UPDATE ON STIs

46TH VAIL OB/GYN CONFERENCE
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VAIL, CO
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• I have no conflicts to declare

Learning Objectives
• Apply recommended screening guidelines
• Implement EPT as appropriate
• Describe Pre-Exposure mitigation of STIs
• Recognize threat of antimicrobial resistance
The Bad News

• WHO: 357 M new infections w Ng, Ct, Tv, or Syphilis/yr or IM/ID

• US: 35,000 new cases syphilis 2018, steady increase from historic low 2000: 36% 2017-18
  71% since 2014
• Congenital syphilis on the rise, 1300 cases in 2018 40% increase

• US: 800,000 Ng/yr 75% since 2009 low.
  20% since 2016

• US: 1.8 M new cases of Ct infections in 2018 19% since 2014
• Cost $700M/year
• One half (if not more) occur in persons aged 15 to 24 years.

Why Are STI Rates on the Incline?

• Drug Use- Opioid epidemic
  – Directly to shared drug paraphernalia use
  – Associated lifestyle
• Limited access to care for disenfranchised populations
• Budget cuts/financial constraints placed on STD programs. Limits Tx, Screening and Follow-up
• Reduced safe sex practice and condom use in vulnerable populations
How to Correct This?

- Identification of infected persons: Screening
- Evaluation, Tx and Counseling of partners: EPT
- Pre-Exposure Prophylaxis and Immunization
- Effective Dx and Tx ( Threatened by resistant organisms)

2015 CDC STD Screening Recommendations

[Table Image]

2015 CDC STD Screening Recommendations

[Table Image]
Special Populations

**Pregnancy** - Routinely screen:

- **HIV**. retest 3rd tri. if high risk, and rapid HIV in labor w/o documentation
- **Syphilis**. retest 3rd tri. if high risk
- **Hep B**. Retest at admission for L&D if high risk (mult partners, IVDA, other STIs, partner with Hep etc.)
- **Ng**. retest 3rd tri. if high risk and if tx’d early in preg.
- **Ct**. retest 3rd tri. if high risk, <25 and if tx’d early in preg.
- **Pap**- as indicated per screening guidelines (?HPV)
- **Hep C**. if high risk- IVDA, Transfusion or Transplant <92

Special Populations cont’d

**Female Adolescents**: (Demographic with highest rate of Ct and Gc. Very high if not highest for HPV)

- Confidential care for STIs can be provided in all states. (dependents in health insurance plans may not remain confidential)
- Yearly screening for Ct. <25
- Yearly screening for Ng. <25 at risk. (age being a risk)
- HIV should be discussed

Partner Management: Expedited Partner Therapy (EPT)

- Data limited for benefit of reducing prevalence/incidence w/ partner *notification*
- When partners are tx’d patients have reduced re-infection rate
- EPT: Partners are tx’d without evaluation or counseling
- Evidence for Ct. reduced by 20% and Gc. by 50% with EPT. ? Benefit for TV.
Pre-Exposure Strategies

- PrEP. Although evidence is can backfire: providers withhold, fearing increase # partners or reduce barrier contraception efforts
- HAART to undetectable VL U=U
- HPV Vaccine: Nonavalent vaccine approved for females and males 9-26-45
- Hep B Vaccine for all uninfected pts evaluated for STIs.
- Hep A & B vaccine for MSM, IVDA and HIV
AMR: Antimicrobial Resistance

- WW 10 Million Deaths in 2050, $100Trillion
- 35,000 deaths/yr in US currently (increasing)
- Stewardship on Abx guidance in agriculture, aquaculture, industry, manufacturing, sewage/disposal and healthcare
- Global awareness on infection control, advances in hygiene, improved vaccination and diagnostics, appropriate provision
- R&D on future Anti-Biologics
  - Support, collaboration and recruitment scientists
- Awareness

CDC: Antibiotic Resistance Threat

- Highest Risk:
  - *Clostridioides difficile*
  - *Acinetobacter*
  - Candida auris
  - *Enterobacteriaceae*
  - *Neisseria gonorrhoeae*
- Serious Threats:
  - *MRSA*, S pneumoniae, M tuberculosis, Salmonella, VRE*, *P aeruginosa*, Shigella, Campylobacter
- Potential Risks:
  - Aspergillus, *M genitalium*, B pertussis, GAS, GBS

Antibiotic-Resistant N. gonorrhoeae (ARNG)

- Sulfa, PCN, 1st Ceph, Tetracycline, Macrolides all Hx.
- CDC had recommended single dose quinolones beginning 1993.
- By 2006, resistance or intermediate resistance had increased to 14% (compared with 2% in 2000) for United States
- 2007 Quinolones no longer recommended
Antibiotic-Resistant N. gonorrhoeae (ARNG)

- Gonococcal isolate Surveillance Project (GISP)
- 2014-2017 Ng isolates with elevated MIC Azithro doubled 2.5-4.4%
- 2017: 0.2% Ng isolates with elevated MIC to Ceftriaxone
- Oral cephalosporin Tx failures reported in Asia
- Because of concern 250 mg Ceftriaxone is recommended dose.

Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum*

**Recommended Regimens**

Ceftriaxone 250 mg in a single intramuscular (IM) dose
OR, IF NOT AN OPTION
Cefixime 400 mg in a single oral dose
PLUS
Azithromycin 1 gm po

Dual therapy recommended even if Ct negative for greater effectiveness with possible resistance.

N. gonorrhoeae

- Follow-up – If diagnosed with uncomplicated gonorrhea and treated with recommended regimens, no test of cure routinely needed.
  Retest at 3 months for re-infection (not failed therapy).
- **Any person should be rescreened 3 mos. After Tx for Gc, Ct, Tv.
  (If pregnant- TOC and retest3rd trimester)
- Partners –EPT: Dual therapy with oral agents (Cefixime and Azithro) or Instruct patients to refer partners for evaluation, testing, and treatment.
**N. gonorrhoeae: What if?**

- **Severe allergy**
  - Gentamicin 240 mg IM + azithromycin 2 g PO, or
  - Gemifloxacin 320 mg PO + azithromycin 2 g PO

- **Increasing resistance?**
  - Zoliflodacin
  - Gepotidacin
  - Solithromycin
  - Delafloxacin
  - Fosfomycin

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**Gonorrhea Tx**

- Zoliflodacin- Inhibits DNA synthesis
- 179 & 179 RCT 2 or 3 g Zoliflodacin Vs 500 mg IM Ceftriaxone. 3 g Zol and Ceft 100% vs 98%
  - 2 g Zol cured by negative Cx.
- All 3 regimen cured 13 pts with anorectal Ng
- However Pharyngeal site: 67% 2 g zol
  - 78% 3 g zol
  - 100% Ceft
- In phase III testing

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**Gonorrhea Tx**

- Gepotidacin: Bacterial Topoisomerase inhibitor
- RCT 69 & 69 received 1500 or 3000mg
  - Microbial eradication 96%uro-gen
  - 50% pharyngeal
  - 100% rectal
- All of the Tx failures were Resistant to Cipro and harbored mutations for abx binding site
- In phase III studies
Gonorrhea Tx

- Solithromycin: fluoroketolide w activity against Ng, Ct, and M gen.
- Phase 2 study with 100% efficacy in urogen/rectal and oral sites.
- Limiting liver effects and infusion site infection
- NIAID phase III study revealed no difference compared to Ceftriaxone/Azithro

Gonorrhea Tx

- Ertapenem: Carbapenem
- Comparable efficacy to Ceftriaxone and Cefixime
- Ongoing phase III study comparing Ertapenem/Fosfomycin/Gentamycin/Ceftriaxone for anogenital Ng
- Concern for exposure to non-target organisms and resistance

Gonorrhea Tx

- Fosfomycin
- Encouraging In-Vitro activity against multi-drug resistant Ng.
- Has led to resistant Gram-negative organisms when used as monotherapy
- Ongoing studies for combination use with Cipro and Azithro
Gonorrhea Tx

- Spectinomycin: originally used in 60s but resistance evolved and its use D/Cd
- New class Aminomethyl Spectinomycin has demonstrated greater efficacy for Ng and also Ct and being tested

Prevention Developments

- NIH renewing interest and resources for Vaccine development.
  - 2018 $9M RFA for 3-5 awards
- PrEP and PEP for other STIs

Doxycycline

- Pilot study demonstrating efficacy as STI-PrEP
- Small study 30 MSM and Transgender Women
- 70% decrease in Tx group for Tp/Ct/Gc
- Substudy of Ipergay with Post exposure Doxy:
  - 232 MSM, Tx group 200 mg Doxy after episodes
  - 70% decrease in Tp/Ct but not Ng
Doxycycline

- BC CDC
  - Study using Doxy PrEP for Syphilis in HIV negative MSM also on HIV-PrEP
  - Study using daily Doxy for Syphilis prevention in 288 MSM HIV+
- Australia
  - Study using 100mg Doxy daily in 125 MSM or BM to reduce Tp/Gc/Ct

Vaccine Research

- Retrospective case-control study of 15,000 young adults received MnB vaccine during an epidemic and were 31% less likely to be Dxd with Ng compared to Ct.
  - Same study demonstrated 45% decrease compared to Non-vaccine recipients
- Research at OHSU have identified proteins from cell envelope and cytoplasm that are present in all resistant strains of Ng and using these as targets for new therapies

Vaccine Research

- Researchers believe natural Ct infection can lead to immunity and explains why adolescents have higher infections rates than older persons
- Some data show young women with spontaneous clearance are resistant to re-infection
- Potential promise with Chlamydial antigen BD584 as vaccine candidate
Vaccine Research

- UK has several phase I chlamydial vaccine trials.
- Efforts have identified common antigens on Treponema outer membrane which are preserved across strains and may serve as a vaccine target.
- Cross protection among syphilis strains seems to be lacking and previously infected individuals are susceptible to future infection with different strains.