OVERVIEW
The key to approaching any dermatology case is to have a systematic diagnostic plan established. It is important to remember that the skin can be the “window” to the general health of the patient. The goal of this lecture is to review a few of the skin conditions that can be seen in our aging patients.

SUPERFICIAL NECROLYTIC DERMATITIS
Superficial necrolytic dermatitis (a.k.a. hepatocutaneous syndrome, metabolic epidermal necrolysis, necrolytic migratory erythema) is a rare disease in dogs and very rare in cats. The disease primarily affects old dogs, with the average age being 10.7 years. Small breeds seem to be over-represented. Clinical signs are most commonly associated with liver disease in dogs, although glucagonomas and hyperadrenocorticism may also lead to superficial necrolytic dermatitis. Idiopathic liver disease is the most common cause in dogs, although the liver disease may also be drug or mycotoxin induced. Glucagonomas are the most common cause of the disease in humans.

General clinical signs of superficial necrolytic dermatitis in dogs include anorexia, depression and weight loss. Dermatologic signs are the hallmark of the disease and usually precede evidence of internal disease. Skin lesions are characterized by erythematous crusting and erosions/ulcerations primarily affecting the mucocutaneous junctions, ears, feet, axillary and inguinal regions, genitalia and pressure points. Secondary bacterial and yeast infections are very common and can significantly worsen the condition of the patient. Pruritus can vary from minimal to intensely pruritic. Cutaneous signs may precede evidence of internal disease by weeks or months.

The disease should be suspected on the basis of the history and physical examination. Examination of skin biopsies of lesions on affected dogs reveals a unique combination of diffuse parakeratotic hyperkeratosis, epidermal necrosis, marked superficial epidermal edema, irregular epidermal hyperplasia and mild superficial perivascular dermatitis. The epidermal edema is both intercellular and intracellular edema and is localized to the upper half of the epidermis. Severe edema may result in intraepidermal clefs and vesicles. In dogs with hepatic disease associated with necrolytic migratory erythema, a unique "honeycomb" pattern is found on ultrasonographic evaluation of the liver. This pattern consists of variable sized hypoechoic regions surrounded by highly echogenic borders. These hypoechoic regions correspond to regenerative nodules bounded by severely vacuolated hepatocytes, numerous bile ductules and a network of reticulin and fine collagen fibers representing remnants of collapsed hepatic lobules. Clinicopathologic abnormalities vary, depending on the specific inciting organ system and the progression of the disease. Complete blood count abnormalities include anemia, neutrophilic leukocytosis and toxic
neutrophilic changes. Serum biochemical abnormalities may include increased liver enzymes, total bilirubin, and bile acids. Hypoalbuminemia is a common finding and many dogs develop hyperglycemia as the disease progresses. Glucagon concentrations are increased in some cases. In dogs with liver disease, severe, profound hypoaminoacidemia is often seen.

Treatment is aimed at correcting the underlying metabolic disease. If the dog is diabetic, insulin therapy is indicated. In most cases however, regulation is difficult. Surgical excision of a glucagon-secreting tumor of the pancreatic alpha cells may be possible. Unfortunately, most cases are associated with irreversible chronic liver disease and hepatic cirrhosis, making treatment largely unrewarding. Therapy for dogs with severe hypoaminoacidemia (commonly seen with dogs with hepatic diseases) is nutritional support to include intravenous amino acid supplementation. The diet should consist of a good quality protein diet. Fatty acid, zinc and niacin supplementations have been utilized with some success. IV amino acid supplementation regimens vary from 250–500 ml IV of an 8–10% amino acid supplement given daily until dermatologic signs improve, to these doses given weekly for an extended period of time. IV amino acid supplements are re-administered in many patients when dermatologic signs return. Antibiotics and/or antifungal agents should be used to treat secondary skin infections.

Hydrotherapy and shampoo therapy can help remove crusts and lessen the pruritus and pain that may be present. Glucocorticoid therapy has been associated with improvement in cutaneous signs, but should be used with caution as it may worsen the underlying metabolic disease.

**PARANEoplastic Alopecia**

This is rarely seen in cats affected by pancreatic carcinoma or, less frequently, bile duct adenocarcinoma. These patients are usually systemically ill, anorexic, may present with vomiting, diarrhea, lethargy and weight loss. Results of biochemical blood analysis are usually within normal range. Radiographs and ultrasound usually fail to identify the tumor. The alopecia usually starts on the abdomen and legs. The hair is easily epilated and leaves a typically smooth shiny skin. In some cases there is pruritus and excessive licking, which exacerbates the alopecia. Secondary *Malassezia* infection may be seen in the clawbeds. Histologically, there is profound atrophy and miniaturization of hair follicles and mild hyperkeratotic hyperplasia of the epidermis, with occasionally a mild lymphocytic exocytosis. There is no treatment currently available. The prognosis for the cats once a diagnosis has been made is grave. The neoplasia is usually advanced by the time of diagnosis and the cats either die or are euthanized soon after.

**Squamous Cell Carcinoma**

Squamous cell carcinomas are common in the dog and cat and are malignant epithelial tumors. They occur most frequently in sun-damaged skin. In dogs, squamous cell carcinoma occurs at an average age of 9 years, with no sex predilection. Claw bed origin squamous cell carcinomas are usually seen in black-coated dogs of large breeds, especially Labrador Retrievers, Standard Poodles, Giant Schnauzers, Dachshunds, and Bouvier de Flandres. Because of an affinity for lying around in the sun, short coated breeds with white or piebald ventral coat and skin color (Dalmatians, American Staffordshire Terrier, Bull Terrier and Beagle) have a high incidence of solar-induced tumors. The average age of cat inflicted with squamous cell carcinoma is also 9 years with no sex or breed predilection. However, white cats are 13 times more likely to present with these tumors.
In dogs, these tumors may be proliferative or ulcerative. Proliferative types are papillary masses of varying size that can be cauliflower in appearance that are ulcerated and bleed easily. The ulcerative types initially appear as shallow, crusted ulcers that become deep and crateriform. Squamous cell carcinomas can be located on the trunk, limbs, digits, scrotum, lips, anus, and nose. Lesions in cats may also be proliferative or ulcerative and is usually characterized by a deep ulcer covered that is crusted. Occasionally, lesions in cats have overlying cutaneous horns. The most common sites are the external nares, pinnae, eyelids and lips.

Prognosis in cats is dependent on histopathologic differentiation but not with location of the lesion. Location does affect the prognosis in dogs. About 70% of lesions of the claw bed invade the bony tissue of the third phalanx and metastasize more frequently (about 20% invade regional lymph node). One study reported 95% of dogs with lesions under the nail survived at least one year, while 60% of dogs with lesions elsewhere on the digits survived one year. Treatment may include surgical excision, cryosurgery, electrosurgery, hyperthermia and radiotherapy with laser therapy a consideration.

MULTICENTRIC SQUAMOUS CELL CARCINOMA IN SITU

Bowen's disease is a rare disease of cats older than 10 years of age. Exposure to ultraviolet light is not a causal factor as the lesions are reported more commonly in dark-skinned cats or in areas of the body that receive little solar exposure. Papillomavirus antigen has been demonstrated in feline skin lesions.

Lesions are multifocal and occur most commonly on the head, neck, shoulders, and forelimbs. They are well-circumscribed, melanotic, hyperkeratotic macules and plaques, 0.5 to 3 cm in diameter. The older lesions become thick, crusted, and ulcerated plaques that tend to bleed easily.

On histopathologic examination, the lesions resemble actinic keratoses. There is a very abrupt onset from unaffected to dysplastic epithelium. Multiple coalescing small aggregates of dysplastic keratinocytes are seen. These can be differentiated from squamous cell carcinoma in situ that involves entire sheets of surface epidermis and superficial parts of the follicular epithelium (from the infundibulum to the isthmus.)

Treatment options include surgical excision, the use of a CO2 laser, topical application of 5-fluorouracil cream (use with extreme caution on cats), or imiquimod (Aldara 5%, 3M pharmaceuticals, a local human antiviral topical medication) has been anecdotally successful in some cases.

The prognosis for cats with this disease is guarded. The incidence of developing infiltrative squamous cell carcinoma in cats with Bowen's disease is much lower than in cats with solar-induced actinic keratoses. No metastases have been recorded

EPITHELIOTROPIC (T-CELL) CUTANEOUS LYMPHOMA (MYCOSIS FUNGOIDES)

Epitheliotropic lymphoma or mycosis fungoides (MF) is a special variant of cutaneous lymphoma. It is dominantly a T-cell tumor of atypical lymphocytes. This tumor has a strong
affinity for the epithelium so that the epidermis and follicular epithelium are typically heavily infiltrated by lymphocytes where the underlying/surrounding dermis may be only sparsely involved. In very early stages, the lymphocytic infiltrate can be extremely difficult to differentiate from that of a non-specific allergic reaction or a mild, subtle *Malassezia* dermatitis. Later in the development of the disease the characteristic intraepidermal microabscesses (Pautrier's micropustules) may be found. The tumor development is typically slow: it may be present for several years from start to finish in some animals.

The clinical appearance of MF varies enormously in animals. Initially, however, it presents as a subtle, erythematous, scaling and mildly alopecic lesion. These may be solitary or multifocal. The later stage—which clinically resembles a mycosis—is the source of the name. The scaly, erythematous lesions are frequently associated with pruritus and very easy to confuse clinically with allergies and other inflammatory dermatoses. The scales and erythema may even encourage a mild secondary overgrowth of *Malassezia* or bacteria, further confusing the diagnosis as they will then partially respond to the appropriately given antimicrobial therapy. The average survival time following a confirmed diagnosis ranges from 4–7 months. Nodules occur in the end stage, at which time, in animals, a clinical cure is not to be expected.

When many different stages are present on the same animal, the clinical appearance can be highly suggestive of this diagnosis. Biopsy at that late stage should be diagnostic. However, when the lesions are early and there is pruritus with the erythema and scale, the diagnosis can be tricky. At this clinical stage there may be a diagnostic biopsy finding. However, there may also be mild interface dermatitis, a lymphocytic exocytosis or a mild superficial perivascular dermatitis with exocytosis. These are all relatively non-specific findings, often taken in an itchy animal as representing a likely hypersensitivity. In humans there are documented cases of MF arising in sites of chronic allergy. It is possible this is also the case in animals. It is therefore more than theoretically possible that an original diagnosis of allergies may indeed transform into this tumor.

A number of treatments have been reviewed. Response to standard chemotherapeutic protocols used in lymphosarcoma of other organ systems has been disappointing. Lomustine (CCNU), an alkylating agent, has been effective in the treatment of dogs with cutaneous lymphoma, at a dose of 50mg/m² q 21–30 days. Remission lasted from 2–15 months. Neutropenia may be seen, and is most likely to occur 1–2 weeks after treatment, although this has usually been noted with higher doses. While generally a safe drug, irreversible hepatic toxicity (again, generally at higher doses) has been reported. The use of essential fatty acid supplementation at the rate of 3 ml/kg twice a week has been reported to be associated with clinical success. In practice, for a number of dermatologists, this has not been successful.

**PARANEOPLASTIC EXFOLIATIVE DERMATITIS (THYMOMA-ASSOCIATED DERMATITIS)**

Cats present with a severe scaling and alopecia which typically begins on the head and neck and may extend over the entire body. Pruritus is a common feature, although the grade of pruritus is lower than the grade of the scale-crust formation. Many of these cases were initially reported in older cats with thymoma.
METASTATIC PULMONARY ADENOCARCINOMAS
This syndrome has been reported in cats: the lesions occur on the distal extremities, especially the front feet, and look more like inflammatory pododermatitis than a neoplastic process. Their presence may be noted before pulmonary signs are noted. The neoplasm may be either a bronchogenic or squamous cell carcinoma. Palliative treatment to reduce the discomfort may be attempted (topical or systemic corticosteroids to reduce edema, etc).

CONCLUSION
Allergic skin disease and endocrinopathies were not discussed in detail in this presentation but should also be on the list of differential diagnoses when presented with a geriatric dermatology case. Many dermatological conditions can mimic one another so it is important to have a systematic plan in order to prevent misdiagnosis. It should also be remembered that malignancies of all kinds may metastasize to the skin, even mimicking inflammatory dermatoses.