WHAT IS NEW IN THE TREATMENT OF CANINE AND FELINE DEMODICOSIS

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1. **Canine Demodicosis** (Red Mange)

   There are now **three** species of demodex known to cause clinical disease in the dog:

   1. *Demodex canis*
   2. *Demodex injai*[^1][^3]
      a. All life stages are larger than *D. canis*
      b. Resides primarily in the Sebaceous gland
   3. *Demodex cornei*[^3][^4]
      a. 50% shorter than *D. canis*
      b. Resides primarily in the stratum corneum

   **A brief review of clinical features** - there are 2 different clinical forms: localized and generalized. Prognosis and therapy varies for each condition. Each form may have a juvenile or adult onset. There are slight variations in the clinical presentation depending on the species of Demodex. *Demodex injai* presents primarily as a dorsal seborrheic dermatitis. To date, clinical presentation of *D. cornei* is similar to *D. canis*.

   **Localized** - lesions in **one** body area based on skin scrapings of 3-5 sites.

   1. Usually **young dogs** (3-12 mos): may be squamous or pustular.
   2. **Squamous**
      a. Benign, self-limiting
      b. One to several patches of circumscribed, erythematous, scaly alopecia
c. Usually head and/or extremities

d. Prognosis good; over **90% undergo spontaneous remission** in 6-8 weeks *in spite* of therapy.

e. **10% will become generalized** (regardless of treatment!)

3. **Pustular**
   a. Especially feet, periorbital
   b. Deep pyoderma present
   c. MUST treat with antibiotics

4. **Differential diagnosis:**
   a. Dermatophytosis
   b. Seborrheic dermatitis
   c. Pyoderma
   d. Abrasion
   e. Puppy pyoderma (Impetigo)
   f. Juvenile cellulitis

5. **Diagnosis:**
   a. Survey scrape (scrape a minimum of 5 places), **DEEP** (review introductory notes)
      i. Lesions, lip fold, ventral feet
      ii. Avoid scars
      iii. Record life cycle stages (#'s)
      iv. Skin biopsy may be necessary if: Shar-pei breed, foot involvement or chronic
   b. Culture and sensitivity (C+S) if pustular
   c. CBC, fecal, HW antigen
   d. Complete physical exam
   e. Family history of demodex
   f. Formulate prognosis based on the above information
6. **Treatment**

   a. None necessary except occasional antibiotics (topical +/- oral)

   b. Treat the bacterial folliculitis: systemic antibiotics + topical antimicrobial shampoo
      
      Benzoyl peroxide gel, shampoo

   c. **Never use miticidal treatment for localized demodex for various reasons:**
      
      - It is important to know which dogs progress into generalized disease as prognosis is different.
      - Treatment does not affect the likelihood of a dog progressing into generalized as *this is genetically predetermined.*
      - You need to know if the disease is localized versus generalized so you can make the proper recommendation for spaying/neutering the pet.

   d. No steroids!!

   e. Make sure general health status of dog is good: routine health maintenance, deworming, vaccines.

   f. Recheck in 2-4 weeks or sooner if lesions progress. DEEP SKIN SCRAPE AGAIN. After 4 weeks, skin scrapings from healing cases should show fewer mites, fewer immature forms and sometimes no live mites. If lesions are spreading and the mite count (including the ratio of immature to adult) is high, the condition may be progressing to generalized demodicosis.

**GENERALIZED DEMODICOSIS:**

1. Definition (any or all of the following):

<table>
<thead>
<tr>
<th>Localized</th>
<th>Generalized</th>
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<tr>
<td>Only 1 body location involved</td>
<td>More than 1 body location involved</td>
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<tr>
<td>5 or fewer lesions at that location</td>
<td>More than 5 lesions if only 1 location involved</td>
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<td>&lt; 50% area affected if only 1 location involved</td>
<td>&gt; 50% area affected if only 1 location</td>
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<td>2 or more feet</td>
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2. Generalized demodecosis is one of the most severe, most difficult to treat, and most common dermatoses of dogs.

3. Any sex or breed, but is more common in some and more severe in some breeds:

<table>
<thead>
<tr>
<th>Dobie*</th>
<th>Shar pei*</th>
<th>Lhasa Apso*</th>
<th>OESD*</th>
<th>Boxer*</th>
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<tbody>
<tr>
<td>Shih-Tzu*</td>
<td>Collie</td>
<td>Pit bull</td>
<td>Bulldog</td>
<td>Dachshund</td>
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<tr>
<td>Pointer</td>
<td>German shep</td>
<td>Afghan</td>
<td>Dalmation</td>
<td>Pug</td>
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<tr>
<td>Chihuahua</td>
<td>Rottweiler</td>
<td>Boston Terrier</td>
<td>Beagle</td>
<td>Great Dane</td>
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(* = high risk breeds) (OESD = Old English Sheep Dog)

4. May be squamous or pustular
   a. Squamous - scaly, **alopecic**, patches which coalesce to form large areas of alopecia. Skin is erythematous (reddened), or can be **hyperpigmented** (darkened (black) skin). The scale is brown, grayish. **Comedones** may be prominent.
   b. Pustular: **a life threatening disease**. Generalized hair loss, deep pyoderma (deep folliculitis/furunculosis), progresses to cellulitis, sepsis, death. In some cases, may be confined to the feet (if so, less serious, but harder to treat- see pododemodicosis below).

5. Lesions are complicated by bacterial infection- *Staphylococcus pseudintermedius* (previously known as *S. intermedius*) is the most common bacterial organism to complicate generalized demodicosis

6. Pododemodicosis: demodicosis can be present on the feet w/o generalized body lesions, but this is still considered generalized demodicosis.
   The case history reveals whether the dog once had generalized demodicosis that healed, except for the foot lesions or whether the paws were the only part of the body ever
affected. The digital and interdigital lesions are especially susceptible to secondary pyoderma. In some animals, demodectic pododermatitis can be chronic and extremely resistant to therapy.

1. The generalized form may be juvenile onset or adult onset:

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<tr>
<th>Breed</th>
<th>Juvenile</th>
<th>Adult</th>
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<tr>
<td>Small breeds</td>
<td>&lt; 12 months</td>
<td>&gt; 12 months</td>
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<tr>
<td>Large breeds</td>
<td>&lt; 18 months</td>
<td>&gt; 18 months</td>
</tr>
<tr>
<td>Giant breeds</td>
<td>&lt; 24 months</td>
<td>&gt; 24 months</td>
</tr>
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</table>

a. Juvenile-onset, generalized
   i. 50% self-cure (will clear without anti-mite treatment) – although we treat all cases of generalized demodecosis
   ii. 50% require anti-mite treatment
   iii. Of those that need anti-mite treatment, 10% will need life long anti-mite treatment - usually by pulse therapy
   iv. Hereditary: all dogs with generalized demodecosis should be neutered, even if they cleared spontaneously without treatment.

b. Adult-onset, generalized
   i. Usually secondary to another disease or steroid use.
   ii. Rule out internal disease, neoplasia, immunosuppression, hypothyroidism, iatrogenic/spontaneous Cushing's.
   iii. In more than 50% of cases, no underlying disease can be documented at the time demodicosis is diagnosed. In these cases, the dog should be monitored carefully because the malignancy or systemic illness may become obvious weeks to months into treatment. Although the condition may resolve
spontaneously in some mildly affected dogs with the resolution of the underlying disease, most will require treatment. If no cause for the demodicosis can be found, the odds of successful treatment are reduced.

iv. Differentiate adult-onset from a juvenile-onset that never cleared or was never diagnosed

v. Keep in mind- infectious disease in younger adult-onset cases and endocrine or neoplasia in older dogs.

8. Diagnosis

a. Deep survey skin scrapings (capillary oozing)
   - There are 3 cases in which you may not see the mites despite scraping → thus you may need to biopsy:
     1. Shar-Pei breed (due to their thick skin and excessive mucin)
     2. Fibrotic skin (e.g. scar tissue or lick granuloma)
     3. Pododermatitis/ pododemodicosis (painful, tend to bleed easily giving rise to false negative result)

b. Thorough physical examination

c. CBC, fecal, HW antigen test, chemistry panel, urinalysis
   - In adult dog: don’t forget to evaluate for underlying cause with additional diagnostic tests.

d. Culture and sensitivity if pustular

e. Mites can be seen on biopsy

f. Formulate prognosis

g. Response to treatment is not a diagnostic test!

TREATMENT – GENERALIZED CANINE DEMODECOSIS

40-50% of dogs < 1 year old will undergo spontaneous remission (except certain breeds). In dogs with a familial history of demodicosis, the condition may resolve spontaneously, but the rate probably is much lower than that seen with no familial history. However, most cases of generalized demodecosis
should be treated with anti-mite therapy. For those not on anti-mite therapy, remember to recheck in 2-4 weeks and reassess lesions and mite counts. If mite counts are increasing or lesions expanding-then will likely not self cure and will need to treat with miticide.

Four concepts essential to treatment:

1. Kill the mite → topical or systemic miticidal agents
2. Treat for secondary bacterial folliculitis → systemic antibiotics
3. Flush the follicle → shampoo containing Benzoyl
4. Ensure systemic health → adequate nutrition, control underlying disease, etc

Miticidal therapy: hundreds of treatments are available, most have questionable efficacy. Some young dogs may spontaneously resolve without treatment; therefore, be cautious of therapies claiming efficacy without controlled studies to support.

1. **AMITRAZ** (Mitaban®, Upjohn→ Pharmacia→ Pfizer)

*The only approved treatment for generalized demodicosis*

- An emulsion in water and organic solvent, clip hair of medium coated breeds to maximize penetration.
- A broad spectrum miticide, mechanism = monoamine oxidase inhibitor, alpha-2 adrenergic agonist, inhibits prostaglandin synthesis.
- Label says effective in > 98% of cases (not quite, one study showed long term efficacy of 60-80%, Paradis 1999).
- The labeled use protocol:
  - 1 vial (10.6 mls)/2 gallons H₂O = 0.025% sol.= 250 ppm of active drug
  - Clip animal all over
  - Bathe with benzoyl peroxide shampoo, rinse
  - Sponge dip all over affected and nonaffected areas every 1-2 weeks.

- **Dip until 3 consecutive scrapings are negative!** By 6-9 properly performed dips you should start seeing improvement in mite count.
♂ If not improving, consider other anti-mite treatment.

♦ Do not allow dog to get wet between dips. Especially the feet in pododemodicosis cases.

♀ The off label use protocol (routinely recommended)

♦ Same protocol as above except: perform weekly.

♦ Use greater volumes for large breed dogs (i.e. 2 vials/4 gal H₂O).

♦ Be careful in toy breeds: use ½ to ¼ strength.

♀ Side effects: expect even if dipping appropriately!

♦ Depression, anorexia, vomiting, pruritus, hypothermia, ataxia, bradycardia, sedation (do not sedate and dip on same day!), hyperglycemia, possible death.

♦ Transient sedation for 12-24 hours, esp after the first treatment.

♦ Some dogs become severely pruritic after the first few applications.

♦ Precautions: owners, veterinarians, technicians with asthma, diabetes mellitus or Parkinson’s disease should not apply amitraz dip. The individual applying the dip should wear gloves and apply the dip in a well ventilated area.

⇒ Treatment of side effects:

▪ Yohimbine - reversal agent for xylazine (α₂ adrenergic agonist) and amitraz. Use label dose subcutaneously pre- and/or post-dip.

▪ Atipamezole- reversal agent for medetomidine (α₂ adrenergic agonist) and amitraz.

▪ Diphenhydramine for pruritus (avoid hydroxyzine/Atarax).

♀ Availability: Mitaban® is made by Pfizer Animal Health, Inc.. It is available as 10.6 ml bottles. Cost: approximately $35 / bottle.

♀ Taktic (large animal Amitraz product)- This product is not endorsed by the University of Florida Dermatology Department because of adverse side effects that have been reported and because of the availability of other treatments (i.e. Ivermectin and Milbemycin).
2. **MILBEMYCIN** (Interceptor®): 1-2 mg/kg/day until 3 negative skin scrapings. Not approved for this use.

- One x 23 mg tablet of Interceptor® costs approximately $6.50: to treat a 30 kg dog costs approximately $200-300 per month depending on the dose required for disease control.

- Doses greater than 2.5 mg/kg day have been associated with neurological side effects in any breed of dog.

- The dog MUST BE heartworm negative. Watch for adverse effects: vomiting, loss of appetite, lethargy/weakness, trembling, ataxia, stupor, seizures, coma death.

- **BUILD UP TO FINAL DOSE**: 0.5mg/kg/day then 0.75. 1.0 …. Do this during the first (7-10) days of treatment to identify sensitive animals.

- **Reported time to first negative scrape**: 8-26 weeks[v]

- **Success rate for treatment of juvenile, generalized demodex**: at dosage of 0.5-1.0 mg/kg/day = 42%, at a dosage of 2.2 mg/kg/day = 84.6%[vii]

3. **IVERMECTIN** - Success with high dose (400-600 ug/kg) daily therapy in otherwise amitraz resistant cases until **3 negative skin scrapes**.

- **Do not use in**: Collies, Shelties, Border Collies, OESD, and Australian shepherds! Any genetically predisposed breed, herding or non-herding, may develop neurological signs from toxic accumulation of ivermectin in the central nervous system.

- Toxic CNS levels arise due to a defective p-glycoprotein pump whose normal function is to extrude ivermectin and many other drugs/toxins out of the CNS.

- The specific mutation has been identified in the gene encoding this pump: the multi-drug resistance gene-1 (MDR1).

- A screening test is available to determine if dogs are homozygous, heterozygous or unaffected for the MDR1 mutation. This is strongly recommended for all dogs, especially herding breeds. The test requires a buccal mucosa swab. [http://www.vetmed.wsu.edu](http://www.vetmed.wsu.edu)

- Click on Research>Veterinary Clinical Pharmacology Laboratory > Test your dog
• The dog MUST be heartworm negative

• Watch for adverse effects: ataxia, mydriasis, lethargy- can be seen at any time into treatment.

• **Build up to the final dose:** i.e. 50 µg/kg/day then 100, 200 and 300…Do this during the first (7-10) days of treatment to identify sensitive animals.

4. **METAFLUMIZONE PLUS AMITRAZ** (Promeris Duo®, Fort Dodge Animal Health)

   • Labeled use is for once a month, topically applied flea and tick control

   • Metaflumazone 150 mg/ml, mechanism of action: blocking neuronal sodium channels, which results in paralysis and death of the flea

   • Amitraz 150 mg/ml, mechanism of action: monoamine oxidase inhibitor, alpha-2 adrenergic agonist, inhibits prostaglandin synthesis.

   • Eucalyptus smell for canine product, novel applicator

   • Potential adverse reactions: vomiting, drowsiness, neurological abnormalities (lethargy, hypersalivation, ataxia), allergic reactions (urticaria/angioedema), pemphigus foliaceous (rare, anecdotal)

   • Clients with diabetes mellitus or those taking monoamine oxidase inhibitors should not touch the product ingredients or the pet for 24 hours after application.

   • A clinical study has been done to evaluate efficacy against demodex[vii]

     - 3 month clinical trial, all dogs had generalized demodecosis
     - Number of dogs: 16 total, 8 per group
     - Concurrent therapy: none
     - Applied at 0.133 mL/kg (20 mg kg of each of metaflumizone and amitraz/kg)
     - Interval of recheck scrapes: day -3 to-1, 28, 56, 84
     - Promeris Duo® was applied topically q 28 days (group 1)
or q 14 days (Group 2)

- **Time to parasitological cure**: 1- 3 months (end of study)
- **Success rate** (proportion of dogs negative for mites at end of study): group 1 (q 28 days) = 42.9%; Group 2 (q 14 days) = 62.5%
- Problem with clinical study: many dermatologists observe that 50% of generalized demodecosis will spontaneous resolve- difficult to evaluate effect of drug. There were no untreated controls in this study.

5. **IMIDACLOPRID 10% PLUS MOXIDECTIN 2.5%** (Advantage Multi®, Advocate®, Bayer)

- Labeled use is for once a month, topically applied for heartworm prevention and treatment of: fleas, hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), roundworms (*Toxacara canis*, *Toxascaris leonina*)
- Also effective against: lice (*Trichodectes canis*, *Otodectes cynotis*, *Sarcoptes scabiei*), lungworms (*Angiostrongylus vasorum*)
- Moxidectin, mechanism of action: interacts with gaba-aminobutyric acid (GABA) and glutamate-gated chloride channels. This causes the chloride channels on the post-synaptic junction to open and influx of chloride ions → flaccid paralysis of susceptible parasites, followed by their death and/or expulsion.
- Imidicloprid, mechanism of action: has a high affinity for the nicotinic acetylcholine receptors in the post-synaptic region of the nervous system of fleas. Inhibits cholinergic transmission in insects → paralysis and death.
- A clinical study has been done to evaluate efficacy against demodex[viii]
  - 84 day clinical trial, all dogs had generalized demodecosis
  - Group 1: Advantage Multi applied monthly 0.1 ml/kg
  - Group 2: Milbemycin given PO 0.5-2 mg/kg/day
  - Number of dogs per group: group 1 = 30 dogs; group 2= 33 dogs,
• Concurrent therapy: none
• Interval of recheck scrapes: 1 month
• Control group: milbemycin
• **Time to parasitological cure:** 2 - 4.6 months
• **Success rate:** 86.7% parasitological cure rate (n=26/30), in milbemycin controlled study (n= 29/33)
• **Adverse reactions:** 1/36 dogs had an episode of vomiting during clinical trial. Considered safe in ivermectin sensitive Collies.

**How to monitor therapy**

1. Start by making scrapings from 5 representative sites, always including muzzle and 2 ventral interdigital locations
2. Record mite counts - live, dead, nymph, egg – under a coverslip
   - Demodex skeletons are translucent and can be overlooked with full illumination
   - The diaphragm on the condenser should be closed down to increase the contrast and visibility of the skeletons.
3. Rescrape these sites and new lesions every 30 days

*REMEMBER THAT DOGS CAN ACHIEVE CLINICAL CURE BEFORE PARASITOLOGIC CURE- this can lag behind by 0.5- 6 months- if owner stops treatment too soon, a relapse will occur.*

4. Continue treatment until you have achieved three, consecutive, negative skin scrapings at 2-4 week intervals.
   - A minimum of 5 sites should be negative at the same time to declare parasitologic cure.
   - After 3 negative scrapes, stop miticidal therapy and recheck: 1, 3, 6 months and then 1 year after the date of the third negative scrape. Cannot truly declare CURE until at least 12 months after treatment is stopped.
5. Of all dogs with juvenile onset generalized demodicosis remember that **40-50% will self cure.** Of all the dogs that require treatment, about 5% are never cleared and require lifelong therapy.

- **Prognosis** - guarded for complete cure. It still is not an *easily* treated disease and owner should be informed of the level of commitment and prognosis. With intense treatment nearly 90% can be cured, but it may take nearly a year.

- Tell owners at the beginning - it costs $1000 (or more depending on outcome/duration of treatment) to treat generalized demodicosis.

*This is just one scenario... dogs may have their first negative scrape 6-28 weeks after starting therapy*
• Difficult to cure - OESD, Afghan Hound, Shih Tzu or Lhasa Apso.

• Old dogs with Demodex - prognosis depends on underlying cause. If it is iatrogenic Cushing's prognosis is good.

• Recommend spaying/neutering when pyoderma clears and before or at first negative scrape (i.e. as soon as safely possible). Intact females may experience exacerbation or relapse of disease during estrus and may be more resistant to treatment. If demodex is cleared prior to spaying/neutering, the stress of surgery is likely to induce relapse. The dog must be receiving a miticide at the time of surgery.

Therapy that is considered INEFFECTIVE:

1. Rotenone (Goodwinol, Drs. Foster & Smith, Inc.). Anecdotal reports only.
   • Parasiticide- rotenone is derived from the root of the derris plant
   • Available: ointment or shampoo
     Goodwinol ointment: DOGS ONLY: Apply once every 24 hours. Massage in until absorbed. Do NOT use in cats nursing puppies or kittens.
   • Rothenone shampoo: Dogs and Cats: Wet hair, apply 1-2 ounce of shampoo, lather well, leave on for 10 minutes, and rinse thoroughly. Repeat weekly as needed.
   • Possible side effects: Skin irritation.
   • Drug Interactions: Do not use with other pesticides or topical treatments.
   • Toxicity: drooling, vomiting, diarrhea, increase then decrease in breathing rate, muscle twitching, seizures, coma, and death.

2. Vitamin E 400 IU QID: not effective

3. EPA fatty acid capsules - as an addition to any therapy: not effective

FELINE DEMODEX- Uncommon disease in the cat

1. Two species of mites (Genus= Demodex, species= cati or gatoi)
   a. Demodex cati
- Narrow, long body
- Lives in the hair folicle of the host
- Diagnosed by DEEP skin scrapings
- Associated with underlying immune suppression
- More commonly found on head and neck, however, may generalize
- Variable pruritis, may be non-pruritic

b. *Demodex gatoi*

- Broad, short body
- Lives in the stratum corneum/ on the skin surface
- Diagnosed by superficial skin scrapings
- Contagious and more commonly pruritic
- More common in Texas
- More commonly found on trunk, however, may generalize
- Variable pruritis, may be SEVERELY pruritic

2. Clinical features common to both species

a. Localized or generalized disease (as in the dog)

b. Alopecia, scaling, macules, erythema, hyperpigmentation. Some cats will have a thin hair coat, and greasy skin.

c. Some cats with *D. gatoi* will present as alopecia without erythema

d. Ceruminous demodectic otitis externa has been reported.

3. Diagnosis

a. Skin scrapings - superficial (*D. gatoi*) and deep (*D. cati*)

b. Multiple sites:

1) To enhance your ability to find *D. gatoi*

2) To differentiate localized from generalized for *D. cati*

c. Generalized *D. cati*: search for underlyng disease (routine blood work +/- FeLV, FIP, FIV, Diabetes etc...
d.  *D. gatoi* can be difficult to find because: the mite lives on the surface and cats often groom excessively from pruritus.

*Scrape in places such as the lateral antebrachium and dorsal neck, where the cat’s tongue cannot reach.*

4. Therapy

a.  *D. gatoi*— treat all cats in contact, contagious.

   i.  2.5% lime sulfur dip (Lymdyp®; DVM Pharmaceuticals): weekly dips for 6 weeks.

      * Some cats become really pruritic with lime sulfur--start with 1% solution and workup.

      * Treatment of choice for *D. gatoi*.

      * E-collar to prevent licking dip before it dries- will cause hypersalivation, gastritis and vomiting if ingested.

      * Treat all animals in contact with affected cat.

b.  *D. cati*

   i.  Ivermectin (off-label use! Do not use in kittens) - 300 µg/kg SQ or PO once weekly for 6 consecutive treatments.

   ii.  Amitraz @ ½ to ¼ strength: **Not recommended!!** Monitor for side effects (anorexia, depression, diarrhea) if cure not achieved, try another treatment.

   iii.  LymDyp - 2% lime sulfur, weekly dips for 6 weeks, unknown benefit.

   v.  Spontaneous resolution has been documented.

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<tr>
<th></th>
<th><em>D. cati</em></th>
<th><em>D. gatoi</em></th>
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<tbody>
<tr>
<td><strong>Habitat</strong></td>
<td>Hair follicle</td>
<td>Stratum corneum</td>
</tr>
<tr>
<td><strong>Dx</strong></td>
<td>Deep skin scrapes</td>
<td>Superficial skin scrapes</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
<td>Immunosuppression</td>
<td>Contagious</td>
</tr>
<tr>
<td><strong>Rx</strong></td>
<td>Ivermectin</td>
<td>1-2% lime sulfur Dip +/-</td>
</tr>
<tr>
<td>Prognosis</td>
<td>( \text{Poor} \rightarrow \text{unable to Dx/Rx cause} )</td>
<td>( \text{Excellent with Rx} )</td>
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<td>-----------</td>
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<tr>
<td>( \text{Good} \rightarrow \text{Dx &amp; Rx cause} )</td>
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<tr>
<th>Morphology</th>
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<tr>
<td>( \text{Narrow} )</td>
<td>( \text{Wide} )</td>
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