PATHOGENESIS:

**Immunologic**
- Type I, II, III, IV hypersensitivity reactions

**Nonimmunologic**
- Related to pharmacology of the drug
- Predictable, dose dependent

**Route of administration**
- Oral
- Topical
- Injectable
- Inhalation

**Clinical Presentations:**
- Erythema multiforme
- Toxic epidermal necrolysis
- Pemphigus foliaceus
- Vaccine reaction
- Cutaneous vasculitis
- Lichenoid Drug Eruption

**Unique Feline Reactions:**
- Miliary dermatitis reaction
- Vaccine reaction
  - Injection site fibrosarcomas

**ERYTHEMA MULTIFORME**

- Drug-induced apoptosis
  - Programmed cell death
- Acute onset of lesions
- Erythematous macules
- “Target lesions”
- Urticarial plaques
Vesicles and bullae
Concurrent systemic illness
   Fever, depression, anorexia
Mucous membrane involvement
   Vesicles, bullae, ulcers
   Erythema multiforme major or Stevens-Johnson syndrome
Can be life threatening

**Drugs implicated**
   Aurothioglucose
   Cephalexin, chloramphenicol, gentamicin, trimethoprim sulfas, ormetoprim sulfas, tetracycline
   Diethylcarbamazine, levamisole
   L-thyroxine, phenobarbitol

**TOXIC EPIDERMAL NECROLYSIS**

Severe erythema multiforme?
Massive and sudden apoptosis
Diffuse erythematous rash
Vesicles and bullae
Full thickness skin sloughing and ulcers
May affect footpads, mucous membranes
Lesions usually painful
Concurrent fever, anorexia, lethargy, depression
Secondary sepsis a problem
Often a fatal disease

**Drugs implicated**
   Penicillins, cephalosporins, trimethoprim sulfas
   Griseofulvin
   Levamisole
   5-fluorocytosine
   Topical flea dips (D-limonene)

**DRUG-INDUCED PEMPHIGUS**

Mimics Pemphigus foliaceus
Acute, transient pustular eruptions
Subsequent crusts, scales, erosions, epidermal collarettes
Variable distribution patterns
Systemic illness rare
**Drugs implicated**
- Ampicillin, cephalosporins, sulfonamides
- Diethylcarbamazine, thiabendazole
- Cimetidine, procainamide

**VACCINE REACTIONS**
Most commonly observed at site of a subQ or IM vaccination
- Rabies, DHLP- Parvo
  - Can occur from weeks to months post-vaccination
Focal area of alopecia and hyperpigmentation

**Breed predisposition**
- Poodle, Bichon Frise
- Shih Tzu, Lhasa Apso
  - Miniature Schnauzer, Yorkshire Terrier, Bedlington Terrier, Silky Terrier
Most spontaneously resolve over several months
Lesion may remain static
Area of alopecia and hyperpigmentation can gradually enlarge over months to years

**Treatment**
- Tincture of time
- Surgical excision
- Pentoxifylline (Trental)
  - 15 mg/kg TID x 3 months

**CUTANEOUS VASCULITIS**
Palpable purpura, hemorrhagic bullae
Craterform ulcers, full thickness skin sloughing
Acrocyanosis of distal extremities
Large areas of erythematous or purplish skin
  - Does *not* blanch on dioscopy
Lesion often painful
Pitting edema of distal extremities
Concurrent systemic illness
  - Anorexia, depression, fever

**Drugs implicated**
- Penicillins, sulfonamides, cephalosporins, dexamethasone
- DHLP- Parvo vaccine
**LICHENOID DRUG ERUPTION**

Solitary to multiple papillomatous or plaque-like lesions  
Drugs implicated:  
  - Cyclosporine (Atopica, Neoral, Gengraf)

**MILIARY DERMATITIS REACTION**

Miliary lesions  
Affects head, face, neck regions  
Intense pruritus  
Mimics “food allergy”  
Drugs implicated:  
  - Methimazole (Tapazol), Propranolol

**VACCINE REACTION**

**Injection site fibrosarcomas**  
Interscapular and femoral regions  
  - Associated with either subQ or IM injections  
  - Tumor may develop 1-2 years post-vaccination  
Vaccines implicated:  
  - FeLV, Rabies, FVRCP

**DIAGNOSIS OF CUTANEOUS DRUG REACTIONS**

**History**  
Observed reaction does not resemble pharmacologic action  
Prior exposure to drug may have been well tolerated  
Reaction can be reproduced by small amounts of drug  
Reaction consistent with a known hypersensitivity response  
Reaction occurs within several days of drug exposure  
Resolution within several days of drug withdrawal

**Drug rechallenge**  
Proves cause and effect relationship  
Clinical signs often more severe  
Outcome can be fatal

**Erythema Multiforme**  
**Histopathology**, 
Hydropic interface dermatitis
Dyskeratotic keratinocytes with satellitosis
Superficial perivascular infiltrates with mononuclear cells

**Toxic Epidermal Necrolysis**

**Histopathology**
- Hydropic degeneration of basal cells
- Coagulation necrosis of epidermis
- Absence of dermal inflammation
- Dermoepidermal separation and bullae formation

**Clinical Criteria**

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<tr>
<td>Flat or raised, focal</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
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<td>or multifocal, target lesions</td>
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<td>Number of mucosa involved</td>
<td>&lt;1</td>
<td>&gt;1</td>
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<td>Erythematous or purpuric, macular or patchy eruption</td>
<td>&lt;50%</td>
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<td>Epidermal detachment</td>
<td>&lt;10%</td>
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<td>10-30</td>
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**Pemphigus Foliaceus**

**Histopathology**
- Subcorneal pustules
- Acantholytic cells
- Neutrophils, eosinophils
- Involvement of hair follicles

**Vaccine Reaction**

**Histopathology**
- Vasculitis, panniculitis
- Dermal edema
- Atrophic hair follicles
- Hydropic degeneration of basal cells

**Cutaneous Vasculitis**

**Histopathology**
Most commonly leukocytoclastic
  Neutrophils in vessel walls
  “Nuclear dust”
Fibrinoid degeneration, thrombi
Perivascular hemorrhage and edema

**LICHENOID DRUG ERUPTION**

**Histopathology**
Psoriasiform lichenoid dermatosis – with or without papillomavirus

**UNIQUE FELINE REACTIONS:**

**Miliary dermatitis**

**Histopathology**
  Epidermal crusts, spongiosis
  Neutrophilic, eosinophilic vesicopustules
  Eosinophilic perivascular infiltrates

**Vaccine Reactions**

**Histopathology**
  Fibrosarcoma

**TREATMENT**
Discontinue suspected drug
Avoid chemically related or similar drugs
When multiple drugs are present: all should be discontinued
Best advice: “Do no harm!”
For Idiopathic cases (Erythema multiforme, cutaneous vasculitis, miliary dermatitis) –
consider hydrolysate treated or home-cooked elimination diet trial

**Supportive Therapy - IV Fluids**
  Systemic antibiotics in septic patients
    Broad spectrum initially
      Cephalexin - 10 mg/lb TID
      Based on culture and sensitivity
    Gram negative organisms
      Ciprofloxacin - 22 mg/kg SID

**Immunosuppressive Drugs**
Extremely controversial
  May actually be contraindicated
Increased risk of infections, delayed healing
Indicated in drug induced Erythema Multiforme major

Corticosteroids:
  Prednisolone
  1 mg/lb SID-BID

Immune Modulating Drugs:
  Cyclophosphamide - 1 mg/lb SID
  Cyclosporine (Neoral, Gengraf, Atopica) - 5 mg/kg SID-BID
  Azathioprine (Imuran) - 1 mg/lb SID, Pentoxifylline (Trental) – 15 mg/kg TID