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Diagnosis of uveitis, how to proceed?

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Size of the problem

- 15/100000 in US every year.
- 10% of blindness
- Prevalence varies by age, location and study date.
- ? Females
- Anterior uveitis most common (location?)

Challenges

- Uveitis is caused by diverse etiologies
- Often, clinical signs are shared by most entities
- Sometimes, uveitis is a part of a disease developing elsewhere in the body and it is the first evidence of this disease

Failure to diagnose can lead to death

- Even in the setting of isolated ocular disease misdiagnosis can have a devastating consequences
- A patient with fungal endophthalmitis thought to have a sterile traumatic reaction may lose the eye if treated with corticosteroids

Principles of our work as uveitis specialists

1- Distinguish infectious from non infectious uveitis

2- Distinguish purely ocular disease from systemic conditions

3- Obtain additional testing only if results will influence your plan e.g. refer to the first principle

- Uveitis specialist must have thorough knowledge of all uveitis entities and the work up has to be complete
- In addition few other challenges are specific to practice in our locality:

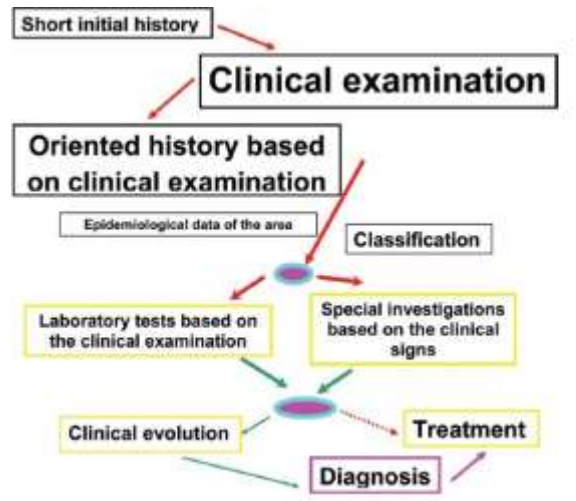
1. Lack of good primary health care
2. Poor affordability
3. Poor compliance

- Establishing an algorithmic approach in reaching etiologic diagnosis might help overcome these challenges by defining the pathway to be taken

- Steps in building an algorithmic approach are:

1. Defining the problem by naming technique
2. Review all possible causes of the problem which fit the existing pattern
3. Proving the diagnosis by using the diagnostic modalities in a logical matter

- General history--→ Ocular examination→ focused systemic history and exam-→ liaise with rheumatologist/ pulmonologist.. etc → now you should reach provisional diagnosis and DDs-→ lab and imaging modalities and sometimes therapeutic response will confirm diagnosis



- Diagnosis relies on a process of *recognition of pattern*

Collection of findings from

- History
- Clinical exam
- Investigations

It is helpful to ask yourself 8 questions

1- Is the disease acute or chronic
2- Is inflammation granulomatous or Non granulomatous
3- Unilateral Vs. Bilateral disease?
4- Where is the inflammation located in the eye?
5- What associated signs are present of examination?
6-What systemic symptoms does the patient have?
7 -What type of patients do I deal with ?i.e. demographics
8-What is the time course of the disease and response to previous therapy?

- By answering the previous questions you could effectively name the uveitis e.g. bilateral acute anterior recurrent nongranulomatous iritis in a 28 year old male patient with history of inflammatory low back pain, oral ulcers and diarrhea with marked improvement on steroid eye drops.

- Now, you should have a limited list of possible differential diagnoses for this particular scenario.
- Then, it is time for targeted specific investigations

1- Is the disease acute or chronic

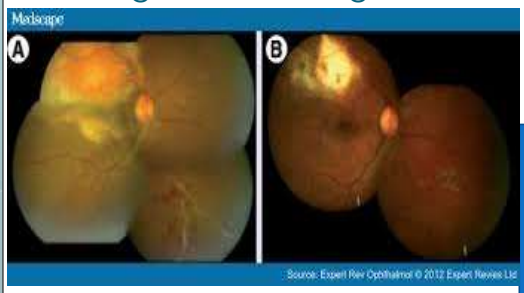
- SUN criteria: course

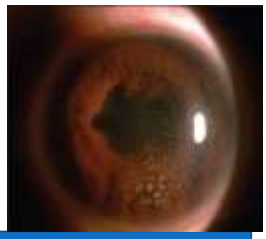
- Onset: sudden vs insidious
- Duration: limited (< 3 months) vs persistent(> 3 months)
- Course:
- ✓ Acute (sudden onset+ limited duration)
- ✓ Recurrent (flareups at intervals > 3 months after stopping treatment)
- ✓ Chronic (persistent OR flareups in < 3 months after stopping treatment)

- ***Acute disease***: e.g. HLA-B27 AAU, idiopathic AAU, some white dot syndromes such as AMPPE, MEWDS, VKH (early), ARN, Toxoplasmosis
- ***Chronic*** E.g. JIA, birdshot, serpiginous, TB, fungal, sympathetic ophthalmia, lymphoma, MFC, sarcoidosis and pars planitis

2- Is inflammation granulomatous or Non granulomatous

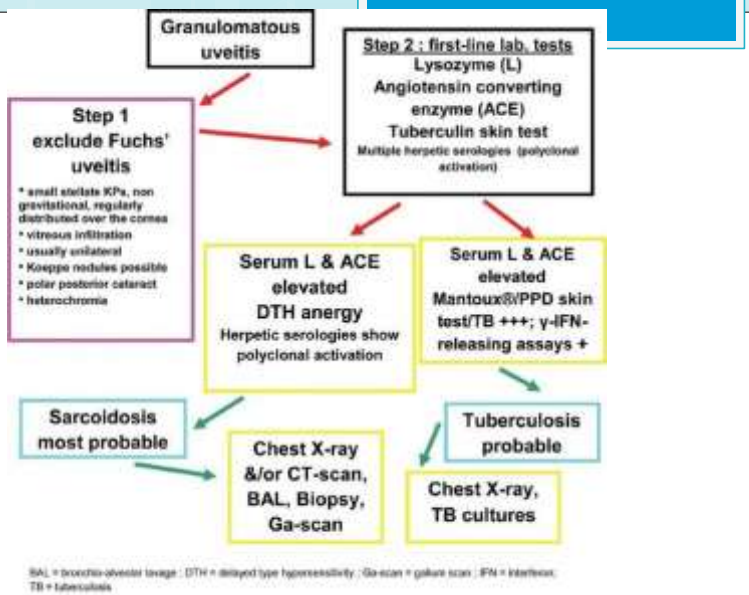
- Distinction based mainly on:
  - the appearance of KPs
  - Finding a choroidal granuloma





Finding granulomatous inflammation suggests a unique set of possibilities

- Infections e.g. TB, syphilis
- Sarcoidosis
- Sympathetic ophthalmia
- Lens-induced uveitis
- Multiple sclerosis
- VKH



3- Unilateral Vs. Bilateral disease?

SUN dimensions: laterality

- ✓ Unilateral
- ✓ Unilateral alternating
- ✓ Bilateral simultaneous
- ✓ Bilateral asynchronous

- HLA- B27 associated AAU is classically alternating i.e. flip flops
- Most cases of uveitis are bilateral within few months of presentation
- Therefore, a history of a disease that is both chronic and unilateral may point towards some culprits

- Post surgical uveitis
- IOFB
- Sarcoidosis
- Pars planitis
- Behcet's (Asian type)
- Parasitic infestations (except toxo)
- ARN

4- Where is the inflammation located in the eye?

- Different causes for different locations
- However, the diagnosis of intermediate uveitis is the most helpful in establishing diagnosis because it limits the possibilities to few entities

- Sarcoidosis
- IBD
- Multiple sclerosis
- Pars planitis
- Lyme disease

IUSG	Tessler	SUN group
---------	***Sclerouveitis***	--------
--------	***Keratouveitis***	--------
• ***Anterior uveitis*** ➢ Iritis ➢ Anterior Cyclitis	• ***Anterior uveitis*** ➢ Iritis ➢ Iridocyclitis	• ***Anterior uveitis*** ➢ Iritis ➢ ridocyclitis
Iridocyclitis	----------	Anterior cyclitis
• ***Intermediate uveitis*** ➢ Posterior cyclitis ➢ Hyalitis ➢ Basal retinochoroiditis	• ***Intermediate uveitis*** ➢ Cyclitis ➢ Vitritis ➢ Pars planitis	• ***Intermediate uveitis*** ➢ Pars planitis ➢ Posterior cyclitis ➢ Hyalitis
• ***Posterior Uveitis*** ➢ Focal, multifocal or diffuse choroiditis ➢ Chorioretinitis or retinochoroiditis	• ***Posterior Uveitis*** ➢ Choroiditis ➢ Retinitis	• ***Posterior uveitis*** ➢ Focal, multifocal or diffuse choroiditis ➢ Chorioretinitis or retinochoroiditis - ➢ Retinitis
Neuroretinitis	--------	***Neuroretinitis***
Panuveitis	----------	***Panuveitis***

Notes

- Macular edema is a structural complication and not per se osteriou uveitis
- Also, SUN criteria didn't put retinal vasculitis as posterior uveitis
- Sometimes there is spill over of cells
- So, intermediate uveitis with macular edema or peripheral retinal vasulitis and mild AC cells MAY BE labelled as panuveitis by mistake

5-What other symptoms does the patient have?

- A thorough medical history is often a key to diagnosis.
- Examples of useful data from ROS
- Headaches, SNHL → Behcet's, Vogt–Koyanagi–Harada syndrome, Sarcoidosis, Cogan's syndrome , and Susac syndrome
- Paresthesia, weakness → Intermediate uveitis associated with multiple sclerosis, Behçet's syndrome, steroid myopathy

- Skin rash → Behçet's syndrome, sarcoidosis, viral exanthem, syphilis, herpes zoster, psoriatic arthritis, Lyme disease
- Oral ulcers → Behçet's syndrome, IBD
- Genital ulcers →Behcet's, Reiter's and STDs

- Diarrhea → Whipple's disease, IBD
- Cough, shortness of breath → Sarcoidosis, tuberculosis, malignancy
- Sinusitis → Wegener's granulomatosis
- Sacroiliitis → Ankylosing spondylitis, Reiter's syndrome, inflammatory bowel disease
- Chemotherapy or other immunosuppression →

  Cytomegalovirus retinitis, Candida retinitis, other opportunistic organisms

- Arthritis → Behçet's syndrome, Reiter's syndrome, sarcoidosis, juvenile rheumatoid arthritis, rheumatoid arthritis, Lyme disease, IBD, Wegener's granulomatosus (GPA), SLE, other connective tissue diseases

6- What associated signs are present of examination?

- Psychosis → Vogt–Koyanagi–Harada syndrome,sarcoidosis, Behçet's disease, steroid psychosis, systemic lupus erythematosus.
- Cerebrospinal fluid pleocytosis → Vogt–Koyanagi–Harada syndrome, sarcoidosis, acute posterior multifocal placoid pigment epitheliopathy, Behçet's syndrome

Salivary or lacrimal gland swelling → Sarcoidosis, lymphoma

Lymphoid organ enlargement → Sarcoidosis, AIDS

Vitiligo, poliosis → VKH

Skin nodules → sarcoidosis, onchocerciasis

Alopecia → VKH

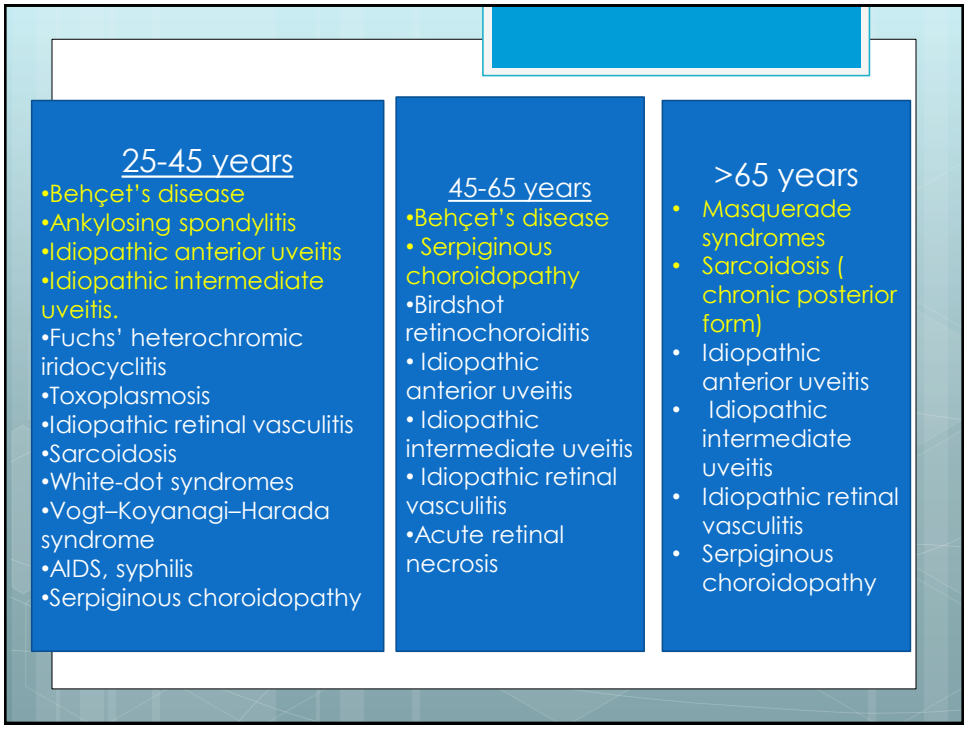
7 -What type of patients do I deal with ?i.e. demographics

- Age is the most notable example
- However, exceptions can occur

Age 5 years or less
- JIA
- Pars planitis
- Toxocariasis
- Post viral neuroretinitis
- Retinoblastoma, JXG, leukemia

5-15 years
- JIA
- Endophthalmitis
- Pars planitis
- Toxocara
- Post viral neuroretinitis
- Sarcoidosis
- Leukemia

15-25
- Pars planitis
- Juvenile Behcet's
- Ankylosing spondylitis
- Idiopathic anterior uveitis
- Toxoplasmosis
- Sarcoidosis (acute, mainly anterior)
- Acute retinal necrosis



8-What is the time course of the disease and response to previous therapy?

- Steroid resistance or unusual steroid dependence- → think infection
- Relapsing cases e.g. HLA B27
- Chronic downhill course with frequent exacerbations that frequently burn out spontaneously many years after onset e.g. Behcet's

When to investigate

- Any uveitis patient except
- 1- Patient with single attack of unilateral acute anterior nongranulomatous uveitis
- 2- Clinical picture very distinctive e.g VKH, toxoplasmosis, Behcet's
- 3- Patient on a drug known to cause uveitis and the clinical picture is not suggestive of another etiology

How to describe/ characterize

Anterior uveitis

- Cells and flare
- Hypopyon
- Keratic precipitates
  - (GR vs non Gr)
  - Diffuse vs Arlt's triangle
- Transillumination / atrophy
- Hypopyon (color, surface, mobility)

Posterior uveitis

- Primary site of involvement
  - Retititis
  - Choroiditis
  - Retinal vasculitis (arterial vs venous)
- Pattern
  - Focal/ paucifocal
  - Multifocal
- Description
  - Placoid, punched-out, amoeboid, ovoid, punctate
  - Color

Other characteristics

- Ocular co morbidities
- Response to treatment
- Ethnicity
- Medical conditions
- Geographic location/ travel

Lab testing

- Bayesian analysis
  - Sensitivity and specificity
  - Positive/ negative predictive value
  - Prior probability of the disease
- Cost
- Will it really matter(affect treatment, prognosis)

- E.g. Cost of ANA pannel is about 700 Dollars and it has low sensitivity and specificity
- TB accounts for less than 0.5% of uveitis in the US . PPD has a sensitivity and specificity of 75% and 85% respectively. So if all uveitis patients in the U.S are screened, the PPV of PPD is 1

Rosenbaum JT, Wernick R. Arch Ophthalmol 1990;108: 1291-1293

- However, in our region TB accounts for about 15% of uveitis, so it is worth to screen all patients with compatible uveitis for TB
- The reverse is true for syphilis

Simplified algorithm

Anatomic location

Infectious vs non infectious

Ocular vs systemic

Possible combinations Anterior uveitis

Infectious		*Non infectious*	
Ocular	***Systemic***	***Ocular***	***Systemic***
Herpetic	Syphilis	FHI	Behcet's
	TB	UGH	HLA related
	Leprosy	Post surgical	Sarcoid
		Traumatic	JIA
			TINU

Intermediate uveitis

Infectious		Non-infectious	
Ocular	**Systemic**	**Ocular**	**Systemic**
	Syphilis	Pars planitis	Sarcoidosis
	Lyme		MS
	Whipple's		IBD

Posterior uveitis

Infectious		Non-infectios	
Ocular	**Systemic**	**Ocular**	**Systemic**
PORN	TB	White dot syndromes	Behcet's
Eale's	Syphilis		VKH
	Fungal		Sarcoidosis
	Toxo		Retinal vasculitis

Panuveitis

Infectious		Non-infectious	
Ocular	**Systemic**	**Ocular**	**Systemic**
ARN	Syphilis	MFC-PU	Behcet's
Toxo	CMV retinitis	IOFB	VKH
Post surgical	TB		Sympathetic ophthalmia
Traumatic	Metastatic endophthal mitis		Lymphoma

Conclusion

- Ask/ examine/ think before your order tests
- Why….. To be cost effective
- Consider PPV and NPV (think of prior probability not just specificity and sensitivity)
- Consider geography

Thank you