of apoptotic behavior throughout the individual. Lesions may ultimately develop as the first noticed evidence that neoplasm is present. Left untended the disease is progressively more debilitating and is commonly fatal.

A tumor that exhibits structure, with a discernable shape and boundaries is, in fact, usually surrounded by tissue that appears normal to visual inspection. This diseased tissue is sometimes judged pre-cancerous or questionable on biopsy and sometimes this diseased tissue escapes notice. It frequently is diseased but not so far advanced as to be readily recognized. Further multiple classifications of diseased tissue are simultaneously present. Therefore since the conclusions based on tissue analysis of a lesion are troublesome and there is little connection between

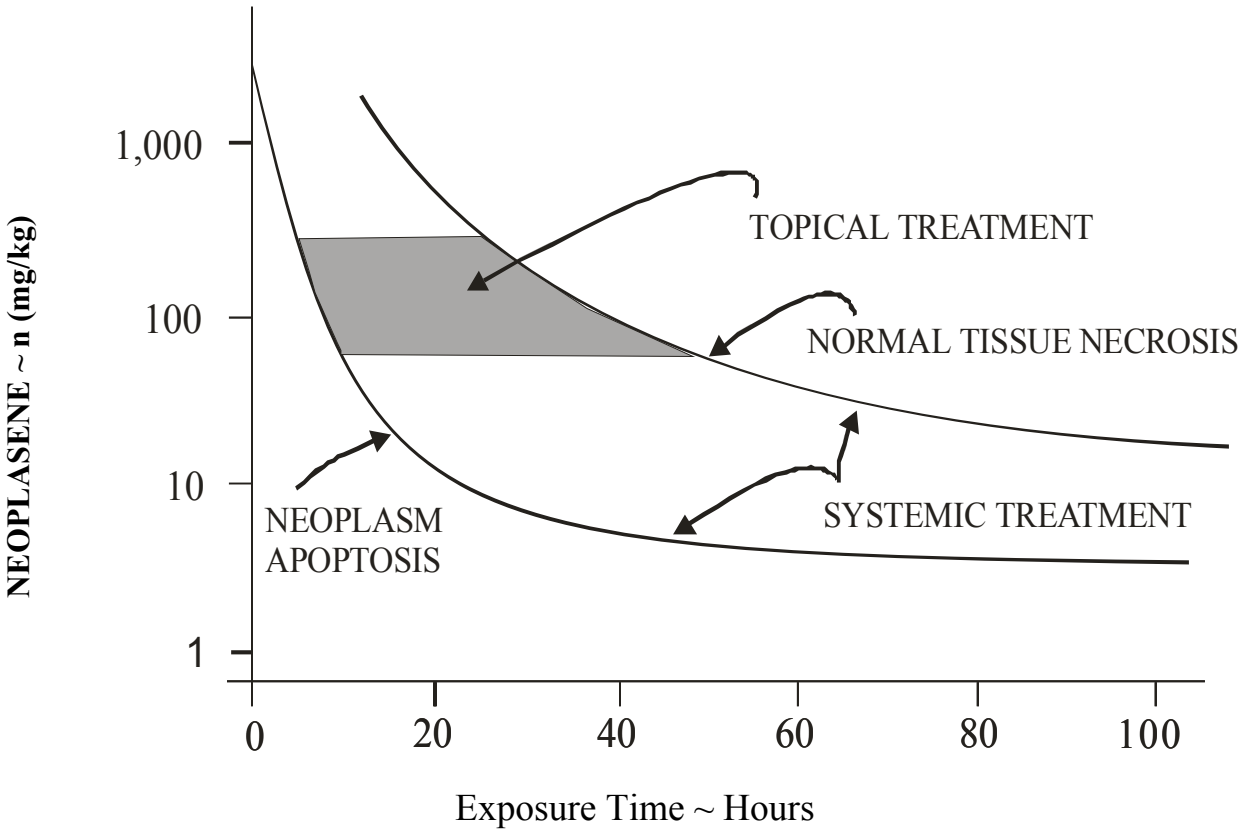
the cell type of a particular lesion and the cell type of other present neoplasm, lesion or not, the value of biopsy is diminished. Biopsy may be destined to become but an academic curiosity and a vestigial remain of the ongoing research into the character of cancer.

If multiple lesions present, it is generally assumed that the disease has metastasized when they more likely developed independently due to degeneration of the apoptotic process. Further, the reappearance of a tumor after resection is frequently thought of as regrowth when more likely a new tumor has simply developed in the neighborhood of the resection from the diseased tissue that escaped detection. The practice of removing a margin around an excised tumor blindly removes a portion of this field of diseased tissue. The closer to the structured tumor the more actively diseased this field is typically observed to be. Resection followed by irradiation and chemical therapy are less than specific and blind to residual neoplasm and collateral damage is done without elimination of all the diseased cells.

Whether tumors arise from connective tissue, melanocyte, fibroblast, basal cell, squamous, epithelial, mast cell, or any other anatomical origination site they do have in common that they are abnormal. They are characterized by a cell membrane that is different from normal cell membrane or the neoplastic cell membrane is different just because it is not fully developed. Either way the neoplastic cells are vulnerable as a result of this characteristic. A single diseased cell or a field of diseased tissue, just as the flagrantly malignant structured tumor, exhibits a different mix of polysaccharides in the cell membrane which lends them vulnerable to preferential attack and they therefore are detectable.

There are some chemicals that do respond to the vulnerable neoplasm preferentially. The viscotoxins in mistletoe are feebly effective; curcumin and epigallocatechin are much better and similar to sanguinarine [reference 1 and the references therein]. Benzyl isoquinoline alkaloids and their salts are however stunning. These alkaloids, including sanguinarine, clearly attack neoplasm preferentially [reference 1 and the references therein]. The cell membrane of neoplasm is permeable to Neoplasene's active principles - benzyl isoquinoline alkaloids and their salts. Healthy cells possess a cell membrane that is resistant to attack unless dosage or exposure times are high, then attack results in necrosis not apoptosis. The active principles interact with DNA and trigger apoptosis. They also inhibit adenosine triphosphatase. Further, nuclear transcription factor NF-κB is potently inhibited [reference 1 and the references therein]. These are the key mechanisms of the affinity of Neoplasene to trigger apoptosis. By adjusting concentration and exposure time neoplasm is condemned and normal cells are spared.

There is a functional relationship between the death of neoplastic cells and exposure to Neoplasene. It is observed that the apoptosis and necrosis resulting in the death of diseased cells is directly proportional to the concentration of the active principles and the concentration required monotonically decreases as a function of exposure time to Neoplasene, figure 1.



APOPTOSIS and NECROSIS – NEOPLASM vs. NORMAL CELLS*

*This figure is quantitatively approximate. Do not rely on the numerical values.

figure 1

When neoplasm is attacked there is localized inflammation and soreness because the immune system which does not readily recognize neoplasm does recognize dead neoplastic cells. Normal bodily processes that eliminate necrotic cells usually will not have trouble ridding the system of the dead cancer cells because the increase in load over normal bodily processing is comparably small due to the dose controlled low rate of apoptosis. If the cancer is large and aggressive and the rate of apoptosis high enough to eliminate neoplasm as fast as it is produced it may overwhelm the ability to digest the necrotic tissue, in this situation debulking is indicated.

The active principles will induce gastrointestinal distress if the concentration is too high or the exposure time is too great. It has been found that if the drug is administered by mixing thoroughly with a wet cooked meal that dosages below eleven milligrams per kilogram are usually beneath the threshold of distress.

General Treatment Protocol

The strategy is to eliminate, by preferentially stimulating apoptosis, the diseased tissue. The task in treatment is to simultaneously get enough of the Neoplasene in contact with the neoplasm to cause apoptosis faster than it is growing by mitosis and restrict the concentration and exposure time so that healthy tissue is not attacked. Further the dose needs to be low enough to allow the body to rid itself of the dead tissue as fast as it is produced and also to avoid anorexia.

There are situations where these tasks are easy, others where they are difficult and still others where they are impossible. On the easy extreme are those cases where the tumor is sloughed or excised and the residual neoplastic tissue is eliminated with long term low dose oral treatment. The difficult situations include aggressive inoperable growths where oral treatment is the only option. Anorexia may be avoided with careful adherence to oral protocol and large doses of metoclopramide or other antiemetics. Impossible situations present when the diseased tissue is being created at such a rate that the required dose of Neoplasene ensuring cell destruction faster than cell creation cannot be accomplished without anorexia and/or overloading the body's ability to eliminate necrotic neoplastic cells.

It is the unusual situation wherein the disease is limited to an observed lesion. The common situation encountered is that diseased cells with compromised ability to self destruct are widespread in the patient. They often involve multiple cell types (e.g. squamous cell, melanocyte, mast cell, etc.). Usually the presence of the disease is not apparent until a debilitating limp, lump, lesion or other signal of debilitated function presents. Elimination of the lesion by resection or use of Neoplasene or NeoplaseneX does not solve the problem. Much diseased tissue remains and is continually produced because of a widespread compromised apoptotic cell destruction mechanism.

Smearing or injecting the margins after resection followed by long term low dose oral treatment is an effective treatment protocol. It takes some measure of time for the redevelopment of widespread tissue with debilitated apoptotic genetics. Hopefully the patient will succumb to old age by a more normal organic shut down prior to the resurgence of cancer. If not, the prophylactic use of Neoplasene continually or at least periodically, for the remainder of the patient's life is indicated.

Many cancers can be treated topically with adjunct long term oral treatment. Osteosarcomas, bladder carcinomas, lymphomas and other internal or widespread neoplasm may be treated orally, by injection or by infusion. The oral dose is initially high and is followed by long term low level oral protocol. Treatment protocols for a wide variety of situations are available.

Several case histories are presented to demonstrate the use of Neoplasene and the developing protocols. Neoplasene salve has been in use topically since mid-2003 and oral and injectable forms have been used widely since early 2006. The methods employed to accomplish effective treatment are varied and limited only by practical realities and the creativity of the practitioner. The presence of a malignant tumor is not as grim a situation as it once was.

Reference: Ahmad et al., Differential Antiproliferative and Apoptotic Response of Sanguinarine for Cancer Cells versus Normal Cells, Clinical Cancer Research, Vol. 6, pgs. 1524-1528, April 2000.

CASE HISTORIES

James H. Bailey, DVM: Associated Veterinary Service: Great Falls, MT

Patches a neutered feline, fourteen pounds, ten years old was referred on April 13, 2004, for non-healing lesion on and in the right nostril one centimeter in diameter. The lesion involved the right nares extending posterior into the nasal cavity with apparent bone involvement. The tissue was identified as a squamous cell carcinoma

On April 26, 2004, Patches was anesthetized and the area was clipped and cleansed. A layer of Neoplasene was applied to the entire area. Patches was maintained on Isoflorane for thirty minutes and then the Neoplasene was cleaned off. The tissue was gray and necrotic after this treatment. The lesion was reevaluated on April 27th. Wound Balm was applied to keep the lesion soft. One week later the lesion was retreated with Neoplasene under Isoflorane anesthesia. On May 6, 2004, fluid drainage from the nostril with frequent sneezing occurred. Clinical exam revealed heavy scab and tissue separation in the middle of the mass. On May 13, 2004, the lesion was retreated. Neoplasene was applied to an area of normal looking healing tissue. On May 25, 2004, a normal healing lesion presented. Three weeks later there were two small areas of raw tissue in the depth of the lesion. It was covered with Neoplasene under Isoflorane anesthesia. Excessive salivation after recovery resolved in thirty minutes without treatment. On July 2, 2004 the raw areas were retreated with the Neoplasene without anesthesia.

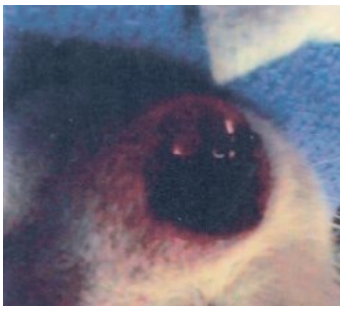
In early August there was a fine line of raw tissue deep into the nares. It was retreated with Neoplasene under Isoflorane anesthesia. On September 13, 2004 no active lesion could be seen and Patches was acting normal. On October 10, 2004 some nasal discharge and excess sneezing occurred. No areas of visible tumor presented but a thin red line deep in the nares was treated with Neoplasene. After three hours the medication was wiped away. No area of reactivity could be seen. The Neoplasene acts as its own confirmation or denial of the presence of diseased tissue.

On November 18, 2004; March 10, 2005 and July 27, 2005 the tumor bed area appeared normal and no treatment was warranted. On August 23, 2005 bloody mucous discharge was reported. There was no active lesion. One week later Patches was normal. The cause for the bloody nose was not identified. On

September 25, 2005, Patches was a normal, happy cat and the owner was very pleased.

Treatment was a protocol dictated by response to the treatment. General anesthesia was used because of the location of the lesion and the patient's ability to do damage with its front claws. At no time during or after the treatment did Patches appear to be uncomfortable or in pain. The response of the tumor to the Neoplasene was dramatic in that minimal tissue was destroyed which would have been impossible with a surgical approach. Normal tissue does not appear to be affected by the Neoplasene. This ability to spare normal tissue is a great asset.

4/26/04



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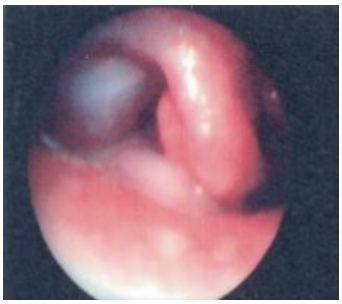


3/10/05

Patches - Squamous Cell Carcinoma Photo Chronology

Figure 2

On January 25, 2007 Gingko, a seven year old, ninety-two pound neutered Rottweiler mix was diagnosed with a mast cell tumor involving the fifth digit of the right hind paw.

The lesion appeared to be confined to a red, raised dermal growth, approximately one centimeter in diameter. On January 26, 2007, Gingko was pre-anesthetized and maintained on Isoflourane anesthesia. The tumor was found to be more invasive than anticipated, encircling the bone and involving the majority of the tissue of the fifth digit. Amputation of the digit to the level of the distal third of the fifth metatarsal was performed.

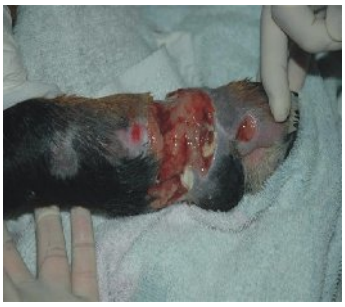
Histopathology supported a morphological diagnosis of grade II mast cell tumor with the appearance of complete excision at the amputation border. After consultation with the School of Veterinary Medicine at Madison, Wisconsin (SVMM), Gingko was started on the Vinblastine/Prednisolone chemotherapy program.

On June 2, 2007, approximately six weeks after the last Vinblastine treatment, a small growth was found involving the same location as the surgery. A referral for cancer staging and radiation therapy was declined. On June 5th an aggressive debridement of the affected region was executed. Histopathology identified perivascular mast cell infiltrates consistent with a grade III Mast cell tumor.

CCNU therapy was started on the 19th of June. Despite two doses the growth was returning, prompting investigation of alternative treatments, which led to Neoplasene. Neoplasene was elected and on the 20th of August Gingko was sedated for NeoplaseneX infiltration. Five cubic centimeters of NeoplaseneX was diluted to ten cubic centimeters with lactated ringers and the entire dorsal and lateral aspect of the foot was injected with three-tenths cubic centimeters volumes of the diluted solution. Following recovery, Gingko was started on Tramadol for pain control. The following day, redness was noted throughout the treated area. Over the next two days, the tissue started to swell and ooze a serous fluid and twice daily applications of Wound Balm was started. Neoplasene 300 at one and six-tenths cubic centimeters twice daily was initiated on August 23rd. Two days later, multiple areas of the affected tissue began to slough and on August 31st, the tissue sloughing continued to the point of concern that the distal aspect of the foot may become devitalized. Cephalexin 1000 milligrams by mouth three times daily and foot soakings with Chlorhexidine was started due to evidence of a gram positive bacterial infection secondary to the tissue damage. Treatment continued throughout

the next two weeks and on September 13, the wound was almost completely filled in with granulated tissue.

On March 27, 2008, Gingko was re-examined and there was no evidence of cancer recurrence at the surgical site. The foot healed nicely with excellent re-growth of the hair coat. Gingko is bright, alert and happy. There is no lameness or pain noted and Ginkgo continues to receive the oral Neoplasene at the normal after care dose.



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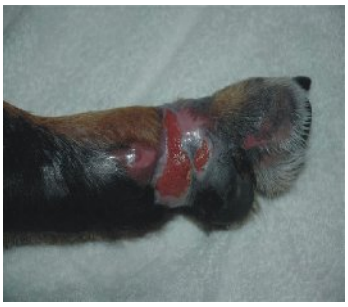

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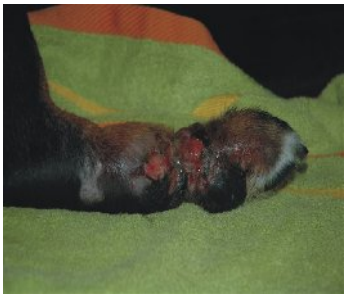

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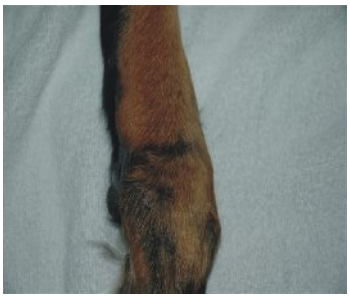


d

Gingko - Mast Cell Treatment Photo Chronology

figure 3

Brandie, a ten year old, thirty-three pound, spayed Cocker Spaniel presented with a seven and one-half centimeter diameter raised, fluctuant, fluid filled mass involving the right side of the anterior chest. The owner noticed it two months prior to presentation but thought that it had the feel and appearance of a fatty tumor. Fine needle aspirate resulted in a determination of a mast cell tumor on December 4, 2006.

On December 15th, a wide excision of the mass and surrounding tissue was completed and histopathology report indicated a Grade II Mast cell tumor with the appearance of clean margins. After consultation with SVMM, Vinblastine/ Prednisolone chemotherapy program was started.

On June 15, 2007, approximately ten weeks after the last Vinblastine treatment, a mass similar to the previously removed tumor involving the same location was found. Surgical removal was elected. Follow-up Histopathology reported the presence of a possible Grade III Mast cell tumor. Two weeks after surgery, CCNU therapy was initiated, but after two doses, three weeks apart, the mass recurred with palpable soft tissue densities and fluid accumulation. Investigation into alternative therapies identified Neoplasene as an option and the owner elected to proceed.

On August 22, 2007, Brandie was pre-anesthetized with Hydromorphone and sedated with IV Telazol and the entire anterior chest region was infiltrated with three-tenths cubic centimeters volumes of a diluted solution of NeoplaseneX. Tramadol was started for post-treatment pain once Brandie was recovered from the anesthesia.

On August 25th, Brandie was started on six-tenths cubic centimeters Neoplasene 300 given twice daily. On August 31st, the infiltrated chest region started to drain a malodorous, cloudy fluid through several small necrotic areas and Brandie was started on 250 milligrams Cephalexin by mouth three times daily. The owner was instructed to keep the area clean with frequent warm soaks with an antiseptic shampoo.

On September 12th, Brandie was re-examined and the area was dry and clean with no evidence of drainage. On October 5th, Brandie was found to be completely healed with no evidence of recurrence of the cancer, although there were a few small areas of thickened skin associated with the drainage sites. On March 24, 2008, Brandie was re-examined and although still overweight, appeared to be alert and healthy. She has no evidence of recurrence of the cancer and the focal areas of thickened skin were resolved. Her owner continues to administer twice daily doses of Neoplasene oral aftercare.

Cedar, an eight year old neutered pit bull terrier mix presented on April 4, 2005 to evaluate a swelling on the dorsal aspect of his right metatarsals. A biopsy revealed soft tissue sarcoma three by four centimeters of fibroblastic origin.

Treatment options include resection with wide margins followed by irradiation. Large tumors on distal limbs pose problems of closure. Where the tumor is locally invasive amputation may be offered as an alternative. The clients did not wish to pursue surgical approach or irradiation. Treatment with Neoplasene was offered.

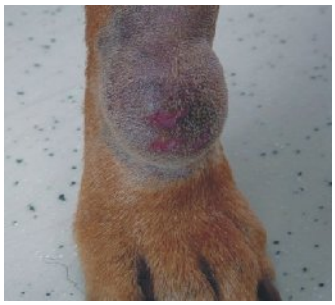
A layer of Neoplasene approximately five millimeters thick was applied to the tumor surface. The treatment site was bandaged for ten hours. The bandages were removed and the area rinsed with hydrogen peroxide. Several areas of tissue necrosis were evident primarily surrounding the biopsy sites. The site was coated with Wound Balm and bandaged. The following morning an additional treatment was performed. By that evening a larger area of discoloration and necrosis was evident. The paw was mildly swollen. Three days later the dorsal and superficial layers of the tumor began to separate and large areas of tumor necrosis were evident.

Four days later the skin overlying the tumor mass had completely separated from the surrounding skin and an extensive area of necrosis was present at the center of the tumor. The tissue at the periphery of the mass appeared viable so an additional application was performed. Three days later the entire tumor mass appeared necrotic and partially separated. The following day the mass sloughed. The client cleansed the area daily with hydrogen peroxide, applied Wound Balm or a triple antibiotic ointment topically and bandaged the area.

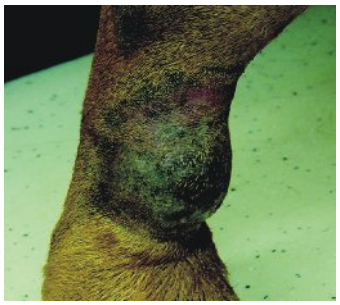
Four days later the tissue appeared healthy. There was no evidence of pain or inflammation. Normal wound contracture was observed. At a six month follow up there was no evidence of tumor recurrence and hair re-growth had occurred over approximately three fourths of the original treatment area.

A follow up biopsy was not performed. The tumor was successfully removed without surgery or irradiation. This author (SLG) has subsequently used Neoplasene in the treatment of hemangiopericytoma, nerve sheath, squamous cell carcinomas, oral melanoma, and an apocrine cell carcinoma, as either the sole method of therapy or following surgical debulking of the tumor mass. These experiences and those of other practitioners indicate that Neoplasene differentiates between neoplastic and non-neoplastic tissue, causing rapid necrosis of neoplasm

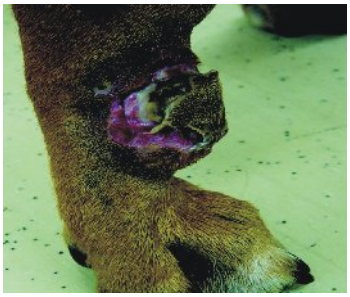
without harming the adjacent healthy tissue. The use of this compound is an effective alternative to surgery and irradiation in the removal of small to medium size cutaneous and subcutaneous neoplasms and a useful adjunct to surgery in the removal of larger masses. The potential benefits of a therapeutic agent that differentiates neoplastic from non-neoplastic tissue at the cellular level are enormous. These would include not only the successful eradication of neoplastic cells beyond the visible margins of a mass, but also elimination of the need to remove large amounts of healthy tissue to ensure 'clean margins'. In situations where this treatment is used as the sole therapeutic modality, anesthesia is generally not needed, with the possible exception of intraoral neoplasms, or those in very close proximity to the eye.



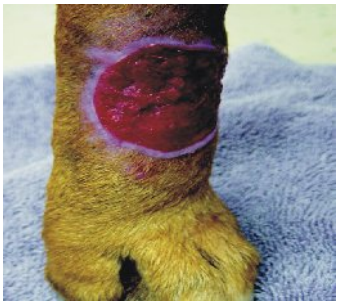
4/28/05 pre-treatment



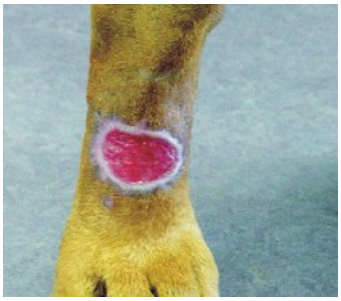
4/29/05 post treatment



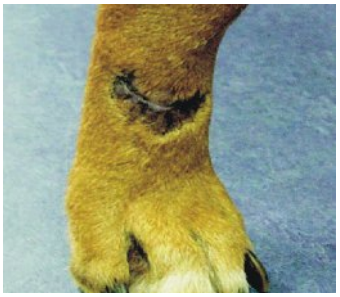
5/2/05 separation



5/23/05 granulation



6/3/05 healing



11/8/05 end result

Cedar - Soft Tissue Sarcoma Treatment Photo Chronology

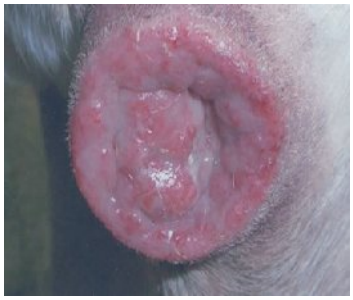
figure 4

This author (ABL) has treated many patients with Neoplasene. In all the cases the Neoplasene has been applied in a thin layer. In a few cases the salve has been reapplied in twenty-four to forty-eight hours.

Ali a seven year old spayed female yellow Labrador Retriever, presented on December 9, 2004 with a six centimeter spherical mass on her front left leg. The skin over the lump appeared normal. Twenty cubic centimeters of blood were removed with a syringe. A hard mass palpated in the lesion. Surgical removal was accomplished. Histopathology identified that the mass was a spindle cell tumor. The tumor returned aggressively and within seven days had regrown to nearly the size as it was at the time of surgical removal, figure 5.

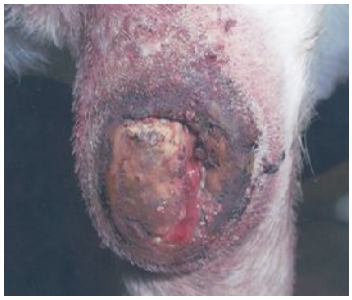
Neoplasene was applied and the leg bandaged. At eighteen, twenty-five and thirty-seven hours the Neoplasene was reapplied. At sixty-four hours a large plug of necrotic tissue fell out of the treated area. The area in and around the tumor bed was inflamed and showed signs of healing at the end of seven days. A ridge of granulation tissue looked suspicious and was retreated. The ridge sloughed and the area continued to heal. After initial treatments which were bandaged for about twenty-four hours each, the patient was allowed to remove devitalized tissue with lingual abrasion. After fourteen months, the area that had tumor tissue appeared normal and was hair covered. As of January 2008 the patient was doing well.

12/21/04



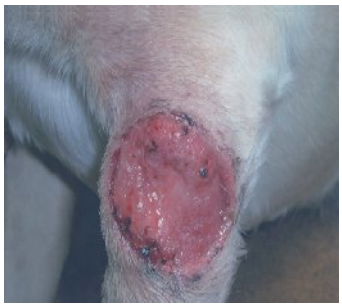
Seven days post surgery

12/22/04

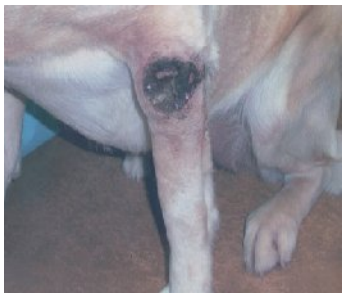


Twenty-five hours later

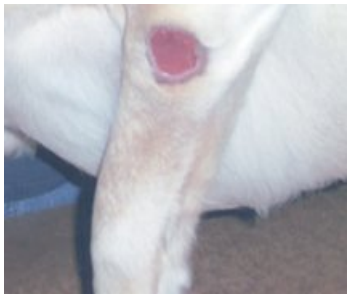
12/28/04



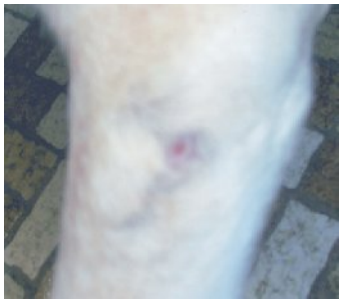
Sloughed Off



12/28/04 The end is near



Ali Healing



The End

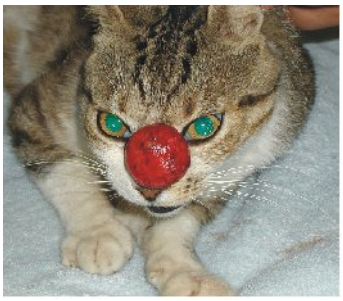
Ali - Spindle Cell Carcinoma Treatment Photo Chronology

figure 5

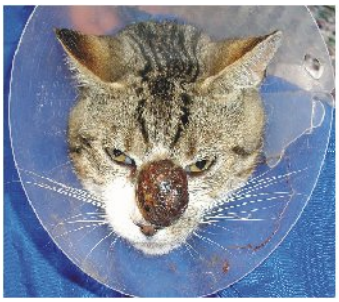
A feral cat with a tumor covering the bridge of its nose was presented. The duration of the condition was unknown. Histopath was not performed on this tumor however neurofibroma is presumed.

Neoplasene was applied on days one, two and four for twelve hours. After the twelve hours the salve was cleaned off with hydrogen peroxide and Wound Balm was applied. Because the cat was fractious, sedation was required for each treatment. The tumor was kept protected with Wound Balm. The tumor began to separate from the normal adjacent tissue by day six and fell off on day ten.

Once the tumor sloughed the wound was treated daily with Wound Balm without sedation for almost a week until the patient was too fractious to treat further and was discharged. Skin margins were migrating in at that time. Treatment at home did not continue because of his fractiousness, figure 6.

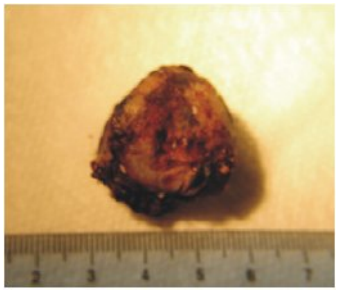


Day one prior to treatment

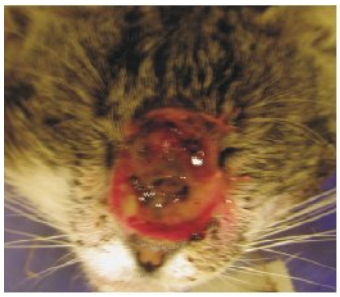


Day two of treatment

Day six of treatment



Day ten of treatment



Nasal cartilage intact

Eight months from start of treatment

Rudolph - The Fractious Feral Feline Treatment Photo Chronology

figure 6

Maggie an eight year old, spayed female, Scottish terrier was diagnosed with transitional cell carcinoma of the bladder at Kansas State University on September 10, 2007. The patient was ultrasounded then and again on October 8, 2007 to find that the tumor was growing and also causing hydronephrosis of the left kidney. Treatment with Neoplasene 300 orally and NeoplaseneX with sterile saline bladder infusions were elected. The patient was placed on Neoplasene 300 orally at a dose of 125 milligrams twice daily, and Astragalus extract orally at one-quarter milliliter twice daily. Maggie was also placed on an all natural, preservative and additive free food, and supplemented with fruits and vegetables. The patient was anesthetized each time for bladder infusion.

On October 9, 2007. Maggie was anesthetized and infused with fifty milliliters saline/one milliliter NeoplaseneX intrabladder.

On October 12, 2007. Maggie was anesthetized and infused with thirty-five milliliters saline/two milliliters NeoplaseneX intrabladder.

On October 15, 2007. Maggie was anesthetized and infused with thirty-five milliliters saline/five milliliters NeoplaseneX intrabladder.

On October 19, 2007. Maggie was anesthetized and infused with thirty-five milliliters saline/seven milliliters NeoplaseneX intrabladder.

On October 26, 2007. Maggie was anesthetized and infused with ten milliliters saline/three milliliters NeoplaseneX intrabladder.

Ultrasound on October 31, 2007 showed reduced transitional cell carcinoma mass. Ultrasound on November 7, 2007 showed further reduction of transitional cell carcinoma, narrow band of tumor tissue and no fingerlike projections had been previously noted.

On November 14, 2007. Maggie was anesthetized and infused with six milliliters saline/two milliliters NeoplaseneX intrabladder.

On November 21, 2007. Maggie was anesthetized and infused with six milliliters saline/two milliliters NeoplaseneX intrabladder.

An ultrasound on December 19, 2007 showed no evidence of a bladder tumor. Ultrasound on January 16, 2008 showed no evidence of a bladder tumor. Ultrasound was repeated on 4/1/08 and no evidence of a tumor was found.

Maggie will continue to be monitored using ultrasound and urinalysis. So far she is doing well, has a good energy level, and urine output. Seven months has elapsed since treatment began. The plan is to do bladder infusions as needed and to maintain her on Neoplasene 300 and Astragalus by mouth daily.

This author (LKM) has been using the Neoplasene drugs for over a year.

Zoey a rescued spayed Labrador retriever approximately seven years old presented 10/30/06 at seventy-nine pounds for what was assumed an abscessed tooth at the buccal aspect of #307. There was a two centimeter, ulcerated, firm, erythematous mass that was painful and bleeding. Tooth #307 had been displaced by the mass. A firm, bony mass extended lingually from #305-309. Radiographs were performed and lysis noted in the left mandible from the apex of the lower left canine #304 to #308. Histopath results were osteosarcoma.

Referral consultation resulted in recommendation of hemimandibulectomy, radiation and chemotherapy. Neoplasene treatment was elected. On 11/14/06 Zoey was presented and general anesthesia induced with Isoflourane, figure 7.a., pretreatment of buccal mass. Neoplasene salve was applied to the buccal mass for thirty minutes and then was rinsed away with hydrogen peroxide and water, figure 7.b. Zoey was released with Tramadol and Chlorhexidine rinse. Neoplasene Oral 300 at a dose of six and one-half milligrams per kilogram by mouth three times daily was started. Some salivation and oral hemorrhage was observed.

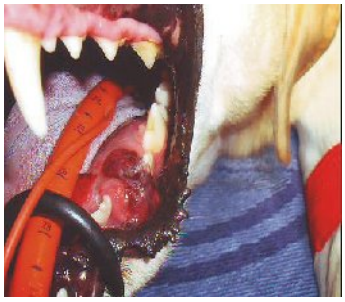
One week later a second topical treatment was administered. Indicators were normal. General anesthesia was induced and the mass evaluated, figure 7.c. It fell apart exposing the alveolar socket for #307. The displaced #307 was extracted. Salve was again applied for thirty minutes and then rinsed away. Zoey was sent home with astragalus extract at a dose of one and one-quarter milliliters three times daily.

Zoey presented 11/28/06 for a third treatment. Health indicators were normal and general anesthesia was induced. There was no buccal mass present. Neoplasene was applied to the lingual mass for thirty minutes. Prior to this third treatment there had been substantial hemorrhage, which resolved.

A fourth treatment was performed on 12/5/06. The oral Neoplasene dose was increased to eight milligrams per kilogram by mouth three times daily. She was rechecked on 12/12/06, figure 7. d., and appeared stable. Another recheck on 12/18/06 demonstrated no new visible tumor growth. Zoey's owner reported she was back to eating hard food. The Neoplasene Oral 300 dose increased to ten and one-half milligrams per kilogram by mouth three times daily. Famotidine forty milligrams was also dispensed at one-half tablet with each Neoplasene dose. A

fifth Neoplasene salve treatment was performed on 1/22/07 under general anesthesia.

Zoey was rechecked on 2/5/07, 5/10/07 and 10/15/07. She is at this writing well over a year post diagnosis. She has a normal life, catches a Frisbee and is doing very well. She continues on the Neoplasene Oral 300 three times daily and astragalus two times daily. Her disease is controlled and she has an excellent quality of life.



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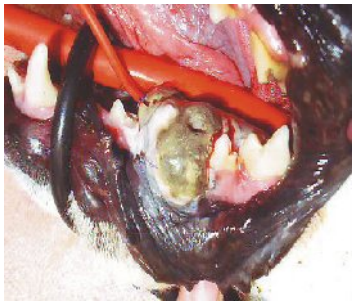

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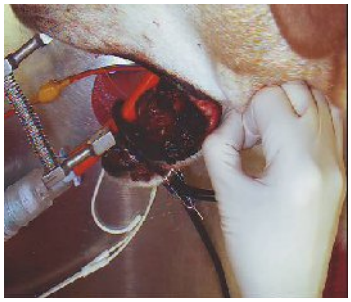

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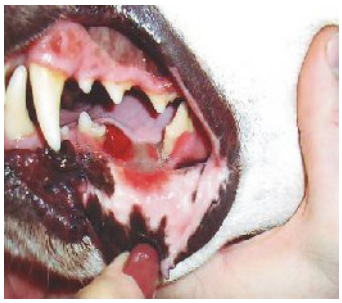

d

Zoey - Osteosarcoma Photo Chronology

figure 7

Jesse, a female brindle boxer, birth date 5/14/98 originally presented 7/6/05 for vaccinations and evaluation of a pink, depigmented area medial to the nares opening on the left side of her nose of approximately three month's duration. Biopsy revealed a well-differentiated mast cell tumor.

On 9/23/05 Jesse was accepted into a double blind study to evaluate a chemotherapy drug for mast cell tumors. She had a second tumor on her right shoulder. She began the program on 10/18/05. At the conclusion of the study it was learned that she received the drug, not the placebo. She now had four tumors, was inappetent and her weight had dropped from near eighty pounds to seventy pounds. The study ended in December, 2006.

She began Neoplasene therapy on 1/15/07. Two milliliters of NeoplaseneX injectable was diluted in two milliliters of lactated ringers solution and one-half milliliter was injected into eight sites around a two centimeter mast cell tumor on her left lateral thorax. This procedure was repeated in a mass on her left hind leg as well. She had immediate swelling and appeared uncomfortable. She was sent home to start Neoplasene Oral 300 three days later at a dose of nine and four-tenths milligrams per kilograms by mouth two times daily and one and one-quarter milliliters of astragalus by mouth two times daily on her food. If there were no signs of vomiting or anorexia, the owner was to increase the Neoplasene Oral dose to three times daily.

Jesse was rechecked on 1/24/07. The mass on her left side had ruptured and was draining serosanguinous fluid. A wrap was devised to absorb the exudates. Her weight had increased to seventy-one pounds. Her left hind leg was markedly swollen. Her Neoplasene dose was increased to eleven and three-tenths milligrams per kilogram by mouth three times daily. Metoclopramide was also dispensed to give with each Neoplasene dose. She returned on 1/26/07 with further swelling of her left hind leg the leg was hot packed and drained twice. Copious amounts of serosanguinous fluid drained from the tumor area. She was sent home with a mild pressure bandage and instructions to continue hot packs. The leg returned to normal size and function within twenty-four hours.

Jesse has continued on the oral protocol ever since. Her weight as of 8/31/07 was eighty-seven and two-tenths pounds. She is active, happy and has excellent quality of life. She does not act her ten years.