THE CLINICAL VS. HISTOPATHOLOGICAL DIAGNOSIS OF VKH: ARE WE GETTING IT RIGHT?
Immune mediated disorder

- Postulated delayed type hypersensitivity towards melanocytes
  - In humans CD4+ Th1 cells (Gocho et al. 2001)
  - 2 dogs, minimal T-cell and predominantly B-cell in eye, opposite in skin (Carter et al. 2005)
- Suspected viral trigger to immune response to self molecules
- Melanin dispersion and phagocytosis are the hallmark
- Strong genetic predisposition
  - More common in humans from Japan
  - More common in northern breed dogs and the Akita breed (DQA1 allele predisposes?)
- More severe in darkly pigmented individuals
1882 – Hutchinson
1906 – Vogt
1926 – Harada (bilateral posterior uveitis and exudative retinal detachment)
1929 – Koyanagi (headache, fever, bilateral mostly anterior uveitis, poliosis and vitiligo)
Named Vogt-Koyanagi for nearly two decades until realized it was one entity
Other names:
- Uveo-cutaneous syndrome – failed to describe meningitis features
- Uveo-encephalitis – failed to describe integumentary changes
Questions regarding sympathetic uveitis/ophthalmia
- Sympathetic uveitis --- VKH --- Phaco-anaphylaxis (Chan)
CLINICAL PRESENTATION: THREE PHASES (HUMANS)

- **Meningeal Stage – Prodromal (1-2 weeks)**
  - Headaches, nausea, fever, vomiting, malaise, vertigo, photophobia
  - Meningismus
  - CSF pleocytosis and encephalitis

- **Ophthalmic Stage**
  - Panuveitis
  - Scleritis
  - Exudative retinal detachment
  - Dysacusis

- **Convalescent Stage (weeks to months)**
  - Alopecia
  - Vitiligo
  - Poliosis
  - Chorioretinal scarring and depigmentation
DIAGNOSING VKH IN PEOPLE

- History
- Clinical signs – usually recognized earlier
- Skin signs and biopsy
- Ocular signs:
  - Exudative retinal detachment
  - Anterior or posterior uveitis
- Ocular histology- rarely performed
  - Granulomatous vs. non-granulomatous
  - Choroidal scaring
Bilateral immune mediated ocular disease of young Akitas and Northern breed dogs.

Unilateral Uveitis in a dog with uveodermatologic syndrome (Sigle et al. 2006)

Diagnosed in breeds:
- Dachshund (Herrera et al. 1998)
- Fox Terrier (Delta 1999)
- Cockapoo (Godoy et al. 2003)
- Brazilian Fila dog (Laus et al. 2004)
- American Akita (Angels et al. 2005)
- Siberian Husky (Sigle et al. 2006)
- German Shepherd Dog (Catoi et al. 2007)
- Jack Russell Terrier (Baiker et al. 2011)
- Rat Terrier (Blackwood et al. 2011)
- Border Collie (Horikawa et al. 2013)
- Samoyed- often indicated, no reports
NOMENCLATURE IN DOGS

- Granulomatous panuveitis and dermal depigmentation (Bussanich 1982)
- Mucocutaneous ocular syndrome (Hasegawa 1985)
- Uveitis associated with poliosis and vitiligo (Kern et al. 1985)
- Generalized leukoderma and poliosis following uveitis (Campbell et al. 1986)
- Uveodermatologic syndrome (Furlong et al. 1989)
- Vogt-Koyanagi-Harada-like syndrome (Lindley et al. 1990)
PERSPECTIVE

Revised Diagnostic Criteria for Vogt-Koyanagi-Harada Disease: Report of an International Committee on Nomenclature

RUSSELL W. READ, MD, GARY N. HOLLAND, MD, NARSING A. RAO, MD, KHALID F. TABBARA, MD, SHIGEAKI OHNO, MD, LOURDES ARELLANES-GARCIA, MD, PAOLA PIVETTI-PEZZI, MD, HOWARD H. TESSLER, MD, AND MASAHIKO USUI, MD
TABLE 1. Diagnostic Criteria for Vogt-Koyanagi-Harada Disease

Complete Vogt-Koyanagi-Harada disease (criteria 1 to 5 must be present)

1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis.
2. No clinical or laboratory evidence suggestive of other ocular disease entities.
3. Bilateral ocular involvement (a or b must be met, depending on the stage of disease when the patient is examined).
   a. Early manifestations of disease.
      (1) There must be evidence of a diffuse choroiditis (with or without anterior uveitis, vitreous inflammatory reaction, or optic disk hyperemia), which may manifest as one of the following:
         (a) Focal areas of subretinal fluid, or
         (b) Bullous serous retinal detachments.
      (2) With equivocal fundus findings; both of the following must be present as well:
         (a) Focal areas of delay in choroidal perfusion, multifocal areas of pinpoint leakage, large placoid areas of hyperfluorescence, pooling within subretinal fluid, and optic nerve staining (listed in order of sequential appearance) by fluorescein angiography, and
         (b) Diffuse choroidal thickening, without evidence of posterior scleritis by ultrasonography.
   b. Late manifestations of disease.
      (1) History suggestive of prior presence of findings from 3a, and either both (2) and (3) below, or multiple signs from (3):
      (2) Ocular depigmentation (either of the following manifestations is sufficient):
         (a) Sunset glow fundus, or
         (b) Sugira sign.
      (3) Other ocular signs:
         (a) Nummular chorioretinal depigmented scars, or
         (b) Retinal pigment epithelium clumping and/or migration, or
         (c) Recurrent or chronic anterior uveitis.
4. Neurological/auditory findings (may have resolved by time of examination).
   a. Meningismus (malaise, fever, headache, nausea, abdominal pain, stiffness of the neck and back, or a combination of these factors; headache alone is not sufficient to meet definition of meningismus, however), or
   b. Tinnitus, or
   c. Cerebrospinal fluid pleocytosis.
5. Integumentary finding (not preceding onset of central nervous system or ocular disease).
   a. Alopecia, or
   b. Poliosis, or
   c. Vitiligo.
DIAGNOSING VKH IN CANINES
CLINICAL DIAGNOSIS

- **Ocular**
  - Sudden blindness
  - Chronic uveitis, anterior or posterior, mostly granulomatous
  - Serous/exudative retinal detachment
  - Secondary glaucoma
- **Skin- affecting mostly muzzle, lips and periocular skin**
  - Vitiligo
  - Poliosis
- **Meningic and Auditory – not recognized?**
Ophthalmologist will often suspect VKH in appropriate breed.

Ophthalmologist are often suspicious of other disease processes in other breeds and are very surprised when they get our report.

Consequently there are lots of papers of case reports per breed.

Skin lesions are great for confirming a case with chronic bilateral uveitis.
- 190 cases
- 54% male, 42% Female, 4% unk
- 30% OD – 36% OS – 34% OU
- Approximately 20 cases a year since 2007
BREED DISTRIBUTION

- Akita: 16.2%
- Husky: 5.2%
- Australian Shepherd: 2.6%
- Boxer: 5.2%
- Chihuahua: 2.1%
- Chow Chow: 3.7%
- German Shepherd: 4.2%
- Jack Russell Terrier: 3.1%
- Labrador Retriever: 2.6%
- Samoyed: 2.1%
- Mixed: 26.2%
- Other: 26.8%
## BREED DISTRIBUTION

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<tr>
<th>Overrepresented Breeds</th>
<th>Percent VKH</th>
<th>COPLOW%</th>
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<tr>
<td>Akita</td>
<td>16.2</td>
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<tr>
<td>Husky</td>
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<td>Australian Shepherd</td>
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<td>Boxer</td>
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<td><strong>Labrador Retriever</strong></td>
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<tr>
<td>Mixed</td>
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<td>17</td>
</tr>
</tbody>
</table>
AGE DISTRIBUTION

- Average age 6.75

Cases by Age
GROSS PATHOLOGY

Blue Eyed Dog

Brown Eyed Dog
GROSS PATHOLOGY

Depigmenting VKH

Depigmenting VKH
HISTOLOGICAL DIAGNOSIS: SYMMETRY
HISTOLOGICAL DIAGNOSIS

Depigmenting

Granulomatous
HISTOLOGICAL DIAGNOSIS
MENINGITIS

Granulomatous

Lymphoplasmacytic
THE DILEMMA

- We are hesitant to diagnose VKH without a bilateral disease.
- Sometimes the clinical signs aren’t symmetric – not only in heterochromic animals.
- Sometimes there is a 2-3 year lag between enucleation of one eye and the next.
- What to do when you get histology of an eye with pathology typical of VKH, but history of a healthy contralateral eye?
- We see meningitis histologically, therefore should the name be VKH, rather than VKH-like, or uveodermatologic syndrome?
NEW INSIGHT

- Not a young dog disease (Gellatt, 2013)
- Akitas and northern breeds overrepresented, but also, Chow, JRT, Corgi, Boxer, GSD and perhaps Chihuahua.
- Northern breeds show more of a lymphoplasmacytic depigmenting disease as opposed to granulomatous.
- May be a long lag until deterioration in other eye, nonetheless, is impressively symmetrical.
- Different presentations pathologically.
- Although meningismus is not recognized clinically it should be searched histologically.
- If suspected, could be beneficial to include eyelid in histosection.