The Eyes Are Going Viral

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1

Cecelia Koetting Disclosures

"All relevant relationships have been mitigated."

- Ocular Therapeutix
- Glaukos
- Horizon
- Quidel
- Eyevance
- Ivantis
- Orasis
- Claris Bio
- Aldeyra
- RVL
- Oyster Point
- Allergan
- Alcon
- Visus
- Thea
- Bruder
- Glaukos
- Avellino

2

Nothing makes the office more nervous than when this walks in. . .

3

Multiple Causes of "Red Eye"

- Sub-Conjunctival hemorrhage
- Allergic Conjunctivitis
- Viral Conjunctivitis
- Bacterial Conjunctivitis
- Episcleritis
- Scleritis
- Ocular Surface Disease

4

Herpes

5

All in the family. . .

- Herpes virus
  - Herpes simplex virus type 1 (HSV-1)
  - Herpes simplex virus type 2 (HSV-2)
  - Varicella-zoster virus (VZV)(HZV)
  - Cytomegalovirus (CMV)
  - Epstein Barr virus (EBV) (Mono)

6

HSV-1 and HSV-2

- HSV-1 Fever blisters on lips and mouth
  - Watery blisters on the skin or mucous membranes, will scab over and ooze
  - Most likely cause of lesions on cornea and eyelids
- HSV-2 Genital blisters, transmitted during sexual contact
  - Passed during birth from mother to child, risk of ocular infection

7

Herpes Simplex Virus

- Can be contagious through contact with saliva or an open blister
  - HSV-2 periodically sheds the virus
- Primary vs. recurrent infections
  - More common as a recurrent HSV
- Remain dormant in cell bodies of neurons in the sensory ganglia
  - More than 90% carry the latent virus
- Active phase can lead to destructive inflammatory phase

http://shaitheodore.com/neuroscience/drug-addiction/neuron-the-nerve-cell/neuron-the-nerve-cell/

8


https://en.wikipedia.org/wiki/Herpes_labialis


Diseasesforum.com

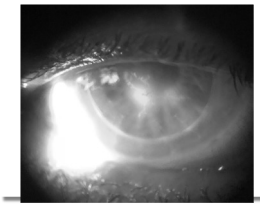

http://www.herpesland.com/herpes-on-eyes/


http://eyemicrobiology.upmc.com/Images/Sub/PhotoGallery/Virology/Photos/SVDendrite.jpg

9

HSV Ocular Signs and Symptoms

- Symptoms
  - Pain
  - Photophobia
  - Blurred VA
  - Tearing
  - Redness
  - FB sensation



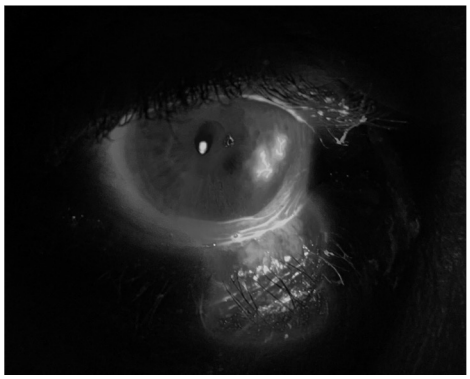
- Signs
  - Recurrent
  - Unilateral
  - Eyelid vesicles
  - Epithelial dendrites
  - Decreased K sensitivity
  - K edema
  - KPs
  - Iris stroma / sphincter
  - High IOP
  - Vitritis
  - Retinitis
  - Papillitis

10

Ocular HSV

- Cornea:
  - Epithelial keratitis: only the top layer of the cornea is affected
    - Dendrite with vesicles
  - Stromal keratitis: deeper layers of the cornea involved, more serious and will lead to scarring
- Less common can affect the inside of the eye and the retina
- Recurrence 27% at 1 year, 50% at 5 years, 63% at 20 years
  - Increased risk with each occurrence
  - Increased risk with DES and CL use

11



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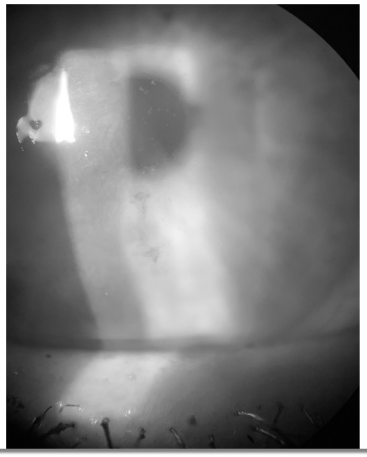

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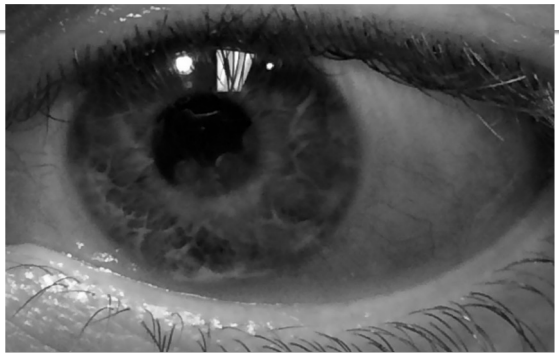


14

Treatment for HSV Epithelial Keratitis

- Dendritic keratitis usually resolves within 3 weeks
- Goal to minimize stromal damage and scarring
  - Consider epithelial debridement
  - Topical / Oral antivirals
  - Topical steroids

15

HSV UVEITIS:

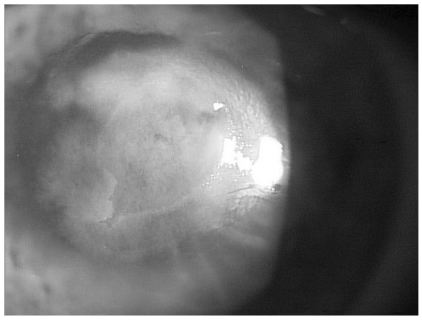
- Herpes Simplex Virus cause of up to 5-10% of all uveitis cases[2]
  - More common in patients with previous history of HSK[1]
  - 40-50 years old, both genders[1]
- Clinical signs[1-3]:
  - Unilateral most common, but can be bilateral
  - Moderate anterior chamber reaction
  - Medium sized keratic precipitates
  - Elevated IOP due to trabeculitis and blockage of trabecular meshwork by inflammatory cells
    - Occurs in 46-90% of cases[2]
  - Sectoral iris atrophy is pathognomonic for viral anterior uveitis[1,2]
    - Acute event → sectoral flattening of pupil border in involved area
    - After resolution → sectoral atrophy

16

TREATMENT:

- Oral antiviral:
  - Acyclovir: 400mg 1 PO 5x/day
  - Valacyclovir: 500mg 1 PO TID
- Topical IOP-lowering drops
  - Aqueous suppressant
  - Not needed long-term once trabeculitis resolves

17



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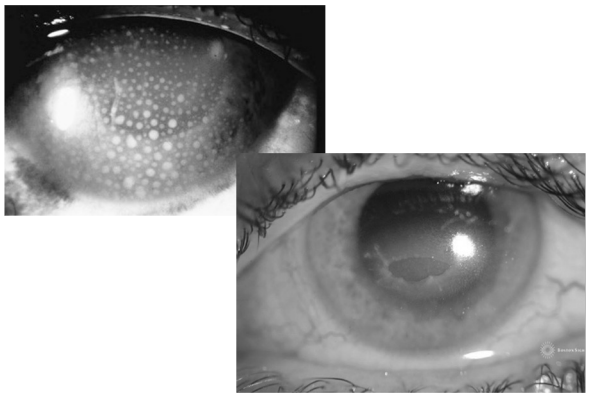

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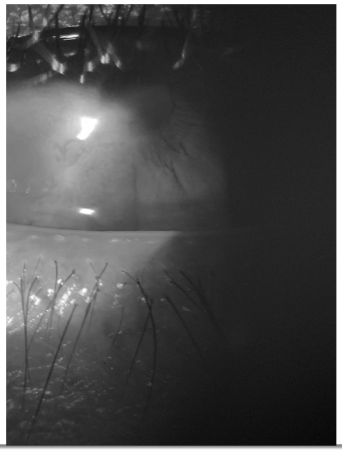

20

Studies

- HEDS I and II
  - Stromal Keratitis: Steroids use had a faster healing time, oral acyclovir did not make an improvement when added to topical antiviral
  - Iridocyclitis: oral antiviral beneficial
- Acyclovir Prevention Trial
  - *Reduced by 41% the probability of recurrence*
  - *50% reduction in the rate of return of the more severe form*

21

VZV

- Aka Shingles, HZV, chicken pox
- Primary Infection: often occurs in childhood as chicken pox
  - Usually leaves the person immune to recurrence, but the virus will lay dormant within the neurons and can reactivate
- Later Infection: reactivation is called Zoster or Shingles
- If ocular involvement with Zoster, called herpes zoster ophthalmicus (HZO)

22

VZV

- Vesicle placement respects the midline of the face
- Follows dermatome of the nerve
- Very painful!!
- Traditionally in people >60 YOA
  - Increase incidence in younger people since introduction of chicken pox vaccine
  - Decreased incidence overall since introduction of Shingles vaccine
  - Increase risk in people w/ decreased immune system, HIV, on immunosuppressive drugs

23

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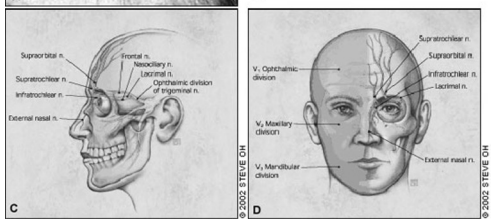


SAAD SHAIKH, M.D., and CHRISTOPHER N. TA, M.D., Stanford University Medical Center, Stanford, California
Am Fam Physician. 2002 Nov 1;66(9):1723-1730.

24

Herpes Zoster Ophthalmicus

- HZO accounts for 10-25% of all cases of shingles
  - 90% of U.S. population infected with VZV by adolescence
  - 100% of U.S. population by 60 years of age****
  - 1.5-3.4 cases per 1,000 individuals

25

HZO

- Conjunctivitis
- Scleritis
- Pseudodendrites
  - No terminal bulbs
- Keratic precipitates
- Iritis
- Synechiae
- Elevated IOP
- Potential vascular occlusion
- Bells Palsy
- Nerve palsies
- Glaucoma (longer-term)

26

HZO

- Prodromal phase: fatigue, malaise, low-grade fever
- Unilateral rash over the forehead, upper eyelid, and nose
  - 60% of patient have dermatomal pain prior to rash
  - Erythematous macules to papules to vesicles to pustules to crusts
  - Hutchinson's sign
- Similar to HSV, can affect different layers of the cornea
  - Stromal Keratitis
- Can also affect anterior chamber and retina
  - Uveitis, Episcleritis, Scleritis
  - Acute retinal necrosis (ARN), progressive outer retinal necrosis
- Postherpetic neuralgia: >12 months for 50%

27

HZO

- Treatment
  - Oral and topical antiviral drugs
  - Topical steroid vs oral steroid
  - Wound care

28

Vaccines for HZO - Zostivax

- Zostivax is live attenuated herpes zoster (HZ) virus
  - 50% reduction in the incidence of HZ
  - 60% reduction in symptom severity in patients who developed HZ
  - 66.5% reduction in postherpetic neuralgia.
- Must have chicken pox as a child
- May help patients who've had HZO already

1. Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med. 2005 Jun 2;352(22):2271-84.

29

Vaccine for HZO-Shingrix

- 2 dose vaccination recombinant zoster vaccine
  - Separated by 2-6 months
- 90% effective in preventing shingles and post herpetic neuralgia
  - 85% for the first 4 years post vaccination
- 50 years of age or older
  - Ok if have had shingles
  - Received Zostavax
  - Are not sure if had chickenpox

30

UVEITIS WITH ELEVATED IOP → THINK VIRAL!

- Herpes Simplex Virus
- Herpes Zoster Virus
- Cytomegalovirus
- Rubella
- Anterior chamber tap or polymerase chain reaction can make definitive diagnosis[1]
  - Diagnosis often made on clinical findings and patient history

31

	HERPES SIMPLEX	HERPES ZOSTER	CYTOMEGALOVIRUS	RUBELLA
AGE	<50	>60 or immunocompromised	40-60	20-40
GENDER	No predilection	No predilection	Males	No predilection
LATERALITY	Unilateral (18% bilateral)	unilateral	Unilateral	Unilateral (14% bilateral)
COURSE	Acute, recurrent	Acute, recurrent	Chronic	Chronic
KERATITIS	Common	Common	None	None
CORNEAL SCARS	Present 33%	Present 33%	None	None
KERATIC PRECIPITATES	Small to medium Same distribution as inflamed cornea; often central, paracentral, diffuse, or in Arlt's triangle	Small to medium Same distribution as inflamed cornea; often central, paracentral, diffuse, or in Arlt's triangle	Small Diffuse or coin-like nummular lesions	Fine and stellate Diffuse

Chan & Chee (2019)[1]

32

Epstein Barr

33

Epstein Barr

- Aka mononucleosis when primary exposure in adolescence
- Part of the Herpes virus family
  - >90% of population
  - Subclinical infection with exposure infancy and childhood
- Systemic condition with rare primary infection of the eyes
  - Periorbital edema

34

EBV

- Lays dormant in latent nonproductive state
  - Can reactivate in many ways throughout the body
  - One study found far reaching links to MS, Lupus, RA, JIA, IBD, celiac disease and Type 1 DM
  - Ocular manifestation rare
    - Bilateral uveitis
    - Optic disc swelling
    - Macular edema
  - Responds well to topical steroids, acyclovir and systemic acyclovir

35

Bell's Palsy

36

Viral Conjunctivitis

37

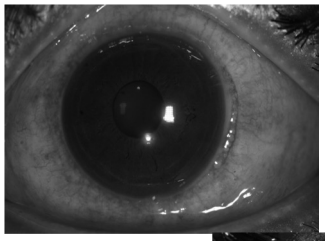
Hmm that looks contagious. . .

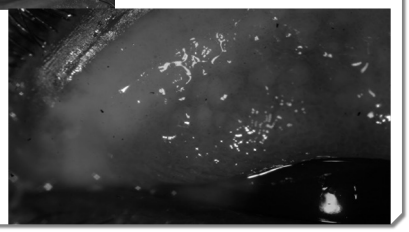
38

Adenovirus

- Caused by a virus
  - 6 subgenera and 53 serotypes
- Symptoms: redness, itching, photophobia, tearing, aching, foreign body sensation, blurred vision
  - Fever, headache, fatigue (flu like symptoms)
- Signs: chemosis, follicles, swollen lymph nodes, discharge, sub epithelia infiltrates, pseudomembranes

39





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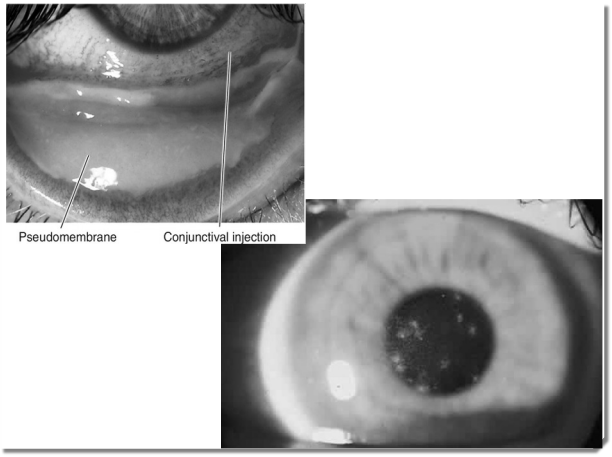


41

- Highly contagious.
- Adenoplus
  - Tests for most common serotypes 3,4,8,11,19,37
- Rule of 7's
  - Contagious for 7 days prior to signs and symptoms
  - Contagious for 7-14 days after signs and symptoms
  - Signs and symptoms will persist for 21 days after they start

42

Treatment

- In office
  - Betadine wash
  - Removal of pseudomembranes
- Topical antivirals
  - Decrease viral load?
- Topical NSAID
- Topical Steroid
  - Prolong viral shedding?
- Lubrication with artificial tears

43

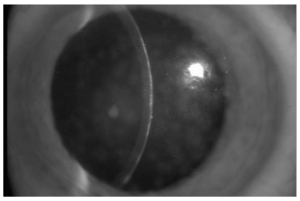
Current Treatment Studies

- Viral conjunctivitis treatment study
  - 0.01% hypochlorous acid
  - Avenova efficacy in treatment of viral conjunctivitis
- Topical Dexamethasone vs AT for treatment of viral conjunctivitis
  - 0.1% dexamethasone/povidone-iodine 0.4%
  - Shire, phase 3 clinical trial
    - Was terminated May 2019

44

Persistent side effects

- Typically occur with the Epidemic Keratoconjunctivitis serotypes
  - Sub epithelial infiltrates
- If signs and follicles persist for over 3-4 weeks, consider starting on oral antivirals
  - May actually be Herpes
  - HSV 1 and 2 IgG and IgM



45

Is It COVID?

46

COVID 19

47

Ocular Manifestation Primary Exposure

- Can present as follicular conjunctivitis
  - Red, watery, FBS, itchy, chemosis, follicles, possible CEI, possible pseudomemebrane
- Episcleritis and scleritis
  - Direct effect?
  - Reactivated uveitis?
- Posterior vascular problems
  - CRAO BRAO
  - CRVO BRVO
  - Acute macular neroretinopathy or paracentral actue middle maculopathy (ischemia deep retinal capillary plexus)
  - Purtscher like retinopathy

48

Continued!

- NMO and MS patients reactivation of optic neuritis
- Papilledema from increased intracranial pressure
  - Widespread inflammation and dural venous sinus thrombosis
- Cranial nerve palsies
- Pupil changes
  - post-ganglionic parasympathetic pupillary nerve fiber damage
- Nystagmus and oscillopsia
- Acute stroke affecting posterior visual pathways
  - Increase risk of stroke 7.6X more than the flu
- **These present with or with systemic symptoms**

49

Ocular Manifestations of COVID

- Still poorly understood
- Long term complications unknown
  - Anecdotally
    - More neurological
      - Migraines
      - Pupil changes
      - Accomdative spasms
      - CN palsies
      - Brain FOG

50

COVID Vaccine Shingles

- Shingles reactivation with Pfizer vaccination
  - Very small number in those with autoimmune inflammatory rheumatic diseases
  - 1.2 % of patients
  - Occurred within the first several days of receiving vaccination
  - 4/6 had Rheumatoid arthritis

51

Zika Virus

52

Zika

- Virus that is transmitted primarily by Aedes mosquitoes
  - Mosquitos that bite both during day and night
  - Can be passed from a pregnant woman to her fetus
  - Can be sexually transmitted
  - Can be transmitted through blood transfusion (not confirmed)
  - No current vaccine
- United states, Mexico, Cuba have all reported cases
- Canada at this time has no reported cases or mosquitoes that spread the virus
- Consult CDC or WHO website for risk level when traveling

53

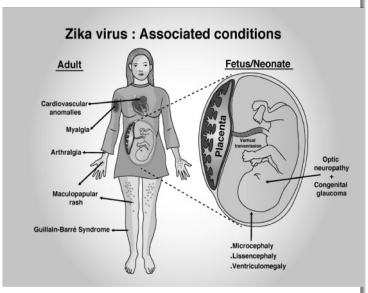
Initial Zika Infection

- Symptoms lasting several days to a week
  - Fever
  - Rash
  - Headache
  - Joint pain
  - Conjunctivitis
  - Muscle pain

54

Zika and Pregnancy

- Zika contracted by a pregnant women
  - Early fetal loss
  - Intrauterine fetal demise
  - Intrauterine growth restriction

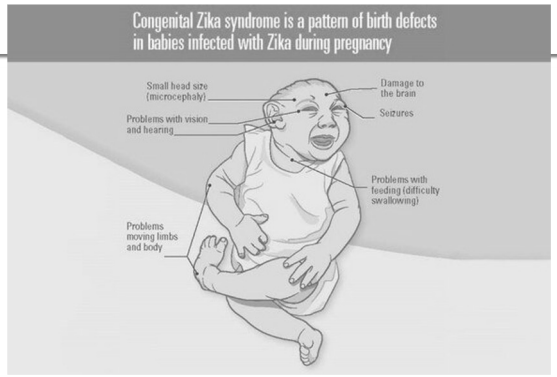


55

Congenital Zika Syndrome

- Fetus's exposed to the Zika virus while in utero develop CZS
- Rate of birth defects declines with each trimester of infection
  - 1^{st} – 8%, 2^{nd} – 5%, 3^{rd} – 4%
- Brain developmental abnormalities
- Ocular manifestation
- Extremities defects

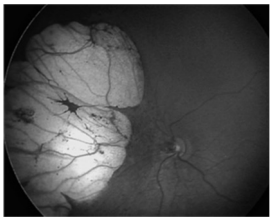
56



57

Ocular Manifestation of CZS

- Posterior Segment
  - Retina, optic nerve, retinal vessels
    - Pigment mottling
    - Chorioretinal atrophy
  - Glaucoma
  - microphthalmia
- Iris coloboma
- Lens subluxation, cataracts
- Oculomotor
  - Strabismus
  - Nystagmus



58

Sexually Transmitted Diseases

59

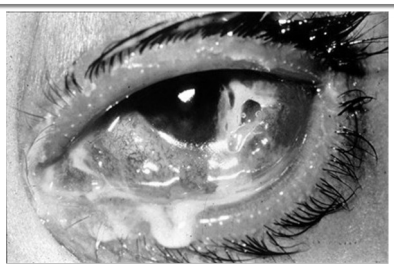
- Herpes Simplex Type 2 (discussed previously)
- Gonorrhea
- Syphillis
- Human Immunodeficiency Virus (HIV)

60

Gonorrhea

- Hyperacute bacterial conjunctivitis by Neisseria gonorrhoeae
  - STD, may not have concomitant genital infection
  - Direct sexual contact
    - Doesn't survive more than a few minutes outside human body
  - Attaches to and penetrates epithelial cells of mucosal surfaces
- Mucopurulent discharge
- Lid edema
- Conjunctival injection and chemosis
- Lymphadenopathy
- Globe tenderness

61



62

Neonatal

- Gonococcal ophthalmia neonatorum
- Passed from mother at birth
  - Contained within mucosa of cervix and urethra of infected mother
- Acute conjunctivitis, chemosis, lid edema, mucopurulent discharge
- Corneal epithelial edema and ulceration
  - Perfed cornea and endophthalmitis

63

64

Neonatal Prophylaxis

- Erythromycin 0.5% ophthalmic ointment
- Tetracycline 1% ophthalmic ointment
- Symptomatic or high risk
  - Ceftriaxone IV or IM

65

Testing

- Gram stain
  - Gram negative intracellular diplococci
- Culture on Thayer Martin and chocolate agar
- PCR
- Should have STD screening for HIV and chlamydia

66

Treatment

- **For Neisseria gonorrhoeae and Chlamydia trachomatis, systemic antibiotics**
- Chlamydia:
  - Azithromycin (1gm single dose) or Erythromycin
  - Doxycycline or Tetracycline (Avoid in pregnant, nursing mothers)
- Neisseria gonorrhoeae:
  - Ceftriaxone Intramuscular injection + Azithromycin PO single dose

67

Syphilis

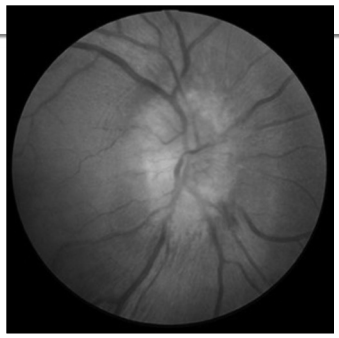
- Infection by the spirochete *Treponema pallidum*
- The great masquerader!
- Signs/Symptoms
  - Conjunctivitis
  - Decreased vision
  - Follicles
  - Scleritis, episcleritis
  - Persistent red eye
  - Posterior ocular involvement
  - Interstitial keratitis and crystalline lens dislocation (congenital)

68

Diagnosis

- RPR and VDRL
  - Test antibodies against host antigens which are released following tissue damage by T. pallidum
  - quantifiable and reflect both disease activity and response to therapy
  - Use to test for reinfection
  - Poor sensitivity
- FTA-ABS and MHA-TP
  - Measure serum antibodies for T. pallidum
  - Highly sensitive
  - Can't monitor response to treatment

69



70

Neurosyphilis

- Swollen optic nerve
- Visual field defects or vision loss
- Argyll Robertson pupil
- Must be diagnosed based on an MRI and a lumbar puncture to confirm

71

Treatment

- Penicillin
  - Neurosyphilis IV penicillin G for 10-14 days
- Penicillin allergy
  - Tetracycline, doxycycline, chloramphenicol, ceftriaxone
  - Macrolide antibiotics
- Systemic corticosteroids in conjunction with antibiotic
  - Interstitial keratitis
- Topical steroids for anterior uveitis

72

HIV/AIDS

73

HIV / AIDS

- Human immunodeficiency virus (HIV) is a blood bourne retrovirus
  - Acquired immune deficiency syndrome (AIDS) is cause by HIV when profound immune suppression occurs and allows for opportunistic infections, neoplasms, neurological manifestaions, possible death

74

HIV/AIDS

- Transmission
  - Sexual intercourse
  - Shared IV drug use
  - Mother to child via breastfeeding or birth
  - Very little/no viral load found in ocular secretions

75

HIV

- After initial exposure self limited acute illness with flu like symptoms
  - Rash, sore throat, vomiting, myalgias, fever, weight loss, fatigue
- Chronic stage the patient may be asymptomatic and last for years
- Final stage is progression to AIDS
  - CD_4 T cell count less than 200/ul
  - Viral load reflects activity

76

HIV/AIDS

- Most frequent ocular complaints
  - Irritation of the conjunctiva
  - Keratoconjunctivitis sicca
  - HIV-related retinal microangiopathy
  - Cytomegalovirus
  - Immune recovery uveitis
  - Acute retinal necrosis
  - Progressive outer retinal necrosis
  - Molluscum contagiosum
  - Syphilis
  - Toxoplasmosis
  - Pneumocystis jiroveci
  - Mycobacterium tuberculosis
  - Neoplasm (Kaposi sarcoma)

77

78

HIV/AIDS

- 80% HIV patients will be treated for an HIV associated eye disorder
- Control of immune system using antiretroviral therapy helps to decrease incidence and improve response to treatment of occurrences
- Should undergo regular ocular evaluations

79

Questions?

80

Thank you!
Dr.CeceliaKoetting@gmail.com

81