UPDATES ON CHRONIC ALLERGIC DERMATITIS (CAD)

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Etiopathogeny

**Genetics**
No clearly identified genes. CAD is a polygenic syndrome.

<table>
<thead>
<tr>
<th>Genes</th>
<th>Breed</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>S100A8</td>
<td>All breeds</td>
<td>Inflammation</td>
</tr>
<tr>
<td>rTSLP</td>
<td>All breeds</td>
<td>Inflammation, pruritus</td>
</tr>
<tr>
<td>Filaggrine</td>
<td>Labrador (UK)</td>
<td>Skin barrier</td>
</tr>
<tr>
<td>INPPL1 et MS4A2</td>
<td>Labrador &amp; West Highland white terrier (UK)</td>
<td>Inflammation</td>
</tr>
<tr>
<td>RAB3C, PROM1</td>
<td>German shepheard (UK)</td>
<td>Skin barrier</td>
</tr>
<tr>
<td>RAB7A</td>
<td>Labrador</td>
<td>Inflammation</td>
</tr>
<tr>
<td>SORCS2</td>
<td>German shepheard (UK)</td>
<td>Inflammation</td>
</tr>
<tr>
<td>CD83</td>
<td>West Highland white terrier</td>
<td>Immune response</td>
</tr>
<tr>
<td>PKP2</td>
<td>German shepheard</td>
<td>Skin barrier</td>
</tr>
</tbody>
</table>

**IgE synthesis**
Largely influenced by *Toxocara* infestation

**Allergens structure**

<table>
<thead>
<tr>
<th>Allergens</th>
<th>Major allergens for the dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatophagoides farinae</td>
<td>Der f 2, Der f 15, Der f 18, Zen 1</td>
</tr>
<tr>
<td>Dermatophagoides pteronyssinus</td>
<td>-</td>
</tr>
<tr>
<td>Ragweed</td>
<td>Amb 1</td>
</tr>
<tr>
<td>Grasses</td>
<td>Phi p 5, Dac g 5</td>
</tr>
<tr>
<td>Cryptomeria japonicum</td>
<td>Cry j 1, Cry j 3</td>
</tr>
</tbody>
</table>

**Cross allergenicity**
Identified for house dust and storage mites and also grasses pollens (group 5)

**Influence of environment**
Urban environment is involved in the very few published epidemiological studies.

**Mediators of pruritus**
Main mediator is IL31. It can induce pruritus by IV, SC or IM routes
There is other mediators but they are not yet identified:
- TSLP does not seem to be involved
- Potential role of cathepsine S (CTSS), neuromedine B (NMB), NGF and some mast cells proteases (CMA, tryptase et mastine)
- Histamine is not involved

**DIAGNOSIS OF CAD**

Allergy testing is NOT a diagnostic tool as results are the same for atopic and non atopic dogs for a same breed. Different diagnostic criteria can be used but accuracy depends on clinical form.

**TREATMENT**

**Allergen specific immunotherapy**

- New allergens
  - Allergoids: safe but no evidence of efficacy
  - Recombinant house dust mite allergens: rDerf2 is efficient in small clinical studies on atopic dogs sensitized to *Dermatophagoides farinae* in Japan & Europe

- New adjuvants
  - Pullulan is used as adjuvant for Derf2 ASIT
  - CpG: not efficient in a small short open clinical study

- New protocols
  - Simplified SC protocols: safety of SC protocols with calcium phosphate adjuvanted allergenic extracts using no progressive increase of doses.
  - Intralymphatic protocols: very small amount of allergen with spectacular efficacy in small open clinical trials.
  - Sublingual protocols: no evidence of efficacy

**Ciclosporine**
- CsA is still the first line systemic treatment of AD
- Low dose (2-3 mg/kg/d) is not efficient.
- Efficacy comparable to IL31 targeted treatment on day 60.
- In human AD association of ciclosporine with ASIT gives the opportunity to stop ciclosporine after less than one year of treatment.

**JAK inhibitors**
- Oclacitinib which is mainly a JAK1-inhibitor is widely use to control pruritus in CAD.
- It is efficient a few hours after administration with mean reduction of pruritus of 61% on Day 1
- It can be used in acute AD and for long term treatment
- Short term side effects are rare (behavior)
- Long term side effects are rare but can be severe with immunodeficiency or leucopenia. This is why clinical and biological follow up are mandatory for long term administration
- Lack of efficacy is often due to skin infection (bacteria or Malassezia)

**Anti-IL31 monoclonal antibody**
- Lokivetmab is highly efficient on the control of pruritus in atopic dogs with:
  - good response after less than 24 hours
- mean duration of efficacy of 1 month at 1 mg/kg et 2 months at 2 mg/kg
- almost no adverse effect
- some important individual variations
- efficacy comparable to ciclosporine on day 58

It can be used for the long term treatment of CAD when pruritus is the main clinical signs and systemic
treatment is needed or when immunosuppressive treatment cannot be used.

**Anti-NGF monoclonal antibody**
Not efficient in a small open clinical trial

**Anti-IL31 vaccine**
A VLP-based vaccine showed promising results on pruritus in an experimental open trial

**Vitamin D**
Administration of colecalciforol or paricalcitol to atopic dogs significantly decreases pruritus score but
dogs are still itchy after 2 months of treatment

**Palmitoylethanolamide**
PEA is a nutraceutical product which demonstrated spectacular effect in very small studies: 30% non
symptomatic animals after 2 months therapy in moderate form of CAD.

**Stem cells**
Not efficient in one small open clinical trial with low dose autologous cells

**Flea control**
Treating dogs with CAD against flies can reduce dramatically (2/3) clinical scores…