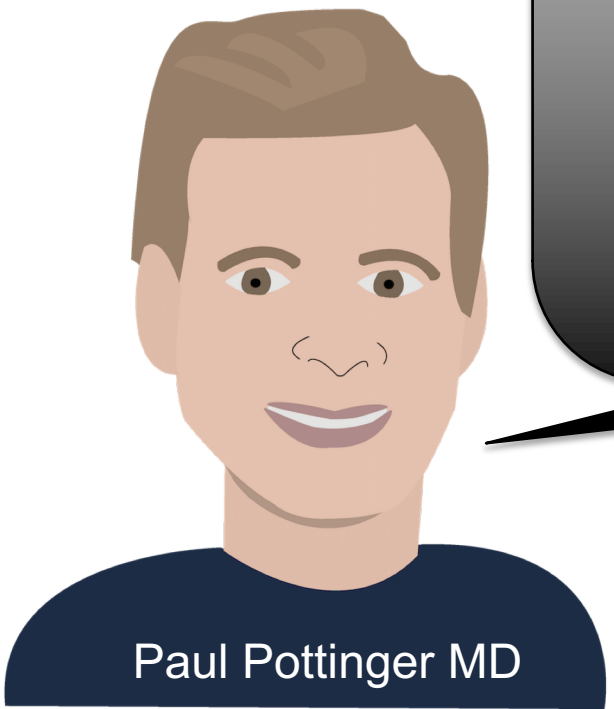
UW TASP tele-antimicrobial stewardship program | echo

Anaerobic Coverage: *Use Just What You Need*

Paul Pottinger, MD, FACP, FIDSA
Professor
University of Washington School of Medicine
UW Medical Center

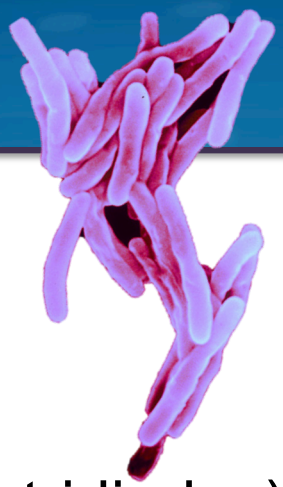
October 8, 2019

Disclosures



- No financial conflicts of interest
- Everything we discuss is QI, thus protected from legal discovery under WA State Code

Anaerobes: *Our Helpful Friends*



Bacteria that thrive in low oxygen tension

1. "Strict"
   Must live in absence of oxygen (Bacteroides, Clostridiodes)

2. "Capnophilic"
   Tolerate oxygen but prefer only small amounts (Oral strep)

3. "Facultative"
   Groove on oxygen, can go anaerobic if they must (E.coli)

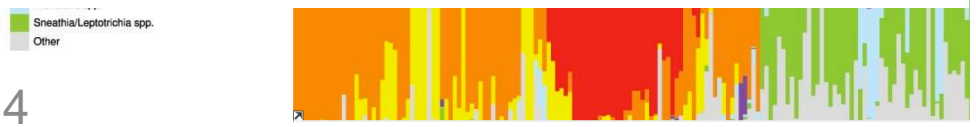
Anaerobes: *Our Helpful Friends*

Vital Part of the Human Microbiota

Benefits…

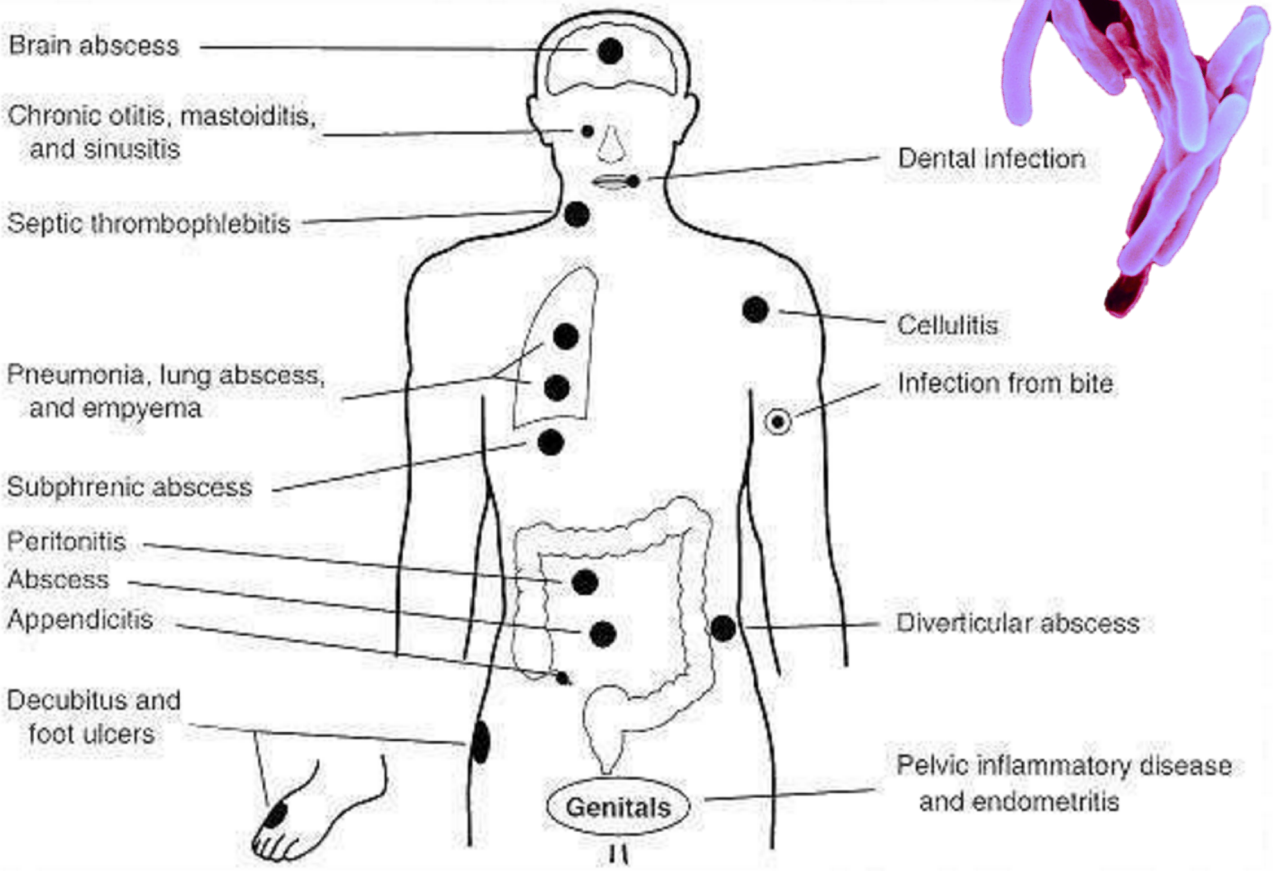
1. Digestion of food
2. Repel candidiasis
3. Reduce UTI risk
4. Reduce *C.difficile* risk
5. ?Autoimmune reduction?

Abx Collateral Damage?



Anaerobes: *Frenemies?*

Problems may arise…



Anaerobes: *When to Kill Them?*

"Only when you must"

1. <u>Guided Therapy</u>
   Proven anaerobic infection
   (culture-positive from sterile site)

2. <u>Empiric Therapy</u>
   Suspected anaerobic infection
   (e.g. abdominal source of sepsis)

1. <u>Above Diaphragm</u>

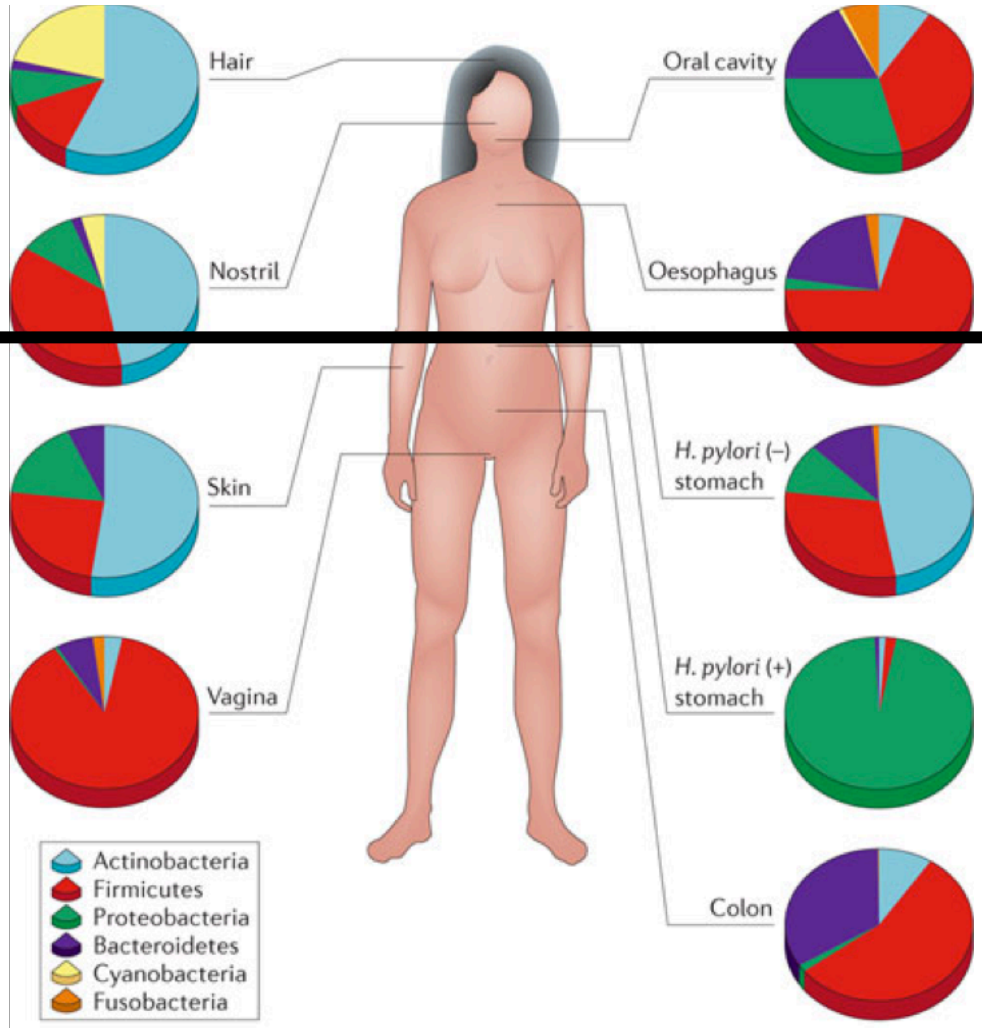
   Oral, Respiratory

   (Strep, Eikenella, Fusobacterium)

2. <u>Below Diaphragm</u>

   Colon (Bacteroides)

Anatomic Diversity of Anaerobes



1. <u>Above Diaphragm</u>
   Oral, Respiratory
   (Strep, Eikenella, Fusobacterium)

PO	IV
Amox-Clav	Amp-Sulbact
Clindamycin	Clindamycin
+/- Moxiflox	+/- Moxiflox

2. <u>Below Diaphragm</u>
   Colon (Bacteroides)

PO	IV
Metronidazole	Metronidazole

IV
Pip-Tazo
Ertapenem
Imipenem
Meropenem
Doripenem

Anaerobes: *Coverage Reliability?*

"Almost Perfect Reliability"

- Oral anaerobes "virtually always" susceptible to clindamycin or amox-clav.

- *B.fragilis* "virtually always" susceptible to metro, pip-tazo, carbapenems.

Pan-Resistant Organism: *B.fragilis*

That ain’t right…

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 62 / No. 34
August 30, 2013

Multidrug-Resistant *Bacteroides fragilis* — Seattle, Washington, 2013

The *Bacteroides fragilis* group consists of species of obligate anaerobic bacteria that inhabit the human gut. They are among the leading pathogens isolated in the setting of intra-abdominal infections. *B. fragilis* strains, especially in the United States, are virtually always susceptible to metronidazole, carbapenems, and beta-lactam antibiotics (*1*). Although isolated cases of resistance to single agents have been reported, multidrug-resistant (MDR) *B. fragilis* strains are exceptionally rare (*1,2*). In May 2013, an MDR *B. fragilis* strain was isolated from the bloodstream and intra-abdominal abscesses of a patient who had recently received health care in India. This is only the second published case of MDR *B. fragilis* in the United States. This report summarizes the case and highlights the need for awareness of multidrug-resistant organisms (MDROs) in returning travelers who have received inpatient medical care outside the United States, both for timely implementation of proper infection control measures and to ensure administration of appropriate antimicrobials.

count of 25,000/μL. Blood cultures were obtained but yielded no growth. A CT scan of the abdomen revealed multiple fluid collections suggesting abscesses. Vancomycin and piperacillin/tazobactam were initiated, and the patient underwent radiographically guided percutaneous drainage. The fluid grew a pan-susceptible *Escherichia coli,* and antibiotics were narrowed to ceftriaxone. The leukocyte count improved initially, but then increased again several days later. Repeat blood cultures drawn through a central catheter showed anaerobic gram-negative rods, and piperacillin/tazobactam coverage was restarted. Follow-up blood cultures drawn 2 days later demonstrated no growth. A repeat CT scan for persistent fever, 10 days after drain placement, demonstrated a ring-enhancing fluid collection in the abdomen and right flank and pelvic fluid collections. Vancomycin was added to the patient's antimicrobial regimen, and an additional percutaneous drain was placed. Fluid was sent immediately for microbiologic testing. Gram stain of the fluid revealed 4+ polymorphonuclear cells and 3+ gram-negative bacilli, with a pure culture of anaerobic

Characterizat
Novel Bac

**Stephen J. Salipante,[1] Aley K
Paul S. Pottinger, Daniel R. Ho
Lisa Cummings, Jeffrey S. I
Dhruba J. Sengupta, Steven A
Brad T. Cookson, and Susan M.**

Metronidazole- and carbapenem-resist *fragilis* are rare in the United States. We drug-resistant anaerobe from the bloodstr dominal abscesses of a patient who had Whole-genome sequencing identified the novel *Bacteroides* genomospecies. Phys aware of the possibility for concomitant c metronidazole-resistant *Bacteroides* infec

We previously reported a 2013 case c abscesses and bacteremia caused resistant anaerobe identified as *Bacteroid* brief, unremitting abdominal pain develo old man who had been traveling in India man was hospitalized locally and subseq diagnosis of metastatic colon adenocarcin to Seattle, Washington, USA, for treatme cycles of chemotherapy, followed by righ and right hepatectomy. On postoperative showed marked leukocytosis, and abdc were noted on computed tomographic s tured percutaneous drainage fluid grew that was resistant to ampicillin, trimethop azole, and fluoroquinolones. Therapy wa ceftriaxone, and the patient's leukocyte to rise and fever returned. Blood culture gram-negative rods identified as *B. frag* TOF (matrix-assisted laser desorption ic flight) mass spectrometry and 16S rRNA rim-enhancing fluid collections in the abc were noted on computed tomographic s percutaneous drainage fluid from these 3+ (moderate) quantities of *B. fragilis*. Is culture and abscess fluid were resistant tc

Author Affiliations: University of Washington, Se USA (S.J. Salipante, A. Kalapila, P.S. Pottinger, Hoogestraat, L. Cummings, J.S. Duchin, D.J. S Pergam, B.T. Cookson, S.M. Butler-Wu); and F Cancer Research Center, Seattle (A. Kalapila, S

DOI: http://dx.doi.org/10.3201/eid2101.140662

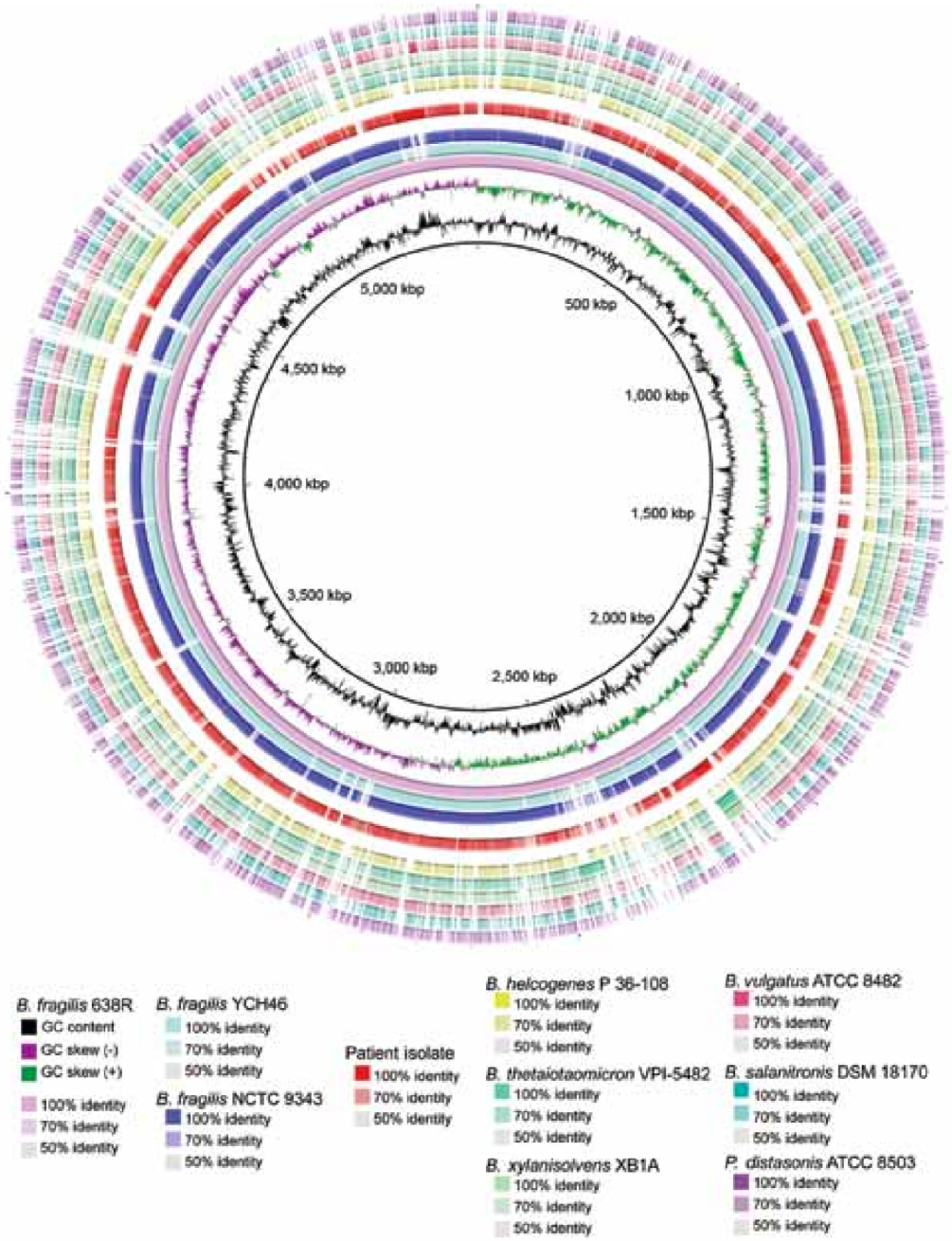


Figure. Characterization of circular plot of genome diversity between the clinical isolate of a multidrug-resistant, novel *Bacteroides* genomospecies and other *Bacteroides* spp. isolates. Reading from the center outwards, the map, GC content, and GC skew of the *B. fragilis* reference strain 638R are depicted. The white and colored regions of the following outer rings indicate regions absent and present, respectively, in genomes of the indicated organism compared with the genome of *B. fragilis* reference strain 638R. Intensity of coloration is proportional to the degree of sequence identity relative to the reference genome. The innermost 3 rings indicate the 3 *B. fragilis* reference genomes. The genome of the clinical isolate, separated from other rings by white space, follows. Non-*fragilis Bacteroides* species and a *Parabacteroides* species comprise the outermost rings. ATCC, American Type Culture Collection; DSM, Deutsche Sammlung von Mikroorganismen; NCTC, National Collection of Type Cultures.

The WHO priority list

PRIORITY: CRITICAL

- **Acinetobacter baumannii** carbapenem-resistant
- **Pseudomonas aeruginosa** carbapenem-resistant
- **Enterobacteriaceae** carbapenem-resistant, ESBL-producing

PRIORITY 2: HIGH

- **Enterococcus faecium** vancomycin-resistant
- **Staphylococcus aureus** methicillin-resistant vancomycin-intermediate and resistant
- **Helicobacter pylori** clarithromycin-resistant
- **Campylobacter spp.** fluoroquinolone-resistant
- **Salmonellae** fluoroquinolone-resistant
- **Neisseria gonorrhoeae** cephalosporin-resistant fluoroquinolone-resistant

PRIORITY 3: MEDIUM

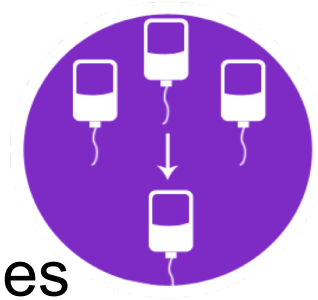
- **Streptococcus pneumoniae** penicillin-non-susceptible
- **Haemophilus influenzae** ampicillin-resistant
- **Shigella spp.** fluoroquinolone-resistant

Source: WHO

WHO's list of the 12 most threatening pathogens includes (from left) *Staphylococcus aureus* (causing skin infections, pneumonia and bloodstream infections), *Pseudomonas aeruginosa* (causing blood infections, pneumonia, infections after surgery) and *Neisseria gonorrhoeae* (causing the sexually transmitted disease gonorrhea).

NIAID, NIH Image Gallery/Flickr

Anaerobes: *De-Escalation Opportunities*



"One and Done"

- Very rarely necessary to "double cover" anaerobes

  Pip-Tazo + Metro is one drug too many!
- Exotic, rare exceptions aside, please consider stopping one (or both!) drugs
- Reduce risk of diarrhea!
- Reduce risk of metro-induced neuropathy & nausea!

INTRA-ABDOMINAL

A. Community-acquired, mild-moderate
(Enteric Gram-negative rods, anaerobes)

- **HMC only:** Ertapenem 1g IV q24h
- **UWMC only:** Ceftriaxone 2g IV q24h **PLUS** Metronidazole 500mg PO/IV q8h
- For uncomplicated ***biliary*** infections, anaerobic coverage usually not necessary, use Ceftriaxone alone

Typical Duration: 4 days following source control

B. Hospital-acquired, severe physiological disturbance, advanced age, immunocompromised

- Vancomycin** **PLUS**
- Piperacillin-tazobactam 4.5gm X 1, then 4 hours later, start 3.375gm IV q8h infused over 4 hours

Typical Duration: 4-7 days from source control; if source control is not attained, then duration is variable.

C. Intra-abdominal infections:

⇒ **Double anaerobic coverage is not required (i.e. metronidazole + piperacillin/tazobactam)**

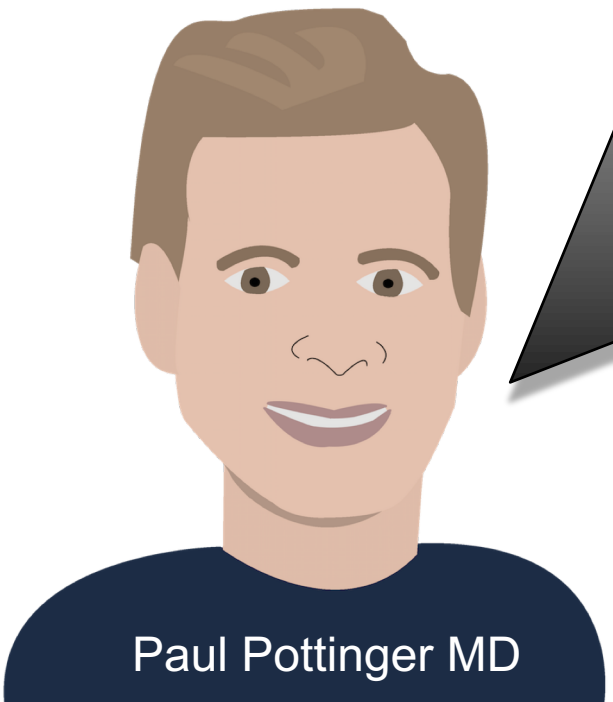
⇒ **Abdominal Transplant patients: Same as above and consult Transplant Infectious Diseases**

osyn?

n a short course
metronidazole)
(ceftriaxone for
ss)

infection

Conclusions



1. Anaerobes come in 2 flavors (above & below diaphragm)
2. Only kill them when necessary
3. Only kill them with one drug at a time
4. Low(ish) hanging fruit

References

- Brook et al. Antianaerobic antimicrobials: spectrum and susceptibility testing. *Clin Microb Rev* 2013 (PMID: 23824372)
- Schuetz AN. Antimicrobial resistance and susceptibility testing of anaerobic bacteria. *Clin Infect Dis* 2014 (PMID: 24867792)
- Hastey CJ et al. Changes in the antibiotic susceptibility of anaerobic bacteria from 2007-2009 to 2010-2012 based on the CLSI methodology. *Anaerobe* 2016 (PMID: 27427465)