What’s New in Infectious Disease Rx?

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What Happened to the Arbovirus Threat?

Chikungunya

- Fever, arthralgia/myalgia, headache, maculopapular eruption
- 2006-2013 average ~30 US people; returning travelers from Africa, Asia, Indian Ocean
- Late 2013: Few local cases in travelers from Caribbean
- 2014: Local cases in Puerto Rico, Caribbean and Florida (12)
  Total USA cases 2811
- 2015: One local case in Texas; Total USA cases 896
- 2016: NO local cases in USA; Total USA cases 248
- 2017: NO local cases in USA; Total USA cases 104
  Only 33 local cases in PR

Zika

- Fever, arthralgia/myalgia, headache, maculopapular eruption, conjunctivitis; babies: microcephaly, eye & CNS problems


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<th>DRUG</th>
<th>APPROVAL DATE</th>
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<tr>
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<td>Dec 14, 2016</td>
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<tr>
<td>Dupilumab (Dupixent®)</td>
<td>Mar 28, 2017</td>
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<tr>
<td>Guselkumab (Tremfya®)</td>
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**New Antibiotic: Delafloxacin (Baxdela®)**

- Fluorinated quinolone
- MOA: Inhibits bacterial DNA replication
- Wide spectrum activity Gr+ and Gr- organisms
- Includes: MRSA, MSSA, Strep pyogenes, E. coli, Pseudomonas aeruginosa, Enterobacter, Klebsiella
- Approved ABSSSI in June, 2017
- Available IV (unit dose 300mg) and Oral (unit dose 450mg)

**Utility?**

- Tested IV (300mg Q12h) or oral (450mg Q12h)
- Oral followed 3 days IV loading dose
- Active comparator: Vancomycin + Aztreonam
- N = 1510 in both studies combined
- Statistically non-inferior to combination
- AEs: Nausea, vomiting, diarrhea, headache, ↑LFTs
- BLACK BOX: Tendinitis and tendon rupture, Peripheral neuropathy, CNS effects

**Why Is New Impetigo Drug Important?**

- High level resistance to mupirocin reported
- Conjugal (mupA) and nonconjugal (mupB) genes in Streptococci and Staphylococci confer resistance (alternate isoleucyl-tRNA synthetases)
- Mupirocin resistance is a worldwide phenomenon: recent papers from China, France, India, Chicago

**Ozenoxacin (Xepi®): Approved 12-14-17**

- Non-fluorinated quinolone
- Developed as 1% ointment for impetigo
- Dosed: BID x 5 days
- Wide spectrum of activity against relevant Gram+ microbes, including MSSA, MRSA, mupirocin and ciprofloxacin resistant Staphylococci, Strep. Pyogenes
- Superior to placebo, and non-inferior retapamulin
- N=875 in two international studies, age ≥ 2 months

**Chagas Disease**

- "American trypanosomiasis"
- T. cruzi
- Spread by reduviid bugs
- 10-30% risk progressive dis
- Megacolon
- Megaesophagus
- Cardiomyopathy
- Rarely dementia
**Benznidazole (No brand name)**

- Rx children 2-12 (and adults) w/ Chagas disease (acute or chronic)
- Parasitological cure better: younger age and acute disease (vs chronic) 60-90%
- Destroys parasite DNA
- 5-8 mg/kg/d in divided doses for 60 days
- 12.5 and 100mg tablets
- Peripheral neuropathy
- Bone marrow depression
- Hypersensitivity reactions

**New Zoster Vaccine (Shingrix®)**

- VZV subunit vaccine for shingles (not live attenuated)
- Glycoprotein E antigen + adjuvant; TWO doses, IM @ 0, 2-6mo
- ACIP voted (8-7) to FAVOR use of this over existing HZ vaccine
- Indicated for 50; EVEN if given prior vaccine, OK to revaccinate
- 91-97% effective across ALL AGES; 4 year study (6 year Ab+)
- 88% effective reduction of PHN
- Use in HIV+ inconclusive, although appears positive
- AEs: injection site reactions, systemic side effects (Gr 3: 5-10%)

**Therapeutic Concepts**

- Hurricane Harvey
- Hurricane Irma
- Hurricane Maria
Leptospirosis

- Common, serious zoonosis; Leptospira spp (21 species)
- ~1,000,000 cases and 60,000 deaths yearly worldwide
- 5-15% mortality rate
- Exposure to water contaminated with animal urine
  - Most commonly rodents (rats, mice)
  - Swallow contaminated water; exposure via skin cuts
- Most common in SE Asia; Associated with floods!
- Initial: Fever, chills, headache, myalgia, conjunctivitis, non-specific maculopapular eruption (90% resolve)
- Progressive: Hepatic and renal failure, pulmonary hemorrhage, meningencephalitis; death!

Leptospirosis: Chemoprophylaxis

- Comprehensive review and meta-analysis
- Doxycycline most widely used drug
- Single dose 200mg OR 200mg/week for 2-4 weeks
- PRE-exposure dosage significantly reduces morbidity and mortality
- POST-exposure dosage trends toward benefit but often not statistically significant

Flood is coming? Take 200mg Doxycycline!

Post-Exposure Bacterial Prophylaxis?

- French study; MSM who have condomless sexual contact
- All receiving PRE-exposure HIV prophylaxis w/ antiretroviral
- Randomized: Single dose doxycycline 200mg within 24 hours versus no antibiotic within 24 hours of sexual contact (n=316 per group)
- Followup: 10 months; Occurrence of chlamydia, GC, syphilis
  - 22% presented with bacterial STD in prophylaxis group
  - 42% presenting with bacterial STD in NO prophylaxis group (p =0.007)
- Adverse GI events: 53% PEP vs. 41% NO PEP (not stat signif)
HIV DNA levels in 229 varied autopsy tissues from 20 HIV+ cART-treated study participants with low or undetectable plasma VL.

HIV-DNA found in brain, spleen, liver, lung and kidney.

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cART and HIV

- Three year prospective US study: ALARMING
- Followed serially 230 HIV+ men on appropriate cART
- ALL had CD4 counts > 600, NONE were symptomatic
- Undetectable HIV-RNA in blood in ALL subjects, BUT.....
- 35% of subjects had AT LEAST ONE HIV-RNA+ semen
  - Regardless of type of cART
- Message: Current antiretroviral treatment strategies do not eliminate HIV from semen as effectively as they eliminate HIV in blood.

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What ABOUT SMALLER Abscess?

Is surgery (Incision/drainage) sufficient, without ABX?

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Is surgery enough?

- Multicenter, prospective, double-blind trial involving outpatient adults and children
- Surgically drainable abscesses ≤ 5 cm (smaller for kids: 3-4 cm)
- After I&D: randomly assigned clindamycin (150mg BID), TMP-SMX (standard BID), or placebo BID for 10 days
- Clinical cure assessed 7-10 days after treatment
- n = 786 participants: 64.2% adults, 35.8% children
- S. aureus 67%, with MRSA isolated from 49.4%
- Clinical cure: Clinda 83.1%, TMP-SMX 81.7% No Abx 68.9%

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What’s New in ID? Thanks for your attention!

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