Posterior uveitis: introduction

Non infectious posterior uveitis

RAIO 6-7 JUL 2019
REUNIÃO ANUAL INTERNOS OFTALMOLOGIA
HOTEL DOLCE CAMPO REAL

Inês Leal

Summary

Introduction

Sarcoidosis

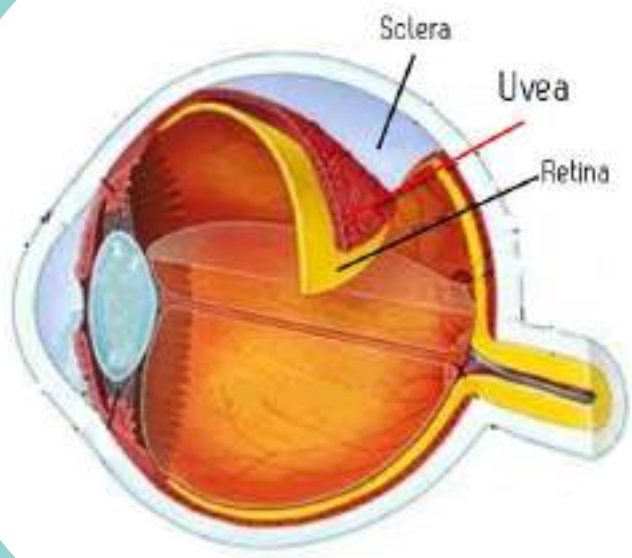
Behçet

VKH

Introduction

The Uvea

- Uvea (from the Latin uva, meaning “grape”): intermediate vascular pigmented layer of the eye
- **Uveitis: group of intraocular (iris, ciliary body or choroid) inflammatory diseases**
- Shared physiopathological mechanisms with systemic inflammatory diseases



Fundamentals and Principles of Ophtalmology, 2015-2016, American Association of Ophtalmology, Singapore, 2015
Intraocular inflammation and uveitis, 2015-2016, American Association of Ophthalmology, Singapore, 2015

Uveal Inflammation

Caused by diverse stimulus

Same kinds of cellular subsets as in inflammation in other organs

Protective response – ultimate goal: get rid of the initial stimulus

But… potentially harmful!

Fundamentals and Principles of Ophtalmology, 2015-2016, American Association of Ophtalmology, Singapore, 2015
Intraocular inflammation and uveitis, 2015-2016, American Association of Ophthalmology, Singapore, 2015

Uveitis Etiologies: examples

Infectious

Toxoplasmosis

Tuberculosis

Syphilis

Lyme disease

Non-infectious (NIU)

With known systemic association

- HLA-B27 uveitis
- Behçet disease
- Vogt-Koyanagi-Harada
- Sarcoidosis

Unknown systemic association

- Idiopathic uveitis
- White dot syndromes
- Sympathetic ophtalmia

Fundamentals and Principles of Ophtalmology, 2015-2016, American Association of Ophtalmology, Singapore, 2015
Intraocular inflammation and uveitis, 2015-2016, American Association of Ophthalmology, Singapore, 2015

Non-infectious uveitis (NIU)

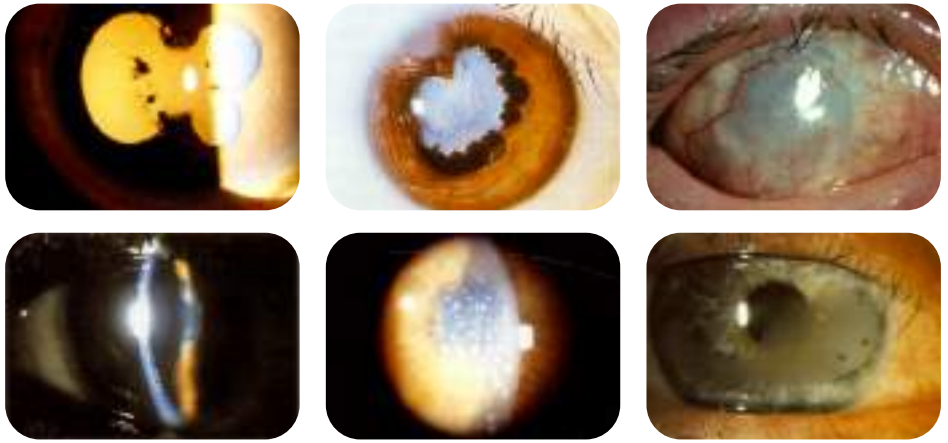
NIU immune-mediated response to ocular antigens (+++ uveal melanin and proteins)

Most affected population: 20-60 years – Immense social burden

In developed countries: 4th leading cause of blindness

Late complications: **SIGH-THREATENING!**

- Synehchiae
- Band keratopathy
- Cataract
- Glaucoma
- Macular oedema
- Retinal ischemia
- Chronic eye pain/ Pthisis bulbi



Durrani, O. M. et al. Br. J. Ophthalmol. **88**, 1159–1162 (2004). Pavesio C. et al. Ophthalmology 2010; **117**: 567–75. Arcinue CA. et al. Saboo US, Foster CS. Corticosteroids in uveitis. Nanomed 2012; **2**: 55–64. Giuliari GP. et al Int Ophthalmol 2014; **34**: 145–56. Nussenblatt RB. et al. Invest Ophthalmol Vis Sci 1991; **32**: 3131–41. Dick AD et al. Ophthalmology 2016;123:665-662

Uveitis Classification: Standardized Uveitis Nomenclature

Anatomic Classification

Type	Primary site of inflammation
Anterior uveitis	Anterior chamber
Intermediate uveitis	Vitreous
Posterior uveitis	Retina or choroid
Panuveitis	Anterior chamber, vitreous and retina or choroid

The SUN Working group descriptors of uveitis

Category	Descriptor	Comment
Onset	Sudden	
	Insidious	
Duration	Limited	≤ 3 months duration
	Persistent	> 3 months duration
Course	Acute	Episode characterized by sudden onset and limited duration
	Recurrent	Repeated episodes separated by periods of inactivity without treatment 3 months in duration
	Chronic	Persistent uveitis with relapse in 3 months after discontinuing treatment

Perspective: Standardization of Uveitis Nomenclature for Reporting Clinical Data. Results of the first international workshop – The Standardization of Uveitis Nomenclature (SUN) Working Group
Jabs DA. Am J Ophthalmol 2005;140:509–516

Uveitis Classification: Standardized Uveitis Nomenclature

The SUN Working Group Grading Scheme for Anterior Chamber Cells	
Grade	**Cells in field**
0	< 1
0.5 +	1-5
1 +	6-15
2 +	16-25
3 +	26-50
4 +	> 50

The SUN Working Group Grading Scheme for Anterior Chamber Flare	
Grade	**Description**
0	None
1 +	Faint
2 +	Moderate (iris and lens details clear)
3 +	Marked (iris and lens details hazy)
4 +	Intense (fibrin or plastic aqueous)

Field size is a 1 mm by 1 mm slit beam.

Uveitis Classification: Standardized Uveitis Nomenclature

The SUN Working Group Activity of Uveitis Terminology	
Inactive	Grade 0 cells
Worsened activity	Two step increase in level of inflammation (e.g. anterior chamber cells, vitreous haze) or increase from grade 3 to 4
Improved Activity	Two step decrease in level of inflammation (e.g. anterior chamber cells, vitreous haze) or decrease to grade 0
Remission	Inactive disease for 3 months after discontinuing all treatments for eye disease

Problems in posterior uveitis

Clinical signs may be

UNSPECIFIC

… And **SHARED** by different diseases

Posterior uveitis represents **diseases that are developing elsewhere** in the body

(and ocular signs may be the 1st evidence)

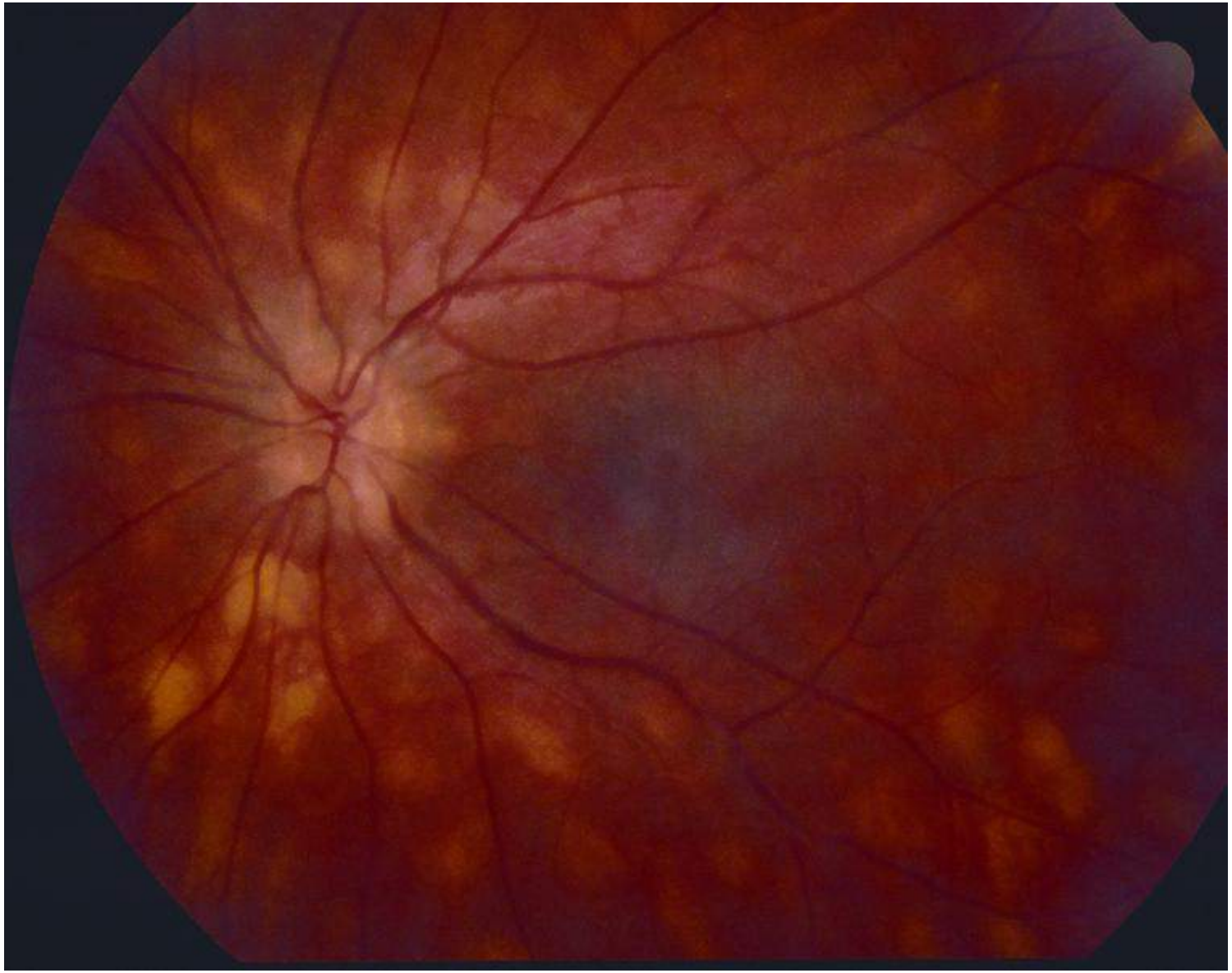
Uveitis specialists need to have a **thourough knowledge** of all entities and their work up has to be systematic and complete

DIAGNOSING IN POSTERIOR UVEITIS

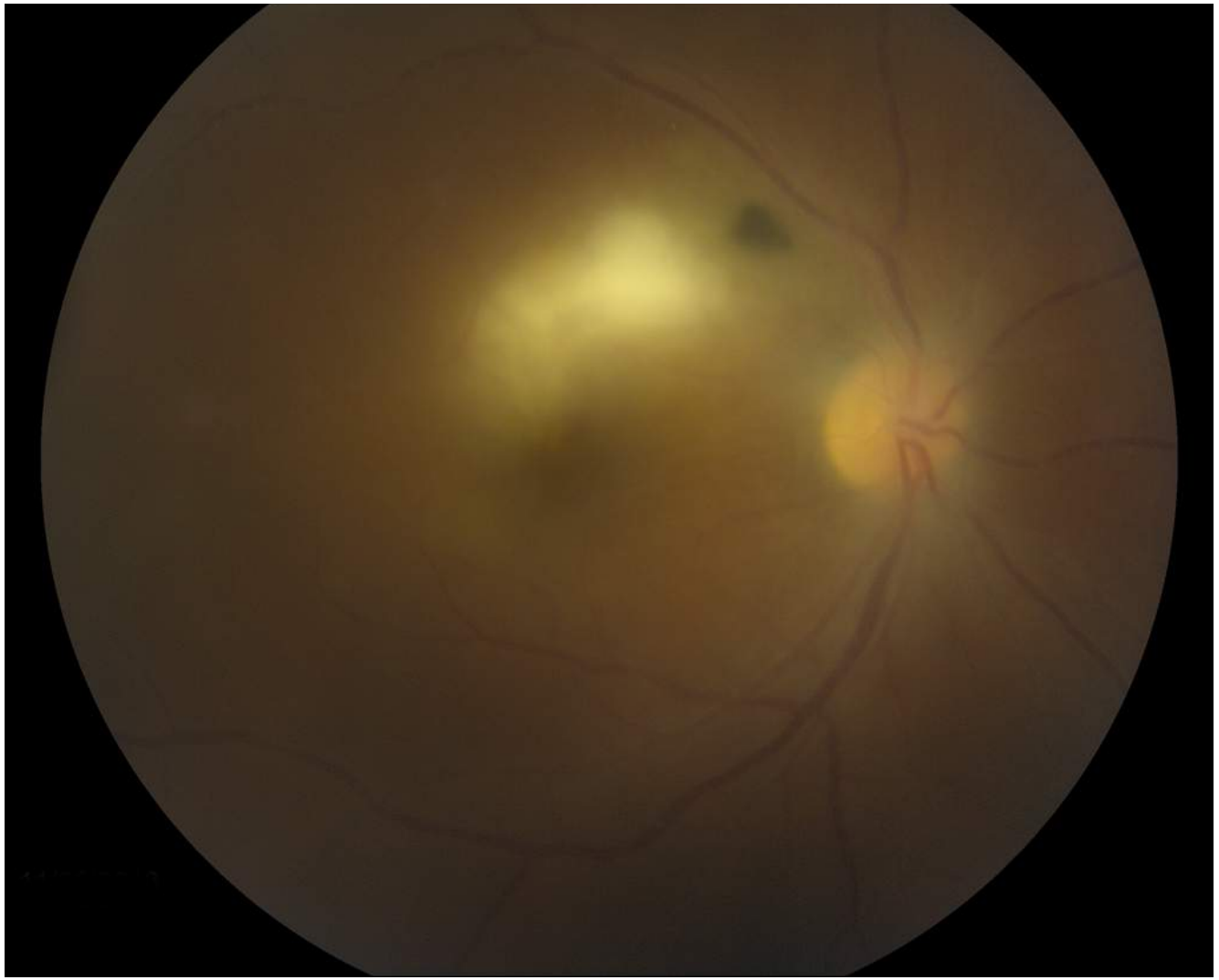
IS ALL ABOUT PATTERN

RECOGNITION

DIAGNOSING IN UVEITIS IS ALL ABOUT PATTERN RECOGNITION



DIAGNOSING IN UVEITIS IS ALL ABOUT PATTERN RECOGNITION



General algorithm

1) Defining the **PROBLEM** and deriving a clinical diagnosis

2) Reviewing all possible causes of the condition and comparing with **existing known uveitis patterns** (meshing technique)

3) Proving the **DIAGNOSIS** by presenting diagnostic modalities in a logical manner

Good strategy: assume **INFECTIOUS CAUSE**

1) Infections often respond well to antibiotic/viral

2) If infections can be ruled out early on → safe to proceed to steroids/immunossupression


ABC.
Always Be
Curious.

Investigating in posterior uveitis

Includes ALL aspects of the clinical history and environment, not just what we find in the eye

Investigating in uveitis

What to look for

Age, sex, race

Country, latitude, season, epidemics

Travel, sexual behaviour

History of systemic disease

Ophthalmological concurrent or preceding disease (ametropia!!)

Benhar I. et al. Front. Immunol. 2012 Sep 21;3:296

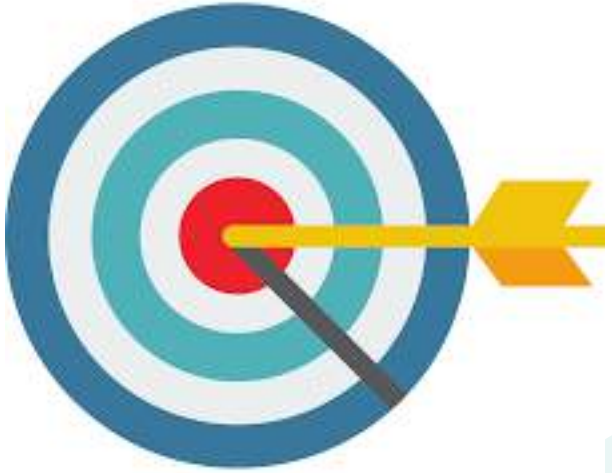
Investigating in uveitis

Investigation is usually to support or confirm a

CLINICAL SUSPICION

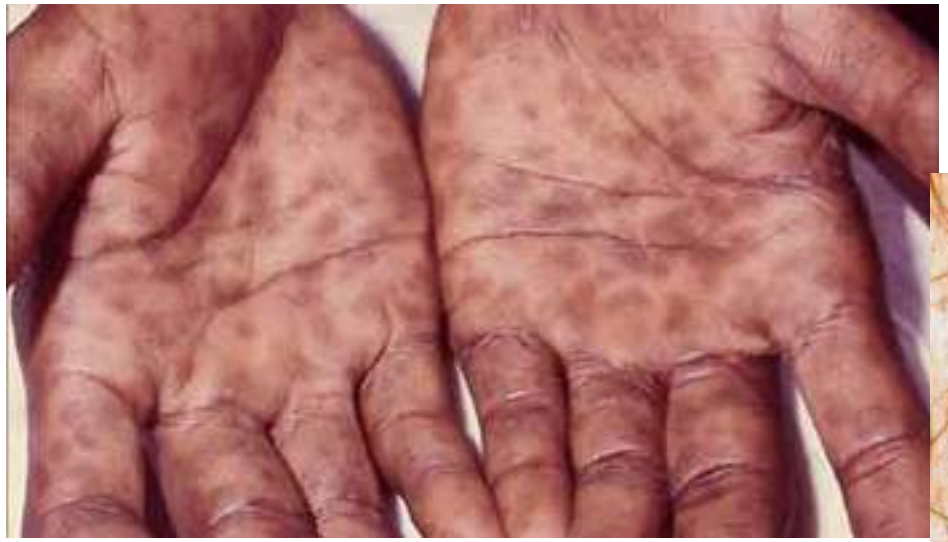
TARGETED INVESTIGATION

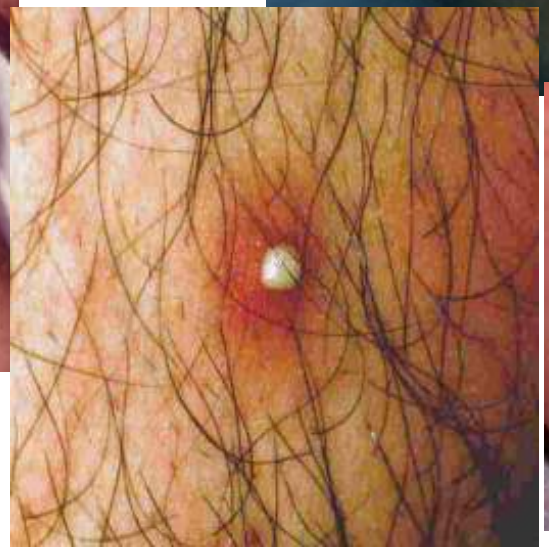
after pattern recognition!

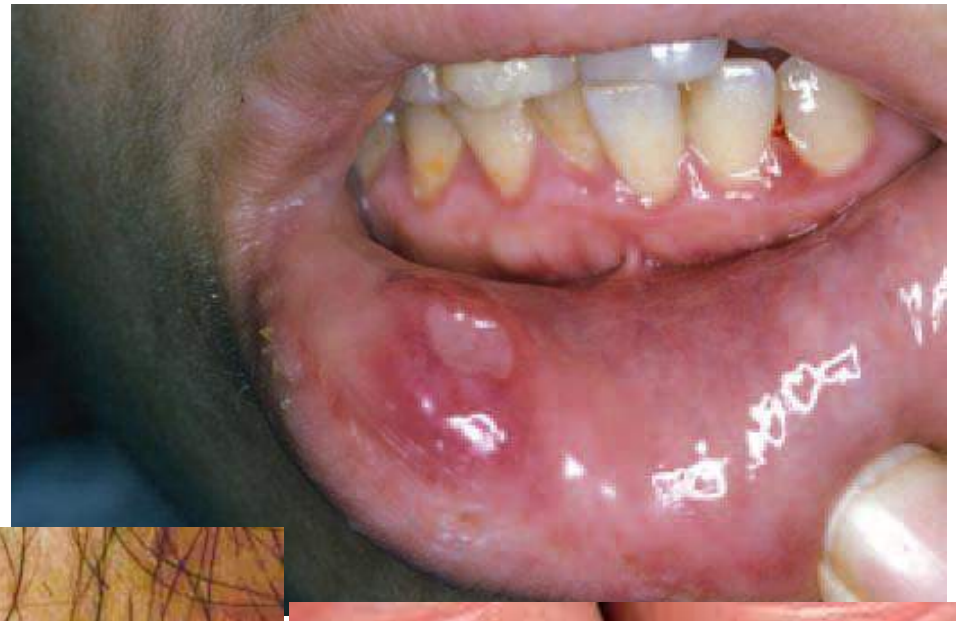


Pearls of investigating uveitis!

Examining the patient (PROPERLY!!)







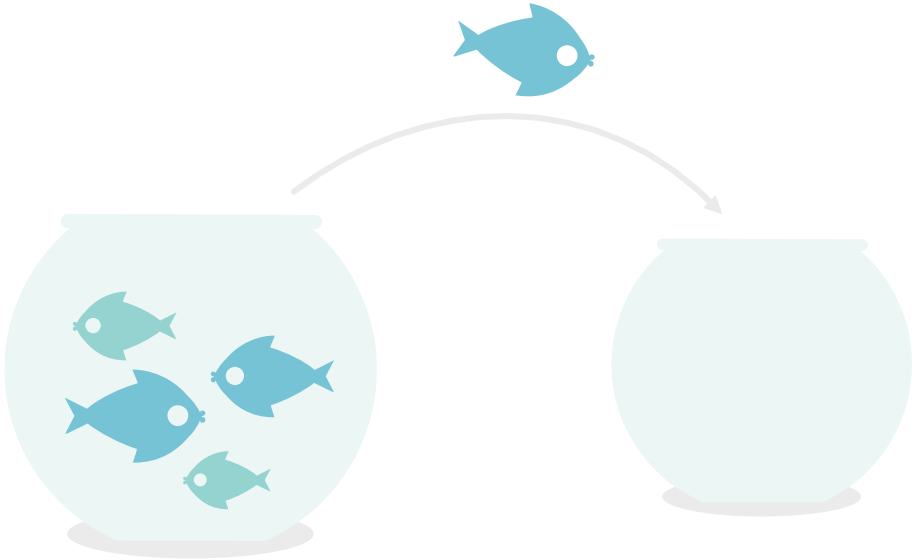
Treatment

Reduce inflammation

Prevent damage to ocular structures and visual loss

Goals of therapy for uveitis

Changing the dogma…



Suppressing immune responses in the eye

Boosting beneficial immunity / Immunomodulation

Benhar I. et al. Front. Immunol. 2012 Sep 21;3:296
Taylor AW. Wyw (2009) 23, 1885-1889
Forrester JV. et al. Front. Immunol. 2012 Nov 3;338

BATTLE CRY

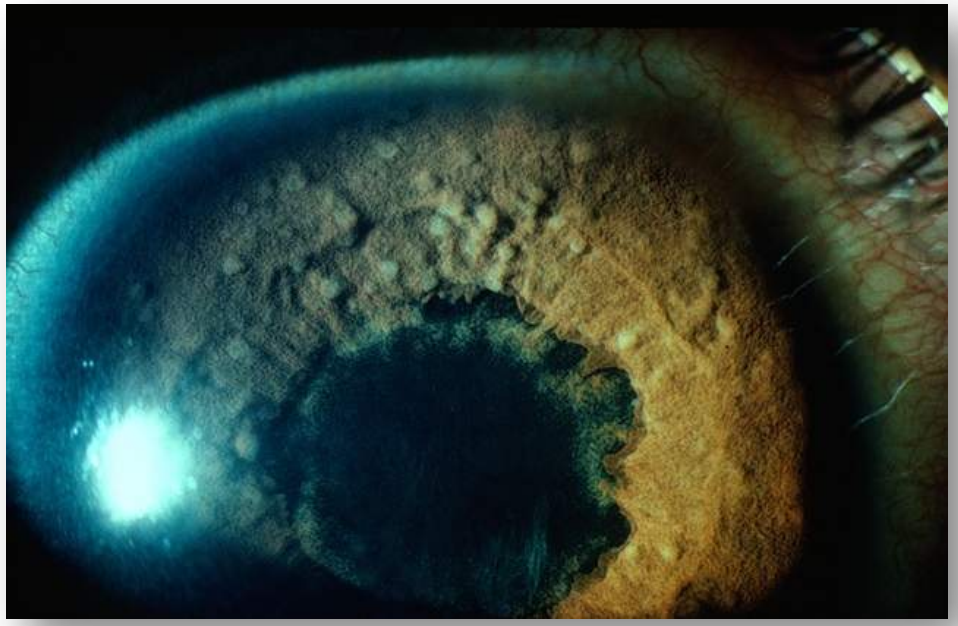
THE MISSION IS REMISSION

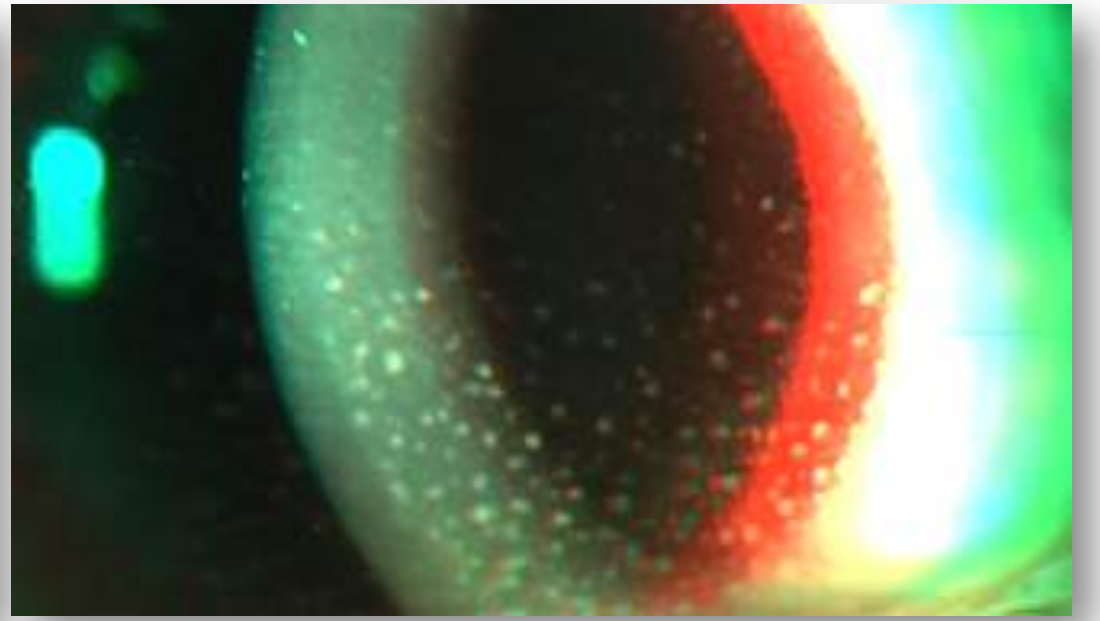
Steroid-free!

Sarcoidosis

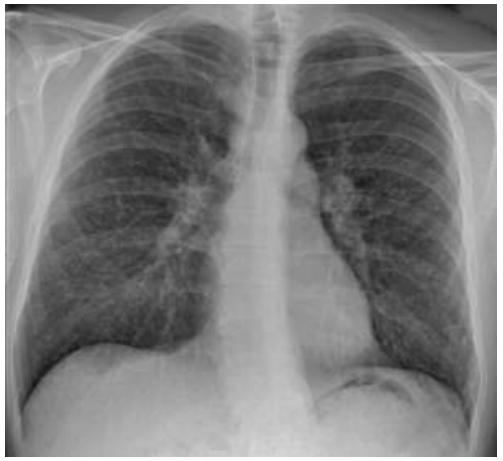
Sarcoidosis

- Systemic inflammatory disorder, unkown etiology, non-caseating granulomas
- Palpebral granulomas
- Lacimal gland infiltration





Sarcoidosis PEARLS



- Up to 95% with chest involvment (++bilateral hilar lymphadenopathy without lung involvment)
- Unilateral lymphadenopathy: uncommon
- Lymphopenia
- If normal X ray → HRCT
- Mikulick's syndrome
- Acute non-ganulomatous uveitis (younger)
- Chronic granulomatous uveitis (older)

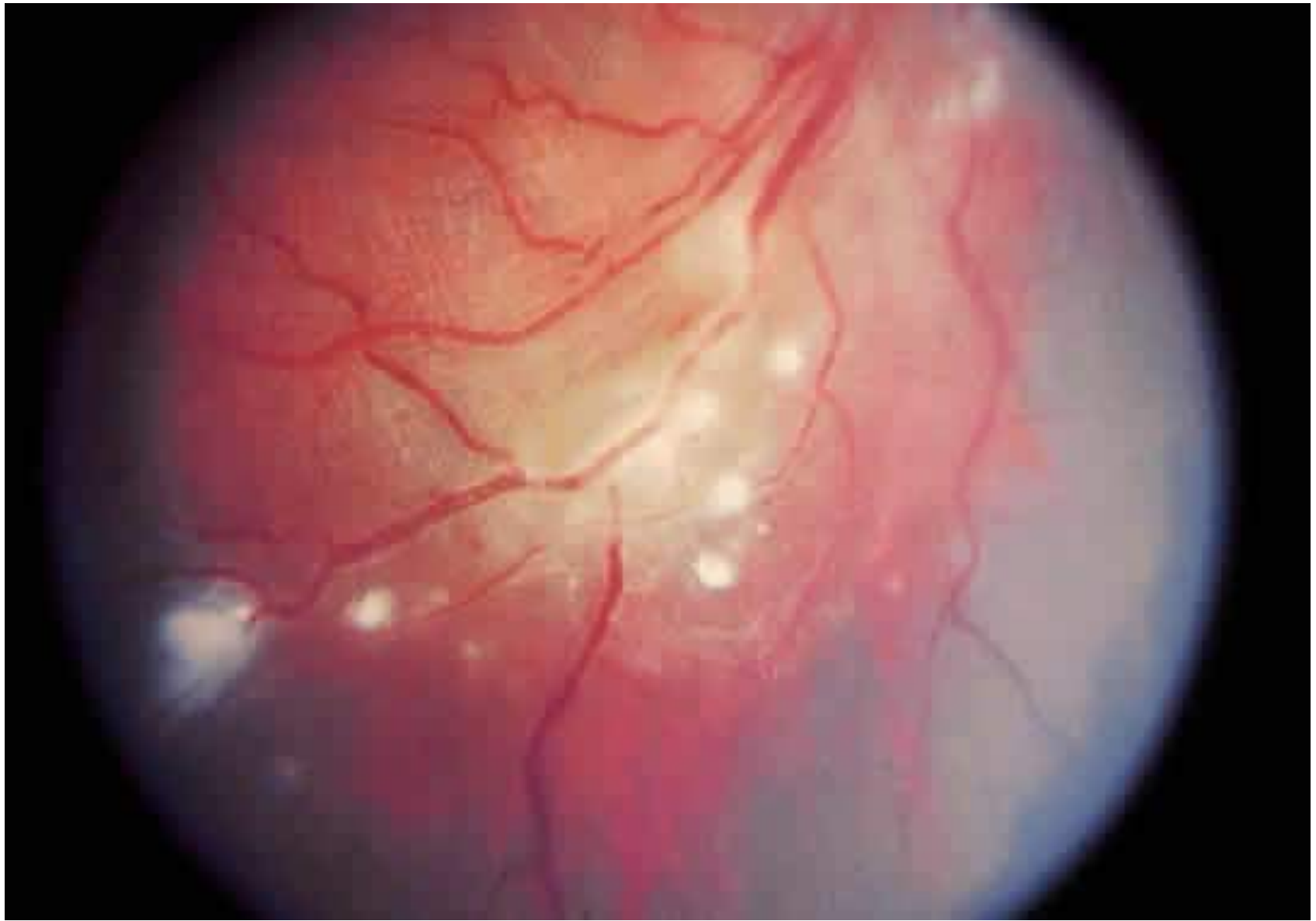
Sarcoidosis PEARLS

- Multifocal choroidits +-SRF
- Vasculitis typically patchy, non-occlusive
- Optic nerve involvement
- Macroaneurysms

Box 1 Revised International Workshop on Ocular Sarcoidosis (IWOS) criteria for the diagnosis of ocular sarcoidosis (OS) (2017)

I. Other causes of granulomatous uveitis must be ruled out.
II. Intraocular clinical signs suggestive of OS.
   1. Mutton-fat keratic precipitates (large and small) and/or iris nodules at pupillary margin (Koeppe) or in stroma (Busacca).
   2. Trabecular meshwork nodules and/or tent-shaped peripheral anterior synechia.
   3. Snowballs/string of pearls vitreous opacities.
   4. Multiple chorioretinal peripheral lesions (active and atrophic).
   5. Nodular and/or segmental periphlebitis (±candle wax drippings) and/or macroaneurysm in an inflamed eye.
   6. Optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule.
   7. Bilaterality (assessed by ophthalmological examination including ocular imaging showing subclinical inflammation).
III. Systemic investigation results in suspected OS.
   1. Bilateral hilar lymphadenopathy (BHL) by chest X-ray and/or chest computed CT scan.
   2. Negative tuberculin test or interferon-gamma releasing assays.
   3. Elevated serum ACE.
   4. Elevated serum lysozyme.
   5. Elevated CD4/CD8 ratio (>3.5) in bronchoalveolar lavage fluid.
   6. Abnormal accumulation of gallium-67 scintigraphy or 18F-fluorodeoxyglucose positron emission tomography imaging.
   7. Lymphopenia.
   8. Parenchymal lung changes consistent with sarcoidosis, as determined by pulmonologists or radiologists.
IV. Diagnostic criteria.
Definite OS: diagnosis supported by biopsy with compatible uveitis.
Presumed OS: diagnosis not supported by biopsy, but BHL present with two intraocular signs.
Probable OS: diagnosis not supported by biopsy and BHL absent, but three intraocular signs and two systemic investigations selected from two to eight are present.

Sarcoidosis



Sarcoidosis PEARLS Diagnosis

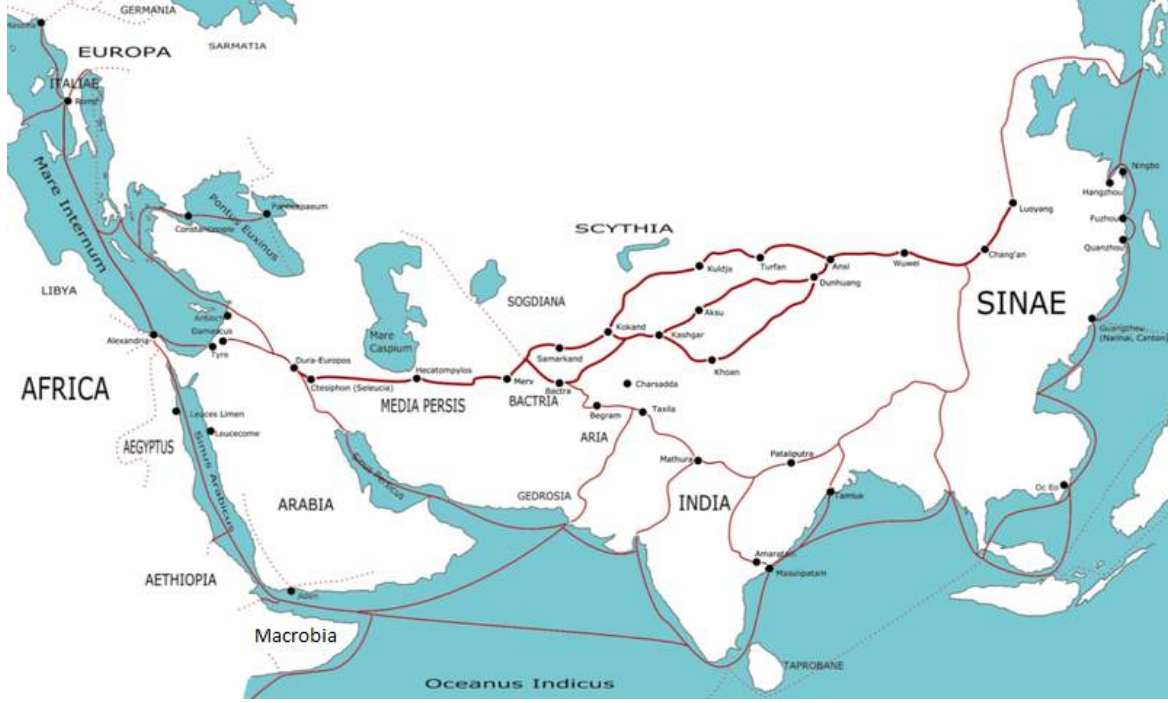
- Bronchoscopic cytology
- Transbronquial, endobronchial or mediastinal biopsy
- Conjunctival and lacrimal gland biopsy
- Biopsy of skin
- Immune changes: Mantoux
- ACE (children!!) >100 IU/L – 100% sarcoidosis
- Lysozyme
- Gallium-67 scintigraphy / PET

Sarcoidosis - treatment

- Anterior uveitis: topical steroids
- Periocular steroids
- Minority: systemic steroids
- Imunnossupression: little evidence
  - Biologics: etanercept No!

Behçet disease

Behçet disease

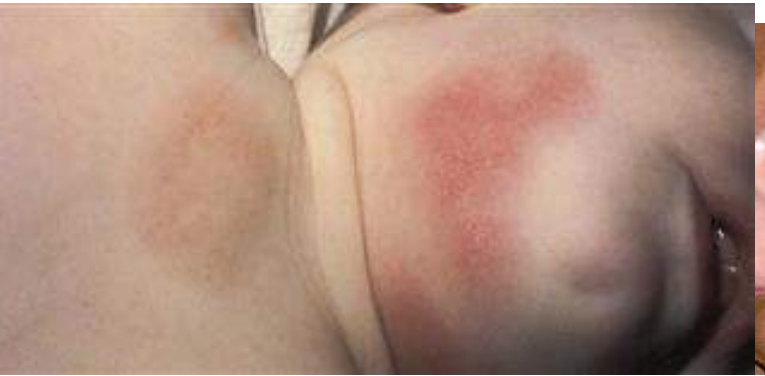
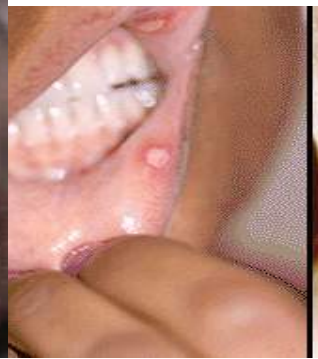
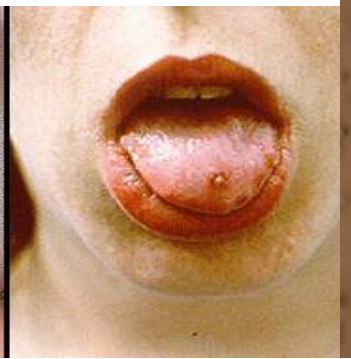
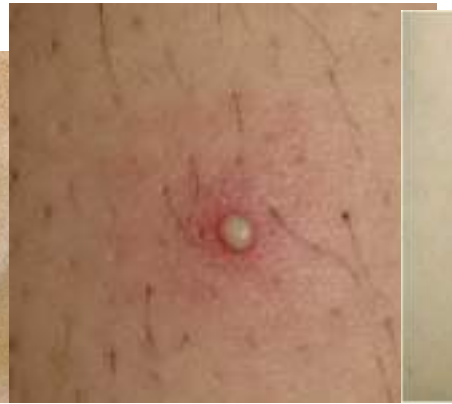
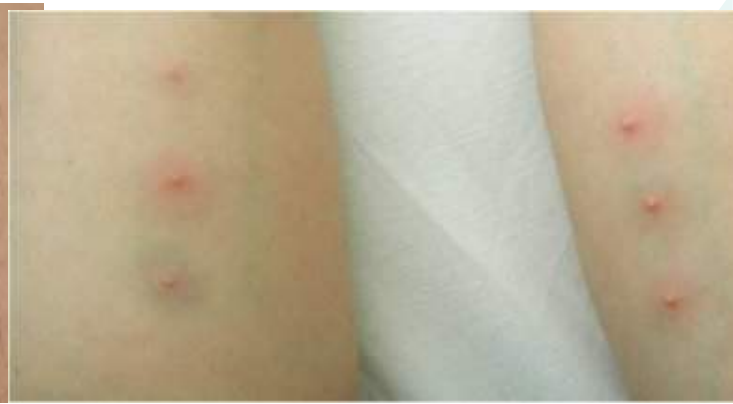


- Systemic occlusive vasculitis
- Etiology?
- Silk route, +++ Turkey
- 25-35 yrs, ++ Male
- Multissystemic: neuro Behçet, intestinal Behçet, Vascular Behçet
- Articular symptoms
- Thrombotic episodes

Behçet disease

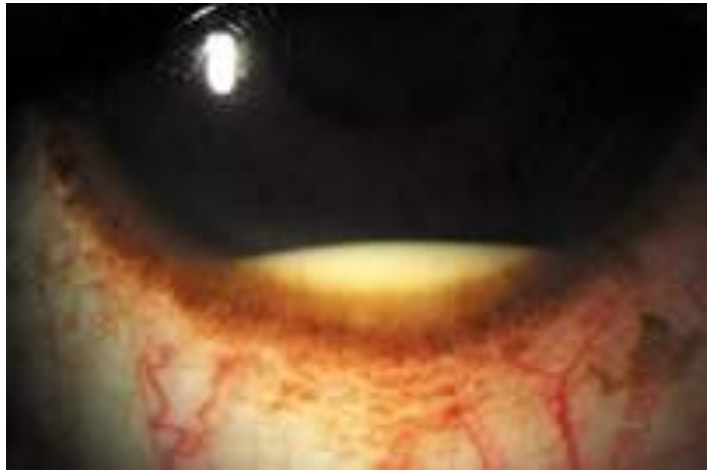
International Study Group for Behçet's Disease Criteria
Oral aftous ulcers (at least 3 x/year) + 2 of the following:
1. Recurrent genital ulcer
2. Ocular inflammation
3. Skin lesions
4. Positive pathergy

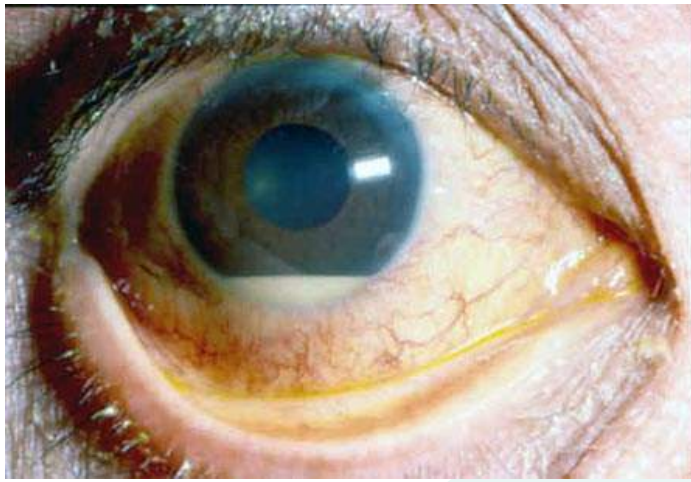
Diagnostic System for Behcet Disease (Japan)
Major Criteria:
• Recurrent Oral aphthous ulcers • Skin lesions (erythema nodosum, acneiform pustules, folliculitis) • Recurrent genital ulcers • Ocular inflammatory disease
Minor Criteria
• GI ulceration • Arthritis • Epididymitis • Systemic vasculitis or associated complications • Neuropsychiatric symptoms
Types of Behcet Disease
• Complete (4 major criteria) • Incomplete (3 major criteria or ocular involvement with 1 other major complication) • Suspect (2 major criteria with no ocular involvement) • Possible (1 major criterion)

Behçet disease – ocular manifestations

- 70% of patients
- Irreversible damage, poor prognosis
- Worse in men, more frequente if close to disease onset
- Anterior uveitis:
  - Shifting hypopion
  - Explosive?





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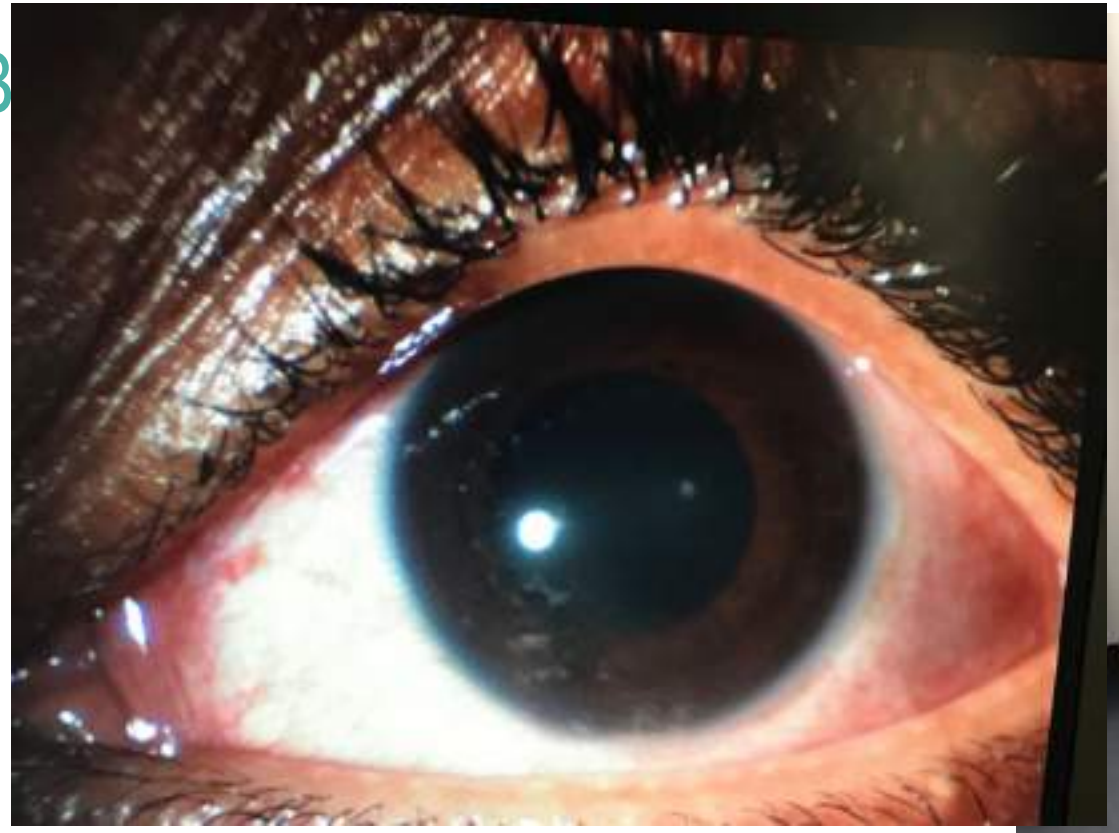


Behçet disease

- Posterior uveitis: obliterative vasculitis, non granulomatos, necrotizing
  - Vitritis
  - Vessel occlusion
  - CMO
  - Vasculitis nad ischemic retinitis
  - Papilitis / optic atrophy

Behçet disease

- Treatment
  - Steroids
  - IMT: AZA, CSA, TAC, MMF
  - EULAR: 1st line for ocular DB: steroids + AZA
  - Biologics: ADA (IFX)
- Consider immunossupression in isolated anterior uveitis in BD

Recommendation

2018 update of the EULAR recommendations for the management of Behçet's syndrome

Gulen Hatemi,[1] Robin Christensen,[2] Dongsik Bang,[3] Bahram Bodaghi,[4] Aykut Ferhat Celik,[5] Farida Fortune,[6] Julien Gaudric,[7] Ahmet Gul,[8] Ina Kötter,[9] Pietro Leccese,[10] Alfred Mahr,[11] Robert Moots,[12] Yesim Ozguler,[1] Jutta Richter,[13] David Saadoun,[14,15,16,17] Carlo Salvarani,[18] Francesco Scuderi,[19] Petros P Sfikakis,[20] Aksel Siva,[21] Miles Stanford,[22] Ilknur Tugal-Tutkun,[23] Richard West,[24] Sebahattin Yurdakul,[1] Ignazio Olivieri,[25] Hasan Yazici[1]

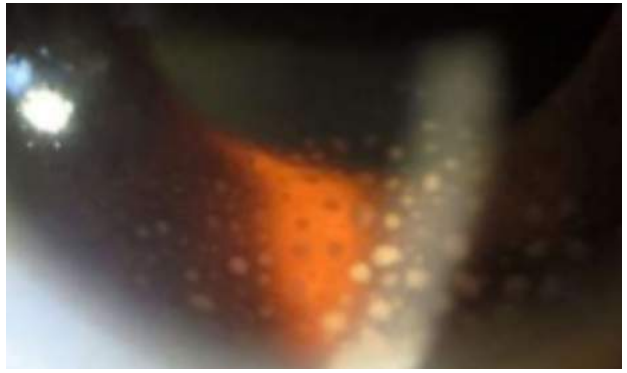
VKH

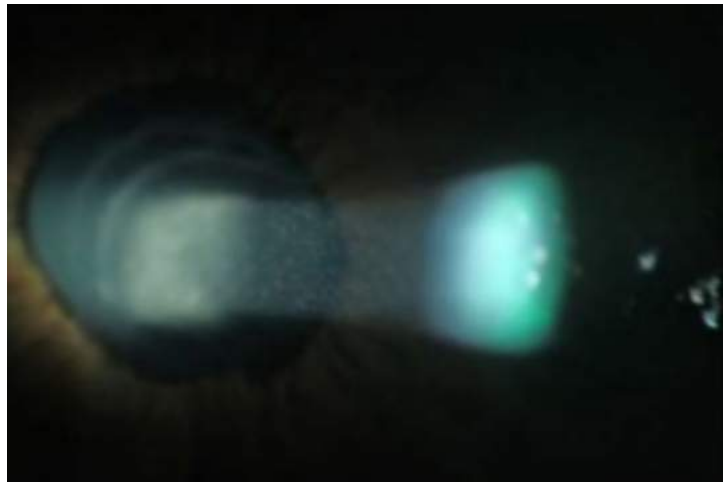
VKH

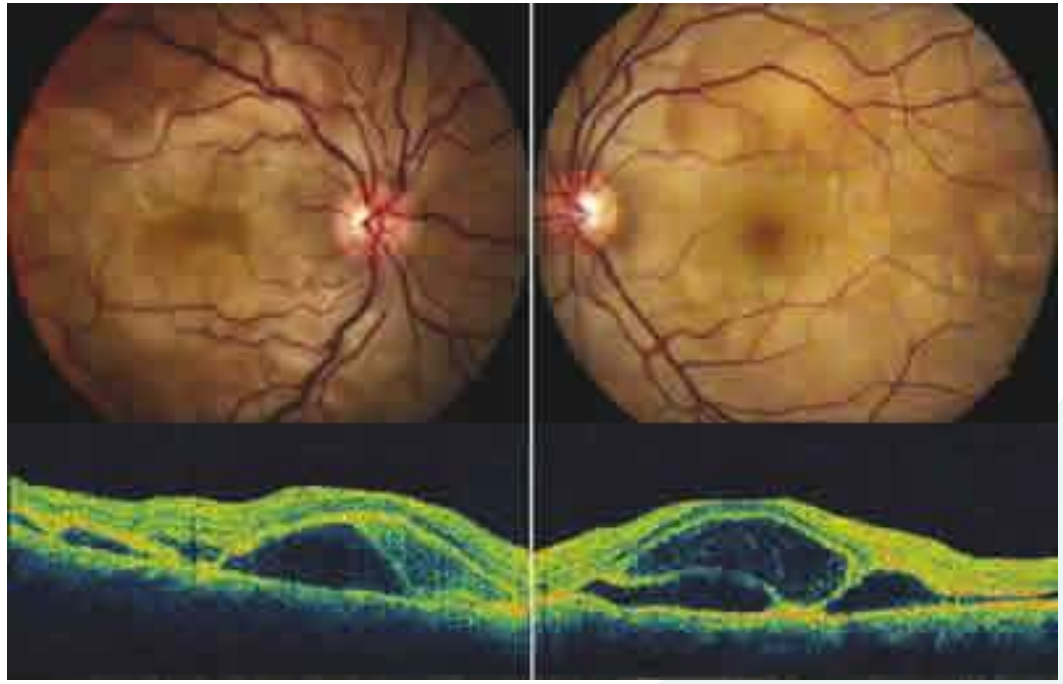
- Multisystemic disorder, autoimmune process T lymphocytes against antigens associated with melanocytes
- Granulomatous panuveitis with exsudative retinal detachments
- Neurological and cutaneous manifestations
- Asian, Middle Estearn populations
- HLA associations
- Female predilection
- 2^{nd}-5^{th} decades of life

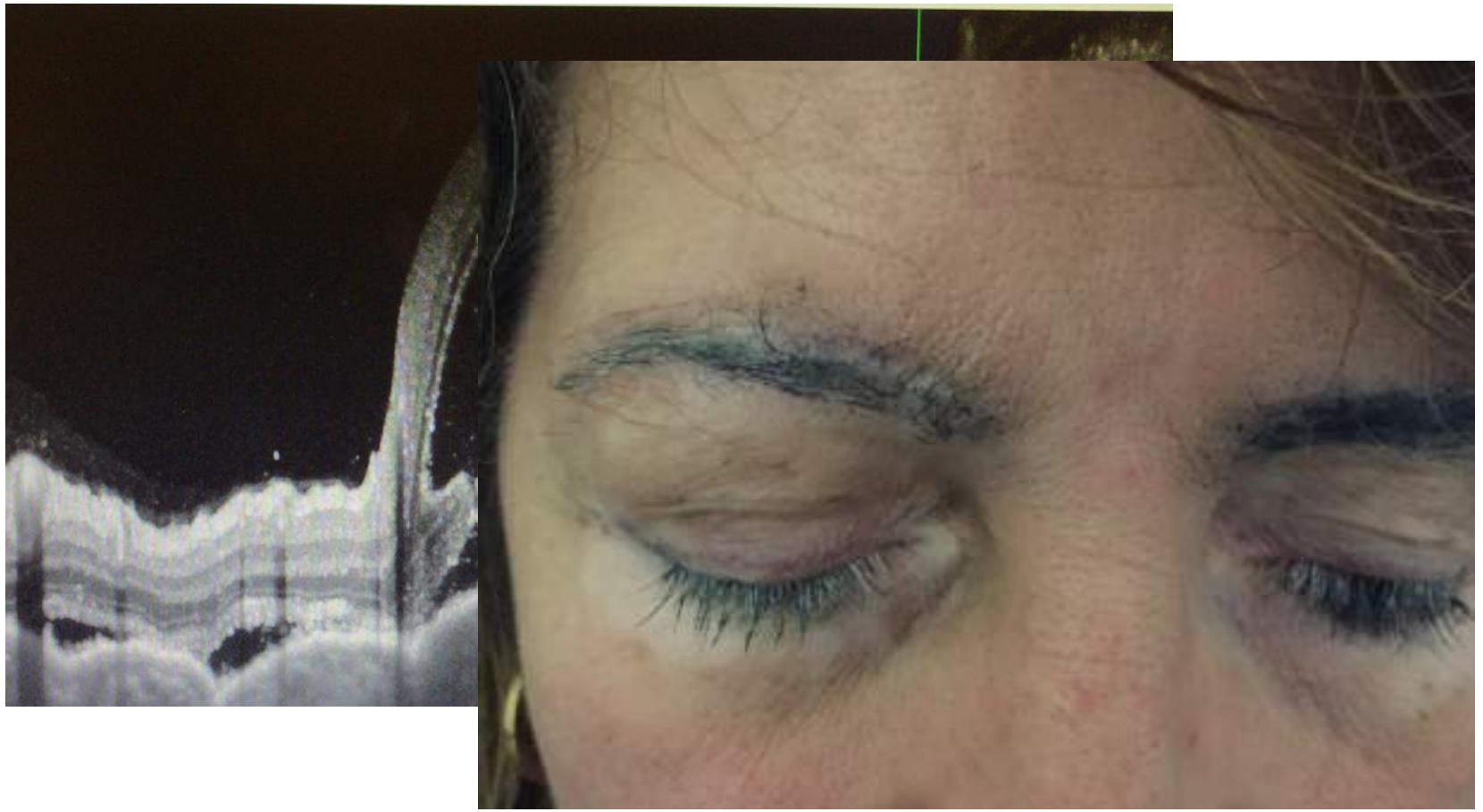
VKH

- Prodromal stage
- Uveitic stage
- Chronic stage – convalescent/recurrent





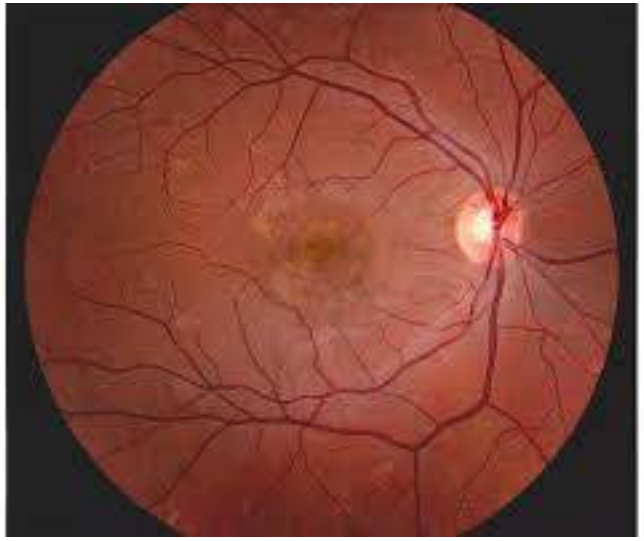


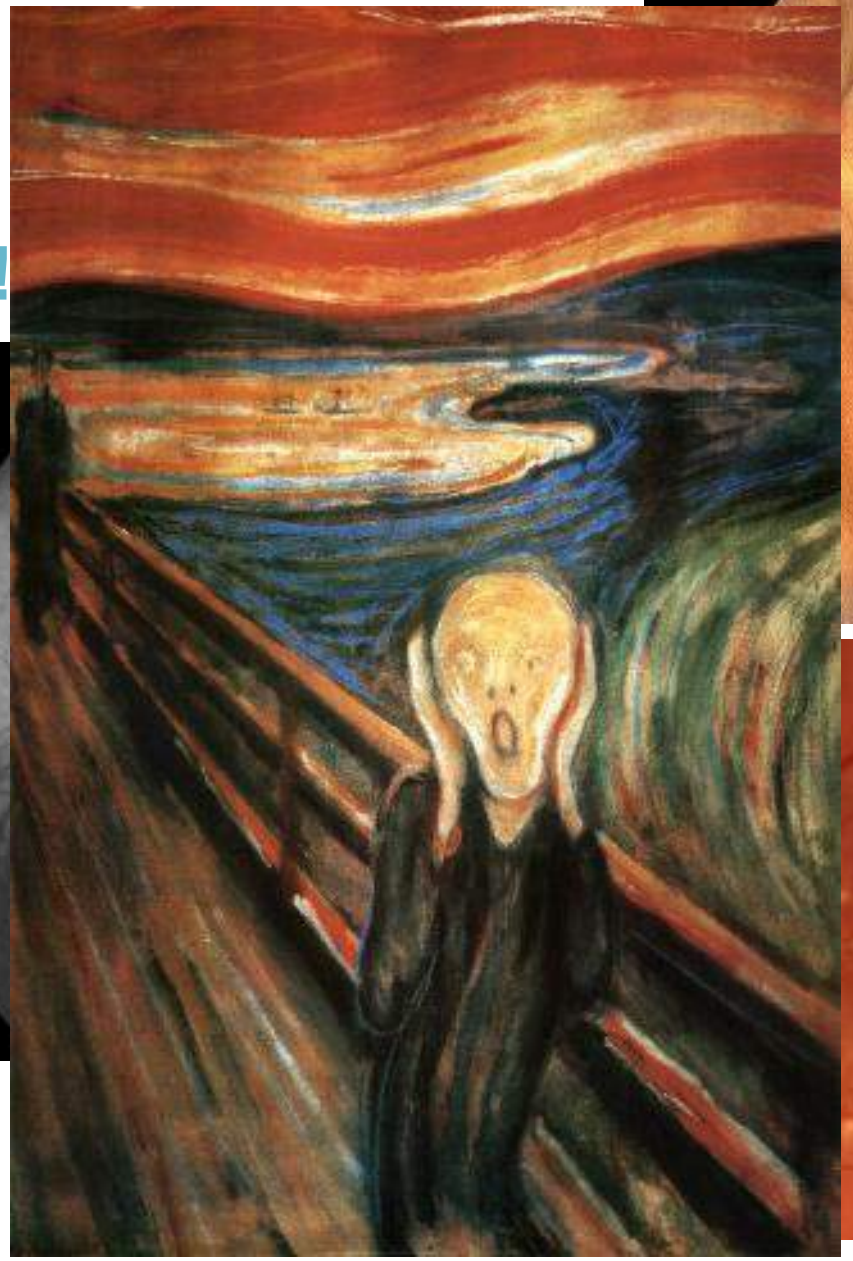


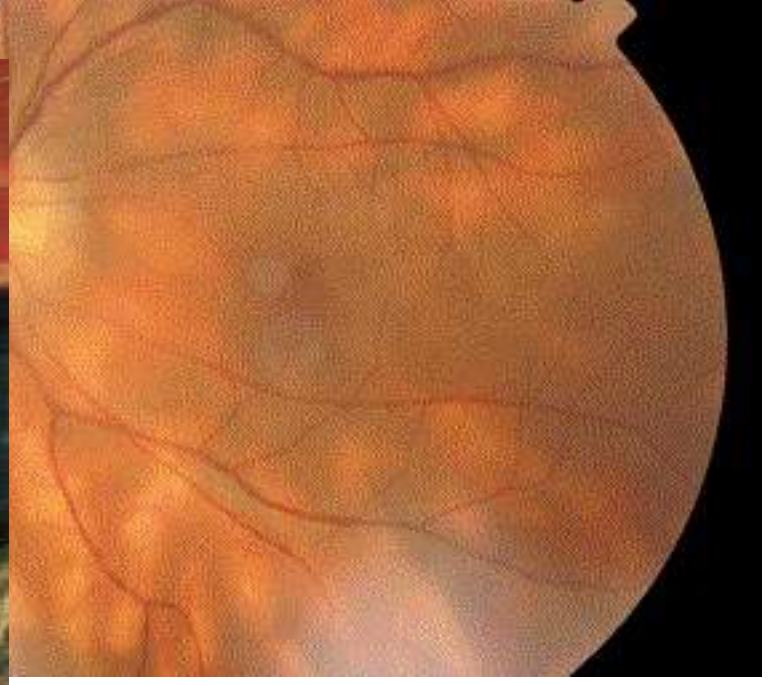
VKH Treatment

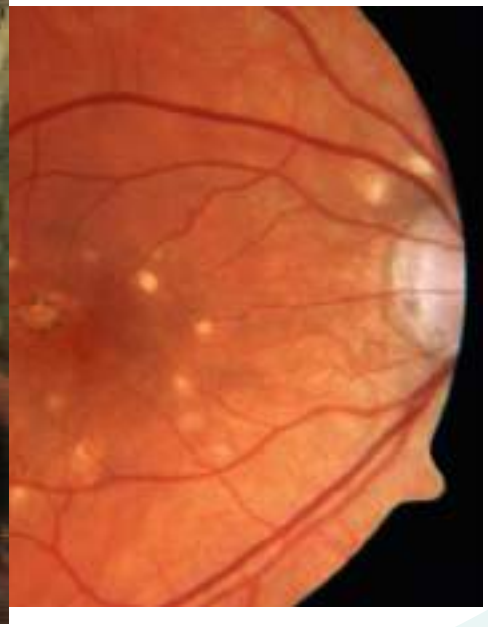
- Agressive management of acute VKH
  - High-dose systemic steroids
  - Immunossupressants: beggining?
- Treatment of complications

White dot syndromes!









OBRIGADA!

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