I've Got What?
Sexually Transmitted Diseases: Infections with Ocular Manifestations

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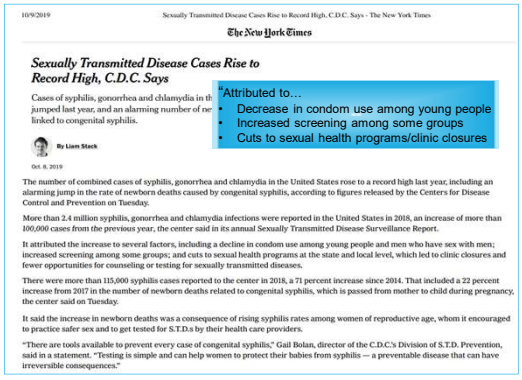
Let's Talk About STIs and STDs

Julie A. Tyler, OD, FAAO - Disclosures: ***None***

Terms:

- **STI** -"sexually transmitted infection" refers to a pathogen that causes infection through sexual contact, whereas..
- **STD** - "sexually transmitted disease" refers to a recognizable disease state that has developed from an infection



10/9/2019 Sexually Transmitted Disease Cases Rise to Record High, C.D.C. Says - The New York Times

The New York Times

Sexually Transmitted Disease Cases Rise to Record High, C.D.C. Says

Cases of syphilis, gonorrhea and chlamydia in th
jumped last year, and an alarming number of ne
linked to congenital syphilis.

"Attributed to…
- Decrease in condom use among young people
- Increased screening among some groups
- Cuts to sexual health programs/clinic closures

By Liam Stack

Oct. 8, 2019

The number of combined cases of syphilis, gonorrhea and chlamydia in the United States rose to a record high last year, including an alarming jump in the rate of newborn deaths caused by congenital syphilis, according to figures released by the Centers for Disease Control and Prevention on Tuesday.

More than 2.4 million syphilis, gonorrhea and chlamydia infections were reported in the United States in 2018, an increase of more than 100,000 cases from the previous year, the center said in its annual Sexually Transmitted Disease Surveillance Report.

It attributed the increase to several factors, including a decline in condom use among young people and men who have sex with men; increased screening among some groups; and cuts to sexual health programs at the state and local level, which led to clinic closures and fewer opportunities for counseling or testing for sexually transmitted diseases.

There were more than 115,000 syphilis cases reported to the center in 2018, a 71 percent increase since 2014. That included a 22 percent increase from 2017 in the number of newborn deaths related to congenital syphilis, which is passed from mother to child during pregnancy, the center said on Tuesday.

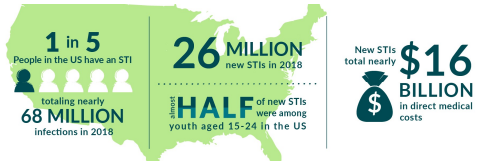
It said the increase in newborn deaths was a consequence of rising syphilis rates among women of reproductive age, whom it encouraged to practice safer sex and to get tested for S.T.D.s by their health care providers.

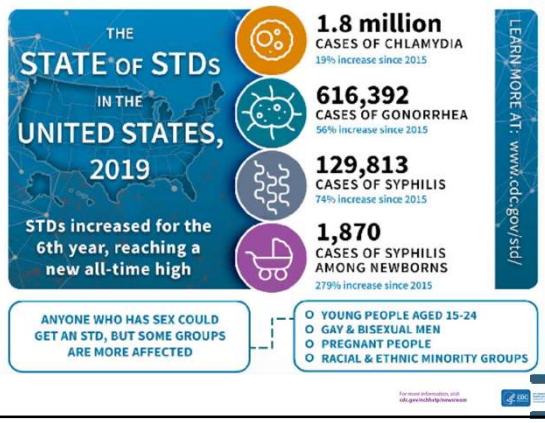
"There are tools available to prevent every case of congenital syphilis," Gail Bolan, director of the C.D.C.'s Division of S.T.D. Prevention, said in a statement. "Testing is simple and can help women to protect their babies from syphilis — a preventable disease that can have irreversible consequences."

STD Rates are Rising – Relevancy…

Rates for chlamydia, gonorrhea & syphilis are at a modern high:
MORE than 2.5 MILLION new cases of all three infections reported in 2019 →

**2020 Sexually Transmitted Disease Surveillance Report*
by the Centers for Disease Control and Prevention *2019*





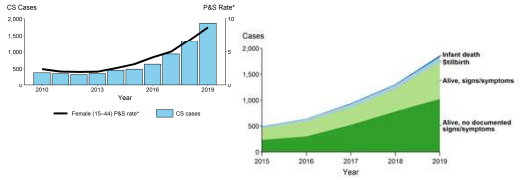
The Basics

- 15-24 year-old account for half of new sexually transmitted infections
- Men who have sex with men have a higher rate of sexually transmitted infections (STI)
- Increasing concern: Congenital syphilis rates ….

The Basics

July 23, 2021: Congenital syphilis rates increased by more than 267% during 2013-2019. Numbers In 2019,

- 36% (up from 28%) cases due to a lack of timely prenatal care
- 40.2% cases because pregnant women didn't get appropriate Tx (Despite Dx)



Relevancy…

- CDC surveillance (2019) rates per 100k – most recently updated (as of 4/10/2022)

Indiana

Chlamydia Cases	24	Indiana	35,430	529.4
Gonorrhea Cases	23	Indiana	11,926	178.2
Syphilis Cases	41	Indiana	336	5.0

- Chlamydia & gonorrhea most common among people <30 YO

Seeing resurgence →

Indicative of issues with education, closing of clinics and failures within "public health safety net" and further anticipate BIG surges associated with COVID-19 pandemic due to decreased testing

Considerations on our role…

- All STDs have a potential for ocular complications
- Pts may not recognize the associations with ocular findings and systemic issues
- **Primary care eye care professionals can identify issues and work to provide interdisciplinary care/ interprofessional/collaborative care**

Case I:
This Rash Just Won't Go Away….

19 Year Old White Male

Case co-managed with optometric colleagues

- CC: Irritated, painful, red eye OS
  - HPI: Sensitivity to light with mild decreased VA, "FBS", *Onset: 1 day prior*

- Ocular History:
  - (+) Contact lens wearer – Acuvue two week disp.
  - *FBS increased with CL use*

Case I:
This Rash Just Won't Go Away….

19 Year Old White Male

Medical History/Review of Systems

- **Persistent Rash on torso**
  - Dx elsewhere as: *pityriasis rosacea*

- No medications or medical allergies noted

Case I:
This Rash Just Won't Go Away….

- Persistent Rash on body (here shown on leg)
  - Hx of Dx elsewhere: *pityriasis rosacea*

Case I:
This Rash Just Won't Go Away….

Ocular Examination

- VA entering cc: 20/20 OD and OS
- EOM: FROM OU
- CF: FTFC OD, OS
- Pupils: Anisocoria (OD>OS [miosis]), (-) APD
- **Slit Lamp: OD within normal limits**
  - OS: 3+ conjunctival injection, 1x1 corneal defect superior to visual axis, (+) Nafl staining
    - Fleeting views: Unable to visualize cells, flare

Case I:
This Rash Just Won't Go Away….

Initial Diagnosis → Impression/Plan

- **Corneal "ulcer" associated with CL overwear**
  - Moxeza ™ 1 gt q15min x 1hr OS, then 1gt q1hr until 1 day follow-up
  - 1 gt Cycloplegia in office OS
  - Non-preserved AT q1hr OS

Case I:
This Rash Just Won't Go Away….

Social History

- Risk behaviors
  - Extended wear CL use
  - Swimmer
  - Just finished first year in college … "away from home"
- Environmental considerations

Case I:
This Rash Just Won't Go Away….

Follow-up Exams

- At one day follow-up pt noted decrease in redness and discomfort
  - Now visible → *Significant anterior chamber reaction*
  - *Maintain antibiotic and cycloplegia*

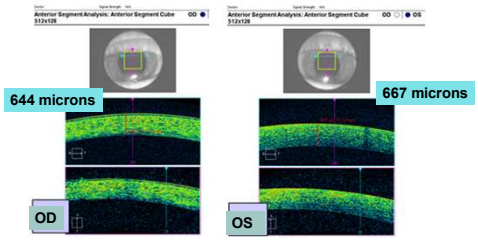
- **Over the next two weeks**
  - Quality of vision improved and corneal epithelium/ "ulcer" resolved….

BUT

Case I:
This Rash Just Won't Go Away….

Follow-up Examinations

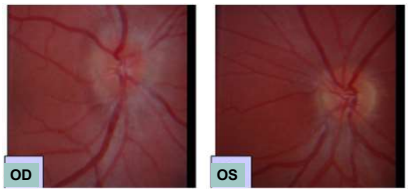
- ***Interstitial keratitis*** *ensued and AC reaction persisted despite aggressive topical steroid regimen*



Case I:
This Rash Just Won't Go Away….

Follow-up Examinations

- At the two week follow-up with observation →
  - *OPTIC NERVE HEAD ELEVATION with blurred disc margins and obscuration of vessels in the right eye*



Case I:
This Rash Just Won't Go Away….

Additional questioning….

- Systemic changes
  - Rash had spread to his trunk and arms

Case I:
This Rash Just Won't Go Away….

Additional questioning….

- Further Assessing Risk behaviors
  - Just finished first year in college … "away from home"…and
  - **Unprotected sexual contact**
- Environmental considerations
  - **From Lyme, Connecticut** *(Literally!)*

Case I:
This Rash Just Won't Go Away….

Differential Diagnosis

- Syphilis
- Lyme disease
- Underlying rheumatologic condition with secondary dermatologic manifestation
- *Others?*

Serology ordered

Case I:
This Rash Just Won't Go Away….

Differential Diagnosis

- Syphilis
- Lyme disease
- Underlying rheumatologic condition with secondary dermatologic manifestation

Serology Testing and results

- CBC with differential
- RPR
- FTA-ABS → **ELEVATED (1:256) and History suggest Syphilis Dx**
- Lyme titers
- ANA

Case I:
This Rash Just Won't Go Away….

Follow-up Management

- IM PCN provided by Primary Care Physician
- Co-management for ocular presentations was initiated

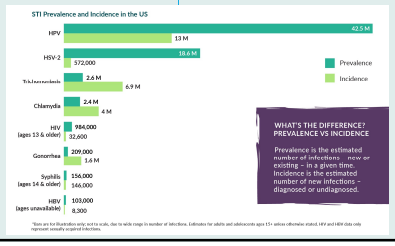
Additional Testing

PCP: "Syphilis doesn't usually come to the party alone"….

- Serology:→ **CLEAR results**
  - HIV
  - Chlamydia
- MRI: Due to optic nerve head elevation
  → **CLEAR results**

Conditions considered– Review of Sexually Transmitted Disease (STD)

- Human Papilloma Virus (HPV)
- Herpes Simplex Virus strains
- **Human Immunodeficiency Virus (HIV)**
- **Chlamydia**
- ***Neisseria Gonorrhea***
- **Syphilis**



STD Statistics for the USA and the World

- This information represents statistics reported for Chlamydia, Gonorrhea, Syphilis from the **CDC website** and HIV at http://www.avert.org and http://www.cdc.gov/hiv/statistics/basics.html

Case II:

I noticed this bump on my eyelid….

23 yo Black Male

CC: Red eye & mildly decreased VA OS

- HPI: Onset three months ago; Also noticed bump on superior lid margin around the same time

(-) discharge, (-) pain, (-) photophobia

Ocular History:

(-)injury, surgery, infection

Case II:

I noticed this bump on my eyelid….

23 yo Black Male

Medical History/Review of Systems

- (+) Dx and treated for Chlamydia 6 months prior
- Negative for other STD's 6 months prior

Denies use of medications or allergies

Case II:
I noticed this bump on my eyelid….

23 yo Black Male

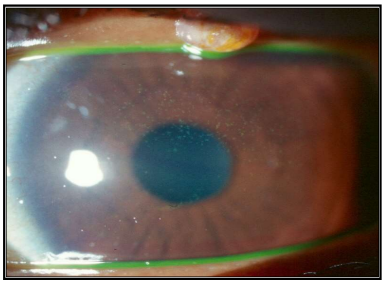
Social History

- Clinical evaluation & Findings
  - BCVA: 20/20 OD, 20/50 OS
  - Preliminary testing: Normal
  - Slit Lamp Exam
    - OD: Without pathology
    - OS: See images

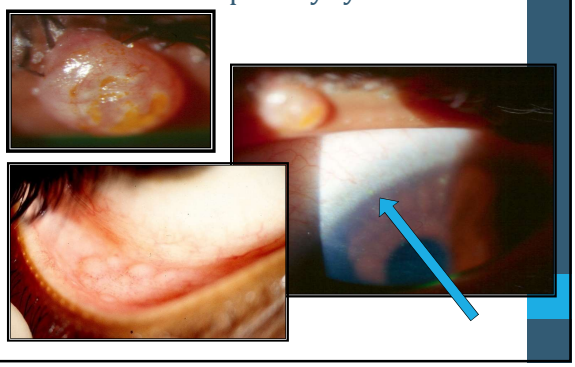
Case II:
I noticed this bump on my eyelid….

- At first glance:

Note diffuse corneal staining associated with superior lesion



Case II:
I noticed this bump on my eyelid….



Case II:
I noticed this bump on my eyelid….

- **LEFT EYE**
  - (+) Superior lid lesion ~1mm round, flesh-colored, elevated with umbilicated center
  - (+) Follicles – grade 2
  - (+) Focal sup. keratitis w/ limbal corneal infiltrates
  - (+) Conjunctival injection – grade 3

Case II:
I noticed this bump on my eyelid….

Dilated Fundus Exam:

- Without pathology 360 degrees OD, OS

What do you want to know?

- Upon questioning, the patient acknowledged an awareness of the lesion with a recent change in size

Case II:
I noticed this bump on my eyelid….

Differential diagnoses -

- Papilloma (HPV)
- Molluscum Contagiosum
- Herpes Simplex vesicle with secondary conjunctivitis
- Herpes Zoster (….?)

Case II:
I noticed this bump on my eyelid….

Impression/Plan

In office management

- Ocular management
  - Artificial tears for supportive therapy
  - Discussed necessity of removing lesion to prevent further ocular irritation
- Systemic Referral & serology considerations
  - **Discussed necessity to repeat serology = R/O HIV**
  - → Seroconversion considerations…

Case II:
Ocular Management Considerations

Part I: Remove….

- Refer to remove lid lesion surgically (Oculoplastics)
- Remove in timely fashion to avoid secondary complications….

But what can WE do now?

Case II:
Ocular Management Considerations

Part II: Treat ocular surface, including prophylaxis

- Artificial tears
- No topical anti-viral med available for this condition
  - **Consideration of Zirgan**
- Prophylactic treatment considerations
  - Protect the cornea with antibiotic
- **Combination med if keratitis is significant**

Case II:
Ocular Management Considerations

Part III:

Ed. patient & consider referral for systemic tests

- STDs including HIV testing
  - *Seroconversion period considerations*
- May need to treat co-morbidity

Case II:
I noticed this bump on my eyelid….

One week follow-up…..

- VA improved but still not 20/20
- SLX: Cornea clear
- Plan:
  - Maintain AT for supportive therapy and provided **steroid** and antibiotic together

- **Following steroid - VA improved to 20/20 OS**
  - Tapered & patient was re-educated on importance of oculoplastic consult for surgical excision

Associated with STD/STI:

Molluscum Contagiosum

- Highly contagious dermatologic condition
- Most commonly seen in childhood
- Associated with **HIV** infection in adults

Ocular complications if occurring on lid margin →

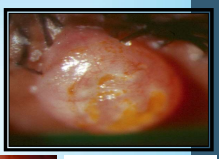
- "Viral shed" = immune response
  - Secondary follicular conjunctivitis
  - Possible infiltrates and keratitis
  - May develop significant ocular surface complications

What may be seen →
Anterior Segment Manifestation Overview

- **Lid and Face Lesions**
  - Herpes Simplex Virus (HSV) Vesicles
  - Molluscum Contagiosum
- **Conjunctivitis/Keratoconjunctivitis**
  - Conjunctival Findings
    - Follicles vs. Papillae or combined….

Anterior segment signs

- **Differential Diagnosis of lid**



Herpes Simplex Lesions – *Nasal canthus vesicles*

Molluscum Contagiosum – *Superior lid, umbilicated center*

Anterior segment signs

- **More Differential Diagnosis of lid lesions**

In some presentations, Kaposi's Sarcoma may look like a subconjunctival hemorrhage (SCH)

Kaposi' s sarcoma involving conj

Kaposi' s sarcoma involving lid

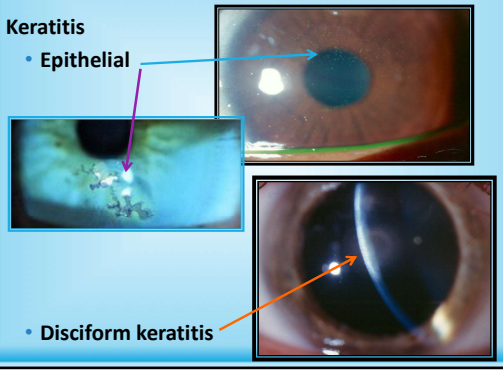
What may be seen →
Anterior Segment Manifestation Overview

- **Keratitis**
  - May be diffuse or focal areas of inflammation
  - Epithelial – Positive NaFl staining
  - Stromal –associated with edema
    - Interstitial
    - Disciform = Generally deeper
  - Associated findings of adjacent tissues
    - Injection may be diffuse or focal (corresp. to defect)
    - Secondary uveitis if severe

Anterior segment signs: Keratitis

Keratitis

- **Epithelial**

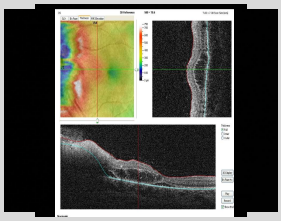


- **Disciform keratitis**

What may be seen →
Posterior Segment Manifestation Overview

Retinal Complications

- **HIV Retinopathy**
- **Retinitis** → Opportunistic
  - **CMV**
  - Toxoplasmosis



- **Retinal Necrosis**
  - Acute Retinal Necrosis (ARN)/ Bilateral ARN (BARN)
  - Progressive Outer Retinal Necrosis (PORN)

What may be seen →
Posterior Segment Manifestation Overview

Retinal Complications

- **Retinal Necrosis**
  - **Acute Retinal Necrosis (ARN)/ Bilateral ARN (BARN)**
    - *Focal, well-demarcated **w/rapid circumferential progression***
    - ***Occlusive vasculopathy** with arteriolar involvement*
    - *Areas of necrotic peripheral retina, sparing the posterior pole = (+)Vitritis, (+)Vasculitis*
  - **Progressive Outer Retinal Necrosis (PORN)**
    - *→Areas of necrotic retina **without** vasculitis and vitritis*

What may be seen →
Posterior Segment Manifestations

Retinal Complications

- **Vasculitis**
  - **Periphlebitis – Inflammation of the outer coat of a vein or the tissue surrounding**
  - **Frosted branch angioitis**

What may be seen →
Posterior Segment Manifestation Overview

Neurologic/Neuro-retinitis

- Neuritis
  - Optic nerve inflammation
- **Neuro-retinitis**
  - **Optic nerve and retinal involvement**

Sexually Transmitted INFECTIONS (the bugs) with STD Ocular Manifestions

Viral Infections associated with sexual transmission

- *1. Herpes Simplex*
- *2. Molluscum Contagiosum (secondary/opportunistic)*
- *3. HIV/ AIDS*

Bacterial and Other Systemic Infections spread by sexual transmission

- 1. *N. Gonorrhea* → *ANTIMICROBIAL resistance issues*
- 2. Chlamydia → A return to Doxy….
- 3. Syphilis

*** And an interesting note on Zika*

Sexually Transmitted Infections– Serology/Testing

Serology

1. **CBC with Differential**
2. **ESR**
3. **EIA** – **E**nzyme **I**mmuno**A**ssay initial testing *for syphilis** → New standard "reverse sequence screening"
4. RPR and FTA-ABS

Sexually Transmitted Infections – Serology/Testing

Serology (continued)

5. **HIV testing**
   - Dx: HIV immunoassay (antibody screening)
   - Monitoring: Viral load & CD4 testing
   - Additional HIV testing options → More sensitive, Tests using antibody and antigens (~3 wks, only blood)

Sexually Transmitted Infections – Serology/Testing

Serology (cont)

6. **IgG & IgM specific antibody titers for HSV-1 and HSV -2**
   - **IgM indicates acute infection →**
     may not be detectable early in the infection (Seroconversion)
   - **IgG *(not generally used for diagnosis)*** → *indicated previous exposure but not necessarily cause of acute infection*

Sexually Transmitted Infections– Serology/Testing

(continued)

7. Plating & Titers for specific condition →

Chlamydia & *N. Gonorrohea* often together

- Chocolate Agar or Thayer-Martin culture for *N. Gonorrohea*
- Chlamydia = Nucleic acid amplification test (NAAT)
  - *More sensitive & specific than other chlamydia tests*
  - **May use urine for both men & women (no pelvic exam rqd)**

Herpes Simplex and related

How should these conditions be classified?

Herpes Simplex Virus

- Double stranded DNA virus
- *Two forms:*
  - HSV-1 ("respiratory") and HSV-2 (direct contact)
  - First exposure between 6mo and 5 yrs for HSV1
  - **First exposure for HSV2 from 18-25 yrs**
    - **"Sexually Transmitted"**
  - Initially infects end point, then to ganglia where it's latent
  - **More than 80% of adults have antibodies but only 20-25% manifest disease**
  - Reactivation of latent virus
    - ***Occurs in 50% of patients in five (5) years***

Herpes Simplex – Other Considerations

- ***Keratitis → Epithelial (dendrite), Stromal (IK, disciform)***
- ***Uveitis***
- ***Trabeculitis → HIGH IOP Common***
  - Proposed assn with Glaucomatocyclitic crisis (GCC)/PSS
- ***Posterior segment/Opportunistic Infection associations***
  - Definite assn with ARN/BARN → Acute retinal necrosis/ Bilateral acute retinal necrosis
    - Rare
    - Exact pathological mechanism not completely understood
    - Postulated to be caused by one of the neurotropic human herpesviruses: HSV (type 1 or 2), VZV, or Epstein-Barr virus → Generally in IMMUNOCOMPROMISED individuals

Other Viral Etiologies: Conjunctivitis & Keratoconjunctivitis

Molluscum Contagiosum – Management

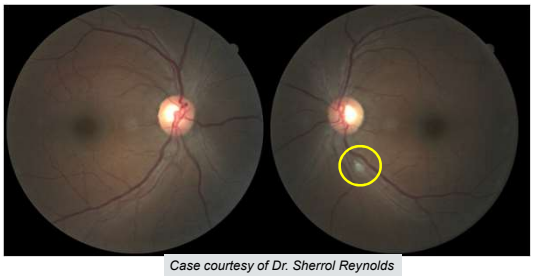
Ocular - Discussed previously in Case II

A Spot: Second opinion request

23-year-old African-American female

Presented after a doctor told her she had a "spot" on her retina of left eye one-week prior.

- *Denied symptoms of pain, floaters, flashes of light, trauma, systemic disease, medication use or smoking*



Case courtesy of Dr. Sherrol Reynolds

May end up as a case like this….

It started with some floaters I couldn't swat away….

32 yo African American Male

CC: …and now, Sudden loss of vision OS x 6 days

- HPI: Pt stated that four days - before visual loss - saw "floaters"-that he "tried to swat out of the way"
- (-) Flashes
- (-)HA, Ocular pain

Diagnosis →

Cytomegalovirus Retinitis OS & HIV Retinopathy

Pt immediately referred for retinal consult and Ganciclovir implant

Case courtesy of Dr. Julie Rodman

Case courtesy of Dr. Julie Rodman

HIV Infection

Human Immunodeficiency Virus (HIV) – retro-virus

- Results in immuno-compromised patient
- Different types and strains
  - HIV-1 and HIV-2 are two main types of HIV
  - HIV-1 = more prevalent & more pathogenic (*over 60 strains of HIV-1*)
    - Finding new strains of HIV-1 all the time
    - **The HIV-1 B strain most common in US.**
    - HIV-1 C strain most common Worldwide
  - HIV-2 found principally in western Africa

HIV Infection

Human Immunodeficiency Virus (HIV 1 and HIV 2)

–Current systemic standards

- CD 4 count
  - Healthy person = 500 to 1500 cells/mm^3
  - HIV positive: 300-500mm^3
  - AIDS = **200 or less mm^3***(OR Presence of AIDS defining OI)*
- Viral Load
  - *Goal = undetectable*

Acquired Immune Deficiency Syndrome (AIDS): Diagnosis

Originally an Acute disease →Now, Chronic disease

AIDS is defined as:

- CD 4 count = 200mm^3 or less

OR

- Presence of AIDS defining opportunistic infection

HIV Statistics for the USA

Number of people living with HIV:

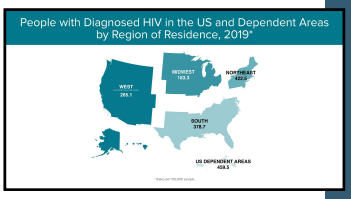
https://www.cdc.gov/hiv/testing/index.html

- United States – Est. 1,189,700 million people aged 13 and older had HIV in the US (*CDC Jun 2021 publ*)
  - **Over ONE in EIGHT are unaware of dx (~13%)**
  - **New Infections Diagnosis – Highest rate categories:**
    - Age group: 25-29
    - Among gay or bisexual men: 69% (decreasing from 83%)
    - Black/African-Americans: 42% new Dx, followed by Latin@ at 28.5%
    - Woman: 19%, esp of women of color

HIV Statistics for the USA

2019 – 36,801

- Florida leading the way in NEW Dx: 4, 378
- **Tend to concentrate in high risk groups… but the NATURE of these groups are changing**



HIV Infection & the Eye

Anterior segment manifestations –

- **DRY EYE symptoms**
- Opportunistic infection(OI)- Microsporidia
  - On cornea seen as (+)NaFl stain, diffuse and very small
  - **A group of unicellular intracellular parasites closely related to fungi**
- Another O.I. - *Molluscum contagiousum*
- Kaposi Sarcoma
  - Lid and/or bulbar & palpebral conjunctiva
  - Focal treatments
- Conjunctival microvasculopathy & *conjunctival squamous cell*
- Iridocyclitis

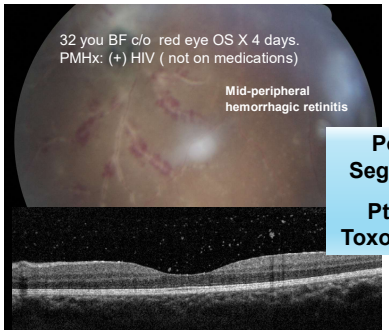
HIV Retinopathy – *MORE than just cotton wool spots*

- Microaneurysms
- Intra-retinal hemorrhages
- Telangiectatic vascular changes
- Areas of capillary nonperfusion
- Noninfectious optic nerve involvement: papilledema, anterior ischemic optic neuropathy, and optic atrophy

HIV Opportunistic infections (OI) – Posterior Segment Differential Dx

- **Cytomegalovirus Retinitis**
  - "Pizza fundus" with grossly hemorrhagic exudative necrotizing retina
- **Toxoplasmosis**
  - Classically presents w/ "yellow fundus lesion" (+) w/ vitritis
- **Acute Retinal Necrosis (ARN)**
  - Areas of necrotic peripheral retina, sparing the posterior pole
  - Prominent Vitritis & Vasculitis
- **Progressive Outer Retinal Necrosis (PORN)**
  - Areas of necrotic retina without vasculitis and vitritis

HIV Infection & the Eye



Posterior Segment OI –

Pt dx with Toxoplasmosis

Image/case courtesy of Dr. Sherrol Reynolds

HIV:
Posterior segment signs

Retinal Complications

- **Vasculitis**
  - **Periphlebitis – Inflammation of the outer coat of a vein/ tissue surrounding**
  - Frosted branch angioitis
- **Retinal Necrosis**
  - Acute Retinal Necrosis (ARN)/ Bilateral ARN (BARN)
  - Progressive Outer Retinal Necrosis (PORN)

CMV Retinitis Update (2019)

Still the most common intraocular opportunistic infection in HIV-infected patients

- Without proper treatment, CMV retinitis may result in blindness in less than SIX (6) months
- Overall prevalence of CMV has decreased
  - Yet persists, with between 10% and 20% of HIV-infected pts worldwide losing vision in one or both eyes as a result of CMV

CMV retinitis

Cytomegalovirus Retinitis

- Visual symptoms present in vast majority of cases, including decreased vision, **floaters**, or scotoma
- **Classic presentation =** Starts: Slow progression
  - Anterior segment → White and quiet
  - Posterior segment → Starts in periphery long vessels
    - Moves towards P. Pole = Lesions appear as full-retinal thickenness area of white granular opacification with associated retinal hemes
    - **Vitritis is minimal despite severe retinitis** (*secondary to low CD4 count*)
  - Unilateral initially → if untreated, 50% development in contralateral eye

CMV Retinitis Update (2019)

Diagnostic modalities - early detection & monitoring CMV

- **Fundus autofluorescence (FAF)**- differentiates active and inactive CMV retinitis
  - Specifically, **Hyper**FAF **at border of past CMV retinitis**
- **SD-OCT-** many possible findings:
  - Vitreoretinal interface (traction) and inflammatory precipitates, macular edema, foveal thickening or infarct, destruction of inner and outer retinal tissues from retinitis and RPE elevation or thinning, indicating choroidal involvement

Longitudinal Studies of the Complications of AIDS (LSOCA) – 1998-2013

- Initiated to study the occurrence of ocular complications among AIDS pts during HAART era, multiple publications
- Review and Results
  - Pre-HAART era, Hoover et al investigated the incidence to be ~ 25% (CD4 <100 mm^3) compared to LSOCA incidence of 7%
- ***Greatest risk factor for developing CMV retinitis was "severely immuno-compromised" state, specified as pts with CD4 counts <50 mm^3***

HIV Testing & Management

CD-4 count/ Viral Load provide guidance

- Management:
  - REGULAR testing of CD-4, Viral load
  - Prophylactic Antibiotic & Antiviral Treatments
  - Triple "cocktail" → HAART (*Highly Active AntiRetroviral Therapy*)
  - **Example: Modern HIV med = TRUVADA:** Combines TWO NRTIs (Nucleoside reverse transcriptase inhibitors) for HIV-1; also used for **"PrEP"**

NON-Positive pt/prevention: **PRE-exposure prophylaxis (PrEP) for HIV1 exposure risk/ must be HIV negative**

Neisseria Gonorrhoea

- Bacterial Conjunctivitis associated with systemic condition - *Neisseria Gonorrhoea*
  - Gram (-) diplococcus
- **Bacteria that can invade the intact cornea**
- Transmission
  - Neonatal conjunctivitis
  - Genital-hand-eye contact
- Diagnosis: Staining procedure requires Thayer-Martin or Chocolate agar

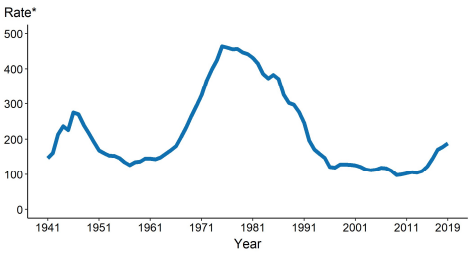
Neisseria Gonorrhoea

Characteristics of *N. Gonorrhoea* Conjunctivitis

- HYPERACUTE with copius mucopurulent discharge
- Lid edema and chemosis
- Anterior chamber reaction
- (+) Pre-auricular node associated w/ very severe acute response *(atypical for bacterial conj)*

Up to 5 days PRIOR to Hyperacute presentation may have mild conjunctivits

Gonorrhea — Rates of Reported Cases by Year, United States, 1941–2018



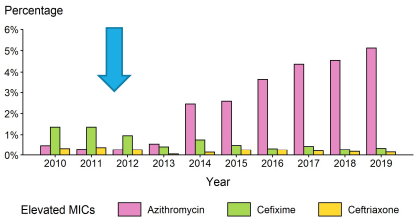
* Per 100,000.
NOTE: See section A1.3 in the Appendix for more information on gonorrhea case reporting.

Neisseria Gonorrhoea

<u>Treatment:</u> REQUIRES systemic AND topical medications

- <u>SYSTEMIC:</u>
  - 125mg IM Ceftriaxone – 1 dose (resistance)
    - *Ideally pt hospitalized for ceftriaxone IV w/in 12 to 24 hrs*
  - Penicillin IM BID x 10 days with 1g of Probenecid or Ampicillin 3.5g daily
  - CDC USED to recommended co-treatment for Chlamydia (1g Azithromycin) → BUT INCREASING RESISTENCE
- <u>TOPICAL:</u>
  - To protect cornea → Lavage and Antibiotic
  - Topical fluoroquinolone for protection (not direct tx)

Neisseria gonorrhoeae — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2010–2019



NOTE: Elevated MIC = Azithromycin: ≥ 2.0 µg/mL; Cefixime: ≥ 0.25 µg/mL; Ceftriaxone: ≥ 0.125 µg/mL

STI Statistics for the US

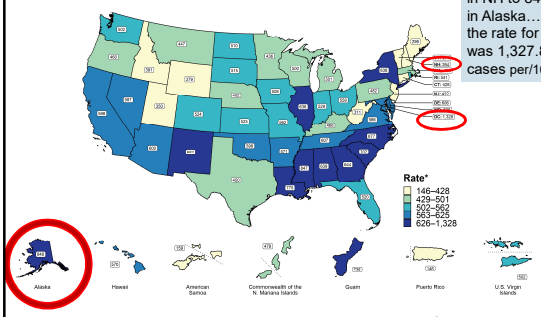
Chlamydia

- Increasing numbers of chlamydia infections lead to it being the most widespread STI in the USA

- May be due in part to expansion of screening:
  - Use of more sensitive screening tests
  - Improvements in the reporting system
  - Especially in women

Chlamydia — Rates of Reported Cases by State, United States and Territories, 2019

263.7 per/100,000 in NH to 848.1 per in Alaska… BUT the rate for DC was 1,327.8 cases per/100,000



* Per 100,000

Chlamydia

An intracellular obligate organism, having properties of both bacteria and virus

* Etiology- Bacterium *Chlamydia trachomatis* (most common), Chlamydia *psittaci, and Chlamydia pneumoniae*

Chlamydia

Chlamydia Related Conjunctivitis

- Different types of ocular manifestations:
  - **NIC = Neonatal Inclusion Conjunctivitis**
  - **AIC = Adult Inclusion Conjunctivitis**
    - Mixed Papillary and Follicular Conjunctivitis
  - **Chronic follicular conjunctivitis**
    - Lasting for > 16-28 days
  - **Trachoma-inclusion conjunctivitis (TRIC) agents**

Chlamydia: NIC

NEONATAL INCLUSION CONJUNCTIVITIS:

- Leading cause of neonatal conjunctivitis in the US
- Incubation 5 to 14 days
  - If mother positive ~ 50% develop conjunctivitis
- (+) watery discharge that becomes copious with thickened palpebral conjunctiva
- NO FOLLICLES / Other symptoms also lacking:
  - (-) fever
  - (-) lethargy
  - (-) irritability
    - *Hahn B, Giunta Y. Ann of Emer Med, Vol 49(6), June 07*

Chlamydia: AIC

ADULT INCLUSION CONJUNCTIVITIS:

- History:
  - Recent "new" sex partner within 4 to 8 weeks
  - Incubation ~5 to 12 days
  - Females often asymptomatic
  - **Often diagnosed because → Non-responsive with traditional antibiotic treatment**

Chlamydia: AIC

ADULT INCLUSION CONJUNCTIVITIS:

- Initial presentation:
  - Unilateral symptoms w/ mucopurulent discharge
  - Most commonly "acute" follicular conjunctivitis
    - Lower fornix
      → Becomes chronic, recurrent
  - *May have mixed response – papillae & follicles*
  - (+)PAN – mild

- **Second week may develop inferior keratitis with infiltrates and pannus. Lower fornix.**

Chlamydia: Trachoma

TRACHOMA – Non-STD variant

- Starts as chronic follicular, sup. palpebral conjunctivitis (and limbus)
- Followed by papillary hypertrophy
- Conjunctival scarring
  - **Bulbar Conjunctival Limbal follicles = HERBERT's PITS**
  - Palpebral = ARLT's Lines
- Conjunctival scarring may cause trichiasis & superior corneal involvement
- May lead to blindness….

Chlamydia

Adult Inclusion Testing = Cultures of conjunctiva

- Giemsa staining *(Basophilic intracytoplasmic epithelial inclusion bodies are seen with conjunctival scrapings)*
- Direct immunofluorescent (DFA) staining of the conjunctival scrapings, also useful (Syva MicroTrak)
- **Enzyme-linked immunosorbent assay**
  - MicroTrak (Syva Company)
  - Chlamydiazyme (Abbott Laboratories)
  - EIA (Pharmacia)
  - Kodak SureCell Chlamydia Test Kit (Kodak)
- Serum immunoglobulin G (IgG) titers to *Chlamydia* species may also be obtained

Chlamydia – Adult Treatment *

- **Trachoma:**
  - Oral Tetracycline: 250mg QID x 3 weeks with topical tetracycline ung 5x/day for one month
    - Avoid milk and DO NOT USE in pregnant patients
- **Adult Inclusion:**

IN JULY 2021 – THESE CHANGED

Doxycycline: 100mg BID x 1 dy
then100mg QD x 21 dys
Zithromax: 1g x 1day

Look for co-morbidity of other STDs

ɪen100mg QD x 21 dys
TDs

ycline in the treatment of inclusion
, 447-451.

Chlamydia – Adult Treatment

Topical → Consider

Azasite: Not specifically approved but….

- Recommended dosage regimen for the treatment of bacterial conjunctivitis :
  - Instill 1 drop in the affected eye(s) BID daily, 8-12 hours apart, for the first 2 days & then instill 1 drop in the affected eye(s) once daily for the next 5 dys
  - http://www.azasite.com/hcp/overview.html

Chlamydia– Vaccine Progress….

Because Chlamydia:

1) Easily treated when identified and
2) If untreated 1/6 women who are infected suffer with pelvic inflammatory disease with complications

HIGHLY beneficial to develop a Vaccine

Phase 1 Studies completed with 35 healthy female→ Aug 2019

- All women who received a vaccine produced antibodies to chlamydia → with one formula out performing the other → produced nearly six times more antibodies
- SE: injection site pain and tenderness, 2-4 days
- But one in six women who get the infection will suffer from

Syphilis

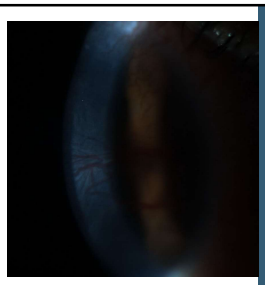
General Information

- Characterized as "the great imitator"
  - Why? Because it can manifest in any area within the eye
  - Other "great imitator" → LYME, also caused by treponema infection
    - *Thus cross rxn with FTA-ABS*
- Caused by a SPIROCHETE, *Treponema Pallidum*
- May be Congenital vs. Acquired

Syphilis

General Information –
The Great Imitator

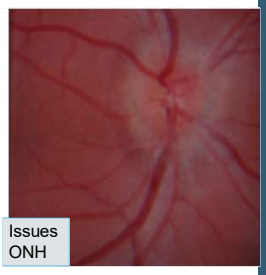
- *Multiple areas of ocular manifestation*
  - Conjunctivitis
  - **Interstitial keratitis (IK)**
  - Episcleritis
  - Scleritis
  - **Uveitis (most common)**
  - Retinitis/Chorioretinitis



Syphilis

General Information –
The Great Imitator

- *Multiple areas of ocular manifestations-->*
  - *Vasculitis*
  - *Vitritis*
  - *Panuveitis*
  - ***ONH changes***
  - *Pupillary anomalies*
  - *VF defects*
  - *CN involvement*



Syphilis

CONGENITAL Infection

- Transplacental transmission
  - 2nd/3rd trimester
  - 60% Mortality rate
  - Manifest at two - ten weeks of age
- Physical findings:
  - Rash & papular lesions around mouth & nose

CDC/ Dr. Norman Cole - The image comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #2246.

Syphilis

ACQUIRED Infection

- Access body through mucous membranes or skin
- Reaches lymph nodes within hours and spreads throughout the body
- Transmission usually through sexual transmission
  - Initial incubation: 1-13 weeks, average 1 mo.
- **THREE ACTIVE stages**

Syphilis

ACQUIRED Infection --Three stages

- Primary: Chancre lesion at inoculation site (~1mo)
  - Spirochete entering blood stream and lymph system
  - Painless
  - Generally, genital area
  - Others (see image) : tongue
  - Appears approximately 1 month
  - Resolves 1 to 2 months

Image credit: CDC/ Robert E. Sumpter, 1967

Syphilis

ACQUIRED Infection --Three ACTIVE stages

- Secondary: Cutaneous rash. (~1.5 to 3 months)
  - May resolve or persist for months
  - Lymphadenopathy, fever & general malaise
  - Generalized rash
    - INVOLVES PALMS OF HANDS/SOLES OF FEET
    - → "Palmar" rash
  - **Ocular presentation ~ 10%**

Syphilis

ACQUIRED Infection –

- Secondary:

https://www.cdc.gov/std/syphilis/images/rash-gbr.htm

Syphilis

ACQUIRED Infection --Three Active stages… but also

LATENT Syphilis

- Clinically undetectable
- Can persist for many years

Syphilis

ACQUIRED Infection --Three stages

- Tertiary:
  - Benign lesions of skin, bone, viscera (Gumma) @ 3 -10 yrs
    - Generalized rash persistence
  - Cardiac issues
  - Tabes Dorsalis
  - NEUROSYPHILIS
    - Argyll-Robertson Pupil, Optic neuropathy, Uveitis

Syphilis

Testing/ Diagnosis → IN THEORY

- *Microscopic bacterial identification:*
  - A surface scraping from the ulcer or chancre may be taken and identified → *Generally not available in most environments*

Testing/ Diagnosis → IN PRACTICE recommend Laboratory SEROLOGY with one of each of the two main categories for testing Non-treponemal tests (NPT) and a Treponemal test (TT)

Syphilis – Serology: Two main categories

Nontreponemal Tests (NTT)

- Measure antibodies against specific antigens released by damaged host cells
- Examples: RPR (rapid plasma reagin), VDRL (venereal disease research laboratory)
- **Most useful test to track active disease and treatment efficacy**

Treponemal Tests (TT)

- Measure antibodies against specific *Treponema pallidum* proteins, **Positive for life**
- Examples: **EIA** (enzyme immunoassay), **FTA-ABS**
  - TPPA (*T pallidum* particle agglutination), TPHA (Treponema pallidum hemagglutination)

ANOTHER IMPACT OF COVID – Some test/lab kits unavailable

Syphilis – Testing/Diagnosis

Laboratory testing:

Reverse Sequence Screening for Syphilis - The Advantages and Limitations Compared with the Traditional Algorithm

- Theel ES, Binnicker MJ, Clinical laboratory news (Nov 2014)
  - **EIA test = Enzyme immunoassay (updated standard)**

Syphilis – Testing/Diagnosis

Laboratory testing:

- **EIA test = Enzyme immunoassay (updated standard)**
- VDRL (Venereal Disease Research Laboratory) or RPR (Rapid Plasma Reagin)
  - **Tests for active infection → To screen and follow**
- FTA-ABS (Fluorescent Treponemal Antibody-Absorption)
  - **Will ALWAYS be positive throughout a person's life**
  - Blood or spinal fluid
  - **May result in a cross-reactivity/false-positive w/Lyme**
  - **False (+) may occur in females with Lupus (SLE)**
- TPHA = Treponemal pallidum hemaglutination assay
- TPPA

Syphilis – Treatment (adults/ adolescents)

- Primary, secondary, or early latent disease: penicillin G 2.4 mill. units IM, **single dose**
- Late latent syphilis or latent syphilis of unknown duration: penicillin G 2.4 mill units IM, **each at weekly intervals x 3 weeks**
- **Neurosyphilis and ocular syphilis** → Aqueous crystalline penicillin G 18-24 mill units/dy, administered as 3-4 mill units **intravenously** q4h or continuous infusion, 10-14 dy
- Or, Tetracycline 500mg QID PO x 15 *or Erythromicin + **Probenicid***

	Chlamydia	Gonorrhoea	Syphilis
What it is?	Intracellular obligate parasite	Bacteria, N. Gonorrhoea	Spirochete, *Treponema Palllidum*
Clinical findings	Recurrent conjunctivitis, Mixed papillary/follicular response, Herbert's pits	Hyperpurulent conjunctivits, papillary response	Chancre, Skin rash, Argyll Robertson Pupil, IK
Microscopic findings	Inclusion bodies	(+) Thayer-Martin, Chocolate agar	Spirochete

Thank you for your time

References:

1. New CDC analysis shows steep and sustained increases in STDs in recent years. CDC, 2018
2. https://www.cdc.gov/std/treatment-guidelines/wall-chart.pdf (accessed Aug 3, 2021)
3. CDC. Fact Sheet: Today's HIV/AIDS Epidemic: June 2021 (accessed Aug 2021)
4. https://www.cdc.gov/std/treatment-guidelines/gonorrhea-adults.htm (accessed Aug 3, 2021)
5. https://www.std.uw.edu/National STD curriculum (accessed Aug 3, 2021)
6. 2019-STD-Surveillence-All-Slides.PPT (accessed Aug 3, 2021)

Thank you for your attention

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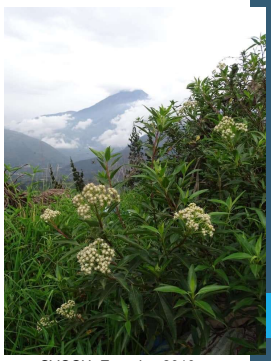

SVOSH, Ecuador, 2019