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Title: THE PATHOGENESIS, DIAGNOSIS AND TREATMENT OF CANINE ALLERGIC AND BACTERIAL DERMATITIS

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The pathogenesis, diagnosis and treatment of bacterial dermatitis and various canine allergic dermatitidies including allergic inhalant dermatitis, contact dermatitis and flea allergy dermatitis were studied. The effect of specific nonprotein and protein components of commercial flea antigens on the gross and microscopic appearance of intradermal injections was investigated. Additionally, a preliminary evaluation of lymphocyte stimulation by mitogens and flea antigen was performed on a limited number of blood samples.

The predominant bacteria isolated from primary or secondary bacterial dermatitis is Staphylococcus auerus (coagulase positive). The history and lesions associated with bacterial dermatitis are quite variable, depending upon the presence of concurrent problems and the nature of the infection such as superficial or deep. Histopathological

changes are not pathognomonic for bacterial dermatitis, but are generally characteristic. Diagnosis is confirmed by bacterial isolation from lesions. Treatment includes long term bactericidal antibiotic therapy based upon in vitro antibiotic sensitivity testing, autogenous bacterins and treatment of concurrent problems.

Allergic inhalant dermatitis is characterized by intermittent or continuous pruritus accompanied by primary or secondary lesions in a young dog, usually one to three years of age. There tends to be a familial history of allergic dermatitis. The distribution of lesions is usually more generalized than other allergic etiologies. Diagnosis is based on history and intradermal skin tests. The predominant allergens identified with intradermal skin testing in the Pacific Northwest include molds, weeds, trees, grass and house dust. In 80 percent good or fair response to treatment by hyposensitization and in some cases minimal maintenance dosages of corticosteroids is expected. Approximately 20 percent of the cases require higher levels of corticosteroids to control allergic symptoms with or without concurrent hyposensitization.

Canine contact dermatitis is characterized by a predominantly ventral dermatitis accompanied by pruritus. Approximately 50 percent of the dogs manifest contact allergies by one year of age, while 25 percent are four years or older. Usually both primary and secondary lesions are

present. Diagnosis is based on history, clinical appearance, isolation from suspected contactant and then provacative exposure to the same contactant. Histopathologic characteristics of allergic contact dermatitis are not specific, but can be helpful in broadly categorizing dermatoses providing direction from further study and treatment. Treatment includes avoidance of contact exposure or corticosteroid administration.

A high incidence of flea allergy dermatitis is commonly found in dogs with a low grade flea infestation. Clinical signs include intense pruritus involving the posterior of the body, especially the dorsal back and abdomen. Both primary and secondary lesions are often present. Diagnosis is usually based on history, distribution of lesions and response to treatment. Intradermal skin tests using flea antigen may help in confirming the presence of a flea hypersensitivity, but are not adequate for making a definitive diagnosis in many cases. The wheal induced by the flea antigen is mainly due to edema without a remarkable inflammatory response. There is no correlation between gross wheal formation and microscopic changes, particularly in the degree of upper dermal edema. Treatment includes control of fleas in the environment by fumigation, continuous flea control on all of the animals in the household and hyposensitization with flea antigen.

The uptake of tritiated thymidine by lymphocytes stimulated with phytohemmaglutinin, concanavalin A, lipopolysaccharides and diluted flea antigen was evaluated on a limited number of blood samples. A wide variation between replicate samples precluded establishment of definite conclusions.

The Pathogenesis, Diagnosis and Treatment of Canine Allergic and Bacterial Dermatitis

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THE PATHOGENESIS, DIAGNOSIS AND TREATMENT OF CANINE ALLERGIC AND BACTERIAL DERMATITIS

I. INTRODUCTION

Canine allergic and bacterial dermatitis constitutes an important group of diseases encountered in veterinary practice. Allergic inhalant dermatitis, flea allergy dermatitis and contact dermatitis are the three most common clinical entities involved in canine allergic dermatitis. Bacterial infection may be primary, but is frequently seen as a secondary problem in association with primary allergic dermatitis (71). The primary symptom of allergic dermatitis is pruritus. The history, symptoms, and lesions are often the same for different etiologies; thus, understanding the pathogenesis, etiology and diagnosis as well as management of the patient can be very difficult. It is not unusual to have more than one primary etiology.

The basic immunological mechanisms associated with these canine diseases are similar to the counterparts in human medicine. Therefore, it is of value to review the normal immune response (40). Mitogen stimulation of peripheral lymphocytes (45, 79) and histopathologic examination of tissue from lesions (1, 71, 72) have been helpful in defining and categorizing various immunological phenomenon in the dog.

In the first section of this thesis, the normal immune response, the pathogenesis of pruritus and normal histology of canine skin are reviewed. Following is a report of a preliminary lymphocyte stimulation study. The remainder of the paper is devoted to the characterization of bacterial dermatitis, allergic inhalant dermatitis, contact dermatitis and flea allergy dermatitis. The pathogenesis, historo-clinical, laboratory and histopathological findings and management of clinical cases are discussed in detail.

II. REVIEW OF LITERATURE

The Immune Response

Immunity is thought of as a state of altered responsiveness to a specific substance, induced by prior contact with that substance. The immune response consists of two functional components (35): cell mediated immunity (CMI) which depends upon the activity of T cells, and humoral immunity, which is dependent upon antibody activity. Humoral immunity developed later in the evolution of defense mechanisms (17).

Immunologically active tissues are principally components of the lymphoid system consisting of three subdivisions: stem cells, primary lymphoid organs and peripheral (secondary) lymphoid system. Stem cells, which originate in the bone marrow may migrate via the circulation to the thymus, a primary lymphoid organ. Here they differentiate into lymphocytes. Approximately 95 percent of these cells die within 3-5 days without leaving the thymus or performing any known function except replication. The other five percent have a life span of months to years. These acquire a characteristic surface antigen, theta, and become the T cells. Many of these leave the thymus and colonize in the thymic-dependent zones of the spleen and lymph nodes (16, 24).

The Bursa of Frabricius in the avian species has been identified as the site of development of cells associated with humoral immunity. Stem cells migrate to the bursa and transform into lymphocytes bearing specifically reactive immunoglobulin determinants on their plasma membrane and possess the ability to divide continuously and to differentiate into plasmocytes and memory cells. These lymphocytes are B cells which are released by the bursa and colonize secondary lymphoid organs, which include the lymph nodes, spleen, tonsils and peyers patches. The mammalian equivalent of the bursa has not been identified. It is suggested by some workers that the antibody production by plasma cells occurs in the gut associated lymphoid tissue (GALT). (24).

The T cells are concentrated in interfollicular and deep cortical areas of the lymph node while the B cells form the germinal centers. The size of germinal centers is proportional to the intensity of antigenic responses. In the spleen, the B cells are found primarily in periarteriolar areas while the T cells are in the periphery of the splenic nodules (24).

Antibodies are produced by plasma cells, which are formed when B cells are stimulated to replicate by contact with antigen. All antibodies are immunoglobulins, but it is not known if the reverse is always true. The principal classes of human immunoglobulins are IgG, IgM, IgA, IgE and

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to supply.

When stimulated by antigen, these cells secrete antibody or proliferate and give rise to antibody forming cells. A wide range of clones arise during prenatal life, but clones that encounter homologous antigenic determinants are immediately destroyed. The postnatal response to contact with homologous antigen may be: 1) inhibition or destruction of the cell, 2) liberation of pharmacologically active agents from the cell, 3) proliferation, or 4) transformation to an antibody producing plasma cell (18, 37).

Macrophages are necessary for an immune response to occur, probably through their role as processors of antigenic material, however, their exact interrelationship with the T and B cell system is not yet known. T and B cells are indistinguishable by ordinary light microscopy. The surface membranes of B cells possess many immunoglobulin receptors that can react with antigenic determinants, and receptors for complement and for aggregated immunoglobulin. T cells have fewer surface immunoglobulin receptors and lack receptors for complement and aggregated immunoglobulins, but may possess binding sites that can attach to heterologous red blood cells and cause the formation of rosettes. Lymphocytic membranes also have receptor sites for various natural substances such as plant lectins (47).

Three subpopulations of T cells with distinct activities have been identified in mice: 1) antigen specific helper cells, 2) antigen cytotoxic effector cells, and

3) nonspecific suppressor cells. T cells exhibit varying degrees of interaction with B cells in the immune response. Helper T cells do not synthesize readily detectable amounts of immunoglobulin, but are needed for differentiation of B cells into antibody producers. Antigens vary in their degree of dependence on T helper cell interaction for the production of specific antibodies. It is generally considered that helper T cells recognize the carrier whereas B cells react to the hapten (57).

Cytotoxic cells are very specialized cells which cause lysis of target cells in vitro and probably rejection of allografts in vivo. They do not appear to cooperate with B cells in the humoral immune response. There is evidence indicating that several cell types may exhibit immunologically specific cytotoxicity and that it may comprise cooperation of several cell types. Lymphocytes activated by agents other than from target cell antigens may be cytotoxic for a wide variety of cells. Mitogens which induce blast transformation and deoxyribonucleic acid (DNA) synthesis in lymphocytes also induce cytotoxicity at the same optimal concentration (29).

Suppressor T cell activity has been associated with many antigens including those which are thymus independent. In specific regulation of the immune response, the induction of suppressor activity appears to be a direct result of antigenic stimulation. It has been shown that IgG, IgM and

IgE are regulated by suppressor T cells. Suppressor activity has been induced in vitro with mitogens. It has been shown that suppressor cells are generated during normal sensitization in delayed hypersensitivity reactions (83).

Lymphocyte transformation induced by an antigen has generally been considered a manifestation of CMI (59). In some cases, lymphocyte transformation has been correlated with antigen specific CMI as measured by skin testing (66, 67, 68, 81). Other studies show that B cells as well as T cells may proliferate in vitro in response to antigens, indicating both humoral and CMI may be measured by lymphocyte assay (65,80).

Gell and Coombs have divided immunologic mechanisms of disease into four categories (38). Type I reactions include all immunologic phenomena involving atopy. They are mediated by antibodies of the IgE or reagin class, which become passively attached to tissue mast cells, basophils and neutrophils. Upon contact with allergen, such reagin sensitized cells rupture, and release pharmacologic mediator substances such as histamine, slow release substance of anaphylaxis (SRS-A), serotonin and proteolytic enzymes (38).

Type II reactions include all immunologic phenomena mediated by cytotoxic antibodies and complement. Autoimmune diseases characterize this reaction (38). The mechanism involved with development of autoimmunity is not well understood. It is known that immunologic responses to exogenous

antigens, both cell mediated and humoral, reflect crucial balance, between extrinsic forces which can either augment or suppress the reactivity of T and B effector cells. It is probable that similar immunoregulatory influences play a key role in maintaining tolerance to some self antigens. Despite the presence of cells potentially capable of reacting to autologous antigens, lack of antoimmunity may reflect either an absence of amplification or a preponderance of suppressive immuno-regulatory forces (77).

Type III reactions include all immunologic phenomena mediated by immune complexes which are composed of circulating antigen joined with circulating antibodies and complement. Serum sickness and the Arthus reaction characterized Type III reactions in many species. Antibody is present in much higher amounts than in Type I reaction and form precipitating complexes with antigen and complement. Components that are chemotactic for neutrophils and which also cause histamine release such as anaphylotoxins are generated during the fixation of complement (38). Food allergies and drug sensitivities are examples of Type III reactions in dogs.

Type IV reactions include all cell mediated immune reactions leading to tissue damage. These reactions are mediated by the thymus dependent lymphoid system (38). Features common to cell mediated immune reactions include: 1) delayed evidence of response (one or more days

as compared to minutes or hours in immediate hypersensitivity reactions) of a sensitized individual to a second experience with the same antigen, 2) inflammatory lesions contain a predominence of mononuclear cells, 3) passive transfer of sensitivity to another individual is accomplished by transfer of lymphocytes rather than antibodies, and 4) inciting agents are of large molecular size such as protein carriers to which the low molecular weight hapten is bound.

The most common clinical manifestation of cell mediated immune reactions is delayed hypersensitivity characterized by allergic contact dermatitis. The hapten contacts the skin, penetrates the corneal layer of the epidermis and froms a covalent union with the epidermal protein. The hapten-protein complex is carried via lymphatics to the regional lymph node where an immunospecific clone of cells is stimulated. Reexposure of the sensitized lymphocyte to more antigen in the epidermis causes release of several soluble mediators (hymphokines) of inflammation and pruritus (27, 38, 40). It has been shown that specific antibody may interfere with the activity of a sensitized T lymphocyte, and, in the process referred to as "immunologic enhancement," cause a decrease in CMI. The enhancing antibody has also been implicated as a basic factor in establishing immunologic tolerance (48, 70).

Many of the cytotoxic reactions mediated by humoral antibody require complement, whereas those caused by the direct action of lymphoid cells or lymphokines liberated from them do not (26). Phagocytic activity of macrophages is enhanced in the presence of lymphokines. Complement and antibody increase the hydrophobic nature of bacterial cells, thereby enhancing phagocytic ingestion.

Pathogenesis of Pruritus

There are two categories of pruritus. Physiologic itch is a sharp and clearly defined pruritic sensation that is a frequent but intermittent everyday occurrence in normal individuals. Pathologic itch is a less well-defined pruritus that is characteristic of dermatitic skin. Pruritus is a primary cutaneous sensation which can be elicited only from the epidermis, the upper dermis and the palpebral conjuctiva. There are no specialized itch receptors, as the itch sensation is carried by the naked nerve endings which are especially numerous at the dermo-epidermal junction. The sensory or "itch points" are specific areas which vary in number from animal to animal and from site to site. After skin damage, they may change in number and respond to a lower threshold or stimulation. Itch sensations originate from naked nerve endings and are carried to the dorsal root ganglion and spinal cord via small unmyelinated C fibers. The fibers decussate a few segments up the cord and ascend

in the ventrolateral spinothalamic tract via the posterior ventral nucleus of the thalamus to the posterior central gyrus of the cortex. There may be a medullary itch center involved (41, 60).

The actual mediators of pruritus are believed to be proteolytic enzymes. Proteases are released by both fungi and bacteria, by mast cell degranulation in allergic diseases and in the course of other antigen-antibody reactions. Extracellular accumulation of proteases can occur with physiologic capillary dilation, e.g. plasmin, or with inflammatory reactions, e.g. leukopeptidase. Cathepsin from epidermal cells has proteolytic activity, and may account for the persistence of the itch sensation after epidermal damage induced by scratching (41, 60).

Itching may be initiated or potentiated by boredom, neuroses and tiredness. Factors such as foreign bodies, insect bites, or parasitisms, allergic reactions, infections and inflammatory reactions, or vasodilation may facilitate access to proteases and thus potentiate pruritus (41, 60).

Normal Histology of the Skin of Dogs

The skin surface is composed of scale-like folds which form irregular depressions into which the hair follicles invaginate. Small knoblike enlargements called epidermal papillae 0.33 to 0.35 mm. in diameter are present on the

surface of the epidermis, projecting from 0.25 to 0.48 mm. above the surrounding area.

The epidermis of hairy skin consists of five layers: 1) basal layer (stratum cylindricum), 2) prickle layer (stratum spinosum, malpighian layer), 3) granular layer (stratum granulosum), 4) clear layer (stratum lucidum), and 5) horny layer (stratum corneum). It varies in thickness from 30 to 40 microns. The granular and clear layers are evident only where keratinization is retarded, as around the hair follicle orifices. The epidermal papillae are covered by a thickened epidermis which is usually six to twelve cell layers thick, about twice as thick as the surrounding epidermis.

The horny layer is the thin outer layer of completely keratinized tissue which is constantly being shed. The clear layer which is usually absent from hairy skin is a fully keratinized, compact, thin layer of nonnucleated dead cells. The granular layer if present is usually only one cell thick. The cells are distinctly flattened parallel to the surface and contain shrunken nuclei and large basophillic staining keratohyalin granules. The prickle cell layer is composed of daughter cells of the basal layer. It is usually two to three cells thick and composed of flattened cuboid cells. The basal layer is a single row of columnar cells resting on the basement membrane (basal lamina) which is a chemical interface between the epidermis and underlying

dermis. It stains with periodic acid-Schiff but not with hematoxylin and eosin. The undersurface of the epidermis of hairy skin is smoothly undulating and more or less parallel to the skin surface. Rete ridges as seen in man are not normally present. Melanocyte humbers vary resulting in inconsistent melanin deposition in the basal layer and dermis (55, 61).

The dermis (corium) is of variable thickness. It is composed of collagenous, reticular and elastic fibers, ground substance and cells. In addition there are epidermal appendages, arrector pili muscles, blood and lymph vessels and nerves. The main component of the dermis is the ground substance. It fills the spaces and surrounds other structures of the dermis, but allows electrolytes, nutrients and cells to traverse it freely in passing from the dermal vessels to the avascular epidermis.

There are three types of dermal cells: fibroblasts, mast cells and histiocytes. The fibroblasts are immature cells with indistinct cytoplasm and spindle shaped nuclei that have a fine vesicular appearance. Mast cells are round to fusiform, but with a round or oval nucleus. They characteristically have numerous large, intracytoplasmic, basophilic, metachromatic granules. Histiocytes are mature lymphoid type cells which are also called wandering or tissue monocytes. They have round or bean shaped nuclei that stain paler than fibroblasts.

The hypodermis or subcutis is subjacent to the dermis and is composed predominantly of adipose tissue with blood vessels, nerves and connective tissue.

There are three types of skin glands. Sebaceous glands are simple alveolar holocrine glands which appears as evaginations of the hair follicle. They are located in the superficial layers of the dermis. Where the hair is dense the sebaceous glands tend to be long and narrow. Where hair is sparse the glands are larger. They are often multilobular, club shaped and coiled. Several glands may enter into the single opening of the hair follicle complex. A ring of sebaceous glands opens into the follicle of the tactile hairs. Each sebaceous gland is connected to the upper part of the hair follicle or to the epidermal surface by a short duct. The gland has a peripheral germinal layer of basal cells which surround a central mass of large, foamy lipid-filled cells.

Apocrine sweat glands are located deep in the dermis. They are serpentine in shape. One gland is associated with each hair follicle complex. Its duct enters the follicle just above the entrance of the sebaceous duct. The body of the gland is composed of widely dilated secretory tubules surrounded by a layer of stellate myoepithelial cells. The secretory epithelium is a single layer of columnar cells with budlike apical projections, finely basophilic cytoplasm containing pigment granules and a spheroid nucleus. At the

completion of secretion the glands have a wider lumen and the secretory cells have become low cuboidal in shape with a flattened nucleus. Apocrine glands are located throughout the body except the planum nasale.

Eccrine sweat glands in the dog are found only in the foot pads. The glands are located deep in the dermis at its junction with the hypodermis. A long duct connects the secretory tubule with a pore on the surface of the pad.

The skin of the nasal planum and foot pads have several unique features. The nasal planum epidermis has rete pegs but no glands. In contrast to other areas, epidermal spinosum cells of the nasal planum apparently do not undergo keratinization as they migrate outward, but their cytoplasm becomes weakly acidophilic and the nuclei become pyknotic as the cells flatten out into the squamous type. As they approach the surface, the cells form a thin atypical nucleated stratum corneum which is surprisingly thin. The foot pads are characterized by an exceptionally thick horny layer and the presence of a stratum lucidum. Ducts of the eccrine sweat glands spiral through the epidermis (55, 61).

Senile changes of dog skin have been reported to include atrophy of the epidermis, appendages and dermis with decreased hair numbers. Senile elastosis and dermal basophilia as seen in man do not occur. Changes are variable in skin from different parts of the body. A characteristic feature of aged apocrine glands is the presence of yellow

refractile granules in the secretory cells. There may be a marked increase in dermal pigmentation (8).

III. LYMPHOCYTE STIMULATION BY MITOGENS AND ANTIGENS

Introduction

Lymphocyte stimulation by mitogens and antigens has been used to evaluate the immunological mechanisms associated with specific diseases such as Demodecosis (45) or in evaluating response to antigens such as tuberculin (66, 67, 68, 79). In a recent study the response of sensitized lymphocytes to antigen was maximum at six or more days of incubation. Lymphocytes from nonsensitized dogs showed progressive increases in tritiated thymidine incorporation as the incubation period was increased from four to seven days. The lymphocyte response to phytohemaglutinin began early and reached a maximum within the first four days of incubation (79).

The commonly used mitogens are the plant lectins phytochemaglutinin (PHA) and Concanavalin A (Con A) which stimulate T cells. Pokeweek mitogen stimulates transformation of T and B cells. Lipopolysaccharides of gram negative bacteria are mitogenic for B cells (28).

A technique for a mixed leukocyte culture test in dogs has shown a lymphocyte recovery rate of 60 percent with 84-90 percent purity (51). A lymphocyte recovery rate of 87 percent with ten to fifteen percent less purity has been reported using a slightly modified technique (79).

The purpose of this study was to become familiar with techniques of lymphocyte separation and lymphocyte stimulation using mitogens and flea antigen. The use of bovine fetal serum and canine serum in culture media was compared.

Materials and Methods

Experimental Animals

Dog number 28 was a three year old, 10 kg Welsh Corgi which demonstrated no clinical signs of disease. Dogs 29 and 30 were obtained from a county dog control shelter. They were maintained at the Laboratory Animal Resources Center (LAR) at Oregon State University. Dog number 29 was a young adult Laborador weighing approximately 25 kg. There were a few fleas on the dog at the time of acquisition, but no evidence of dermatitic reaction. Dog number 30 was a young adult, mixed breed weighing approximately 15 kg. There was evidence of a flea dermatitis on the dorsal, posterior back at the time of admission. Both dogs were sprayed with an insecticidal spray and vaccinated for Distemper, Hepatitis and Rabies at the time of admission to LAR. During the experiment, there was no evidence of infection or flea infestation although dog 29 had a chronically loose stool. Dog number 31 was a 3 year old, 14 kg mixed breed dog with a long history of an allergic dermatitis of undetermined etiology. Dogs 28 and 31 were privately owned.

Hanks Balanced Salt Solution (HBSS)

HBSS was prepared as follows: 1) ten ml. of 10X HBSS (modified) without sodium bicarbonate;[a] 2) 90 md. distilled water; 3) one ml. penicillin-streptomycin (10,000 units of penicillin and 10,000 micrograms of streptomycin/ml.); 4) sodium bicarbonate to adjust pH to 7.4.

Ficoll-Sodium Diatrizoate Solution

Separation fluid was made up of ten parts of sodium diatrizoate[b] (a solution of 33.9 gm/100 ml, final volume: density 1.2000) mixed with 24 parts of ficoll[c] (9 gm/100 ml., final volume). Density of the ficoll-diatrizoate mixture was 1.077.

Blood

Peripheral blood was drawn into heparinized syringes and then placed in beakers containing one ml. of heparin (1000 USP units/ml.)[d] per 50 ml. of whole blood.

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a) Flow Laboratories, Rockville, Md.

b) Hypaque sodium (50% (w/v), Winthrop Laboratories, New York, NY.

c) Ficoll, Mol. wt.-400,000, Sigma Chemical Co., St. Louis, Mo.

d) Burns-Biotec Laboratories, Oakland, California.

Isolation of Mononuclear Cells

Fifteen to twenty ml. of heparinized blood diluted 50 percent with HBSS was layered on 10-15 ml. of ficoll-diatrizoate solution. The tubes were immediately centrifuged at 400X g. for 40 minutes. The cloudy white layer of leukocytes at the interface of ficoll-diatrizoate solution and supernatant fluid were removed with a transfer pipette to another plastic tube. The interface cells were washed with 15-20 ml. of HBSS three consecutive times by centrifuging for ten minutes at 200X g. After final centrifugation the cells were resuspended in 1-2 ml. of HBSS for counting in the hemacytometer. A final dilution of 1 x 10^6 cells/ml. was made using the culture medium as a diluent. The leukocyte viability was measured by trypan blue stain which was excluded by live cells.

Culture Medium

The basic composition of the culture medium/100 ml. was as follows: 1) ten ml. of Medium 199 (modified) with HBSS 10X with L glutamine and without sodium bicarbonate;[a)] 2) one ml. of penicillin-streptomycin solution (10,000 units of penicillin and 10,000 ug. of streptomycin/ml.); 3) four ml. of 2N Hepes prepared with 28.83 gm. of Hepes[e)] dissolved in 50

[e)] Sigma Chemical Co., St. Louis, Mo.

ml. of distilled water and adjusted to pH 8.1 with 2N sodium hydroxide; 4) sterile distilled water (80 ml); 5) 1 ml. Gentamicin;[f] 6) 1 ml. Glutamine (2 mM/100 ml);[a] 7) sodium bicarbonate to adjust pH to 7.4.

One culture medium preparation contained 90 ml. of Medium 199 (modified) with HBSS 10X and ten ml. of Fetal Bovine Serum[a] (FBS). A Second preparation of culture medium contained 90 ml. of Medium 199 (modified) with HBSS 10X and ten ml. of Canine Serum. Two other preparations had the basic composition as noted above and ten ml. of canine serum or Fetal Bovine Serum, respectively. The canine serum was prepared from whole blood from dog number 29. After clotting, the sample was centrifuged and the serum removed. It was prepared by heat inactivation at 56°C for 30 minutes, filtered through a 0.45 um membrane filter and stored at 4°C.

Leukocyte Cultures

A microculture test technique was employed for all samples (51). Using concentrations of 1×10^6 lymphocytes/ml., 0.2 ml. of cell suspension was used and was pipetted into the inside wells of a microplate.[g] The 22 outside wells were filled with a blank and not utilized for data

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[f] Gentamicin, 50 mg./ml., Schering Corp., Kenilworth, N.J.

[g] Microplate, 6 mm. Tissue Culture, Flow Laboratories, Rockville, Md.

tabulation because some evaporation may occur from these wells. All of the empty wells were filled with culture media, HBSS, or diluted cells to prevent excessive evaporation of the test wells. Five-tenths ml. of phytohemaglutin[e] concanavalin A, LPS-055[g] or LPS-111[h] or diluted commercial flea antigen[i] was added to each of the test wells (Table II). The plate was sealed with tape and incubated at 37°C five percent CO_2 in a humidified atmosphere for two days, or five days at which time 0.5 u. curries of $^{3}HTdR$[j] was added to each test well. The plates were resealed with tape and incubated for an additional 12-18 hours. They were then placed in the refrigerator to stop lymphocyte stimulation or were harvested directly.

Culture Harvesting

The cultures were harvested using a microharvester (74). The cells were collected on a glass fiber filter,[k] rinsed with physiological buffered saline (PBS) and dried with ethanol. The filter disc was then placed in a scintillation vial with three ml. of Aquasol.[l]

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h) Lipopolysaccharide E Coli, 055:B5 Difco Laboratories, Detroit, Mich.

i) Flea Extract 1:5000 in 50% glycerin and 0.5% phenol, Hollister-Steir Laboratories, Spokane, Wa.

j) Tridiated thymidine, New England Nuclear, Boston, Mass.

k) Grade 934 AH, Whatman, Inc., Clifton, N.J.

l) New England Nuclear, Boston, Mass.

Cell Counting

The uptake of ^{3}HTdR by lymphocytes was counted in a liquid scintillation spectrometer[m] at 50 percent gain for ten minutes or a maximum of 10,000 counts. The results were reported in counts/minute.

Results

The results of the uptake of ^{3}HTdR by PHA, Con A and lipopolysaccharide stimulated lymphocytes were variable between replicate samples of the same animal as well as between different culture medium (Tables II and III). Some lymphocyte stimulation was observed with diluted flea antigen (Table IV). After three days incubation a pooled sample of dogs 30-31 had higher stimulation ratios than those incubated for 6 days. Dog 30 had signs of flea dermatitis and dog 31 had generalized pruritus. There was no consistent differences in the Con A stimulation response between culture mediums containing either fetal bovine serum or canine serum. The viability of the lymphocytes after isolation was 95 percent or greater in all trials. The culture medium preparations with 90 ml. of Medium 199 (modified) were strongly basic and directly toxic to the cells.

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[m] Packard Tri Carb 2275. Packard Instrument Co., Downers Grove, Illinois.

Discussion

The solution used for washing lymphocytes after separation differed from previous canine studies which used saline solution or a tissue culture medium consisting of Eagle's minimum essential medium, calcium-free salts and three to five percent serum (51, 79) instead of HBSS as used herein. The presence of serum in the wash solution has been shown to influence lymphocyte recovery rates and the proportion of leukocyte types (51, 79). Perhaps the absence of serum in the wash solution has an influence also on the blastogenic activity of lymphocytes and might account for some of the inconsistent results in this investigation. The percent recovery of lymphocytes was not evaluated in this study. Four days has been considered the optimum incubation time for stimulation with mitogens rather than the three days used in this study (51) and may have contributed to inconsistency in this study.

The most striking finding in this study was the variability between replicate samples from the same dog taken at different times. Both nonstimulated (control) and mitogen or antigen stimulated cultures showed this variability. Much of this variation can probably be attributed to laboratory error; however, it is possible that several factors not measured could influence the results, including the presence of suppressor B cells, low dose stimulation or high dose inhibition

by mitogens, loss of macrophages and soluble factors during isolation procedures, and the presence of plasma macromolecules which antagonized the T cell activation.

It is difficult to explain why the B cells of both samples were stimulated with LPS-111 on one occasion but not on the other trials. There was more stimulation noted in the medium containing canine serum than that with fetal bovine serum. Possibly some selection had been made for B cells in the culture preparation process.

Stimulation of lymphocytes with diluted commercial flea antigen was not remarkable. Higher stimulation ratios were seen following three days incubation than after six days. This may reflect the lack of *in vivo* stimulation by flea antigen, since sensitized lymphocytes would be expected to show more stimulation after the six day incubation period (79).

IV. BACTERIAL DERMATITIS

Introduction

Chronic bacterial infections involving the skin and ears are a commonly encountered problem in small animal practice and often are the cause of much frustration for the owner and veterinarian. Pyoderma, the term applied to a pyogenic infection of the skin, can be primary or secondary and superficial or deep. Superficial pyodermas include acute moist dermatitis, folliculitis, acne, skin fold pyodermas and impetigo. The deep pyodermas include callous, nasal, interdigital, juvenile and generalized pyodermas (63).

In animals Staphylococcus aureus is generally considered the primary skin pathogen (6). S. epidermidis predominates on the human skin and S. aureus is isolated from the exposed skin in only five to twenty percent of individuals (78). A recent study found the aerobic flora of normal dogs to consist exclusively of coagulase negative cocci and diphtheroids. Clostridium was isolated on anerobic culture in 60 percent of the cases (63). The coagulase test is used to differentiate S. aureus from S. epidermidis or Micrococcus spp. since S. aureus is the only coagulase positive Staphylococcus (15). For purposes of this discussion, the designation Staphylococcus (coagulase positive) will be used

for pathogenic S. aureus and Staphylococcus (coagulase negative) will denote nonpathogenic Staphylococcus spp.

Antibiotics normally recommended for treatment of staphylococcal dermatitis include penicillin, streptomycin, oxytetracycline, neomycin and chloramphenicol (6). More recently, erythromycin, cephalosporin, lincomycin and Tri Acetyl Oleandomysin (TAO) have been recommended (14). Corticosteroids are generally not recommended for use in bacterial infections. A recent investigation showed less favorable results when prednisone was given concurrently with antibiotics in mice experimentally infected with S. aureus (12). In the same study, there was less mortality with a bactericidal antibiotic (Oxacillin) than with a bacteriostatic antibiotic (erythromycin) and the recovery rate of the S. aureus also increased as bacteriostatic drugs were used. Concurrent prednisone administration further increased the recovery rate of the organism following treatment (12). These results demonstrate two important points concerning therapy of staphylococcal dermatitis. First, bactericidal drugs are superior to bacteriostatic drugs and may reduce the bacterial population more completely even though clinical cures are achieved with either type. Secondly, anti-inflammatory doses of the glucocurticoids decrease the resistance of the host to infection, an effect that is dose related and is much more apparent when a bacteriostatic

drug is used rather than a bactericidal antibacterial drug (4).

Pathogenesis

The pathogenesis of bacterial infection of the skin involves three major elements: 1) the pathogenic properties of the organism, 2) the portal of entry, and 3) the host response to microbial invasion (78). It is suggested that generalized pyodermas are associated with poor host resistance to infections with an alteration of cell mediated immune mechanisms primarily involved (39). The role of hypersensitivity to Staphylococcus toxins in the pathogenesis of bacterial or allergic dermatitis is not clearly understood at this time (7).

Toxins and other substances produced by S. aureus probably contribute to its pathogenicity. Both the capsule and protein are antiphagocytic. A leukocidin acts on the cytoplasmic membranes of many cell types including human neutrophils and macrophages to cause cell lysis. The alpha hemolysin (necrotizing toxin) of virulent staphylococci is highly toxic for human macrophages and epithelial cells. Repeated infections in the skin of rabbits produce local lesions of increasing severity. This increased susceptibility can be passively transferred with lymphoid cells, but not with serum. IgG can combine with protein A and C to form a complex on the bacterial surface. This complex is

chemotactic and lethal for neutrophils. Coagulase is either not an attribute of pathogenicity or is not an essential one since coagulase negative mutants appear to be fully as virulent as coagulase-positive strains. Lipase and esterase permit the staphylococcus to survive the antibacterial action of lipids on the skin (69).

An extensive clinical study of furunculosis (interdigital pyoderma) in dogs has identified some factors important in the pathogenesis of Staphylococcus infection. S. aureus was isolated from 95 percent of the control dogs originating in an animal hospital environment. The carrier percentage of S. aureus among the canine population not originating from environments suspected of being staphylococcal reservoirs was 76 percent. Mannitol fermentation and gelatinase production from furuncles was significantly higher than control isolates. All isolates demonstrated deoxyribonuclease activity, lipase production and protein A occurrence. It was observed that the number of colonies of S. aureus from patient carrier sites growing on a culture plate far exceeded those isolated from normal dogs suggesting that the dermal environment of the dogs with furunculosis had become more favorable to the growth of bacteria.

Results of coagulase tests varied. Strains varied according to the species of plasma used. Strains may appear to be nonproducers of coagulase if relatively large amounts of fibrinolysins are produced which inhibit or resolve any

clot formation. In addition the plasma used can also contain anticoagulase antibodies or a coagulase reacting factor (CRF) on which the coagulability of plasms is dependent.

In studies of pH of the skin it was found that the normal skin and dry furuncles are approximately 6.5-6.5. Wet furuncles had a pH of 7.8. This may have been due to the escape of alkaline subcutaneous tissue fluid during trauma.

A study of the histopathological changes of furuncles showed only 19 percent containing inflammatory cells or having cells migrating through the walls of the hair follicle. In these cases only isolated hair follicles were involved. No cocci or rods were detected within the dermis or its structures. Similarly, no foreign body giant cells were observed. Furuncles may be associated with primary changes of the epidermis, characterized by inflammation associated with acanthosis. Early dermal changes observed were cellular infiltrates around enlarged apocrine glands and enlargement of the associated blood vessels. These appeared to be closely followed by cellular infiltrates around the sebaceous glands and hair follicles. The apocrine glands were the first structures to loose their configuration due to inflammatory cell invasion followed shortly by loss of integrity of the sebaceous glands, the destruction increasing with the increase of dermal cellular infiltrate. In every case plasma cells were the predominanting cells of the dermal infiltrate.

Widely dilated follicular canals containing keratin were seen in some furuncles.

A study of the serum factors in furunculosis showed a significant increase of the alpha-2, beta-1, and gamma globulins on paper electrophoresis. Fifty percent of the furunculosis sera tested were positive for macroglobulins. No differences were noted in the concentration of the oxidizing enzyme associated with phagocytosis between infected and control animals. Total serum complement levels varied significantly below and above control levels.

Antistaphylolysin antibody titers were not demonstrated following the administration of formalin-killed bacterial cell suspensions in saline. Significant titers were found after toxoid administration, but disappeared after four weeks. Presence of antibodies to the S. aureus cell wall antigen, protein A, was found on all dogs with furunculosis and controls using a double gel diffusion precipitation test. Good clinical improvement was observed using high dosages of Staphylococcal toxoid. The improvement was not correlated with antistaphylolysin titers. The duration of immunity was short with recurrence of less severe infection within four-six weeks (75).

Factors associated with the role of hypersensitivity to bacteria in human eczema patients have been discussed. Studies have shown that human skin cells will firmly absorb some bacterial antigens, including those of staphlococci and

that antibacterial antibody and complement reacting with acquired antigen damage the skin cells. For this to occur the patient must have sufficient complement-activating antibody to the appropriate bacterial antigen. The antibody must diffuse through the dermo-epidermal "barrier" and react with bacterial antigen adsorbed to and persistent on epidermal cells. Large numbers of organisms and increased moisture of eczematous skin are likely to predispose to percutaneous adsorption of bacterial antigen. Thus epidermal cells may absorb bacterial antigens which predispose them to damage by antibody to the acquired antigen and complement. Nucleated tissue cells also adsorb some bacterial antigens and thereby become susceptible to damage by antibacterial antibodies and complement. Cytotoxic complement-activating antibodies are mainly IgM.

Bacterial antigen may prepare the epidermis for a cytotoxic reaction in all persons, whether normal or with skin disorders, who have sufficient numbers of bacteria colonizing the skin and who have formed the appropriate antibody. In practice this type of cytotoxic reaction is only likely to occur when the numbers of bacteria and diffusion of antibody into the dermis are greatly exaggerated above normal, as in eczema. In the acute phase of generalized eczema the skin is moist, probably as a result of autolysis of degenerate cells and increased vascular permeability. Hydration of the epidermis provides optimal conditions for growth

of bacteria resulting in excessive amounts of bacterial antigen. Hydration also enhances absorption of some of the soluble bacterial antigen into the epidermis. Concommitantly increased vascular permeability and epidermal inflammatory change increase the diffusion of immunoglubulin, including antibacterial antibody and complement into the epidermis. Epidermal cells which adsorb bacterial teichoic acids or polysaccharides onto their membranes will be killed or damaged when antibacterial antibody and complement react with adsorbed antigen.

Polysaccharides and teichoic acids persist in living tissue for several weeks and may persist in muscle and macrophages in vivo for 6-9 weeks. Therefore, epidermal cells adsorbing persistent antigen would remain susceptible to immunologic cytotoxic damage and the adsorption may be accumulative, thereby increasing the susceptibility.

The cytotoxic effect was observed regularly in vitro tests on monolayers, but not with whole skin explants treated with appropriate bacterial antigens and sera producing damage to monolayers. Cells of organized tissues, like the epidermis, may be protected from such damage by being closely packed. Alternatively, there may be inhibitors of this type of change in tissues which are destroyed in the preparation of monolayers.

For the cytotoxic reaction to occur, the patient must have sufficient complement-activating antibacterial antibody.

However, it is possible that a similar cytotoxic change may be induced by lymphocytes, specifically activated by bacterial antigen, reacting with bacterial antigen adsorbed to epidermal cells. Such lymphocytes could initiate as well as potentiate the exzematous reaction in typical delayed hypersensitivity (73).

Materials and Methods

A retrospective study of 195 cases of chronic canine bacterial dermatitis and otitis was performed. All of the animals were examined at the Animal Skin and Allergy Clinic, a referral dermatology practice in Portland, Oregon and Seattle, Washington. The complete diagnostic workup was performed or supervised by the investigator.

Each individual record was reviewed and data summarized for historoclinical findings, bacterial isolates and senstivity test results, response to therapy, and concurrent problems. The sample was divided into primary and secondary bacterial etiologies. Skin biopsies were obtained using a Keyes Biopsy Punch (71). Histopathological findings of twenty-six cases were reviewed. All of the bacterial cultures and antibiotic sensitivity testing was performed by the Willamette Animal Laboratory in Portland, Oregon. The hematological studies were performed by commercial laboratories in Portland and Seattle.

Historoclinical Findings

The history of an animal presented with a chronic bacterial dermatitis is variable depending upon primary and secondary etiological factors, duration and distribution of lesions and previous treatment. Several of the following observations were usually reported: 1) no systemic involvement, 2) strong odor, 3) pruritus, 4) pustules, 5) scales, 6) scabs without pustules, 7) fistulous tracts, 8) erythema in localized areas or around the periphery of lesions with central clearing, 9) partial or complete focal alopecia, 10) dry or oily skin, 11) excessive shedding, 12) local or generalized distribution, 13) seasonal or nonseasonal occurrence, 14) external parasite infestation, 15) temporary relief (1-3 days) with medicated shampoos, 16) temporary response to short-term antibiotic therapy followed by exacerbation of symptoms one to three weeks following withdrawal of antibiotics.

Historoclincial findings associated with chronic bacterial otitis usually included: 1) acute exacerbations coinciding with other dermatological problems, 2) temporary response to local treatment, 3) foul odor and discharge, 4) pruritus around base of ear, 5) partial occlusion of horizontal ear canal due to edema, thickening of wall, wax, debris or hair, 6) some actue inflammation, especially of the pinna, 7) unilateral or bilateral distribution.

The distribution of lesions in the chronic pyoderma cases was predominantly generalized. Often several different areas of the body were involved at the same time. Age and breeds of the patients were variable depending upon the primary diagnosis. Primary pyoderma cases in this study were evenly distributed in all age groups (Table X). Twenty three different breeds were represented in the study.

Laboratory Findings

Culture results of 159 cases of primary and secondary bacterial dermatitis and otitis, summarized in Table IX, were: Staphylococcus (caogulase positive) isolated from 88 percent of the patients, Staphylococcus (coagulase negative) 7 percent, Streptococcus spp. 26 percent, Clostridium spp. 26 percent and Proteus spp. 13 percent. Staphylococcus (coagulase positive) was most frequently cultured from the ears followed by Clostridium spp., Streptococcus spp., non-pathogenic Candida and Proteus spp. in descending order of frequency (Table VIII). The Staphylococcal isolates were most sensitive to chloromycetin, erythromycin, gentamicin, lincomycin, kannamycin and oleandromycin while significant resistance was reported for ampicillin, tetracycline and streptomycin. The Streptococcal isolates were most sensitive to ampicillin, chloromycetin, erythromycin and oleandromycin. Significant resistance was observed with tetracycline, gentamicin, lincomycin, kannamycin,

streptomycin and neomycin. Gentamicin showed their highest percentage of sensitivity with Proteus isolates. Clostridial isolates were most sensitive to ampicillin, chloromycetin and lincomycin (Table VII).

Hematologic findings from the majority of primary pyoderma cases were normal in all respects; however, three cases had an absolute eosinophilia. A leucocytosis, monocytosis or neutrophilia was infrequently observed in chronic bacterial dermatitides.

Diagnosis

The most difficult problem with a chronic dermatitis is to determine if the pyoderma is primary or secondary and it may also be difficult to differentiate between superficial and deep pyodermas. Success of treatment is often dependent upon one or both of these factors.

A thorough history will help separate primary pyodermas from other potential primary dermatitides such as parasitic, contact, inhalant or food allergies. Pruritus would suggest the predisposition to trauma and secondary pyoderma. Distribution and gross appearance of lesions are very helpful in predicting the presence of other primary factors.

Laboratory tests including microscopic examination of skin scrapings, fecal examinations, fungal cultures, complete blood counts and blood chemistries are helpful screening aids. Specific allergy testing including intradermal

skin tests, isolation and provacative testing, and diet testing are often indicated. Bacterial cultures and antibiotic sensitivity tests should be completed on all chronic dermatitis cases in which there is a history of bacterial involvement. If pustules are not present, a punch biopsy utilizing aseptic procedures can be used to obtain a representative bacteriological culture. Following the removal of the plug, the specimen is opened aseptically and a swab used to obtain the specimen for culture. In other cases, a nontraumatized scab can be removed and the underlying surface swabbed.

Histopathologic Findings

Moderate to marked acanthosis and hyperkeratosis, the most common epidermal changes, were present in approximately two-thirds of the cases (Figure 1). Intraepidermal microabscesses (Figure 1) and abscesses at the dermo-epidermal (D-E) junction (Figure 2) were present in some biopsies. Parakeratosis and keratin plugging of the hair follicles was also present in approximately half of the cases. Surface exudation characterized by crusts or flakes of necrofibrinopurulent material sometimes containing parakeratotic or hyperkeratotic debris and occasional bacterial colonies was present in approximately one-third of the specimens. Intraluminal infection of the hair follicles characterized by accumulation of neutrophils, necrotic debris and occasional

bacteria was also present in approximately one-third of the biopsies, often the same specimens having surface exudation. Focal epidermal edema (spongiosis) was present in a few cases usually accompanied by edema and leukocytic infiltrates in the superficial dermis (Figure 3).

Focal or diffuse edema, often accompanied by moderate fibroplasia, at the D-E junction was present in 18 of the 26 biopsies examined (Figure 4). Perifollicular edema and fibrosis usually accompanied the D-E edema (Figure 5). Perifollicular inflammatory cell infiltrates ranging from slight to extremely dense nearly always accompanied perifollicular edema and fibrosis (Figure 5) and was classifiable as a mixed cell infiltrate in all cases; however, the proportion of each cell type varied from a preponderance of polymorphonuclear (PMN) cells in some cases to dense populations of mononuclear cells with only a few PMN cells in other cases.

A dermal cellular infiltrate was present in all biopsies, ranging in degree from a very slight focal mononuclear accumulation in some cases (Figure 4) to an extremely dense population in others (Figures 2 and 3). The number of cases with predominantely mononuclear cell infiltrates closely approximated those with mixed or primarily PMN cell populations. Distribution of inflammatory cells was both diffuse and focal. Perivascular inflammatory cell cuffing was common and dilated veins containing large numbers of PMN's were

present in some biopsies. Neovascularization, especially in the superficial dermis, and vascular congestion was also often present (Figures 2 and 4). A number of specimens contained focal dermal granulomatous foci associated with degenerating suderiferous glands, or pyogranulomatous foci associated with ruptured hair follicles (Figure 6). Several specimens contained dermal microabscesses. There were large areas of scar formation or fibroplasia replacing normal dermal tissue in several biopsies. There were no significant histopathologic differences between pyoderma cases of primary or secondary nature.

Treatment of Chronic Bacterial Infections

The general protocol used in chronic primary pyodermas includes: antibiotic therapy for three or more weeks in high dosages followed by prolonged maintenance dosages. Antibiotic selection is based on sensitivity tests and bactericidal antibiotics are preferred. Antibacterial shampoos are used as needed. Autogenous bacterins are utilized and continued for at least six months following remission of symptoms. Local treatment including clipping of lesions, foot soaks, topical antibiotics, etc. is prescribed as needed. Atarax[n)] is used in cases of pruritus leading to self trauma. Corticosteroids are used only if

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n) Atarax, J.B. Roerig & Company. New York, N.Y.

other procedures do not decrease pruritus sufficiently and only bactericidal antibiotics are used with glucocorticoids.

The successful treatment of a secondary pyoderma or otitis externa is dependent upon the control of the primary etiological factors. The same basic protocol is normally followed for secondary bacterial dermatitis as described above. If the bacterial infection is easily eliminated with control of the primary factors the autogenous bacterin is not used; however, if the pyoderma is persistent or recurrent due to failure to control the primary etiology, an autogenous bacterin can be very helpful.

The general protocol used for treatment of bacterial otitis cases include: 1) thorough flushing of the ear canal with warm water and disinfectant. A water pik or other flushing device is helpful and sedation is often necessary. 2) If the patient has long ear flaps the ears are taped over the head for several days to allow for drainage and air drying. 3) antibiotics based on antibiotic sensitivity tests are used both locally and systemically until marked improvement is seen, then only local treatment is continued until the infection is eliminated. 3) Autogenous bacterin is usually suggested in a long standing or recurring primary bacterial otitis. 5) Surgery may be indicated when conservative treatment with antibiotics and autogenous bacterin fails.

The responses to treatment with antibiotics and autogenous bacterin[o)] in 40 cases of primary pyoderma are summarized in Table X. Good response was seen in 25 (62.5 percent) of the cases, fair response occurred in 6 (15 percent) of the cases and 7 (17.5 percent) of the patients exhibited poor response. The response to treatment of 97 cases of primary allergic dermatitis with secondary pyoderma is depicted in Table VI. Good or fair results were observed in 80 percent of the patients with primary allergic inhalant dermatitis (AID), 90 percent with primary food allergies, 82 percent with primary contact allergic dermatitis, 39 percent with non-specific allergic dermatitis (etiology not determined), and 67 percent with primary flea allergic dermatitis. Table V summarizes the response to treatment of patients with secondary pyoderma concurrent with primary demodecosis, sarcoptic mange and hypothyroidism. All of the animals with primary sarcoptic mange and hypothyroidism had a good or fair response to treatment of the secondary pyoderma. In cases of primary generalized demodecosis, 54.5 percent good to fair response was reported in control of the secondary pyoderma while 32 percent had a poor response.

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o) Prepared by Willamette Animal-Medical Laboratory, Portland, Oregon.

Discussion

The high percentage of Staphylococcus (coagulase positive) isolated from animals with chronic bacterial dermatitis is consistent with findings of other investigators (63). Clostridia have not been routinely reported as a common isolate from the skin or ears probably because most laboratories do not set up routine anaerobic skin cultures. Clostridia isolated from canine skin lesions are probably nonpathogenic since they are not associated with marked dermal vesicle formation and toxemia. The spores may be skin contaminants which are not activated until placed in the anaerobic environment. Proteus and Pseudomonas were cultured most often from the ears or from the skin of patients who had been on a long term antibiotic therapy.

The antibiotic sensitivity results (Table VI) suggest that ampicillin, penicillin, streptomycin and tetracycline should not be used on a chronic staphylococcal dermatitis or otitis until culture and sensitivity tests are completed, since 52 percent, 47 percent, and 62 percent of the staphylococcal isolates were resistant to ampicillin, tetracycline and streptomycin, respectively. Ampicillin and penicillin were considered to reflect the same sensitivity

results although the present data shows more resistance to penicillin than ampicillin.

While not diagnostic in themselves, histopathologic findings can be of marked significance if interpreted carefully. In general, a much more severe dermal inflammatory cell infiltrate, with greater numbers of PMN cells, was present in this series of chronic pyoderma cases than in a previous series of contact dermatitis cases (71). While edema of the D-E junction and around follicular structures was a common finding in the contact dermatitis cases, the accompanying fibrosis and mixed inflammatory cell infiltrate often seen in the pyodermas was seldom present. Foci of epidermal edema were common in the contact dermatitides and seldom encountered in this pyoderma series.

Therapeutically, a severe inflammatory cell response involving deep dermal zones and structures indicates parenteral antibiotics·administration whereas, topical application may be adequate for mild superficial reactions.

The response to treatment obtained in this study suggests that specific diagnosis and treatment is of major importance. Good to fair responses were reported in 32 (80 percent) of the primary pyoderma cases. Good response was observed in treatment of all secondary pyodermas in conjunction with sarcoptic mange or hypothyroidism. Long term clinical response was observed in 78 animals with primary allergic dermatitis. Of these, 73 percent exhibited good

to fair response to treatment for secondary pyoderma. Good and fair responses were seen with pyodermas associated with allergic inhalant dermatitis (AID) in 66.6 percent of the cases. A favorable response was seen in primary allergic dermatitis in which the specific etiology was not determined in 53 percent of the cases. Many of the primary pyoderma cases and nearly all of the pyodermas secondary to allergic dermatitis had been on long-term corticosteriod therapy. Often the steroid therapy was administered without concurrent antibiotics or with bacteriostatic antibiotics, possibly influencing the success of treatment. The results in Table III suggest that many chronic pyodermas will respond to proper therapy.

It is difficult to evaluate the direct influence of autogenous bacterins on treatment response. One can assume that it is of significant benefit when good clinical response is seen following the initiation of its use in cases where poor response was observed with antibiotics alone. The decision to use autogenous bacterin must be made shortly after culturing since it is not practical for the laboratory to hold a culture for a prolonged time prior to initiating preparation of the bacterin. When secondary pyoderma is present one must make a value judgement on the basis of history, clincial appearance and response to previous treatment. If good control of the pyoderma has not been achieved with routine management the use of an autogenous bacterin

is indicated in all chronic recurrent primary pyodermas.

If good control is not obtained with a specific management program one should reevaluate the patient for other possible etiological factors. It is not unusual to make a diagnosis of primary pyoderma in the late fall only to have symptoms reappear during the next pollen season accompanied by pruritus, indicating that a primary allergic condition was not identified on the initial examination. Reculturing is indicated any time a bacterial infection is not responding to specific therapy based on prior cultures and antibiotic sensitivities. Proteus and Pseudomonas are often pathogenic opportunists which follow prolonged systemic antibiotic or topico-occlusive therapy for staphylococcal dermatitis.

Generally interdigital pyoderma and chronic bacterial otitis show the poorest response to treatment. Autogenous vaccine was reported to be of benefit in this condition (75). Autogenous vaccine appears to have less therapeutic value in otitis than in pyodermas. Treatment of many chronic bacterial dermatitis and otitis cases can be rewarding if an accurate diagnosis is made and specific treatment is initiated.

V. CANINE ALLERGIC INHALANT DERMATITIS (ATOPIC DISEASE)

Introduction

The term atopic disease or atopy designates a familial predisposition to allergic disease which is mediate by immunoglobulin E (IgE) (19,43). The condition in the dog is primarily a dermatologic one manifested by pruritus. This contrasts with primary asthma and hay fever symptoms in man. The most common route of entry of the allergen is the respiratory tract. Ingestion or penetration of intact skin are less frequently involved (40). Intrinsic factors such as hormones and autosensitization may be concurrently involved in the atopic animal (20). Canine Allergic Inhalant Dermatitis (AID) is the preferred term to denote the allergic dermatitis caused by inhaled allergens (2).

The isolation and characterization of canine IgE has confirmed the similarity of the pathogenesis of atopic dermatitis in man and animals. The antigenic similarities of canine and human IgE were confirmed when the absorption of canine reaginic serum with anti-human IgE resulted in a substantial reduction in PK titer to ragweed (44). Also the anti-human IgE was effective in eliciting reversed cutaneous anaphylaxis in the dog. Immunofluorescence studies of IgE in canine skin showed the antibody to be associated

exclusively with mast cells and to be largely cytoplasmically located (42).

The incidence of AID is difficult to determine. One report estimated 15 percent incidence in the canine population (20). Eight five percent of the pruritic dogs referred to a veterinary dermatologist in California were diagnosed as primary AID cases (5). Approximately 30 percent of the patients referred to the investigator's dermatology practice were primary AID cases.

In the last ten years significant progress has been made in the specific diagnosis and treatment by means of intradermal skin testing and hyposensitization. Several methods of hyposensitization have been described (21). Geographical differences in the prevalence of inhalant allergens exist, thus influencing testing and treatment procedures and responses to treatment. There is a lack of information in the literature documenting the importance of various regional allergens from many geographical areas including the Pacific Northwest.

Materials and Methods

Sample

A retrospective study of 230 dogs which had been diagnosed as primary AID was completed. All of these animals had been admitted to the Animal Skin and Allergy Clinic, a referral dermatology practice, located in Portland, Oregon

and Seattle, Washington. The complete allergy workup was performed by the investigator. The direct responsibility for implementation of the treatment programs fell to the referring veterinarian who followed the recommendations given to the client at the time of completion of the diagnostic workup. All followup reports and interpretation of response to treatment were obtained by personal contact with the owner of the animal or in a limited number of cases from the referring veterinarian responsible for treatment.

An initial standard allergy questionnaire was completed on all animals and followup evaluations were completed when possible. Hematological, bacteriological and fungal studies were performed by a commercial laboratory. Data was summarized for age, sex, breed, presenting clinical signs, seasonality of symptoms, concurrent problems, intradermal skin test results and clinical response to treatment.

Intradermal Skin Testing

The most commonly used method of verifying an inhalant allergy is with intradermal skin testing. The 230 dogs included in this study were tested after a sufficient period of time following cortisone withdrawal. This was determined by a recurrence of pruritus and a strong histamine reaction on intradermal testing.

The selection of the antigens to use varied somewhat for each individual dog. In general the antigens were

divided into seasonal and nonseasonal allergen groups (Table XI). The flower pollens were added late in the study. The regionalized pollen group was not routinely used during the winter months (December through February) or if the mixed pollen antigens showed negative reactions in the first group. If the history suggested exposure to other potential allergens, they were included if available.

The dogs were restrained without the use of tranqualization, sedation or anesthesia except in one case in which Rompun[p)] was used with satisfactory results. The lower thoracic wall was clipped carefully with a number 40 blade and lightly disinfected with alcohol. The sites to be injected were marked with a felt pen, leaving three-fourths to one inch between sites. Inflammed areas were avoided. A minimal bleb of .05 ml. of antigen was administered intradermally using a disposable tuberculin syringe and 26 gauge 3/8 inch needle. The syringes and injection sites were identified by number of sequence.

The concentration or dilution of most intradermal test antigens was 1000 protein nitrogen units (PNU)[q)] or 1:1000/ weight volume.[r)] Occasionally a false positive reaction would be suspected on the basis of the lack of correlation

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p) Rompun (Tylazine), Haver Lockhart Laboratories, Shawnee, Kansas.

q) Dome Laboratories, West Haven, Connecticut.

r) Hollister Stier Laboratories, Spokane, Wa.

with a history of exposure to the specific antigen. If very large wheals were seen in several test animals when the majority of other antigen reactions in these patients were weak or negative, a false positive reaction was considered. When false positive reactions were suspected, the antigen was diluted 10 fold to 1:10,000 and another intradermal test made. Staphylococcus and Streptococcus bacterins[p)] were used in varying dilution from 1:10 to 1:100. A histamine phosphate positive control diluted 1:100,000 and a buffered saline negative control were always used.

The size and appearance of the wheal at each antigen injection site was compared to the negative saline control at 15 and 30 minute intervals post injection. A reaction was considered positive if the wheal was three mm. larger or twice the size of the negative control. The relative incidence of positive skin tests to the commonly used antigens are summarized in Table XII.

Treatment

All concurrent problems identified were treated symptomatically or specifically prior to or concurrently with the initiation of specific treatment for AID. The initial treatment of all the dogs included maintenance dosages of oral prednisone or prednisolone. Clients were instructed to strive for alternate day morning dosages. A step down dosage schedule was suggested. When possible the offending

antigen was removed from the environment or exposure was minimized or avoided.

One-hundred-thirty-nine dogs were started on one of four hyposensitization treatment programs. Eleven were initially treated with aqueous antigen[r)] in propylene glycol in a ratio of one part antigen to four parts propylene glycol (Table XIIIA). Nineteen were started with regionalized aqueous pollens[r)] in propylene glycol in addition to nonpollen alum precipitated extracts (Allpyral)[q)] such as epidermals, house dust and molds using the treatment schedule in Table XIIIB. Thirty dogs received Allpyral only following the same schedule. The remaining 79 dogs were started on a rapid hyposensitization schedule using Allpyral (Table XIIIC). Following the initial series, boosters at the maximum PNU dosage were given when pruritic symptoms started to become more severe. The frequency of booster injections were quite variable ranging from three weeks to seven months on the 132 dogs in which progress reports were obtained. All of the dogs on the program at the present time which were initially hyposensitized with aqueous allergen in propylene glycol have been changed to Allpyral boosters. All injections were given subcutaneously.

The animals were hyposensitized against all of the antigens showing positive intradermal skin reactions which correlated with a history of exposure and which were available in Allpyral. Several of the mixed allergens were used

routinely including national weed mix, ten tree mix, seven grass mix and four mold mix.[q)]

The response to therapy was graded on the comparison of corticosteroids required to control pruritus prior to treatment and after hyposensitization. A case that required no maintenance corticosteroids or was controlled by a dosage of 20 percent or less of the original requirement was considered a good response. A case controlled by 20-50 percent of the pre-hyposensitization corticosteroid level was considered a fair response. Dogs showing a poor response required more than 50 percent of the pre-treatment dosage of corticosteroids after hyposensitization.

Historoclinical Findings

All of the dogs included in this study had a primary complaint of pruritis. There was often a history of foot licking, face rubbing and/or axillary pruritus. The specific lesions were characterized by a wide range of pathological changes varying from acute to chronic, erythema and edema to crusting and scaling, hyperpigmentation and lichenification. Superficial or deep pyoderma was observed in a significant number of cases. Most dogs had been on intermittent or continuous long term corticosteroid therapy. The histories usually suggested favorable response initially, but often more refractiveness to recent cortisone therapy. The age of onset of symptoms ranged from six

months to five years with the majority between one and three years of age.

Thirty-two percent reported a seasonal pattern while 68 percent were of nonseasonal or year round problem. Many of the nonseasonal group reported more severe exacerbations of pruritus and secondary lesions during the spring and summer months. There was a wide variation in the distribution of lesions. The most frequent areas involved were the ventral abdomen and thorax. Generally, one or more other areas of the body including lateral or dorsal trunk, ears, face and extremities had lesions.

All patients were submitted to a routine workup to identify allergic etiologies (19). The differential diagnoses most commonly considered were sarcoptic or demodectic mange, flea allergic dermatitis (FAD), contact allergic dermatitis, food allergy, bacterial sensitivity, pyoderma (primary or secondary) and idiopathic seborrheic dermatitis. Appropriate laboratory tests including skin scrapings, elimination, and provacative testing for contact or food allergens, bacterial culture and antibiotic sensitivity testing, complete blood counts and biopsies were performed as indicated by history and clinical appearance. A comprehensive flea control program including indoor environmental control (fumigation) and continuous flea control on all animals in the household was stressed. Flea antigen was used in many cases of concurrent FAD.

The most common concurrent problem was flea infestations. Secondary bacterial infections ranked second. A few concurrent contact allergic dermatitis reactions were seen (71) as was an occasional food allergy. Thirty-five percent of the dogs started on a hyposensitization program were German Shepherds, Irish Setters, Poodles or their crosses. These breeds made up 31 percent of the total clinic population. Other mixed breeds accounted for 13 percent of the total while the remaining 52 percent were distributed among 35 breeds. Fifty-six percent of the AID population were males compared to 50 percent of the total clinic population (Table XIIV).

Complete blood counts were within normal ranges in the majority of cases, even if accompanied by concurrent problems. Infrequently, a mild absolute eosinophilia or mild leucocytosis was reported.

Histopathological characteristics were not specific for AID. Changes typical of subacute or chronic dermatitis were most frequently observed (54). Folliculitis or periadnexal inflammation was seen in some complicated or chronic cases. It was impossible to separate those cases with other concurrent allergic etiologies from those with uncomplicated AID by microscope examination (71).

Treatment Response Summaries

The youngest (2 years) and oldest (7-8 years) age groups exhibited the best responses to hyposensitization with approximately 82 percent good or fair response in both groups. The 6-7 year old group had the lowest rate (53 percent) of favorable responses (Table XV). A high percentage of dogs had a favorable response to hyposensitization within 2-4 months after initiation of hyposensitization. Most of the dogs responding poorly to hyposensitization were identifiable after 6-12 months on the program, hence hyposensitization was discontinued on many of these dogs. Dogs maintained on the treatment program for 18 months or longer generally exhibited good or fair response.

The clinical response to the rapid method of hyposensitization resulted in an 84 percent favorable response within two months after the initiation of treatment. Similar results were observed throughout the first six months of hyposensitization (Table XVII).

Good or fair response was reported in 78.5 percent of the cases hyposensitized. Non-seasonal symptoms predominated in the remaining dogs exhibiting poor response to hyposensitization (Table XVIII). Approximately 27 percent of the poor responders had concurrent flea allergy and several others had contact allergic dermatitis, generalized seborrhea and/or pyoderma. No concurrent problems were

identifiable in the remaining dogs exhibiting poor response to hyposensitization (Table XIX).

Discussion

The history is the most important element in the evaluation of the patient with AID as with the other allergic dermatitidies. The age of onset is usually between 12 and 36 months with extremes of six months to six years. There is usually a familial history of allergic dermatitis although this is often impossible for the owner to ascertain. Several reports confirm the higher incidence in such breeds as the German Shepherds, Irish Setters, Miniature Schnauzers, Silky Terrier, Poodles, West Highland White Terrier, English Bull Dog and Dalmation (5, 13). The present survey agrees with these reports.

It has been reported that the incidence of AID is more common in females (13). In this study males were the predominant sex.

Clinical signs are not specific for AID. Most lesions are the result of pruritus which follows the antigen-antibody reaction. The hereditary susceptibility and the degree of exposure to the antigen are major determining factors in developing a sensitivity. Pruritus tends to be more severe in the facial, axillary and foot areas. However, the inflammation is often seen first on the less protected areas of the body such as the ventral abdomen. There may be

partial or complete alopecia from licking or scatching without significant inflammation. Only hyperpigmentation may be seen. A generalized distribution of lesions is very common in a chronic AID patient. Secondary bacterial infection, most often superficial, but occasionally deep is often observed in chronic cases. An allergic triad of dry skin, seborrheic dermatitis and infectious dermatitis has been reported as a frequent simultaneous occurrence of AID (3). This study would support those observations.

The most common inhaled allergens of AID in the Pacific Northwest are molds, trees, weeds, grass, house dust and kapok (Table XII). The large number of pollen reactions correlate well with an 8-9 month pollen season. Molds are present in the region in significant numbers in the fall, winter and spring (56). It is speculated that the unexpected high percentage of positive reactions to the flower pollens may be due to: 1) cross-reactivity with other pollens, 2) general allergic load which has surpassed the allergic threshold, resulting in exacerbation of reactions when normally they would be weaker, or 3) they are sufficiently antigenic to initiate a positive intradermal reaction.

The percentage of reactions to evergreen pollens is of interest. This pollen has a waxy protective lipoprotein coating. It is a very heavy pollen which does not remain suspended in air. Therefore, there will be a heavy

concentration of the ground surface, providing maximum exposure to the dogs. The waxy coat is very resistant to degradation. The antigenicity of evergreen pollens per gram of material is less than most other pollens, thus requiring a longer period of exposure or larger amount of pollen to elicit the normal allergic response. It may be present in the environment most of the year under favorable conditions.

It is necessary to correlate the positive skin test reactions with a history of exposure before deciding which inhalant allergens are the primary causes. The present study suggests horse dander and trichophyton may be more irritating than allergenic at the 1:1000 w/v dilution since the high incidence of positive reactions does not correlate with the low incidence of known exposure. It is also common to have some cross reactivity among similar proteins. Thus, the three mixed pollen groups (trees, weeds, grasses) and mixed epidermals will often be good screening tests. The cross reactivity can result in strong positive reactions to an individual pollen or animal dander in which there is no known exposure (5).

The interpretation of skin test results may fall into six categories: 1) the animal may be clinically allergic to the allergen; 2) the animal may be sensitized to the allergen, but not necessarily allergic; 3) there may be cross-reactivity; 4) the animal was, but no longer is clinically allergic to the test allergen; 5) false positive due to

allergens too concentrated or too irritating; and 6) false negative due to an allergen too dilute, air injected, or immunosuppressant levels in blood stream (22).

To obtain maximum clinical response, it is necessary to identify and treat all concurrent problems in AID patients. A concept of allergic threshold has been proposed (3). This concept suggests that a certain allergic load may be tolerated by an individual without any disease manifestations, but a small increase in that "load" may push him over the threshold and initiate clinical signs. Each patient has a "threshold" or level of resistance at which combined stresses (immunologic, genetic, climatic, and physiologic) precipitate the disease. The threshold is not fixed, and appears to be raised or lowered by such factors as the general condition of the skin, nutritional state, infections, fleas and environment.

In the geographical area of this study, a significant environmental flea infestation is prevalent throughout the year, often increasing in the spring and fall. In the Pacific Northwest there is little doubt that flea hapten-protein complex is the primary non-inhalant allergen causing exacerbation of symptoms in AID patients. The more sensitive the AID patient appears to be to the inhalant allergens, the more sensitive it is likely to be flea bites. There have been many AID patients that maintain relatively well with minimal treatment until a flea infestation occurs. Then

the allergic threshold is surpassed. In a few cases the clinical sensitivity from inhaled allergens decreased significantly when concurrent food allergies were eliminated. It is almost impossible to adequately control symptoms caused from inhalant allergens when there is a concurrent Sarcoptic Mange or chronic deep pyoderma.

Several criteria influenced the selection of the animal to be hyposensitized once the diagnostic workup was completed. The primary factor was the willingness of the owner to pursue a hyposensitization program and accept the expense and time involved with initial treatment and life-long maintenance. If other significant problems were identified in addition to AID, the owner would often elect to treat the concurrent problems first, particularly if flea infestation, flea hypersensitivity or food allergy was present. If there was a concurrent contact allergic reaction in which exposure to the contact allergen could not be avoided, hyposensitization was not recommended. The exception to this was wool since some favorable response has been observed with hyposensitization (71). In these cases both Allergic Contact Dermatitis and AID may have been present. If the dog was suffering from concurrent systemic or debilitating disease it was not hyposensitized initially.

The response to hyposensitization is variable. Favorable clincial responses have been reported in 80 percent and 86 percent of cases (5, 21). Since all clinical response

evaluations are subjective and the criteria for classification was not reported, it is difficult to make direct comparisons. An attempt was made to determine possible causes of poor response to hyposensitization of the 21.5 percent poor response included in this study (Table XVIII and Table XIX). There was a 15 percent higher proportion of nonseasonal than seasonal patterns in the poor response group. In 38 percent (11) of the poor response cases no concurrent problem or specific reason could be found for a possible failure. In the other 62 percent there were concurrent problems such as severe flea bite allergy (27 percent), contact allergic reaction to rugs (14 percent), and pyoderma or generalized seborrhea, 10 percent each. In two cases (7 percent) had no reaction until coming in direct contact with grass. Then a severe ventral dermatitis would erupt. These may be a contact reaction to plant resins, although this etiology has been questioned. It has been suggested that dogs over eight years of age are poor candidates for hyposensitization (5). Of 15 dogs over eight years old, only 13 percent (2) had poor clinical improvements. The above summary would suggest some selection of patients for hyposensitization is definitely indicated.

The rapid hyposensitization method (Table XIII) using Allpyral has proven to be the most satisfactory of the methods tried by the author. The major advantage is a faster, good clinical response, often by two months (Table

XVII vs. several months on other programs. Several of the dogs in the 2-4 month treatment time had concurrent flea infestations, thus contributing to a slower than expected improvement. The client acceptance of the program is enhanced. The main disadvantage of the rapid schedule using Allpyral is more antigen will be used the first year than with the 24 week schedule, thus increasing expense for vaccine. I have chosen Allpyral as the treatment allergen of choice because of the repository effect (fewer injections), with fewer complications in administration. There is seldom any pain involved, which makes it easier for clients to give the injections if they wish. The main disadvantages are cost and lack of regional production of allergen extracts. There has been an occasional local subcutaneous tissue reaction which are firm and painless. They usually regress in one to three weeks.

Aqueous allergens in propylene glycol were usually painful to inject and often caused a severe local tissue reaction. The advantages were lower cost and a long repository effect, requiring the fewest number of injections.

A level of 10,000 protein nitrogen units (PNU) has been generally accepted as the optimum maximum treatment level for Allpyral. There will be an occasional dog which will require a higher level to achieve clinical response or a lower level to prevent the exceeding of the maximum tolerance level. Regardless of the method of hyposensitization, the clinician

can anticipate a 50 percent good clinical response requiring none or a very low dosage of corticosteroids, a 25-30 percent fair response with a 50-80 percent decrease in post-hyposensitization corticosteroids and a 20 percent poor response at the end of the initial hyposensitization schedule.

VI. CANINE CONTACT DERMATITIS

Introduction

Contact dermatitis is classified into primary irritant and allergic categories. Immunological phenomena are not involved in primary irritant contact dermatitis (ICD) (62), whereas, delayed hypersensitivity is the basis of allergic contact dermatitis (ACD). It is possible for a substance to be a primary irritant on first exposure and cause an allergic response on subsequent exposure. All allergic contact reactions require repeated exposure to the hapten. Plastics, leather, detergents, floor waxes, wool and synthetic rugs, fertilizer and mop sprays are some of the more common substances that induce ACD (76). Once ACD occurs, even if the offending immunogen is removed, the dermatitis may persist for 10 to 21 days if untreated (82).

Several factors are reported to predispose to contact sensitivity including: 1) trauma or irritation to the skin resulting in break of continuity of the epidermal surface, 2) continued or repeated wetting of the skin which softens the keratin layer, 3) addition of wetting agents, 4) the dose-time relationship of exposure to the contactant, 5) the vulnerability of the skin, and 6) environmental factors such as temperature, humidity and prior exposure, 7) nutritional status of the animal with mineral and vitamin deficiencies

altering the responsiveness of the skin, 8) icthyotic and defatted skin being more susceptible to conjugation with a hapten, and 9) endocrine imbalances and metabolic disturbances varying the integrity of the skin or leading to greater susceptibility to infectious dermatitis and thus varying its ability to develop sensitivity to antigenic materials (82).

The incidence of contact dermatitis in dogs is not well documented. A survey of 650 dermatologic cases referred to the Animal Skin and Allergy Clinics in Portland, Oregon and Seattle, Washington revealed an incidence of 5.5 percent of contact dermatitis -- 33 cases of ACD and 2 cases of ICD. In the same sample, approximately 10 percent of the dogs with clinical manifestations of continuous or seasonal pruritus which were corticosteroid responsive were shown to have a contact dermatitis identified by provacative testing and/or elimination of allergen.

The pathogenesis of ICD has been reviewed. The precise mechanism by which most chemicals to which the skin is exposed cause irritation to skin is not known. Many of these materials may not be toxic themselves, but may be carried in a petroleum derivative which is toxic or they may potentiate the toxicity of the otherwise mildly toxic material. The irritating qualities of the petroleum distillate products are directly proportional to their fat solvent properties and inversely proportional to their viscosity. The

oils of the naphthalene series are more irritating than those of the paraffin series.

The substances which contact the skin may cause varying degrees of damage to the epidermis. The heavy metals act as direct toxins to the cells. Mildly irritant substances may dry the skin that becomes more resistant to further insults by the same or other materials. Severe or continued toxic damage by a contactant may result in the development of an acute eczematous reaction, which leads to epidermal necrosis and ulceration. Milder acting toxicants may result in thickened skin with minimal erythema. Very mild toxicants acting over extended periods may cause only hyperpigmentation and slight fissuring.

Severe lesions are characterized histologically by the presence of intraepidermal buttae. The epidermal cells exhibit necrosis and spongiosis and intraepidermal vesicles or microabscesses which contain a few lymphocytes, eosinophils and many neutrophils. In chronic contact dermatitis, hyperkeratosis, acanthosis and occasional areas of parakeratosis are common, but vesiculation is rare.

The dermal changes in acute cases include edema and blood vessel congestion. Pronounced leukocytic infiltrate, mainly polymorphonuclear cells are usually observed at the dermo-epidermal junction. Islands of inflammatory cellular infiltrate may be observed in the dermal layer of severely affected areas (34).

Materials and Methods

Sample

A retrospective study of 35 cases of canine contact dermatitis was completed. All of the animals were examined at the Animal Skin and Allergy Clinic, a referral dermatology practice in Portland, Oregon and Seattle, Washington. The complete allergy workup was performed by the investigator. Each individual record was reviewed and data summarized for age, breed, duration of illness, concurrent problems, primary contactant involved, clinical symptoms and distribution of lesions. Hematological evaluations and bacterial and fungal cultures were performed by a commercial laboratory.

Diagnostic Contact Allergy Testing

The two specific methods of testing for ACD are patch testing and isolation followed by provocative testing (71). Cases 11 and 23 were patch tested as follows. An area was clipped on the lateral thorax with a number 40 blade and cleansed with alcohol. A 2 inch square of carpet with fiber in contact with the skin and a 2 x 2 gauze (control) were placed adjacent to each other on the prepared surface, secured firmly with tape and held in close contact to the body by means of an elastic tape around the chest. The

gauze prevented tape irritation immediately around the test site. Every 24 hours the chest tape was removed to observe for irritation at the test site. Care was taken to replace each square exactly on the original area and to maintain maximum contact between the fiber and skin. The patches were removed after 72 hours with final comparison of the control and test sites.

The most commonly used diagnostic procedure for ACD is isolation of the dog from the suspected contactant substance for two to four days. During this period, if the animal has no exposure to a primary contact allergen or irritant, there should be marked clinical improvement with reduced pruritus and inflammation. As soon as the animal is clinically normal or stabilized at a less reactive state for 24 hours, it should be given maximum exposure to the suspected contactant. Allergic symptoms and lesions should return within 48 hours of reexposure to the allergen. Hospitalization, which often is the most efficient method of isolation, has the advantage of eliminating other environmental allergens present in the home environment. Furthermore, maximum exposure to carpets, bedding, etc. can be achieved by placing remnants of the material in the cage with the animal, thus ensuring continuous uninterrupted contact. Isolation and provocative testing is possible in many homes, however.

Isolation and provocative testing was used to diagnose a contact dermatitis in 31 of the dogs in this study, including the two which were patch tested. Isolation was the only testing procedure used for the primary irritant contact dermatitis cases, numbers 5 and 27, and for ACD case numbers 3 and 18.

Histopathologic Examination

Skin biopsies were obtained from 15 patients with a 4-5 mm. Keyes biopsy punch following local dermal infiltration with lidocaine. The biopsies were fixed in buffered 10 percent formalin, paraffin embedded, sectioned at 6-7 u amd routinely stained with hematoxylin and eosin. Some specimens were also stained with periodic acid-Schiff; Grocott's silver, Gram's or Toluidine blue stains.

Case Histories - Allergic Contact Dermatitis

Case 3

An eight year old German Shepherd male guard dog was presented on March 3, 1975, with a generalized erythematous dermatitis on the ventral abdomen and thorax of three months duration. Moderate pruritus was reported. Approximately four months previously, hay and straw had been placed inside and in front of the dog house for bedding. Questioning revealed that this type of bedding had never been used before. It was recommended that the bedding be removed from inside

the house. Examination one week later revealed a marked reduction of erythema and pruritus; however, the dog was still laying on the wet straw in front of the house occasionally. When this was removed, a complete cessation of pruritic symptoms and lesions followed.

Case 18

A six year old male Chihuahua was presented on October 10, 1974 with chronic papular lesions on the ears of 1-1/2 years duration. A diagnosis of dermatomycosis had been made previously by the referring veterinarian and treatment with grisefulvin and corticosteroids resulted in symptomatic improvement. At the time of examination there were symptoms of ventral dermatitis characterized by marked pruritus and erythematous papules. Questioning revealed that pruritic symptoms persisted whether the dog was at home or in the car for extended periods of time; however, no medication had been required to control symptoms while on a trip to the Midwest. It was further determined that the owner had started salmon fishing two years previously and that all fish were carried home in the back seat of the car. The fish were scaled in a specific location in the backyard and the dog liked to roll and lay in the fish scales. Removal of the fish scales from the yard resulted in a complete remission of symptoms.

Case 20

A seven year old female Sheltie was referred on October 11, 1975 with a history of nonseasonal pruritus and excessive shedding. There was no noticeable alteration of symptoms whether at the owner's home in Washington state or in California where the owners lived for four months each year in a motor home. Lesions were confined to the entire ventrum of the trunk with no lesions on the extremities and were characterized by partial alopecia, erythema and mild secondary superficial pyoderma with a few pustules. A corticosteroid drug response trial resulted in a remission of primary allergic lesions and the secondary pyoderma. Subsequent provacative testing of the carpets in the house and motor home revealed a contact allergic reaction to both.

Case 26

The patient was a 3-1/2 year old intact female Springer Spaniel. The dog had a history of allergic dermatitis since one year of which which initially had been diagnosed as a flea allergy. The first two years there was a history of seasonal moist dermatitis in August. However, the problem did not subside the third winter. Skin scrapings were negative for mites when the dog was examined by the referring veterinarian on July 1, 1974. The history included persistent pruritus, recurrent otitis externa and periodic inflammation of the tip of the tail. Antibiotics,

triamcinolone-acetate, baths for fleas, and dips for sarcoptic mange were prescribed with poor clinical response.

The dog was referred to the Animal Skin and Allergy Clinic on August 30, 1974. Lesions were confined to the ventral aspects of the body including axillary and inquinal areas on ventral abdominal and thoracic regions. The lesions were dry and scaly with moisture beneath the scabs. The hair coat was thin with accentuated alopecia on the contact points of the body. Removal of the dog from its home environment without treatment was recommended. Since 12 days of hospitalization by the referring veterinarian resulted in only moderate remission of symptoms, further diagnostic procedures were indicated. On September 13, 1976 skin scrapings, bacterial culture and sensitivity testing, fungus culture, skin biopsies, and thyroid testing were done. Antibiotic therapy and antiseborrheic shampoos were prescribed until the laboratory tests were completed

The T4 values pre- and post- TSH stimulation were 1.3 ugm% and 4.0 ugm% respectively. Streptococcus spp. was isolated from skin lesions. Histopathologic findings were suggestive of an allergic dermatitis.

Since the primary etiology was still not apparent after environmental isolation and laboratory testing, allergic inhalant dermatitis (AID) was considered and intradermal testing was performed. This was accomplished with difficulty since papular lesions had been generalized leaving few

normal-appearing skin areas of sufficient size on the trunk to conduct the tests. Results showed strong acute hypersensitivity reactions to Streptococcus, mixed trees, mixed molds, mixed grasses, cat hair, and fleas. Moderate reactions to mixed weeds and mild reaction to house dust occurred. These skin tests results correlated well with the history in that the dog played with a cat constantly, rye grass and blue grass were planted in a new yard, and the dog's outdoor environment consisted of open fields, woods, and grass. Furthermore, Streptococcus had been isolated from the skin lesions.

The prescribed treatment included antibiotic therapy, weekly antiseptic baths, autogenous bacterin, maintenance corticosteroids, L-thyroxin, maintenance of good flea control and hyposensitization to mixed trees, mixed molds, mixed grasses, mixed weeds, and cat hair.

There was a good initial response to the treatment protocol, but about December 1, 1974 the dog suddenly regressed with marked pruritus and erythema. The dog was hospitalized and all pruritic symptoms and lesions cleared within two days. Following remission of lesions, provocative testing with nylon carpet resulted in an acute pruritus within 30 minutes of carpet contact. One hour after the dog was isolated from the rug, all lesions were gone. Further questioning of the owners revealed that the dog had been sleeping in the garage until two weeks earlier when the

dog started sleeping in the house with maximum exposure to the carpets. Continuation of the hyposensitization program, avoidance of exposure to carpet and 5 mg prednisone daily have since provided good control of all allergic symptoms.

Case History - Irritant Contact Dermatitis

Case 4

A 10-week-old German Shepherd was presented on June 21, 1975 with generalized papular and pustular lesions which were most severe on the extremities. Pustular dermatitis was present on the outer aspect of both ears. There was partial alopecia and erythema on both the dorsal and ventral surfaces of all feet. Minimal pruritus was observed. The owner reported that two littermates placed in new homes prior to kenneling, remained asymptomatic.

The subject and his two affected littermates had been confined to a concrete block run with a sand pit at one end. Prior to occupancy, the runs had been scrubbed with a phenolic disinfectant[s)] and the washings had drained into the sand pit. The runs had been used with previous litters without any problems; however, the disinfectant had not been used. It was postulated that frequent washings of the runs caused the concentrated disinfectant residue in the porous block

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s) Laro, Whitmoyer Laboratories, Inc., Meyerstown, Pa 17076.

floor to raise to the surface, thus providing maximum contact between the puppies and the disinfectant resulting in a primary contact irritant dermatitis. Removal of the pups from the run and symptomatic treatment for the pyoderma resulted in a rapid clinical recovery.

Clinical Findings

There was no breed predilection with 21 different breeds represented among the 35 individuals. The ages ranged from 10 weeks to 12 years. The age distribution of the dogs was: less than one year - 48 percent, one to four years - 26 percent, greater than four years - 26 percent.

Secondary superficial pyoderma was present in 15 of the 35 cases of contact dermatitis. Concurrent AID, as determined on the basis of history, clinical appearance, and intradermal skin testing, was present in eight cases (23 percent). Thirteen of the ACD cases were allergic to wool as determined by provocative testing. Of these, eight were tested intradermally and all were positive for wool, suggesting that an immediate (Type 1) hypersensitivity was also present. Four of the eight were considered to have concurrent AID.

The clinical appearance was variable, both in character and distribution of lesions. Primary lesions were usually erythematous papules or macules, often lacking bilateral symmetry. Some primary wheals were

observed among more chronic lesions. Several patients had only secondary lesions characterized by excessive scaling, lichenification, hyperpigmentation and partial or complete alopecia of involved areas. Traumatized lesions often had crusts. Two cases, 22 and 23 had focal, acute, moist dermatitis lesions. Most of the secondary pyoderma lesions were a mixture of small pustules and healing hyperpigmented, scaly macules. Case 21 had a marked hyperkeratinization of the front legs. Removal of the scales exposed a moist erythematous surface. Otitis was usually characterized by unilateral or bilateral erythema of the pinna with minimal inflammation of the vertical canal.

The distribution of lesions were predominantly ventral including the extremities. Of those patients with contact dermatitis, only 37 percent had lesions on the sides and 15 percent on the face. Otitis was significant in 33 percent of these patients. The majority of the dogs with concurrent AID had a generalized dermatitis on the ventral, lateral, and dorsal aspects of the body. Only 4 (15 percent) of the 27 dogs with noncomplicated contact dermatitis had dorsal lesions. Historoclinical data is presented in Tables XX, XXI, and XXII.

Laboratory Findings

Peripheral eosinophilia was found in two of twelve (16.6 percent) of the dogs on which laboratory examinations were done. Case 8 had a concurrent AID. Case 12 had a severe staphylococcal pyoderma. All fungal cultures and skin scrapings were negative for parasites and fungi. Staphylococcus (coagulase positive) was the predominant bacteria isolated from secondary pyoderma lesions, but Streptococcus spp. and Proteus were also cultured (Table XXIII).

Treatment

In general, the best method of treatment is avoidance of exposure to the contactant material or chemical (23). If complete avoidance is not possible, minimum exposure and intermittent contact is recommended. Some cases of ACD due to carpets have been controlled reasonably well by covering the rugs with a nonallergenic material. Runners for travel paths have also been provided to reduce direct contact.

Positive intradermal skin tests of cases 8, 9, 27 and 25 are indicative of an immediate hypersensitivity. It was observed in this study that hyposensitization elicited remission of pruritic symptoms and lesions in these cases. Thus it appears that, if primary ACD caused by wool is

accompanied by an immediate hypersensitivity to wool, treatment by hyposensitization may be beneficial.

Many ACD problems will require maintenance corticosteroids and oral prednisone is routinely used. Cases 7, 10, 12, 15, 20, 31, 33, 24, 25, 26 and 29 are maintaining on 5 to 10 mg. prednisone daily or alternate day schedule. All primary ICD should be treated by avoidance of exposure to the irritant contactant. Secondary pyodermas will usually respond to routine antibiotic therapy and avoidance or contact. Autogenous bacterins were used in cases 6, 9, 12, 23, 26, 27 and 30.

Histopathological Findings

Histopathologic changes present in the specimens included parakeratosis, hyperkeratosis, acanthosis, spongiosis (epidermal edema), dermal edema, proliferation and congestionof dermal vasculature and dermal infiltration of inflammatory cells and proliferation of dermal histocytes (Figures 7 and 8). The complete array of histopathologic changes were not necessarily present in each biopsy and there was marked variation in degree of each alteration amongst the biopsies.

The inflammatory cell infiltrate ranged from very mild to extensive and consisted primarily of mononuclear cells, predominantly lymphocytes, with significant numbers of plasma cells and mast cells. Neutrophils were present

in biopsies from all but two cases and varied from a moderate diffuse infiltrate in one case to a slight infiltrate in most cases to only a few scattered cells in several cases. A few eosinophils were identified amongst the neutrophils in the dermis in only two biopsies. Proliferation of histiocytes, present in the dermis in nearly all specimens, ranged from very slight to extensive.

The inflammatory cell infiltrate was primarily in the superficial dermis or at the epidermal-dermal junction which were also the usual areas for the dermal edema. The cells often formed poorly defined, indistinct foci in the superficial dermis with individual cells scattered diffusely in the surrounding dermis. Perivascular and perifollicular mononuclear cell cuffs were prominent in several cases. Polymorphonuclear cells were often seen in dilated blood vessels, in the immediate perivascular tissues or at some distance from a blood vessel in a centrifugal orientation.

The study included biopsies from seven cases of ACD, three cases of ACD and AID, four cases of ACD with secondary pyoderma, and one case of ACD and AID with secondary pyoderma. Generally the cases with secondary pyoderma had greater degrees of epidermal reaction with dilated hyperkeratotic hair follicles and heavier dermal infiltrates of inflammatory cells with more neutrophils than the dermatoses of solely allergic origin. There were no distinctive

histopathologic differences between the solely ACD cases and the cases of combined ACD and AID.

Discussion

The history is the single most important element in evaluation of the patient with dermatitis. The characteristics most suggestive of a primary ACD include: 1) non-seasonal pruritus, 2) predominantly ventral and lateral distribution of lesions, 3) enhanced pruritus noted in particular area(s) of the environment, 4) onset of symptoms 3-12 months following changes in exposure to potential allergic contactants (e.g. new rug, bedding), 5) improvement of symptoms when away from the home environment, and 6) onset at any age.

A sudden onset of pruritus associated with recent exposure to potentially irritant compounds is suggestive of primary ICD. The distribution of lesions may be more variable, depending upon area of contact. For instance, an irritant spray may result in a generalized distribution of pruritic symptoms and lesions or they may be limited to less protected areas of the skin.

The lesions are variable depending on duration. Secondary pyodermas can be expected in at least 40 percent of ACD cases. Acute inflammatory lesions with papules and erythema are present in most cases. Hyperpigmentation, lichenification, and minimal inflammation predominate in

chronic lesions. Lesions, either focal or diffuse, are most commonly found on the ventrum and extremities, followed by lateral surfaces of the trunk, ears, face and dorsum of the trunk in descending order. Dorsal lesions are not common unless concurrent AID or flea allergy dermatitis is present.

The diagnostic method of choice for ACD is isolation of the patient followed by provocative testing of the suspected contactant. Patch testing is successful in some cases (23). Laboratory tests, including complete blood counts, skin scrapings, fungal cultures, bacterial cultures, intradermal skin testing, diet testing, and skin biopsies, should be done to identify concurrent dermatitides.

Histopathologic characteristics of ACD are not specific; however, skin biopsies can be very helpful in broadly categorizing dermatoses, thus providing direction for further study and treatment. Changes of subacute or chronic dermatitis (54) were observed in the ACD cases reported herein. The most consistent epidermal changes were hyperkeratosis and acanthosis. Parakeratosis and spongiosis were also observed in some specimens. Focal and diffuse edema at the epidermal-dermal junction was common. Mononuclear cell infiltrates, composed of lymphocytes and lesser numbers of plasma cells, were consistently present in the superficial dermis as well as perivascularly and perifollicularly. Slight to moderate proliferation of histiocytes in the

superficial dermis was common. Neutrophil infiltration of the dermis was slight in most cases but in several cases of ACD or ACD with concurrent AID it was moderate to rather heavy intensity. Dermal infiltration by eosinophils was present only in two cases. Neovascularization and vascular engorgement was observed in some sections.

Commonly ACD cases have other concurrent primary or secondary complications. The differential diagnoses to be considered when a dog is present with a history and lesions consistent with ACD include: 1) ACD, 2) ICD, 3) food sensitivity, 4) flea allergy, 5) AID, 6) demodecosis, 7) sarcoptic acariasis, 8) mycotic dermatitis, and 9) pyoderma.

The treatment of choice for ACD is isolation from the contactant allergen. If this is not possible, maintenance doses of oral prednisone is usually required. Lesions of contact dermatitis due to wool accompanied by positive intradermal skin tests for wool (immediate hypersensitivity) may be controlled by hyposensitization. Treatment of concurrent primary or secondary problems is necessary.

VII. FLEA ALLERGY DERMATITIS

Introduction

Flea allergy dermatitis (FAD) remainds one of the major clinical dermatological problems in many geographical areas of the world. It is reported as the most important cause of canine skin disease in a study from Ireland (9). Flea hypersensitivity was involved in approximately 35 percent of the dogs referred to the investigator's dermatology practice over a three year period.

It is commonly recognized that an individual living in an area endemic for a specific insect will fail to react to bites after prolonged and repeated exposure. Flea allergy dermatitis often occurs in those dogs with a relatively small number of fleas and those which are frequently defleaed (32, 50).

The clinical signs of a flea hypersensitivity have been characterized. They include intense pruritus in areas of the body where fleas are most often found, namely the ventral posterior abdomen, axilla and dorsal back. The primary lesion is a papule one cm. in diameter, accompanied by erythema of large areas of the dorsum. Secondary lesions result from self-excoriation with breaking of hair, local alcpecia and occasionally, areas of acute, serious dermatitis. Persistent excoriation over a period of many months

in the untreated animal produces diffuse alopecia of the dorsum of the body with acanthosis and hyperkeratinization. Erythema is not noticeable at this state and pruritus is less significant (9, 31).

The diagnosis of FAD is usually possible on the basis of clinical signs and response to eradication of the flea infestation. Intradermal skin testing with the whole flea extract diluted 1:10 in sterile saline has been recommended as a qualitative test in confirming the presence of a flea hypersensitivity. High percentages of reactions have been obtained on dogs tested in geographical areas with heavy flea populations (9,30).

Recommended treatment of flea hypersensitivity includes initial eradication of fleas on the dog using an insecticidal soap, prevention of future infestations with the continuous application of insecticidal powders, sprays or dips and the eradication of fleas from the environment. The latter can be accomplished by destruction or washing of animal's bedding, frequent vacuuming of carpets and fumigation (30).

Hyposensitization by intradermal injection of hapten derived from collected oral secretion of the flea in flea-bit sensitive dogs resulted in a state of nonreactivity lasting from several weeks to several months. Attempts to hyposensitize flea bite sensitive guinea pigs by subcutaneous or intradermal injection of nondialyzable portions of

extracts of whole fleas failed. An acid hydrolysate of the extract induced hyposensitization for several weeks (31, 32). The use of a 1:5000 w/v suspension of ground canine fleas in phenol glycerol saline in a series of three weekly 0.5 cc intradermal injections resulted in good clinical remission of symptoms of allergic dermatitis thought to be caused by flea infestations (49).

Pathogenesis

The association between an ectoparasite and its host is quite varied. It is generally recognized that individuals and animals react differently to insect bites. The four basic reactions of a host to its ectoparasitic invader can be classified in one or more of the following reactions: 1) histamine, 2) enzymatic, 3) hypersensitive or allergic and 4) immune and nonresponsive (33).

A review of the allergic responses to insect bites has provided some insight into the pathogenesis of FAD (32). It has been demonstrated that repeated cat flea bites in guinea pigs elicit a definite sequence of events in the skin reactivity of the host. They are Stage I, induction of hypersensitivity with no observable skin reactions from day 1-4; Stage II, delayed skin reaction from day 5-9; Stage III, immediate skin reactions, followed by delayed reactions from day 10-60; Stage IV, immediate reactions only from day 61-90; and Stage V, no skin reactivity after 90 days. The

distinction between the stages was not clear-cut with a gradual transition observed (32).

The stages of skin reactivity have been correlated with histopathological findings in guinea pigs exposed to cat fleas. During Stage I no changes from the normal were seen. In Stage II there was a diffuse mononuclear infiltration of the dermis and to a much lesser degree, the epidermis at the bite site. Early in Stage II the predominant cell was the small lymphocyte with an occasional monocyte. As this stage matured and approached Stage III, the presence of plasma cells was noted. The immediate reactions of Stage II were characterized by an infiltration of the dermis at the bite site by eosinophils. In the delayed reactions of Stage III, the appearance was that of Stage II. Eosinophils predominated in Stage IV and Stage V appeared histologically normal (53).

Microscopic appearance of skin biopsies from early acute clinical cases of flea hypersensitivity were characterized by vascular dilation in the upper dermis, moderate acanthosis and upper dermal edema. Peri-appendageal and upper dermal infiltration of lymphocytes, histiocytes, mast cells and polymorphonuclear lyekocytes with many eosinophils was observed. In the chronic stage the epidermis was markedly thickened. There was extensive infiltration of the upper dermis by plasma cells, lymphocytes, neutrophils and mast

cells and predominantly eosinophils. Vascular dilation was observed (9).

The substances in the oral secretion of the flea responsible for inducing hypersensitivity is an incomplete antigen or hapten of relatively low molecular weight, stable to heat and acid hydrolysis (11). The hapten contained in collected oral secretion of fleas could not induce hypersensitivity unless injected in combination with Freund's adjuvant, while the flea is able to inject its oral secretion into the skin and induce hypersensitivity. It has been demonstrated that the flea hapten is associated with both salt-soluble and acid-soluble fractions of collagen which acts as the carrier (58).

Following the daily exposure of previously unexposed animals to flea bites no reactions were observed until the fifth day, at which time previously exposed but nonreactive bite sites flared up. It is likely that the hapten having conjugated with the collagen was trapped at the bite site, remaining available as an antigen. When sufficient hypersensitivity finally developed, the antigen present at the previously nonreactive bite sites combined with the newly formed antibody, resulting in a tissue response which was manifested clinically.

Humoral antibodies have been shown to be associated with flea bite sensitivity. Experiments with the transfer of sensitivity to fleas between rabbits and guinea pigs

tend to indicate that nonreaginic antibodies are involved in the hypersensitivity to these insects. In vitro experiments have demonstrated the presence of low quantities of precipitating antibodies in sera of flea bite sensitive rabbits. It is probable that delayed hypersensitivity associated with insect bites does not differ from classical delayed hypersensitivity (46).

Flea Life Cycle

The life cycle of the flea contributes significantly to problems with management of FAD. The female flea lays up to 20 eggs at a time with a total of 400-500 during her lifetime. The eggs are deposited in dust or dirt, or they may be laid on the host, but soon drop off. The rate of development varies greatly depending on the temperature and humidity. The larvae may hatch in two days or up to 16 days after the eggs have been laid. The larvae have masticating mouth parts and feed on dry blood, feces and other organic matter, requiring little food. They are very active, hiding from light, being found in crevices in floors, under carpets and similar places. A moderate temperature and a high degree of humidity are variables in the development of larvae, which lasts 7-10 days or longer. The mature maggot spins a cocoon with a normal span of 10-17 days for the pupal stage under average conditions. A low temperature will cause the

coccon to persist for several months. Fleas frequently leave their hosts (52).

Cross reactivity between bites of different flea species has been demonstrated in Guinea Pigs. It can be expected that a sensitized dog will react to the bits of fleas of several species (46).

Historoclinical Findings

Among the 330 animals in the sample 119 were mixed breed and 211 purebred representing 48 different breeds. There was not a preponderance of one coat type over another represented. Fifty-four percent of the sample were females and forty-six percent males. The clinic population was approximately 50 percent for each sex. The majority (57 percent) were one to three years old, two percent less than six months of age, and approximately twenty percent four years or older (Table XXIV).

The history always included pruritus as the primary complaint. In the majority of cases, flea infestations had been observed by the owners or referring veterinarians in the past. Fleas or flea excrement were usually present someplace on the body, although often not in the most severely involved areas. There were some cases in which the owner had never observed fleas and none were found on examination on the dog but classical FAD lesions were manifested. Many of the primary FAD animals which did not have

other concurrent allergic manifestations had no intermittent pruritus initially accompanied by milder dermatitic lesions. Ofter there was a history of a heavy flea infestation preceding severe exacerabations of generalized pruritus, often allergic otitis and varying degrees of secondary skin changes.

The predominant distribution of lesions was over the posterior back, tail and perineum (83 percent) and in the flanks and posterior ventral abdomen (65 percent) (Table XXV). The clinical appearance of the skin lesions were variable, with the same animal often demonstrating multiple acute and chronic lesions. The primary papules were most often observed as multiple erythematous lesions on the posterior ventral abdomen and in the axilla. There was often a significant zone of generalized erythema on the dorsal anterior tail region accompanied by secondary lesions of scaling, excoriation, hyperpigmentation, hyperkeratosis and/or occasionally lichenification. Alopecia was usually present, varied from focal or partial in the flank or lumbosacral region to a total alopecia of the entire posterior half of the trunk and perinuem. Superficial staphylococcal lesions were observed on the abdomen and in the axilla in approximately 10 percent of the FAD cases.

The season(s) of occurrence of FAD symptoms were as follows: one (majority summer or fall, 17 percent); two (majority summer and fall, 34 percent); three (13 percent)

and all seasons (35 percent) At the time of observation there was a history of intermittent symptoms in 31 percent and continuous symptoms since onset in 69 percent of the dogs (Table XVI). Thirty-three percent of the population of FAD with concurrent AID had manifestations of flea allergy during two seasons of the year while 56 percent had year round symptoms of FAD. Continuous symptoms from time of onset were observed in 80 percent of this population (Table XXVII).

Diagnosis

Most diagnoses of FAD were made on the basis of history, distribution of lesions with posterior dorsal predilection, elimination of other allergic and nonallergic etiologies and evaluation of the response to treatment. Intradermal flea antigen injections were not made unless they were included in the routine testing of antigens for identifying allergens in AID.

The following diagnostic procedures were performed as indicated: skin scrapings, fungus and bacterial cultures, complete blood counts, intradermal testing, isolation and provacative testing for contact allergens, diet testing and biopsies for histopathologic study.

Intradermal Testing Using Flea Antigen

The skin site to be injected was clipped carefully with a number 40 blade and lightly disinfected with alcohol. A stock solution of commercial flea antigen,[t)] 1:5000 dilution of flea extract in 0.5 percent phenol and 50 percent glycerin, was diluted with sterile saline to make a 1:1000 dilution of the starting antigen. A minimal intradermal bleb of 0.05 cc of the 1:1000 antigen was administered using a disposable tuberculin syringe and 26 gauge 3/8 inch needle. A histamine phosphate positive control diluted 1:100,000 and a sterile saline negative control were also used.

The size and appearance of the wheal at the antigen injection site was compared to the negative saline control at 15 to 20 minutes post injection. A reaction was considered positive if the wheal was 3 mm. or larger in diameter or twice the size of the negative control. The elevation and erytherma associated with the wheal were evaluated subjectively.

Of 127 dogs tested which had a history and clinical appearance of AID, 91 percent were positive for flea antigen. Not all of the dogs in this sample had specific symptoms or signs of concurrent FAD. These results raised some

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t) Hollister-Stier Laboratories, Spokane, Wa.

questions about the interpretation of positive reactions to flea antigen when assessing the presence of FAD concurrently with AID.

Evaluation of Commercial Flea Antigen for Intradermal Injections

American commercial flea allergen has been reported to be unsatisfactory for intradermal testing, although the reasons were not given (10). This report together with the finding reported above of 91 percent positive reactions in dogs with AID prompted a study to evaluate the different components of flea antigens in the intradermal test. A primary consideration was to determine whether non-flea components of the commercial test antigen were irritating to the degree of causing a false positive reaction.

The effect of saline, glycerin, phenol and commercial flea extract in 0.5 percent phenol and 50 percent glycerin on the gross and microscopic appearance of intradermal injection sites was evaluated. The following stock solutions were prepared: sterile saline, 50 percent glycerin in sterile saline, 0.5 percent phenol in sterile saline and commercial flea antigen in 0.5 percent phenol and 50 percent glycerin.[t)] The stock glycerin, phenol and flea antigen was then diluted with sterile saline by 10,100,1000 and 10,000 fold.

Six dogs were obtained from a dog control shelter. Dog number 29 had a light flea infestation, but no evidence of

dermatitic lesions. Dog number 30 had significant scaling and hyperkeratosis and breaking of hair over the dorsal tail region, but was not pruritic. Dogs 1-4 had no clinical lesions or evidence of fleas at the time of testing.

All of the dogs were carefully clipped with a number 40 blade and cleansed with alcohol. Duplicate 0.5 cc intradermal injections using saline and four dilutions each of the phenol, glycerin and flea antigen were made on the lateral thorax of each dog. The gross reactions were read approximately 20 minutes post injection. Each dog was then given Rompun[u)] at a dosage of 0.5 cc/20 pounds IV. The first injection sites were then removed using a six mm Keyes biopsy punch and the biopsy site was sutured. In approximately 24 hours, the second set of injections were observed for any delayed reactions. Then a similar dose of Rompun was given and all of the biopsies taken from the injection sites were placed in buffered formalin.

Thirty-five percent of the 78 duplicate tests showed a variation of one mm., nine percent with a variation of five mm. and five percent with a variation of 3 mm. between duplicate injections. Four pairs had one flat and one medium raised wheal. If a positive reaction is defined as 3 mm. larger in diameter than the saline control, all but one

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u) Tylzaine, Haver Lockhart Laboratories, Shawnee, Kansas.

reaction in the phenol group would be negative. In light of the other reactions of 1:10,000 dilution, this would be considered a false positive reaction. The 1:10 dilution of 50 percent glycerin generally caused more wheal formation than the phenol. By definition, six of the twelve reactions would be positive. Case number 30 had positive reactions to 3 glycerin dilutions. The response to commercial flea antigen was more variable. Dogs 29 and 30 had positive reactions to the 1:10 dilution. The other four dogs were negative (Table XXVIII). There were no observed delayed reactions in 24 hours.

All of the biopsies were fixed in buffered 10 percent formalin, paraffin embedded, sectioned at 6-7 microns and routinely stained with hematoxylin and eosin. The biopsies from dogs 1, 29 and 30 were also stained with toluidine blue.

Upper dermal edema of variable degrees was present in most biopsies taken at 20 minutes post intradermal injection (Figure 11). In general, less edema was observed at 24 hours post injection (Figure 12), although there were a few exceptions. The epidermis was missing in approximately five percent of the biopsies, probably due to edema at the dermo-epidermal junction and the subsequent separation during processing.

There were no remarkable differences observed in the dermal cellular infiltration among biopsies from all groups

(Figures 11 and 12). The mild infiltration was predominantly mononuclear, mostly lymphocytes with a few plasma cells. An occasional neutrophil and mast cell was seen.

The results of this trial indicate that most of the wheal formation following intradermal flea antigen injection is due to edema rather than inflammatory reaction. There was no consistent correlation between the degree of edema evident microscopically and the size of the wheal reaction. Thus the glycerin 1:10 group, which showed the most gross reactions, could not be distinguished from the other intradermal injections microscopically.

Histopathologic Findings of Clinical Lesions

Biopsies from four dogs with primary FAD and without concurrent AID were examined. The epidermal changes were characterized by hyperkeratosis and acanthosis (Figure 9). Some sections had marked parakeratosis and surface scabs. The most consistent change in the dermis was a predominantly mononuclear cell infiltration with lymphocytes, histiocytes and plasma cells predominating. Small numbers of neutrophils were often seen. Very few eosinophils and mast cells were routinely observed. There was wide variation in the distribution of the cellular infiltrate including moderate to marked infiltrations at the dermo-epidermal junction, focal upper dermal, periadnexal and diffuse dermal distributions (Figures 9 and 10). Edema

localized at the dermo-epidermal junction was very prominent in some sections while absent in others. Likewise the vascular dilation was variable.

Treatment

The basic flea treatment and control program used had three objectives: 1) break the flea life cycle, 2) minimize flea infestation of all animals in the household by maintaining continuous flea control, and 3) control the allergic reaction to the flea bite.

The protocol recommended started with fumigation of the indoor environment following thorough vacuuming of the carpets and removal of debris and old bedding in the animal's environment. In most instances commercial aerosol insect foggers[v)] were used by the owners. An exterminating service was used in a few instances. It was recommended to repeat the fumigation in 7-10 days if heavy infestations were present initially. Simultaneously, all dogs and cats in the household were bathed with an insecticide or antiseborrheic soap depending on the condition of the skin. For continuous flea control, an insecticide dip[v)] was recommended following the bath and repeated weekly for both dogs and cats. Some small dogs and most cats used flea collars if there was no history of sensitivity to them. The

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v) VIP Insect Fogger, Florida Veterinary Laboratories, Miami Springs, Fl.

collar was used in place of the weekly dipping. Occasionally on a small, short haired dog or cat insecticide powder was used two to three times weekly. It was usually necessary to refumigate every three to six weeks depending on the particular outdoor environment and the number of animals in the household.

One-hundred-eighteen of the dogs with uncomplicated FAD received a series of three weekly flea antigen injections. The dosage was 0.5 cc. subcutaneously or alternatively, 0.1 cc. was given intradermally and the remainder subcutaneously. Most dogs with primary FAD were not given corticosteroids concurrently with the flea control and flea antigen. In severe pruritic cases oral prednisone or prednisolone was given daily or alternate days, decreasing the dosage as possible.

Good clinical response was observed in both groups, those which were hyposensitized with flea antigen (85.6 percent) and those which were treated only with continuous flea control and maintenance of environmental flea infestation (84 percent) (Table XXIX). Good clinical response of dogs with FAD and AID was lower percentage in both groups compared to the noncomplicated FAD. These hyposensitized to the inhalant allergens and fleas had a 55 percent good response and 34.5 percent fair response while the group receiving inhalant allergens with no flea antigen showed a 66 percent good and 33 percent fair response (Table XXX).

The duration of hyposensitization was variable. In general, those animals with FAD which had persistent exposure to fleas required a booster flea antigen injection every three-four months. For those showing FAD symptoms once or twice a year, it was generally recommended to give a booster a few weeks prior to the anticipated flea problem, in addition to the maintenance of continuous flea control all year.

Discussion

The historoclinical findings correlate well with those observed by other workers (9, 30, 31, 64). The classical FAD case was a 1-4 year old dog with a history of pruritus and biting, especially on the posterior dorsal back and perineum. A few fleas or flea excrement were frequently observed. There were usually some lesions over the posterior back, tail and/or perinuem. Often, a few acute papular erythematous lesions were observed on the ventral abdomen and in the axilla. The severity of skin lesions was variable, depending upon the duration of symptoms. In the Pacific Northwest, FAD symptoms were observed in all seasons although there was a slight increase in the summer and fall.

It was common to find FAD concurrently with AID. There was some variations noted in the multiple allergy group. A higher percentage of dogs with AID and FAD had non-seasonal symptoms. Clinically, it was observed that flea

infestations exacerbated the AID symptoms in many cases.

A clinical diagnosis of primary FAD can be made on the basis of history and clinical appearance in most cases. It can be confirmed by a treatment response trial. The recommended treatment consists of controlling the fleas in the indoor environment by fumigation and routine bathing of all animals in the household, followed by continuous flea control consisting of insecticide dips, flea collar or occasionally insecticide powders. It has been generally observed that most flea soaps, insecticide powders or sprays have a very short residual effect, lasting only one-three days. Also, flea collars generally do not provide adequate flea control on the medium or large sized or long haired dog manifesting FAD symptoms. Corticosteroids were not generally needed or used.

The use of flea antigen for diagnosis and treatment is somewhat controversial. Two authors suggest one of the indications for intradermal testing with flea antigen is to confirm the presence of a flea hypersensitivity and a second indication is to help convince the client that flea control is necessary to alleviate the pruritic signs (10, 30). A similar percentage of good response to treatment of primary FAD was obtained in this study with or without flea hyposensitization. A lower and more variable percentage of favorable response was obtained in dogs with concurrent AID,

suggesting that AID was the major factor which was exacerbated by FAD.

Even though similarities were noted in overall percentage results with or without flea hyposensitization, it was observed that many dogs which had not responded to the initial flea control program without flea hyposensitization showed good response with flea antigen added. These observations suggest that in selected cases flea hyposensitization is of definite benefit.

The duration of effect of flea hyposensitization was relatively short, usually lasting from three-six months. The major side effect of intradermal injections of flea antigen was pain at the injection site. If 0.5 cc. was given intradermally, an occasional reaction of induration and epidermal sloughing would occur. This most probably was the result of a strong delayed hypersensitivity reaction.

Several differential diagnoses must be considered. These include sarcoptic mange, pediculosis, AID and contact dermatitis. If good response is not obtained with flea control and flea hyposensitization, one should consider other or concurrent etiologies.

The evaluation of commercial flea antigen for intradermal injection suggested that the 50 percent glycerin component elicits the most edematous response. Phenol and saline showed minimal reactions. The 1:10 dilution of 50

percent glycerin is apparently too strong, resulting in false positive reactions. This study also demonstrated that the reactions to flea antigen extract in 50 percent glycerin and 0.5 percent phenol is variable. Since only two of five stages of skin reactivity to natural flea antigen involves humoral antibodies, it is expected to have many dogs with FAD nonreactive to intradermal tests with flea antigen extract. Gross observations of wheal formation is of more value than microscopic examination in the interpretation of intradermal skin tests.

A variability of duplicate intradermal injections was observed. The majority (35 percent) of the variations between duplicate injections were of a one mm. magnitude. However, five percent showed a three mm. variation. This could lead to problems with interpretation since a positive intradermal reaction was defined as a wheal three mm. larger than the saline control. It would be recommended to make duplicate injections if using diluted flea antigen as a qualitative evaluation of flea hypersensitivity.

Histopathologic findings are not specific. The observations in this study correlate with those of previous authors. In chronic lesions the predominant changes include hyperkeratosis, acanthosis and mononuclear cell infiltration in the dermis. A significant number of plasma cells were routinely observed, but eosinophils were few in number. Edema at the dermo-epidermal junction and vascular dilation

were seen in some biopsies. The most value of biopsies of FAD lesions is to eliminate other non-allergic etiologies or to assess the degree of secondary bacterial involvement in the dermis (72).

SUMMARY AND CONCLUSIONS

Lymphocyte Stimulation by Mitogens and Antigens

The uptake of tritiated thymidine by lymphocytes stimulated with phytohemmaglutinin, concanavalin A, lipopolysaccharides and diluted flea antigen were evaluated on a limited number of blood samples. A wide variation between replicate samples precluded establishing of definite conclusions.

Bacterial Dermatitis

Staphylococcus auerus (coagulase positive) is the predominant bacteria isolated from primary or secondary bacterial dermatitis. The history and lesions associated with bacterial dermatitis are quite variable, depending upon the presence of concurrent problems and the nature of the infection such as superficial or deep. Histopathological changes are not pathognomonic for bacterial dermatitis, but are generally characteristic. They include acanthosis, hyperkeratosis, intradermal and dermal abscesses, edema at the dermo-epidermal junction, and intraluminal or perifollicular mixed leukocyte infiltration with a significant number of neutrophils. Diagnosis is confirmed by bacterial isolation from lesions. Treatment includes long term bactericidal antibiotic therapy based upon in vitro antibiotic

sensitivity testing, autogenous bacterins and treatment of concurrent problems.

Allergic Inhalant Dermatitis

This condition is characterized by intermittent or continuous pruritus accompanied by primary or secondary lesions in a young dog, usually one to three years of age. There tends to be a familial history of allergic dermatitis. The distribution of lesions are usually more generalized than other allergic etiologies. Diagnosis is based on history and intradermal skin tests. The predominant allergens identified with intradermal skin testing in the Pacific Northwest include molds, weeds, trees, grass and house dust. An 80 percent good or fair response to treatment by hyposensitization and in some cases minimal maintenance dosages of corticosteroids is expected. Approximately 20 percent of the cases require higher levels of corticosteroids to control allergic symptoms with or without concurrent hyposensitization.

Canine Contact Dermatitis

This is characterized by a predominantly ventral dermatitis accompanied by pruritus. Approximately 50 percent of the dogs manifested contact allergies by one year of age, while 25 percent are four years or older. Usually both primary and secondary lesions are present. Diagnosis

is based on history, clinical appearance, isolation from suspected contactant and then provacative exposure to the same contactant. Histopathologic characteristics of allergic contact dermatitis are not specific, but can be helpful in broadly categorizing dermatoses providing direction for further study and treatment. The most consistent epidermal changes are hyperkeratosis and acanthosis. Focal and diffuse edema at the dermo-epidermal junction is common. Mononuclear cell infiltrates, composed of lymphocytes and lesser numbers of plasma cells are consistently present in the superficial dermis. Treatment includes avoidance of contact exposure or corticosteroid administration.

Flea Allergy Dermatitis

A high incidence of flea allergy dermatitis is commonly found in dogs with a low grade flea infestation. Clinical signs include intense pruritus involving the posterior of the body, especially the dorsal back and abdomen. Both primary and secondary lesions are often present. Diagnosis is usually based on history, distribution of lesions and response to treatment. Intradermal skin tests using flea antigen may help in confirming the presence of a flea hypersensitivity, but are not adequate for making a definitive diagnosis in many cases. The wheal induced by the flea antigen is mainly due to edema without a remarkable inflammatory response. There is no correlation between gross wheal formation and

microscopic changes, particularly in the degree of upper dermal edema. Treatment includes control of fleas in the environment by fumigation, continuous flea control on all of the animals in the household and hyposensitization with flea antigen.

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APPENDICES

Table I. Biological, immunochemical, and physico-chemical properties of the immunoglobulins of man.[a)]

Ig Class	Sedimentation Value	Where Found in Highest Concentration	Antigen Binding Valence	Complement Fixation	Cross Placenta	Molecular Weight	Carbohydrates	Known Sub-classes
IgG	7S	Serum	2	yes	yes	140,000	2.9%	4
IgA	7S-11S	Seromucous Secretions	2^2-4^3	no	no	170,000[b)] 400,000[c)]	7.5%	2
IgM	19S	Serum	5-$(10)^5$	yes	no	900,000	11.8%	2
IgD	7S	Interstitial Connective Tissue	?	no	no	200,000	14.8%	-
IgE	8.2S	Skin and Epithelium	2	no	no	200,000	10.72	-

a) Serum IgA

b) Secretory IgA

c) From Gordon, B.L.: Essentials of Immunology, 2nd Ed., F.A. Davis Co., Philadelphia, (1974): 48.

Table II. Mean counts per minute (cpm) and stimulation ratios (SR) of lymphocytes treated with concanavalin A (Con A) and phytohemagglutin (PHA).

			Concentrations of mitogen per 2 x 10^5 lymphocytes											
			0.1 ug		0.5 ug		1.0 ug		2.0 ug		5.0 ug		10.0 ug		20.0 ug	
Mitogen	Dog No.	Culture Medium	Mean cpm	SR[a]	Mean cpm	SR[a]	Mean cpm	SR[a]	Mean cpm	SR[a]	Mean cpm	SR[a]	Mean cpm	SR[a]	Mean cpm	SR[a]
Con A	38	FBS[b]	834	3.9	2866	17.9	3971	18.4								
	29	"					226	1.0	206	0.9	236	1.0				
	pooled 30-31	"					210	4.0	106	2.0	113	2.2				
	29	Canine[c]					69	0.6	117	1.0	84	0.7				
	pooled 30-31	"					28	1.0	53	1.9	60	2.1				
	29	"							428	0.5	575	0.6	905	1.0	412	.4
	29	"							150	4.4	280	8.2	123	3.6	81	2.2
	30	"							34	1.1	57	1.9	62	2.0	60	2.0
	29	FBS Ex[d]					13	1.0	14	1.0	11	0.8				
PHA	29	Canine[c]									231	0.2	465	0.5	306	0.3
	29	"									89	2.6	157	4.6	133	3.6
	30	"									27	0.9	106	3.5	125	4.2
	29	FBS Ex[d]	14	1.0	14	1.0	14	1.0	12	0.9	12	0.9				

a) Stimulation ratio calculated by dividing mean cpm of stimulated samples by mean cpm of nonstimulated control sample.

b) Basic culture medium with 10 ml Fetal Bovine Serum/100 ml (see Materials and Methods).

c) Basic culture medium with 10 ml Canine Serum/100 ml (see Material and Methods.

d) Ninety ml. 199 (modified) with HBSS 10X and 10 ml. Fetal Bovine Serum/100 ml.

Table III. Mean counts per minute (cpm) and stimulation ratios (SR) of lymphocytes treated with lipopolysaccharide.

Mitogen	Dog No.	Culture Medium	Concentration of mitogen per 2 x 10^5 lymphocytes							
			10 ug		20 ug		40 ug		80 ug	
			Mean cpm	SR[a]	Mean cpm	SR	Mean cpm	SR	Mean cpm	SR
LPS 055	28	FBS[b]			123	0.6	126	0.6	119	0.6
	29	FBS Ex[c]	11	0.8	12	0.9	10	0.7		
LPS 111	29	FBS[b]	904	4.0	151	0.7	4	0.2		
	pooled 30-31	"	320	6.2	90	1.7	49	0.9		
	29	Canine[d]	14,275	125.7	12,018	105.8	6,814	59.8		
	pooled 30-31	"	3,096	110.6	3,130	111.8	1,451	51.8		
	29	"	21	0.2	17	0.01	23	.02	20	.02
	29	"	28	0.8	36	1.0	24	0.7	24	0.7
	30	"	24	0.8	21	0.7	22	0.7	21	0.7

a) Stimulation ratio calculated by dividing mean cpm of stimulated samples by mean cpm of nonstimulated control sample.

b) Basic culture medium with 10 ml. Fetal Bovine Serum/100 ml. (see Materials and Methods).

c) Ninety ml. 199 (modified) with HBSS 10X and 10 ml. Fetal Bovine Serum/100 ml.

d) Basic culture medium with 10 ml. Canine serum/100 ml. (see Materials and Methods).

Table IV: Mean counts per minute (cpm) and stimulation ratios (SR) of lymphocytes treated with diluted commercial flea antigen and incubated for three and six days.

Days Incubation	Dog. No.	Culture Medium	Dilution of flea antigen[a] (0.05 ml per 2 x 10^5 lymphocytes)											
			1:10		1:100		1:500		1;1000		1;5000		1:10,000	
			Mean cpm	SR[b]	Mean cpm	SR	Mean cpm	SR	Mean cpm	SR	Mean cpm	SR	Mean cpm	SR
3	29 pooled	FBS[c]			249	1.1			204	0.9	243	1.1		
	30-31	"			130	2.5			141	2.7	128	2.5		
	29 pooled	Canine[d]			182	1.6			180	1.6	161	1.4		
	30-31	"			128	4.6			74	2.6	61	2.2		
	29	"			128	4.6			74	2.6	61	2.2	27	0.9
6	29	Canine[d]	32	1.2	24	0.9	21	0.8	32	1.1	25	0.9	29	1.1
	30	"	23	0.1	22	0.1	14	0.04	35	0.1	586	1.9	239	0.8
	29	FBX Ex[e]	11	0.8	13	1.0			10	0.7				

a) Flea extract 1:5000 in 50 percent glycerin and 0.5 percent phenol, Hollister-Stier Laboratories, Spokane, WA.

b) Stimulation Ration calculated by dividing mean cpm of stimulated samples by mean cpm of nonstimulated control sample.

c) Basic culture medium with 10 ml. Fetal Bovine Serum/100 ml. (see Materials and Methods).

d) Basic culture medium with 10 ml. Canine Serum/100 ml.

e) Ninety ml. 199 (modified) with HBSS 10X and 10 ml. Fetal Bovine Serum/100 ml. (see Materials and Methods).

Table V. Response to treatment of patients with concurrent primary generalized demodecosis, Sarcoptes acariasis, or hypothyroidism and secondary pyoderma.

Primary Diagnosis	Treatment	No. of Cases	Response			
			Good	Fair	Poor	Unknown
Demodecosis (Generalized)	AV-Ronnel Dip[a)]	12	7	2	2	1
	Ronnel Only	7	3	-	2	2
	No Treatment	3	-	-	3	-
	Total	22	10	2	7	3
Sarcoptes	Lime-sulpher	8	8			
Hypothyroidism	L-Thyroxine	5	5	-	-	-

a) AV - autogenous vaccine; FA - flea antigen; All animals except those with no treatment received antibiotics; medicated baths and/or corticosteroids.

Table VI. Response to treatment of patients with primary allergic dermatitis and secondary pyoderma.

Primary Diagnosis	Treatment[a)]	No. of Cases	Response			
			Good	Fair	Poor	Unknown
Allergic Inhalent Dermatitis	AV-FA-Hy	3	1	2	-	-
	AV-HY	4	3	-	1	-
	HY only	5	1	1	3	-
	AV only	2	1	1	-	-
	HY-FA	4	1	1	1	1
	HY-ST	1	-	-	1	-
	No treatment	1	-	-	-	1
	Total	20	7	5	6	2
Food Allergy	AV-DR	4	3	1	-	-
	DR only	6	4	1	1	-
	Total	10	7	2	1	-
Contact Allergy	AV-E	5	3	1	-	1
	E only	6	4	1	1	-
	Total	11	7	2	1	1
Non-specific Allergy	AV only	8	2	2	3	1
	AV-FA	7	-	4	2	1
	FA only	6	-	1	4	1
	ST only	2	-	1	-	1
	Symptomatic only	15	2	3	4	6
	Total	38	4	11	13	10
Flea Bite Allergy	AV-FA	4	2	1	-	1
	FA only	14	8	1	-	5
	Total	18	10	2	-	6
Totals		97	35	22	21	19

a) AV - autogenous vaccine; FA - flea antigen; Hy - hyposensitization to inhalant allergens; ST - staphoid A-B, Jensen-Salsbury Laboratories, Kansas City, Mo.; DR - diet restriction; E - elimination of contact with allergen. All animals were treated symptomatically with antibiotics, corticosteroids and/or medicated baths.

Table VII. Results of antimicrobial sensitivity tests on bacteria cultured from patients with chronic bacterial dermatitis and otitis.

Bacteria	Staphylococcus		Streptococcus		Proteus		Clostridium	
Total No. of Isolates	151		41		21		42	
Antimicrobial (concontration)	S	R	S	R	S	R	S	R
Ampicillin (10 ug)	67	74	37	3	14	6	17	5
Penicillin (10 units)	ND[c]		16	8	ND		ND	
Chloromycetin (30 ug)	136	5	38	2	12	8	20	2
Erythromycin (15 ug)	130	11	34	5	ND		15	7
Tetracycline (5 ug)	74	66	11	30	0	20	6	15
Gentamycin (10 ug)	126	7	12	26	19	1	2	20
Cleosin-Lincomycin (2 ug)	91	13	15	12	2	7	12	3
Oleandromycin (15 ug)	82	5	21	1	0	4	9	5
Kanamycin (30 ug)	79	8	7	21	11	7	0	14
Streptomycin (10 ug)	13	21	6	17	ND		1	20
Neomycin (30 ug)	56	10	9	16	17	2	0	22
Cephalothin (30 ug)	3	0	ND		ND		ND	

a) S = Number isolates sensitive to the antimicrobial.

b) R = Number isolates resistant to the antimicrobial.

c) ND = Not done

Table VIII. Results of bacterial cultures from 59 patients with Otitis Externa.

Bacteria	Total Isolates	Percent of Total
Staphylococcus aureus (coagulase pos)	28	47.5
Staphylococcus epidermidis (coagulase neg)	2	3.4
Streptococcus spp.	15	25.4
Clostridium spp.	22	37.3
Escherichia coli	2	3.4
Enterobactor spp.	6	10.2
Proteus spp.	8	13.6
Pasteurella multocida	3	5.1
Candida spp. (not C. albicans)	14	23.7
Pseudomonas spp.	3	5.1
Serratia spp.	1	1.7
Herella	1	1.7
Corynebacterium pseudotuberculosis	1	1.7

Table IX. Results of bacterial cultures from 159 patients with primary or secondary dermatitis or otitis.

Bacteria	Total Isolates	Source		
		Skin	Feet	Ears
Staphylococcus aureus (coagulase positive)	119	119	7	14
Staphylococcus epidermidis (coagulase negative)	11	7	2	2
Streptococcus				
Group A	2	2	-	-
Group B	2	1	-	1
Group C	17	12	3	2
Group D	10	8	1	1
Not serotyped	10	4	4	2
Clostridium spp.[a]	42	37	2	3
Proteus mirabilis	13	3	4	7
Proteus vulgaris	2	1	0	1
Proteus rettgeri	1	1	-	-
Proteus spp.	5	2	2	1
Pseudomonas spp.	3	3	0	-
Pasteurella multoicida	2	1	-	1
Enterobacter spp.	9	5	2	2
Escherichia coli	7	5	1	1
Serratia spp.	1	-	-	1
Mima polymorphia	2	2	-	-
Corynebacterium pseudotuberculosis	1	-	-	1

[a] The majority of clostridial isolates were *C. perfringens*.

Table X. Influence of age of onset and duration of symptoms on the response of 40 cases of primary pyoderma to treatment with antibiotics and autogenous bacterins.

Response to Treatment	Age of Onset	Duration of Symptoms					Total
		<6 mo.	6-12 mo.	1-2 yr.	2-3 yr.	>3 yr.	
Good	< 1 yr.	3	3	-	1	-	7
	1-3 yr.	-	4	1	1	1	7
	3-5 yr.	1	3	2	-	-	6
	>5 yr.	-	3	-	2	-	5
	Total	4	13	3	4	1	25
Fair	<1 yr.	1	1	-	-	-	2
	1-3 yr.	-	-	1	-	1	2
	3-5 yr.	-	-	-	-	-	-
	>5 yr.	-	-	2	-	1[a)]	3
	Total	1	1	3	-	2	7
Poor	<1 yr.	2	-	-	-	1	3
	1-3 yr.	-	-	2	-	1	3
	3-5 yr.	-	-	1	-	-	1
	>5 yr.	-	1	-	-	-	1
	Total	2	1	3	-	2	8

a) Treatment included antibiotics and Staphoid A-B, Jensen-Salsbury Laboratories, Kansas City, Mo.

Table XI. Antigens commonly used for intradermal skin testing.

Routine Screen		Regionalized Pollens	
Histamine 1:100,000	Flea Antigen[b]	Yellow Dock	Cedar
Saline	Streptococcus[c]	Dandelion	Ash
Hormodendrum	Staphylococcus[c]	Sheep Sorrel	Maple
Aspergillus	House Dust	Lambs Quarter	Walnut
Penicillum	Kapok	False Rageweed	Alder
Alternaria	Cat Dander	Pigweed	Oak
4 Mold Mix[a]	Sheep Wool	English Plantain	Blue Grass
10 Tree Mix[a]	Mixed Feathers[a]	Sage	Timothy Grass
National Weed Mix[a]	Horse Dander	Birch Mix[a]	Sweet Vernal
7 Grass Mix[a]		Cottonwood	Rose
		Willow	Daisy
		Fir	Marigold

a) Dome Laboratory, West Haven, Connecticut.

b) Hollister-Stier Laboratories, Spokane, Wa. or Haver-Lockhart Laboratories, Shawnee, Ka.

c) Hollister-Stier Laboratories, Spokane, Wa.

Table XII. Summary of intradermal skin test reactions in 230 dogs with allergic inhalant dermatitis using allergens common to the Pacific Northwest.

Allergen	Total Tested	Total Positive	Percent Positive	Allergen	Total Tested	Total Positive	Percent Positive
4 mold mix	201	177	88	False ragweed	89	63	71
Hormodendrum	108	86	80	Pigweed	116	93	80
Aspergillus	109	92	84	Eng. Plantain	106	79	75
Penicillium	110	92	84	Sage	105	84	80
Alternaria	114	90	79	Birch Mix	122	86	70
10 tree mix	138	107	78	Cottonwood	113	82	73
National weed mix	138	110	80	Willow	86	68	79
7 grass mix	134	114	85	Fir	102	86	84
Cat dander	187	125	67	Mountain cedar	140	115	82
Sheep wool	193	122	63	Evergreen mix	83	74	89
Human dander	24	244	17	Ash	120	85	71
Mixed feather	182	93	51	Maple	33	27	82
Dog epithelium	16	9	56	Walnut	133	74	56
Rabbit epithelium	19	13	68	Alder	117	92	79
Horse dander	154	116	75	Oak	106	83	78
Flea	196	173	88	Orchard	96	79	82
Streptococcus	226	89	39	Blue grass	133	118	89
Staphylococcus	195	53	27	Timothy	62	47	76
House dust	200	141	71	Sweet vernal	127	106	84
Kapok	187	158	84	Velvet	50	38	76
Tobacco	65	18	28	Rye	53	44	83
Trichophyton	74	52	70	Tall oat	50	34	68
Pyrethrin	19	12	63	Bent	62	53	85
Yellow dock	129	101	78	Daisy	29	26	90
Dandelion	125	95	76	Marigold	30	29	97
Sheep sorrel	116	84	72	Rose	29	25	86
Lambs quarter	120	92	77	Cotton	36	5	14

Table XIII. Hyposensitization schedules using aqueous allergens in propylene glycol (A) and alum precipitated extracts (B and C).

A. Hyposensitization schedule using aqueous allergens in propylene glycol

Injection No.	1	2	3	4	5	6	7	Boosters as necessary[a]
Week	1	3	5	9	13	18	24	
PNU[b] per allergen (in thousands)	10	12.5	15	15	17.5	17.5	20	20

B. Hyposensitization schedule using Allpyral[c]

Injection No.	1	2	3	4	5	6	7	8
Week	1	2	3	5	9	13	18	24
PNU per allergen	100	200	400	800	1500	300	6000	10,000

C. Modified (rapid) hyposensitization schedule using Allpyral[c]

Injection No.	1	2	3	4	5	Boosters as necessary[a]
Week	1	2	3	4	8-10	
PNU per allergen (in thousands)	2.5	5	7.5	10	10	10

a) When pruritic symptoms start to increase, a booster is given.
b) Protein Nitrogen Units.
c) Allpyral-alum precipitated extract, Dome Laboratories, West Haven, Connecticut.

Table XIV. Breed and sex distribution of 137 cases of allergic inhalant dermatitis treated by hyposensitization.

Breed	No. of Animals	% of cases	Sex	
			Male	Female
German Shepherd	14	10.2	9	5
Irish Setter	13	9.5	8	5
Poodle	7	5.0	5	2
German Shepherd X	5	3.6	2	3
Irish Setter X	2	1.4	1	1
Poodle X	7	5.0	4	3
Other Mixed Breeds	18	13.0	7	11
All Other Breeds	71	52.0	41	30
Totals	137		77	60

Table XV. Summary of hyposensitization treatment response compared to the age at initiation of treatment of 139 dogs with allergic inhalant dermatitis.

Clinical Response	Age					Total
	<2 yrs	2-3 yrs	4-5 yrs	6-7 yrs	7-8 yrs	
Good	10	27	16	5	6	64
Fair	4	13	11	4	6	38
Poor	2	10	10	6	2	30
No Report	1	1	2	0	1	7
Totals	17	51	39	17	15	139

Table XVI: Summary of the clinical response and duration of treatment in 139 dogs with allergic inhalant dermatitis treated by hyposensitization.[a)]

Clinical Response	Length of hyposensitization treatment time[b)] 2-4 mo	4-5 mo	6-12 mo	13-18 mo	>18 mo	Total
Good	4	10	26	10	14	64
Fair	7	8	16	5	2	38
Poor	1	3	21	5	0	30
No Report	0	5	2	0	0	7
Totals	12	26	65	20	16	139

a) All methods of hyposensitization were used in this sample. Refer to Table XIII.

b) All dogs had been on the treatment program at least 2 months.

Table XVII. Summary of the clinical response and duration of treatment in 65 dogs with allergic inhalant dermatitis treated by a rapid method of hyposensitization[a] using Allpyral[b].

Clinical Response	Length of hyposensitization treatment time				Total
	2 mo	2-3 mo	4-5 mo	6 mo	
Good	11	8	2	14	35
Fair	5	10	1	6	22
Poor	3	0	2	3	8
Totals	19	18	5	23	65

a) Refer to Table XIIIC.

b) Dome Laboratories, West Haven, Connecticut.

Table XVIII. Clinical reponse of dogs with allergic inhalant dermatitis treated by hyposensitization and their seasonal patterns.

Pattern	Total No. of dogs	Clinical Response: Favorable[a] No. of Total	%	Clinical Response: Poor[b] No. of Total	%
Seasonal	44	39	28	5	3.5
Non-Seasonal	95	70	50.5	25	18.0
Total	139	109		30	

a) At least a 50 percent decrease of oral corticosteroids required post-hyposensitization compared to pre-hyposensitization.

b) Less than 50 percent decrease in oral corticosteroids post-hyposensitization compared to pre-hyposensitization.

Table XIX. Percent of 30 dogs with poor clinical response which had concurrent problems with AID.

Concurrent Problem	% of 30 dogs
Contact allergic dermatitis to rugs	14
Flea bite allergy	27.5
Generalized seborrhea	10
Pyoderma-deep	10
Probable contact allergic dermatitis to grass	7
No concurrent problems identified	38

Table XX. Historoclinical data on 33 dogs with allergic contact dermatitis and 2 with irritant contact dermatitis.

Case No.	Breed	Age	Duration of Illness	Secondary Pyoderma	Concurrent AID[a)]	Contactant
1	German Shepherd	5 yrs	2 yrs	no	no	synthetic rug
2	Spaniel Crossbred	10 yrs	5 yrs	no	no	wool rug
3	German Shepherd	8 yrs	1 mo	no	no	straw bedding
4	German Shepherd	10 wks	2 wks	yes	no	disinfectant[b)] (ICD)
5	Dachschund	9 yrs	2 yrs	no	yes	mattress-vinyl
6	Cocker Spaniel	4½ yrs	3 yrs	yes	no	wool rug
7	Scotty Terrier	3 yrs	1 yr	no	no	synthetic rug
8	Golden Retriever	14 mo	3 mo	no	yes	wool rug
9	West High Terrier	6 yrs	5 yrs	no	yes	wool rug
10	German Shorthair	3 yrs	1½ yrs	yes	yes	vinyl-synthetic rug
11	Afghan	14 mo	6 mo	yes	no	wool rug
12	German Shepherd	4 yrs	1 yr	yes	no	synthetic rug
13	German Shepherd	9 yrs	1 yr	no	no	synthetic rug
14	Irish Setter	9 mo	1 mo	no	no	wool blanket
15	Maltese	9½ yrs	2½ yrs	no	no	synthetic rug
16	Sheltie	6½ yrs	2½ yrs	no	yes	wool rug
17	Golden Retriever	1 yr	9 mo	no	no	wool rug
18	Chihuahua	6 yrs	½ yr	no	no	fish scales
19	Schnauzer	7 yrs	3 yrs	no	no	wool rug
20	Sheltie	7 yrs	5 yrs	yes	no	synthetic rug
21	Cocker Spaniel	4 yrs	3½ yrs	yes	no	wool rug
22	Samoyed Crossbred	4 yrs	3 yrs	yes	no	synthetic rug
23	Bassett	10 yrs	2 mo	yes	no	synthetic rug
24	Cocker Spaniel	1½ yrs	10 mo	no	no	synthetic rug
25	Collie	3 yrs	5 mo	yes	yes	wool rug
26	Springer Spaniel	3½ yrs	2 yrs	yes	yes	synthetic rug
27	Pekingese	7 mo	4 mo	yes	no	disinfectant[c)] (ICD)
28	Pomeranian	12 yrs	2 mo	no	no	synthetic rug
29	Cocka-poo	1 yr	6 mo	no	yes	synthetic rug

Table XX (continued)

Case No.	Breed	Age	Duration of Illness	Secondary Pyoderma	Concurrent AID[a]	Contactant
30	Chihuahua	5 yrs	4 yrs	yes	no	synthetic rug
31	Beagle	8 yrs	2 mo	no	no	wool rug
32	Laborador	4 yrs	2 yrs	no	no	synthetic rug
33	Laborador	2 yrs	1 yr	yes	no	synthetic rug
34	Mixed Breed	5 yrs	4 yrs	yes	no	synthetic rug
35	Springer Spaniel	5 mo	3 mo	no	no	wool rug

a) Allergic inhalant dermatitis.

b) Laro, Whitmoyer Laboratories, Inc., Meyerstown, Pa.

c) Malathion.

Table XXI. Distribution of lesions in 27 dogs with contact dermatitis and 8 dogs with contact dermatitis and concurrent allergic inhalant dermatitis.

Distribution of Lesions	No. of Dogs with CD[a)]	No. of Dogs with Concurrent CD and AID[b)]
Ventral/Extremities	27	8
Lateral	10	6
Dorsal	4	7
Otitis	9	1[c)]
Face	9	0

a) CD = contact dermatitis

b) AID = allergic inhalant dermatitis

c) In the author's experience, otitis is more common in AID cases than reflected in this population.

Table XXII. Age of onset of lesions of 35 dogs with contact dermatitis and 8 dogs with contact dermatitis and concurrent allergic inhalant dermatitis.

Age of Onset	No. of Dogs with CD[a)]	No. of Dogs with Concurrent CD and AID[b)]
Less than 6 months	4	0
6-12 months	13	3
1-2 years	4	2
2-4 years	5	2
4-6 years		
greater than 6 years	6	0

a) CD = contact dermatitis.

b) AID = allergic inhalant dermatitis.

Table XXIII. Summary of laboratory findings of 35 dogs with contact dermatitis.

Complete Blood Count

Case No.	PCV %	Hb.	WBC X10^3	Segs X10^3	X10^3	Eos X10^3	Mono X10^3	Lymph X10^3
8	44	14.8	13.8	7.9	.8	1.9	1.0	2.2
12	45	15.4	14.8	8.9	.0	1.5	.9	3.5

Case numbers 2, 3, 9, 15, 20, 22-25, and 29 all had values within accepted normals.

Fungal Cultures

Case No.	Result
4, 6, 15, 20, 27, 31	

Skin Scrapings

Case No.	Result
2, 4, 6-9, 11, 15, 20, 22-27, 29	

Negative skin scrapings were obtained by referring veterinarians prior to referral from most of the other dogs.

Bacterial Cultures

Case No.	Bacteria Isolated
6, 10, 11, 21, 30	*Staphylococcus* (coagulase positive)
12	*Staphylococcus* (coagulase positive); *Streptococcus* group C; *Proteus* spp.
15	*Proteus* spp.
23	*Staphylococcus* (coagulase positive); *Streptococcus* group C
26	*Staphylococcus* (coagulase negative); *Streptococcus* group C
27	*Staphylococcus* (coagulase positive); *Streptococcus fecalis*; *Enterobacter* spp.

Table XXIV. Age of onset of symptoms in 320 dogs with flea allergy dermatitis.

Age of Onset	No. of Dogs	Percent
3 months	4	1
4-5 months	4	1
6-11 months	42	13
1 year	84	26
2-3 years	99	31
4-5 years	44	14
6-7 years	18	5.5
8 years or older	4	1

Table XXV. Distribution of lesions in 266 dogs with flea allergy dermatitis.

Distribution of Lesions	No. of dogs	Percent
Posterior back, tail and perineum	221	83
Flanks, posterior ventral abdomen	172	65
Axilla, anterior trunk	58	22
Generalized	16[a)]	6

a) Ten of this group had concurrent allergic inhalant dermatitis.

Table XVI. Season of onset and number of episodes of clinical symptoms observed in 253 dogs with flea allergy dermatitis compared with the duration of symptoms.

Number of Episodes	1					2	3 or more		
Duration of Episode	Continuous					Intermittent		Total No.	% by Season
	3 mo.	3-5 mo.	6-12 mo	1-2 yrs	2 yrs	1-2 yrs	2 yrs		
Season of onset[a)]									
F	14	-	-	-	-	1	3	18	7.1
W	5	-	-	-	-	-	-	5	2.0
Sp	4	-	-	-	-	1	1	6	2.4
Su	1	-	-	-	-	3	11	15	5.9
Su/F	1	5	8	-	-	13	9	36	14.2
F/W	-	12	8	-	-	2	3	25	9.9
W/Sp	-	2	2	-	-	1	2	7	2.8
Sp/F	-	-	1	-	-	1	2	3	1.2
Sp/Su	-	3	5	-	-	1	7	16	6.3
Sp/Su/F or W/Sp/Su	-	-	14	-	-	2	17	33	13.0
F/W/Sp/Su	-	-	2	35	52	-	-	89	35.2
Total			174			79		253	

a) F - fall; W - winter; Sp - Spring; Su - Summer.

Table XXVII. Season of onset and number of episodes of clinical flea allergy dermatitis symptoms in 55 dogs with concurrent allergic inhalant dermatitis compared with the duration of symptoms.

Number of Episodes	1				2	3 or more		
Duration of Episode	Continuous				Intermittent		Total No.	% by Season
	3-5 mo	6-12 mo	1-2 yrs	2 yrs	1-2 yrs	2 yrs		
Season of onset[a]								
Sp	-	-	-	-	-	1	1	1.8
Su	2	-	-	-	-	-	2	3.6
Su/F	1	4	1	-	1	2	8	19.5
F/W	-	-	1	-	1	-	1	1.8
W/Sp	1	-	-	-	-	-	1	1.8
Sp/F	-	-	-	-	-	1	1	1.8
Sp/Su	-	2	1	-	1	4	7	12.7
Sp/Su/F or W/Sp/Su	-	3	-	-	-	-	3	5.5
F/W/Sp/Su	-	-	15	15	-	-	31	56.4
Totals			44			11	55	

[a] F - fall; W - winter; Sp - spring; Su - summer.

Table XXVIII. Summary of 78 duplicate wheal reactions of intradermal injections of saline, phenol, glycerin and commercial flea antigen. Read at 20 minutes post injection.

Substance Injected	Dilution	Case No. 29 Injection No. 1 Diameter of Wheal mm	Case No. 29 Injection No. 2 Diameter of Wheal mm	Case No. 30 Injection No. 1 Diameter of Wheal mm	Case No. 30 Injection No. 2 Diameter of Wheal mm	Case No. 1 Injection No. 1 Diameter of Wheal mm	Case No. 1 Injection No. 2 Diameter of Wheal mm
Saline	none	6 F	7 F	7 F	7 F	6 F	6 F
0.5% phenol	1:10	7 F	8 F	9 F	8 F	6 F	6 F
	1:100	5 F	7 F	8 F	9 F	6 F	6 F
	1:1000	5 F	5 F	8 F	7 F	6 F	4 F
	1:10000	6 F	4 F	10 M[c]	7 F	6 F	6 F
50% Glycerin	1:10	10 F	10 F	10 M	10 M	6 F	8 F
	1:100	8 F	8 F	10 M	7 M	6 F	7 F
	1:1000	7 F	6 F	8 F	7 F	7 F	7 F
	1:10000	7 F	8 F	10 M	10 M	8 F	7 F
Flea antigen[d]	1:10	9 M	12 M	10 M	10 M	8 F	8 F
	1:100	8 F	8 F	8 F	9 F	5 F	7 F
	1:1000	7 F	4 F	7 F	10 F	6 F	7 F
	1:10000	min.[e]	min.	8 F	7 F	7 F	7 F

Substance Injected	Dilution	Case No. 2 Injection No. 1 Diameter of Wheal mm	Case No. 2 Injection No. 2 Diameter of Wheal mm	Case No. 3 Injection No. 1 Diameter of Wheal mm	Case No. 3 Injection No. 2 Diameter of Wheal mm	Case No. 4 Injection No. 1 Diameter of Wheal mm	Case No. 4 Injection No. 2 Diameter of Wheal mm
Saline	None	7 F	7 F	7 F	7 F	7 F	7 F
0.5% phenol	1:10	8 F	7 F	7 F	7 F	7 F	7 F
	1:100	6 F	6 F	6 F	7 F	7 F	8 M
	1:1000	6 F	8 F	6 F	7 F	6 F	6 F
	1:10000	8 F	7 F	7 F	7 F	7 F	7 F
60% glycerin	1:10	8 M	10 M	8 M	7 M	8 M	9 M
	1:100	8 M	7 M	6 F	6 F	7 F	7 F
	1:1000	7 F	7 F	6 F	7 F	6 F	7 F
	1:10000	7 F	7 F	6 F	6 F	7 F	7 F
Flea antigen	1:10	7 F	7 F	7 F	7 F	8 M	8 M
	1:100	6 F	6 F	7 F	7 F	7 F	8 M
	1:1000	6 F	6 F	6 F	6 F	6 M	7 F
	1:10000	6 F	5 F	6 F	6 F	7 F	6 F

[a] All dilutions made with sterile saline; [b] Flat; [c] Moderately raised from the surface; [d] Flea extract 1:5000 in 0.5 percent phenol and 50% glycerin, Hollister Steir Laboratories, Spokane, Wa.; [e] Too small to measure diameter.

Table XXIX. Response to treatment of 143 dogs with flea allergy dermatitis.

	Treatment			
	Flea control[a] Flea hyposensitization[b]		Flea control only	
Clinical Response	No. of Animals	% of Group	No. of Animals	% of Group
Good	101	85.6	21	84
Fair	14	12.0	1	4
Poor	3	2.5	3	12
Total	118		25	

a) Adequate flea control was recommended for all dogs including weekly baths and insecticide dips or baths and flea collars in addition to fumigation of the indoor environment.

b) Flea antigen, Hollister-Stier Laboratories, Spokane, Wa.

Table XXX. Response to treatment of 35 dogs with flea allergy dermatitis and concurrent allergic inhalant dermatitis.[a)]

	Treatment			
	Flea control[b)] Flea hyposensitization[c)]		Flea control only	
Clinical Response	No. of Animals	% of Group	No. of Animals	% of Group
Good	16	55.0	4	66
Fair	10	34.5	2	33
Poor	3	10.0	0	0

a) All dogs in the study were hyposensitized to inhalant allergens.

b) Adequate flea control was recommended for all dogs including weekly baths and insecticide dips or baths and flea collars and/or inacticide powders in addition to fumigation of the indoor environment.

c) Flea antigen, Hollister-Stier Laboratories, Spokane, Wa.

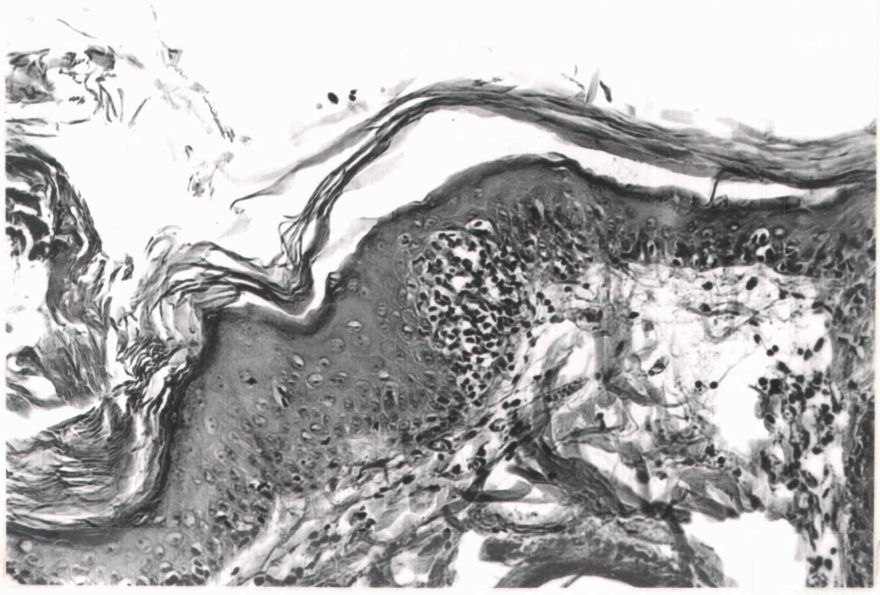

Figure 1. An intraepidermal microabscess in the skin of a dog with chronic pyoderma. There is moderate hyperkeratosis, parakeratosis and a mild subepidermal leukocytic infiltrate. Hematoxylin and eosin stain, 64 x original magnification.

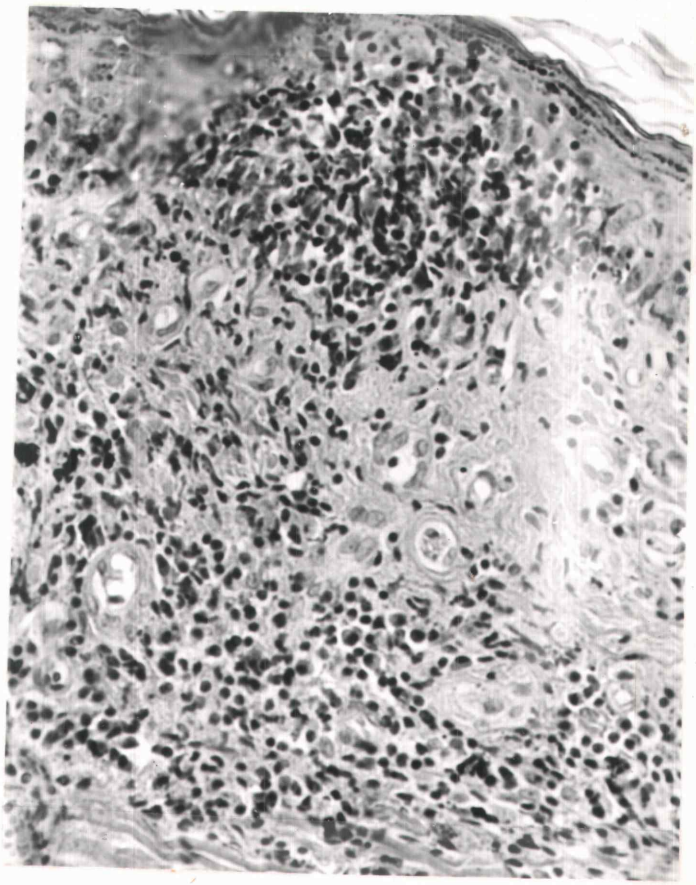

Figure 2. A microabscess at the dermo-epidermal junction of a dog with chronic pyoderma. Note the marked fibroplasia and prominent vascularization in the adjacent dermis and the diffuse mononuclear infiltration in the deeper dermis. Hematoxylin and eosion stain, 102 x original magnification.

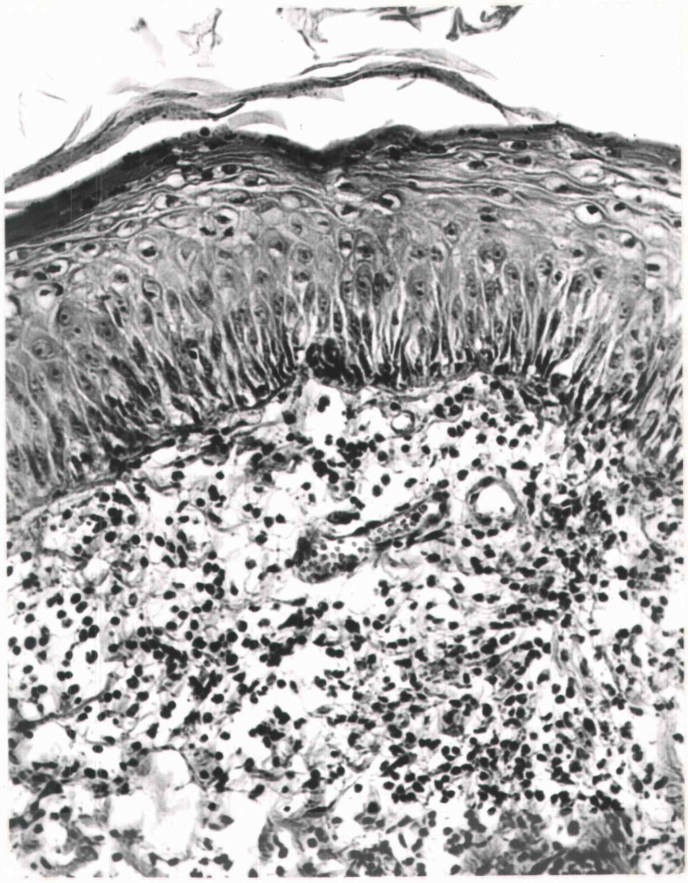

Figure 3. Acute exacerbation of a chronic pyodermatitis showing marked dermal edema, mixed inflammatory cell infiltrate and vascular congestion of the dermis. There is moderate acanthosis, some hydropic degeneration of epidermal cells and slight focal edema in the stratum germination. Hematoxylin and eosin stain, 64 x original magnification.

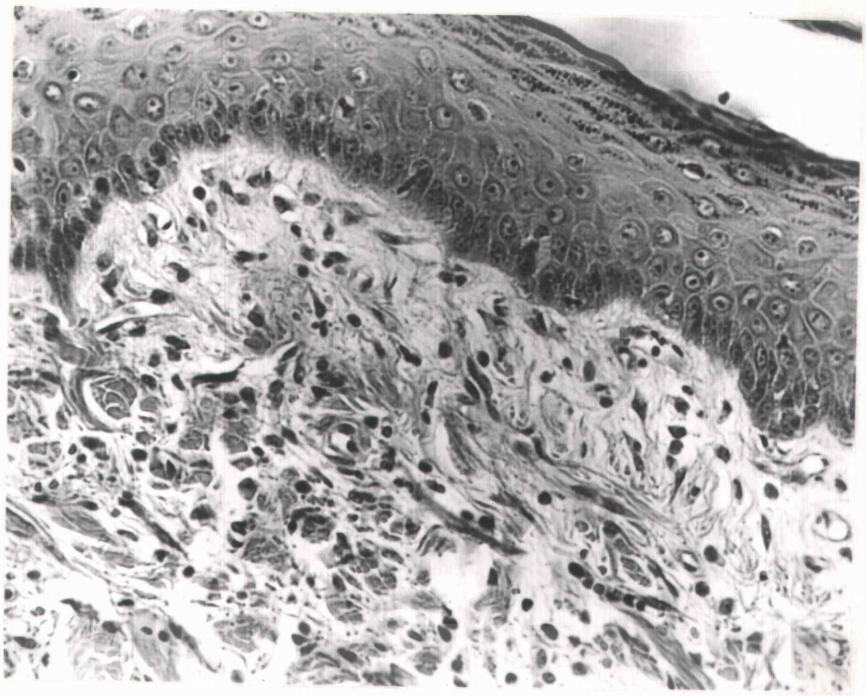

Figure 4. Skin biopsy of a dog with chronic pyoderma showing fibroplasia at the dermo-epidermal junction, accompanied by mild vascular proliferation and slight mononuclear cell infiltrate. Hematoxylin and eosin stain, 83 x original magnification.

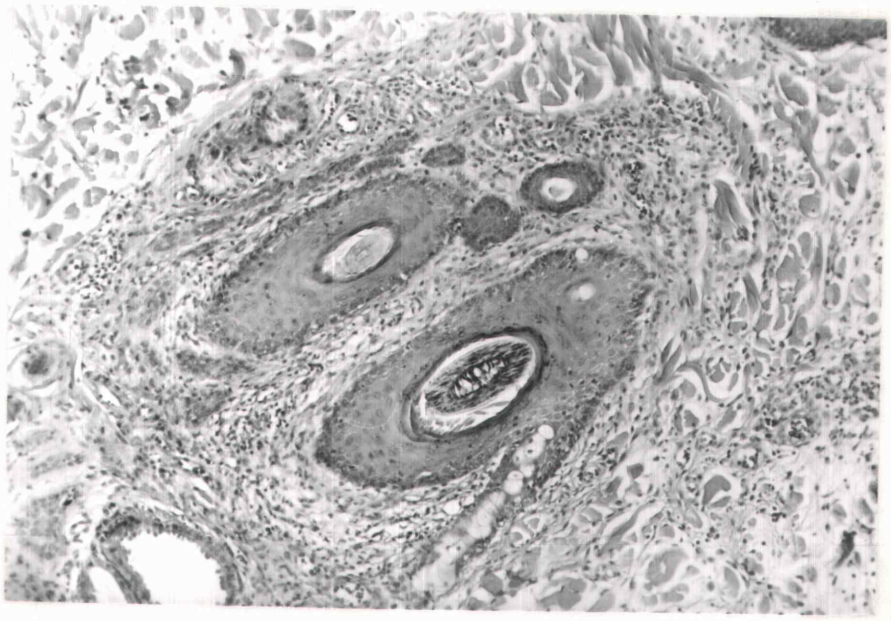

Figure 5. Dermis of a dog with chronic pyoderma showing extensive well-differentiated perifollicular fibroplasia with mild leukocytic infiltrate. Hematoxylin and eosin stain, 32 x original magnification.

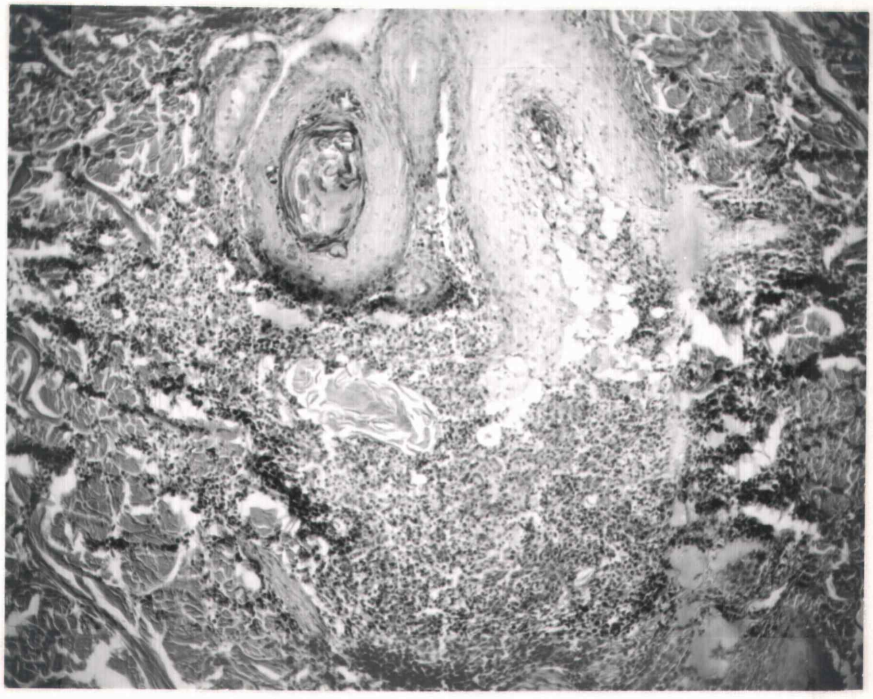

Figure 6. Skin biopsy from a dog with chronic pyoderma showing a ruptured hair follicle with associated pyogranulomatous focus. Note the bits of keratinized debris which are encompassed by the purulent exudate. Hematoxylin and eosion stain, 32 x original magnification.

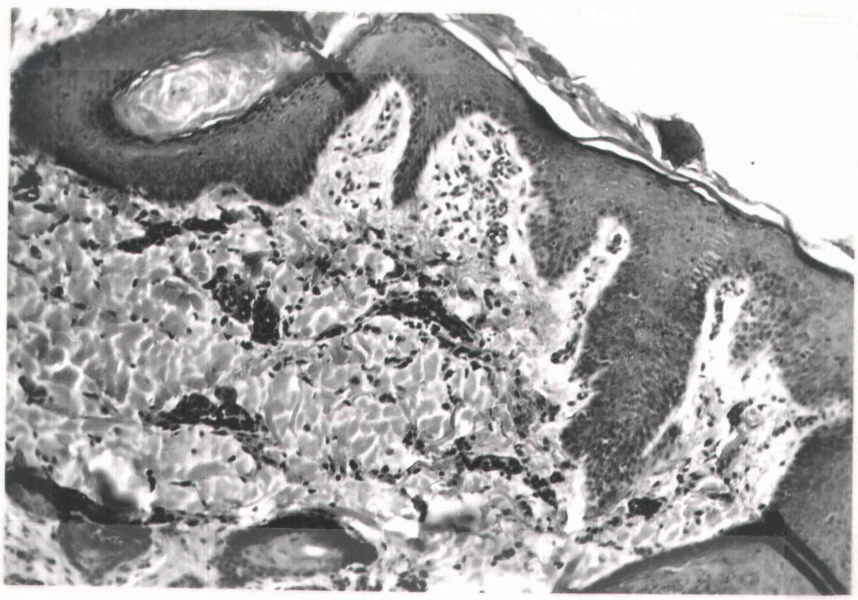

Figure 7. Photomicrograph of a skin biopsy from a dog with allergic contact dermatitis showing acanthosis, hyperkeratosis, keratin plugging of a hair follicle, mild edema of the epidermal-dermal junction, mild diffuse inflammatory (primarily mononuclear) cell infiltrate of the superficial dermis and mild vascular congestion. Hematoxylin and eosin stain, 80 x original magnification.

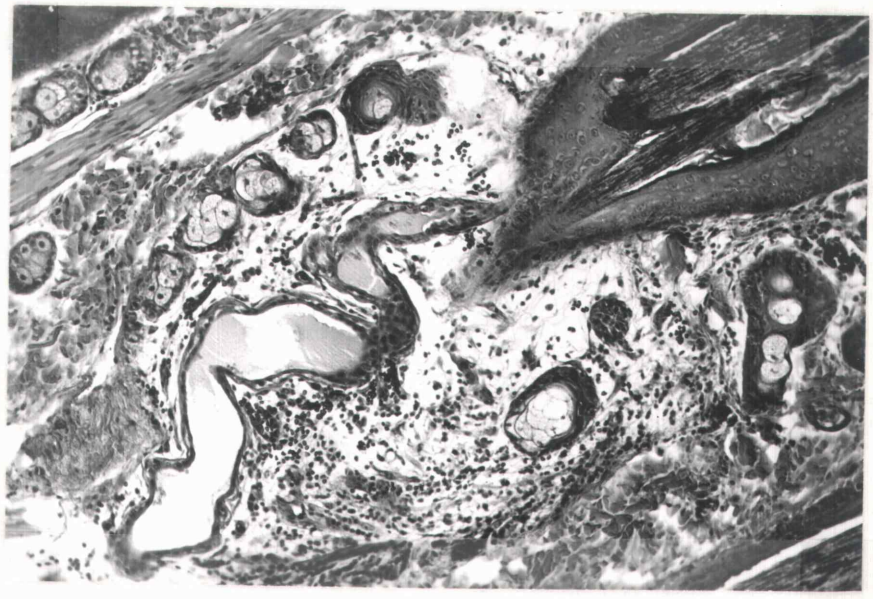

Figure 8. Photomicrograph of a skin biopsy from a dog with allergic contact dermatitis showing a large edematous focus at the base of a hair follicle which contains a moderate infiltrate of inflammatory (primarily mononuclear) cells. Adjacent to the focus is a dilatated suderiferous gland. The epithelim lining the hair follicle is acanthotic. Hematoxylin and eosin stain, 80 x original magnification.

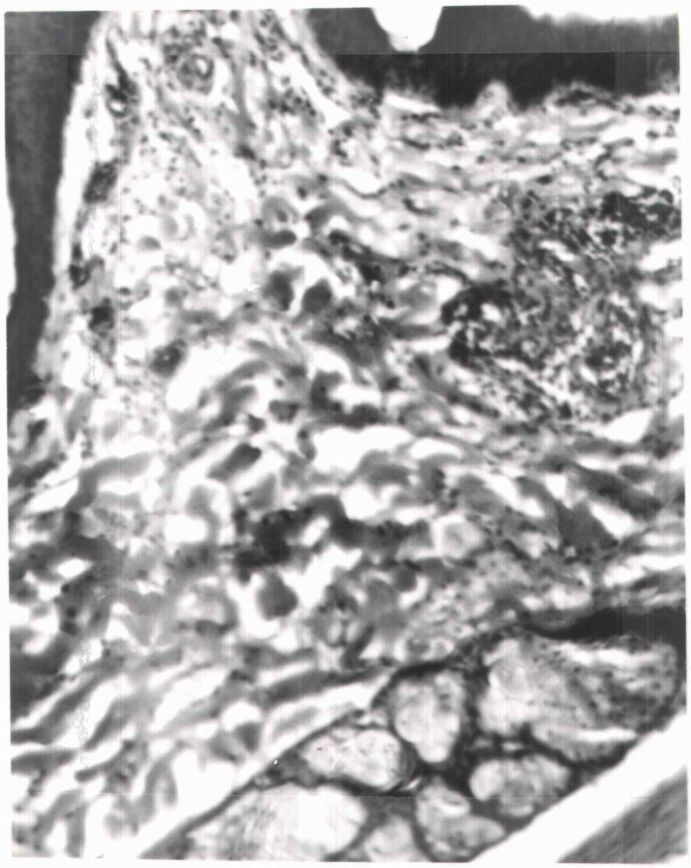

Figure 9. Photomicrograph of a skin biopsy from a dog with flea allergy dermatitis showing mild acanthosis, and mild edema and minimal diffuse infiltration of mononuclear cells at the dermo-epidermal junction. Note the foci of perivascular accumulation of mononuclear cells with a few polymorphonuclear leukocytes. Hematoxylin and eosin stain, 80 x original magnification.

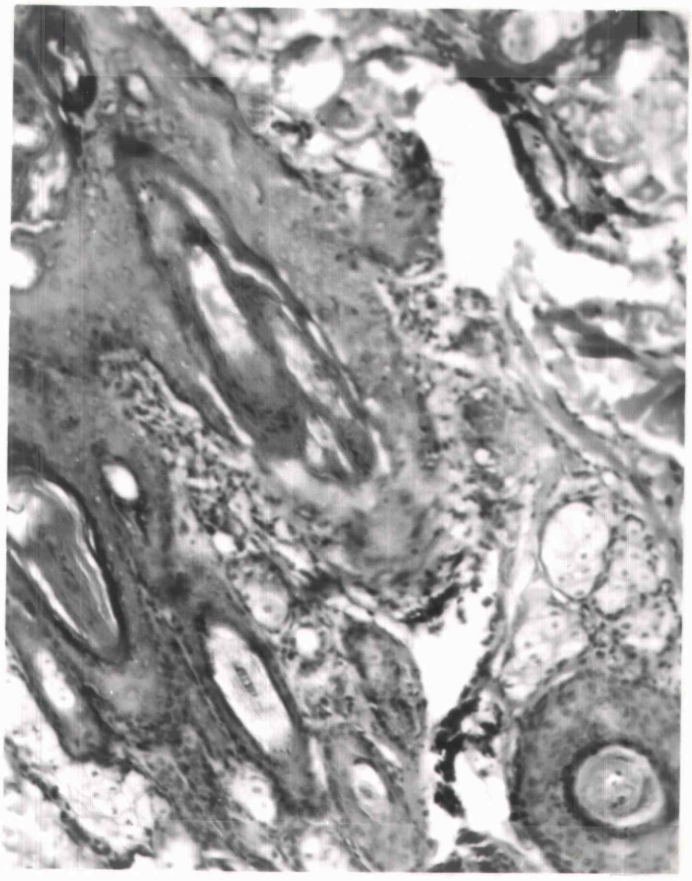

Figure 10. Photomicrograph of a skin biopsy from a dog with flea allergy dermatitis showing perifollicular edema and infiltration of mononuclear cells, mostly lymphocytes and a few plasma cells. Hematoxylin and eosin stain, 80 x original magnification.

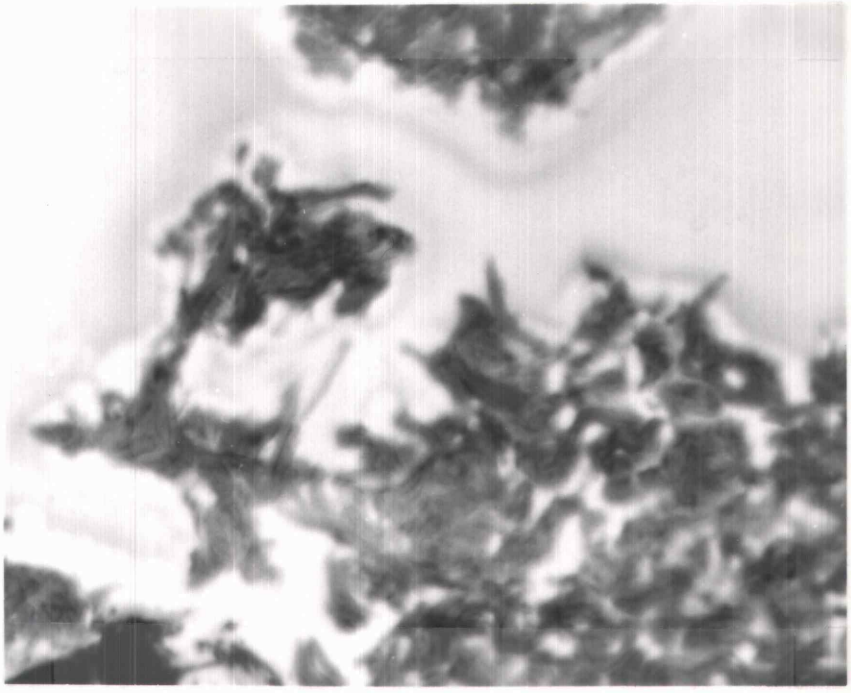

Figure 11. Photomicrograph of 20 minute post injection biopsy from site injected intradermally with 0.05 ml. of 50 percent glycerin diluted 1:10 in saline. Note large spaces filled with edema separating dermal fibers. Hematoxylin and eosin stain, 204 x original magnification.

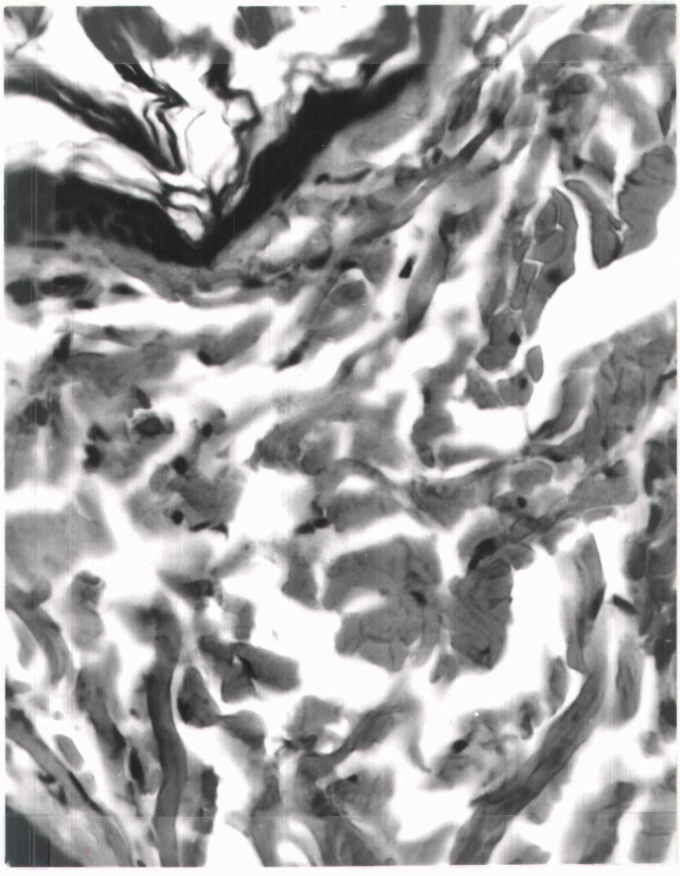

Figure 12. Photomicrograph of 24 hour post injection biopsy from site injected intradermally with 0.05 ml. of 50 percent glycerin diluted 1:10 in saline. Note absence of edema and minimal number of dermal mononuclear cells. Hematoxylin and eosin stain, 80 x original magnification.