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TUMORS OF THE SKIN AND SOFT TISSUES

R. E. Weller

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Pacific Northwest Laboratory
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MASTER

TUMORS OF THE SKIN AND SOFT TISSUES

Dr. Richard E. Weller

Skin covers the largest area of the body, and is often a reflector of many internal disorders. It protects the rest of the organ systems from a variety of environmental insults, but at the same time it is constantly exposed to factors that could ultimately cause chronic diseases and cancer. Since it is relatively easy to recognize skin abnormalities most skin cancers are brought to the attention of professional help earlier in the course of disease than for most other organ system. Many skin neoplasms resemble noncancerous dermatologic disorders that they may be mistreated for months or years. As is true in human medicine, following an accurate diagnosis most skin tumors can be effectively treated with a high rate of cure. Tumors of the skin should be aggressively treated. When causal factors are known, such factors should be removed from the animal's environment or the animal should be removed from repetitive exposure to excessive carcinogenic exposure, i.e., sunlight, known chemical carcinogens.

TABLE 1

COMMON TUMORS OF SKIN AND SUBCUTANEOUS TISSUES OF
DOGS, CATS, HORSES, AND CATTLE

| A. | <u>Epithelial Cell in Origin</u> | Dogs | Cats | Horses | Cattle |
|-----|--|------|------|--------|--------|
| 1. | Cysts | + | | | |
| 2. | Papillomas | + | | + | + |
| 3. | Keratoacanthoma | + | | | |
| 4. | Squamous cell carcinoma | + | + | + | + |
| 5. | Basal cell tumors | + | + | + | |
| 6. | Sebaceous gland adenomas and adenocarcinomas | + | | | |
| 7. | Perianal gland tumors | + | | | |
| 8. | Tumors of hair follicle origin | + | | | |
| 9. | Sweat gland adenomas and adenocarcinomas | ± | ± | | |
| 10. | Ceruminous gland adenomas and adenocarcinomas | ± | ± | | |
| B. | <u>Tumors of Melanin Producing Cell</u> | | | | |
| 1. | Melanoma (benign and malignant) | + | + | + | + |
| C. | <u>Mesenchymal Cell in Origin</u> | | | | |
| 1. | Mast Cell tumors | + | + | + | + |
| 2. | Fibromas (sarcoids in horses) fibrosarcomas | + | + | + | + |
| 3. | Neurilemmoma (Schwannoma) Neurofibroma | + | + | | |
| 4. | Hemangiopericytoma | + | | | |
| 5. | Histiocytoma | + | | | |
| 6. | Transmissible venereal tumor | + | | | |
| 7. | Hemangioma -- hemangiosarcoma | + | + | + | + |
| 8. | Lymphosarcoma -- reticulum cell sarcoma | + | + | + | + |
| 9. | Leiomyoma -- leiomyosarcoma | ± | ± | | |
| 10. | Lipoma -- liposarcoma | + | + | + | + |
| 11. | Myxoma -- myxosarcoma | ± | | | |

+Common

±Found but not common

TABLE 2

COMMON TUMORS OF SKIN AND SUBCUTANEOUS TISSUE OF OTHER ANIMALS
FREQUENTLY SEEN IN VETERINARY MEDICINE

| | Pigs | Sheep | Goats | Poultry |
|---|------|-------|-------|---------|
| A. <u>Epithelial cell origin</u> | | | | |
| 1. Squamous cell carcinoma | | + | + | + |
| 2. Papilloma -- fibropapilloma | | | + | + |
| 3. Basal cell tumors | | + | | + |
| B. <u>Melanin producing cell</u> | | | | |
| 1. Melanoma benign and malignant | + | | | |
| C. <u>Mesenchymal cell origin</u> | | | | |
| 1. Skin leukosis (lymphoid neoplasms) | | + | | |
| 2. Mast cell tumors | + | + | + | + |
| 3. Fibroma -- fibrosarcoma (variety of undifferentiated sarcomas) | | + | | + |
| 4. Lipoma -- liposarcoma | | | | + |
| 5. Leiomyoma -- leiomyosarcoma | | | | + |

+Common

±Found but not common

TABLE 3

FREQUENCY OF DOGS, CATS, HORSES, AND CATTLE SKIN TUMORS OF
EPITHELIAL CELL ORIGIN-RECORDED BY VETERINARY MEDICAL DATA PROGRAM
FROM MARCH 1964 TO DECEMBER 1969*

| <u>TUMOR</u> | Dogs | Cats | Horses | Cattle |
|--------------------------------------|------|------|--------|--------|
| 1. Squamous cell carcinoma | 51 | 6 | 5 | 4 |
| 2. Papilloma | 17 | | 11 | 7 |
| 3. Basal cell tumors | 28 | 9 | | |
| 4. Sebaceous gland adenoma | 60 | 1 | | |
| 5. Sebaceous gland adenocarcinoma | 3 | | | |
| 6. Trichoepithelioma | 15 | 2 | | |
| a. Calcifying and cystic epithelioma | 9 | | | |
| 7. Sweat gland adenoma | 1 | | | |
| 8. Sweat gland adenocarcinoma | 2 | 1 | | |
| 9. Adenexal tumors not specified | | | | |
| a. Adenoma | 83 | 3 | 1 | 1 |
| b. Adenocarcinomas | 51 | 4 | 1 | |
| TOTAL | 330 | 26 | 18 | 12 |

*Data kindly supplied by W.A. Priester - Epidemiology Branch, N.C.I.

TABLE 4

FREQUENCY OF DOGS, CATS, HORSES AND CATTLE SKIN TUMORS
OF MESENCHYMAL CELL ORIGIN-RECORDED BY VETERINARY MEDICAL DATA PROGRAM
FROM MARCH 1964 TO DECEMBER 1969*

| <u>TUMOR</u> | Dogs | Cats | Horses | Cattle | |
|---|-------|------|--------|--------|----|
| 1. Lipoma | 312 | 1 | 8 | 1 | |
| a. Liposarcoma | 1 | | | | |
| 2. Mast cell tumor | 82 | 8 | | | |
| 3. Melanoma (benign and malignant) | 43 | 2 | 11 | 4 | |
| 4. Fibromas (sarcoids horses) | 20 | 4 | 172 | 5 | |
| a. Fibrosarcoma | 15 | 2 | 1 | | |
| 5. Hemangioma | 26 | 1 | | 1 | |
| 6. Neurofibroma | 4 | 1 | 9 | | |
| 7. Hemangiopericytoma | 99 | | | | |
| 8. Histiocytoma | 26 | | | | |
| 9. Transmissible venereal tumor | 1 | | | | |
| 10. Lymphosarcoma -- reticulum cell sarcoma | 3 | 1 | | 2 | |
| 11. Leiomyoma | 1 | | | | |
| a. Leiomyosarcoma | 2 | 1 | | | |
| 12. Myxoma | 1 | | | | |
| a. Myxosarcoma | 3 | | | | |
| 13. Sarcomas not specified | 22 | 1 | 2 | | |
| | TOTAL | 578 | 23 | 211 | 13 |

*Data kindly supplied by W.A. Priester - Epidemiology Branch, N.C.I.

TABLE 5

SOME EXAMPLES OF VIRUSES THAT CAUSE TUMORS OF
THE SKIN AND SUBCUTANEOUS TISSUE

| Virus Classification by Standard Subgrouping | Tumor Types of Skin and Subcutaneous Tissue |
|---|---|
| 1. Pox-like DNA viruses | <ul style="list-style-type: none"> • Myxomatosis of Rabbits • Fibromas of rabbits and squirrels • Histiocytomas of subhuman primates (Yaba tumor)* |
| 2. Papova DNA viruses | <ul style="list-style-type: none"> • Papillomas of man, rabbits, dogs, cattle, horses and solid tumors of hamsters and brain tumors of rabbits |
| SV-40 (vacuolating virus) | <ul style="list-style-type: none"> • Fibromas of deer |
| 3. Oncorna RNA viruses | <ul style="list-style-type: none"> • Sarcomas of poultry • Sarcomas of mice • Fibrosarcomas of cats • Fibrosarcomas of monkeys |

*Only zoonotic virus known.

Chemicals

The first medical documentation of the cause of cancer was in 1775 when Perceival Pott, a British physician, reported that chimney sweeps had a higher incidence of scrotal cancer than the rest of the population. First scientific proof that hydrocarbons cause cancer awaited the demonstration by a Japanese physician, Yamigiwa, and a veterinarian, Ichikawa, in 1914 when they induced squamous cell carcinoma by repeatedly putting coal tars on the tips of rabbit's ears. Other examples of chemicals that cause skin cancer are listed below in Table 6.

TABLE 6
CHEMICALS KNOWN TO CAUSE SKIN TUMORS

1. Tar and Pitch
2. Oil and paraffins
3. Following severe burns (occasionally, following hot iron branding) or chronic exposure to heat such as the use of Kangri in India (a smoldering wood-charcoal burner placed under garments on the abdominal area to provide warmth during the winter months).
4. Industrialization with chronic exposure to chemicals (dyes, hydro-carbons, radioactive isotopes) led to the discovery of several types of carcinogens.

Co-carcinogenesis

Some basic concepts of chemical co-carcinogenesis using skin as the target organ has been described in experimental laboratory animals (Berenblum, 1969).

Berendlum's studies have shown that a chemical factor acts as an "initiator" which set the stage for cell transformation with no clinical signs or abnormality; however, thereafter when the skin is exposed to another chemical factor referred to as a "promoter", overt signs of cancer will occur. It is evident from Barenblum's work that the initiation of ski cancer may be the result of multistage events.

Bovine papilloma virus may cause sarcoid in equine. DNA homologue studies.

Squamous cell carcinoma

1. Vincristine + Cytosan
2. Bleomycin
3. Dinitrochlorobenzene (DNCB)
 - use to sensitize skin, get delayed hypersensitivity rx.
 - limited use

Basal cell tumors

Associated with hair follicles - trichoepith-
transforms toward

| | | |
|--------------|---|--------------------|
| sebaceous | } | elioma |
| sweat glands | | adenoma adenoca |

Usually benign, solitary. More prominent in
dogs, than cats.

sweat glands - usually malignant

sebaceous - "benign lesions on hairless areas
are probably warts, those in haired
areas are sebaceous adenomas."

Diagnosis

Most animal owners recognize skin tumors early for obvious reasons, which is an advantage for effective treatment. An accurate diagnosis is based on cytologic and histologic examinations. A complete clinical assessment is necessary in order to recommend appropriate and corrective therapy.

Therapy

In most instances a veterinarian faced with cutaneous neoplasms, has several alternatives: 1) no treatment, this is particularly advisable where cutaneous tumors occur in young animals originating from DNA virus infections such as papillomas which usually spontaneously regress. Some other tumors with unknown etiologies such as canine histiocytomas and transmissible venereal tumors, 2) surgery using traditional excisional approaches, electrocautery surgery or cryosurgery, 3) radiotherapy, 4) topical chemotherapy, 5) systemic chemotherapy 6) immunotherapy.

Excision Surgery

Wide excisions with traditional surgery are among the easiest and least costly procedures, and most practitioners are equipped to perform such surgery. Healing is also usually fast which is a distinct advantage over other therapeutic approaches. The use of traditional surgery alone when dealing with potentially or known malignant tumors that metastasize is no longer tenable. Therefore, radiotherapy, chemotherapy, or immunotherapy should also be used in conjunction with surgery.

Radiotherapy

There is less information concerning radiotherapy of skin tumors in animals than in humans. The main reason for difference in the two medicines is mainly based on the high cost of radiation equipment and, therefore, costs

for treatment. Nevertheless, the modern veterinary radiotherapists have at their disposal a wide variety of radiation equipment ranging from low voltage to orthovoltage and high energy acceleration machines. Implantation of radioactive materials in the area of the neoplasm is particularly effective in treating skin tumors of large animals. Beta radiation in the form of ^{90}Sr has been particularly effective in treating squamous cell carcinoma of cattle and horses eyes.

Probably there has been more written about radiation treatment of cutaneous neoplasms in large animals than for all other tumors combined. In our clinic, animals with cancer are frequently treated with radiation. Those tumors most frequently treated with radiation are rare squamous cell carcinoma, mast cell tumors, and perianal gland tumors.

Cryosurgery

The topical application of liquid nitrogen to superficial cutaneous neoplasms has been used for some time by veterinarians and physicians. It has several advantages over excisional or electrocautery surgery because the surgery can frequently be done under a local anesthetic. The disadvantages are cost of equipment and accurate freezing to -20°C to insure the destruction of all tumor cells. It is believed that there may be an autovaccination by release of tumor antigen from the cell after freezing which gives to the individual an immunologic enhancement to mount an immune response against its own tumor.

Electrocautery

Cells of some skin tumors such as equine sarcoids or causal viruses such as those of papillomas are easily transferred to incision borders and quickly recur. In addition, the vascular supply of many neoplasms is extremely

abundant resulting in excessive hemorrhage. These difficulties can easily be overcome by using electrocautery for surgical removal of skin tumors.

Topical Cytotoxic Therapy -5-Fluorouracil

Topical treatment of skin cancer has been popularized in human medicine. Its application in veterinary medicine are just as advantageous and should be encouraged for treatment of multiple skin tumors in old geriatric patients where there is extreme anesthetic risk. For difficult invasive tumors, 5-FU cream can be applied for several months at daily intervals. Animals must, of course, be restrained from licking areas where 5-FU cream has been used.

Immunotherapy

Immunotherapy of squamous cell carcinoma of the eye or eyelids and base of the horn in cattle have been investigated. Various types of immunotherapy have been used in treatment of skin tumors of animals (Table 7). One that has received considerable attention in human medicine and little attention in veterinary medicine is use of 2, 4-dinitro-3chlorobenzene (DNCB) which induces delayed hypersensitivity. The sensitizing agent is in a cream base at a concentration of one part per ten thousand. This is classified as a nonspecific active immunization.

Other agents that have been used are triethylene-imino-benzoquinone (TEIB), 5-mercapto-2"-deoxyuridine, purified protein derivative of tuberculin, and several others.

Prognosis

An overall statement concerning the prognosis of skin tumors cannot be made; however, most benign skin tumors respond well to treatment and frequently many malignant tumors are curable, but malignant spindle cell tumors (tumors of mesenchymal cell origin) have a poor prognosis.

TABLE 7
TYPES OF IMMUNOTHERAPY

| | <u>Specific</u> | <u>Non Specific</u> |
|-------------|--|-------------------------------|
| A. Passive | Antisera | Normal Sera |
| B. Adoptive | Stimulated Lymphocytes | Non-Stimulated Lymphocytes |
| C. Active | Tumor Cells, Extracts, or Chemically Altered Antigens | BCG, C. Parvum, Etc. |

TABLE 8
TREATMENT OF SQUAMOUS CELL CARCINOMA

| <u>Tumor</u> | <u>Treatment & Prevention*</u> |
|---|---|
| Squamous cell CA of: nostrils, nasal septum, tips of ears & eyelids and conjunctiva | Excision + radiotherapy (3,500 to 5,000 rads). In large animals may use radioactive implanting devices. |
| Squamous cell CA of sheath, penis vulva, anus & perineal region | Cryosurgery and electrocautery may be used. Chemotherapy. |
| Squamous cell CA of toe nail epithelium and at mucocutaneous junctions | Excision, radiotherapy, maintenance chemotherapy, therapy. |
| Squamous cell CA of ventral abdominal region of dog | Excision + immunotherapy. |
| Squamous cell CA of cornea and sclera | Excision + radiotherapy (⁹⁰ Strontium), immunotherapy |

*Keep light pigmented animals out of sunlight.

TABLE 9

TREATMENT OF OTHER SKIN TUMORS OF EPITHELIAL CELL IN ORIGIN

| <u>Tumor</u> | <u>Treatment & Prevention</u> |
|--|---|
| Papillomatosis | Vaccine; autogenous vaccine. |
| Basal cell tumor electrocautery, radiotherapy | Excision, cryo or multiple tumors - chemotherapy. |
| Sebaceous adenomas (adenocarcinoma) | Excision - multiple tumors - chemotherapy. |
| Perianal gland tumors | Castration, ECP, excision (cryosurgery). Malignant form - combination chemotherapy. |
| Trichoepithelioma | Cryosurgery and/or chemotherapy. |
| Epidermal cyst | Excision. |
| Keratoacanthoma | Excision or chemotherapy. |
| Sweat gland tumors | Excision, radiotherapy, maintenance chemotherapy. |

TABLE 10
TREATMENT OF SKIN TUMORS OF MESENCHYMAL CELL ORIGIN

| <u>Tumor</u> | <u>Treatment & Prevention</u> |
|---------------------------------------|--|
| Benign mast cell | Excision or nothing |
| Malignant mast cell | Excision, radiotherapy, chemotherapy, immunotherapy. |
| Benign melanoma | Excision, multiple cryosurgery or nothing. |
| Canine histiocytoma | Excision or nothing. |
| Fibroma | Excision. |
| Sarcoid | Excision, electrocautery, cryosurgery, immunotherapy. |
| Fibrosarcoma, neurofibroma | Excision, chemotherapy. |
| Hemangiopericytoma | Excision. |
| Lipoma | Excision. |
| Liposarcoma | Excision, chemotherapy. |
| Lymphosarcoma, reticulum cell sarcoma | Chemotherapy, immunotherapy. |
| Hemangioma | Excision. |
| Hemangiosarcoma | Excision, chemotherapy. |
| Canine TVT | Nothing, excision, multiple drug chemotherapy. |

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