Antibiotics Antibiotic Stewardship & Other ID stuff

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Outline

- ID Pearls (scattered throughout)
- All about Dr. Bell
- ABX use in general
- ABX Stewardship
- Resistance mechanisms
- Debunking Myths
- Dealing with the Difficult Patient
- Dealing with the Horrible Physician ABX Steward

About Me

- It's ALL about me! (Diva)
- Sarcastic
- I think I'm cool!
- Socratic method
- Love to teach (lets me talk more!)
- OCD (maybe a little ADHD)

Dr. Bell's Pet Peeves List

1. "mersa"
2. Sanford
3. "bandemia"
4. ABX without the proper cultures & poor judgement
5. Disorganization
6. "it's not my patient"
7. Brand names
8. Poorly requested consults
9. "Urosepsis"
10. Protocols!!

Worst ID Question Ever?

- How do I know when the blood cultures are negative?

Blood Cultures

- When do you order them?
- How do you order them?
- How often do you order them?
- When are they considered contaminants?
- Really, Dr. Bell, how helpful are they?

Isolator® Blood Cultures

- Brand name – they are actually lysis centrifugation cultures
- Ordered for VERY specific reasons:
  - ABX effect
  - AFB
  - *Bartonella*
  - Fungal
  - Intracellular pathogens

Wound Cultures

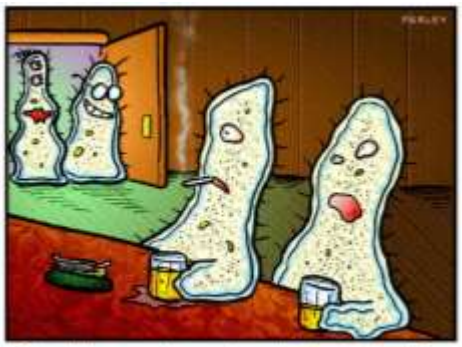
- Can be helpful
- Take with a grain of salt (no pun intended!)
- I usually use them to see if we have a resistant organism or *Pseudomonas* to deal with
- I do NOT go chasing down every bug grown out of them
- Remember – DFU's are polymicrobial – expect a soup!

Sputum Cultures

- GIGO
- Must have rare to few epithelials (any more & you're looking at spit!)
- Should be a respiratory pathogen

Urine Cultures

- Always order with a….
- *Staph*
- Foley (<<shudder>>)
- Men, women & aliens



"Oh gawd - here comes Lenny with something he picked up off the toilet seat!"

Isolation Orders

- What are the different isolations?
- Who goes where?

Antibiotics

- Religious experience
  - Informed consent
  - Interactions
  - Side effects
  - Are you using your PharmD's!!????
- Think 2 steps ahead
- Don't be afraid to stop what you've started!

ABX Use

- That use of antimicrobial agents promotes resistance and ultimately leads to lack of efficacy of the agents used has been called the "antibiotic paradox."
- Some have even discussed the approach of the "post-antibiotic era," in which effective antimicrobial therapy is no longer available.

ABX Knowledge

- There are a number of reasons for the importance of knowledge of antimicrobial therapy.
  - Antimicrobial agents are perhaps used authoritatively by a broader range of clinicians than any class of drugs.
  - Antimicrobial agents have been called "societal drugs," because every antimicrobial prescription potentially has impact far beyond the patient for whom it is prescribed, unlike the selection of an antihypertensive agent
  - Antimicrobial agents comprise 20 – 30% of hospital pharmacy drug acquisition costs
  - A high proportion of physician outpatient visits require decision-making about antimicrobial therapy

Cont…

- Antibiotic misuse continues virtually unchanged over the past 30 years
- 30% of hospital days of antimicrobial therapy were deemed unnecessary in a recent analysis
- Finally, an issue just beginning to attract attention, clinician antimicrobial prescribing habits impact decisions about new drug development by the pharmaceutical industry.

ABX Interventions

- There are five primary interventions health care providers can exercise on the course of disease:
  - observation
  - prophylaxis
  - empirical therapy
  - therapeutic trial
  - specific therapy

Mechanisms of Antimicrobials

- Fewer than 30 proteins have been exploited commercially as targets for antibacterial drugs, despite observations that pathogenic bacteria appear to contain >100 - >600 essential proteins, as determined by footprinting by random transposon mutagenesis.

Table 1: Classification of antibacterial agents by mechanism of action

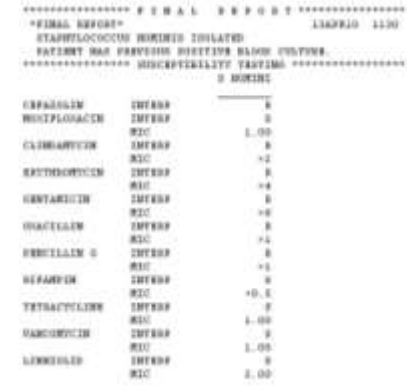
Mechanism of action	Antibacterial family
Inhibition of cell wall synthesis	β-lactam antibiotics (penicillins, cephalosporins, carbapenems, monobactams), glycopeptides
Inhibition of protein synthesis	Aminoglycosides, oxazolidinones, tetracyclines and glycylcyclines, ketolides, the MLS family (macrolides, lincosamides, streptogramins), chloramphenicol
Inhibition of DNA synthesis	Fluoroquinolones
Inhibition of folic acid synthesis	Sulfonamides, trimethoprim, sulfones
Inhibition of RNA synthesis	Rifamycins
Disruption of cell membrane integrity	Daptomycin, polymyxins
Other	Metronidazole, nitrofurans

Pharmacokinetics

- PK describes the time course of what the body does to the drug
  - Absorption
  - Distribution
  - Metabolism
  - Elimination
- Some antimicrobials have equal bioavailability (FQ, fluconazole, metronidazole, linezolid)

Pharmocodynamics

- PD links measures of drug exposure to the microbiological or clinical effects that are observed once an antimicrobial drug has been administered
  - This is truely what we seek
  - Prediction of what will work *in vivo*
- *In vitro* susceptibility testing only provides part of the data
  - For this reason we cannot simply compare the *in vitro* testing data to choose an ABX



********** F I N A L R E P O R T **********
"FINAL REPORT" 13APR10 1130
STAPHYLOCOCCUS HOMINIS ISOLATED
PATIENT HAS PREVIOUS POSITIVE BLOOD CULTURE.
********** SUSCEPTIBILITY TESTING **********
S HOMINI

CEFAZOLIN	INTERP	S
MOXIFLOXACIN	INTERP	S
	MIC	1.00
CLINDAMYCIN	INTERP	S
	MIC	<2
ERYTHROMYCIN	INTERP	S
	MIC	<4
GENTAMICIN	INTERP	S
	MIC	<8
OXACILLIN	INTERP	S
	MIC	<4
PENICILLIN G	INTERP	S
	MIC	<1
RIFAMPIN	INTERP	S
	MIC	<0.5
TETRACYCLINE	INTERP	S
	MIC	1.00
VANCOMYCIN	INTERP	S
	MIC	1.00
LINEZOLID	INTERP	S
	MIC	2.00

ESBL/MDRO

- This is a serious bug!!
- It is resistant to ESBlactam drugs & usually FQ
- DOC now is a carbapenem
- Patient needs contact isolation
- You also need to try & figure out how they got it!

ESBL

- Extended spectrum beta-lactamases
- Certain Gram negative organisms (like *E. coli*, *Klebsiella* & *Pseudomonas*) have developed resistances to enhanced penicillin-like drugs that were developed with additives to enable them to kill bacteria that were resistant to PCN (penicillinases & beta-lactamases)
- These organisms are resistant to beta-lactam antibiotics: piperacillin-tazobactam (Zosyn®), ampicillin-sulbactam (Unasyn®), & ticarcillin-clavulanate (Timentin®)
- No matter what type of culture is positive with these organisms, the patient must be placed in contact isolation

Carbapenems

- Note: not all carbapenems are equal!!
  - Imipenem-cilistatin
  - Meropenem
  - Ertapenem
  - Doripenem

CRE/CP - carbapenemases

- Lot of news lately on CRE
- ESBL Gram negative organisms have taken resistance one step further & are starting to learn to cope with the carbapenem antibiotics, such as:
  - imipenem-cilistatin (Primaxin®)
  - meropenem (Merrem®)
  - doripenem (Doribax®)
  - ertapenem (Invanz®)
- These are highly virulent organisms and any type of positive culture (even if the patient is deemed colonized) must be placed in contact isolation, and current CDC guidelines state they must have an individual RN, last scan of the day, etc…
- we strongly recommend an Infectious Diseases Consultation, and in fact, will invite ourselves to the case if not asked ☹

Agent	**MIC (mcg/mL)**	**Interpretation**
Amikacin	>32	R
Ampicillin	>32	R
Cefazolin	>32	R
Ceftazidime	>32	R
Ceftriaxone	>32	R
Cefepime	>32	R
Ciprofloxacin	>4	R
Gentamicin	4	S
Imipenem	4	S
Meropenem	4	S
Piperacillin-Tazobactam	>128/4	R
Tobramycin	>16	R
TMPSMX	>4/76	R
Automated ESBL test:		**negative**

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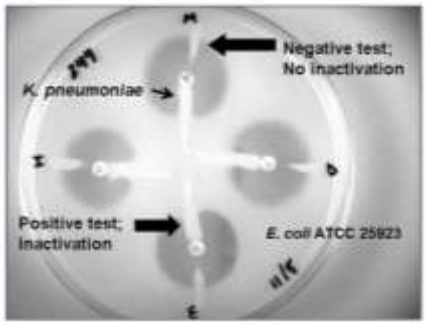
Amikacin	>32	R
Ampicillin	>32	R
Cefazolin	>32	R
Ceftazidime	>32	R
Ceftriaxone	>32	R
Cefepime	>32	R
Ciprofloxacin	>4	R
Gentamicin	4	S
Imipenem	4	S
Meropenem	4	S
Piperacillin-Tazobactam	>128/4	R
Tobramycin	>16	R
TMPSMX	>4/76	R
Automated ESBL test:		**negative**

Modified Hodge Test



XDR – eXtended drug resistance

- These organisms have learned to resist 3+ classes of ABX
- For example, A nursing home patient with recurrent UTI's due to a chronic indwelling foley has a urine cx that has *E. coli* that is reported as resistant to Zosyn®, Merrem®, gentamicin and Cipro®.
- These patients must be immediately placed in contact isolation, and we strongly recommend an Infectious Diseases Consultation

CDI

- MANY recent updates and changes to this infection
  - Bacteria
  - Toxin
  - Definition
  - Category of patient
  - Treatment regimen

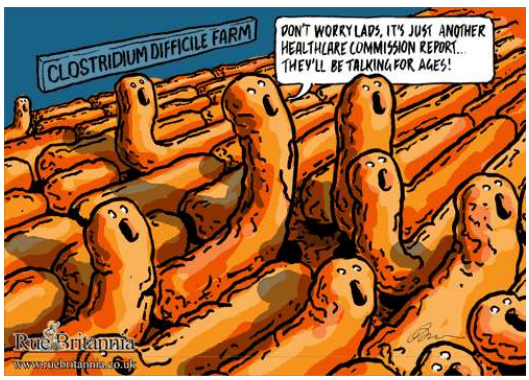
Clostridium difficile

- An increasingly common infection in our ICU's, ward floors and long term care facilities
- *C. difficile* is a common, but aggressive, bowel flora that can emerge to an acute infection in highly stressed patients (broad-spectrum ABX, chemotherapy, burns, trauma, ICU, etc…)
- The guidelines for this are updated just about every 6 months due to new and changing data – this is a VERY dynamic infection that will not be eradicated soon!!

C. difficile

- This infection is characterized by dark green, watery diarrhea, that is usually "crampy" in nature and has a distinctive foul odor
- Contact Isolation must be used for these patients whether they have an actual infection or have a history of shedding toxin at any time during the current admission
- Additional hand-washing with warm water & soap is necessary to slough off the possible spores on your hands – the alcohol-based foams & gels are not enough!

C. Difficile Guideline Updates



Most Recent Update

Clinical Infectious Diseases

IDSA GUIDELINE

Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

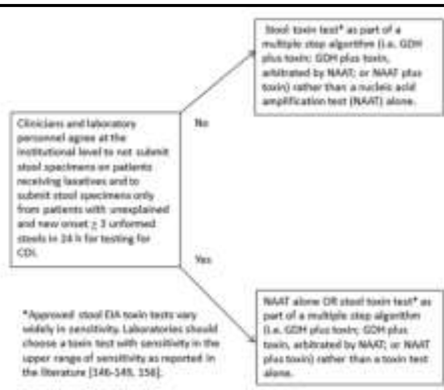


Table 1. Recommendations for the Treatment of *Clostridium difficile* Infection in Adults

Clinical Definition	Supportive Clinical Data	Recommended Treatment	Strength of Recommendation/ Quality of Evidence
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]		[illegible]	[illegible]
[illegible]		[illegible]	[illegible]

Mechanisms of resistance to antimicrobial agents.

- There are 5 basic mechanisms of acquired resistance to antimicrobial agents:
  - Drug inactivating enzymes
  - Modification of existing drug target
  - Acquisition of target bypass system
  - Reduced cell permeability
  - Drug removal from the cell

Resistance

- In virtually all situations, antimicrobial resistance first appeared in hospitals, where antimicrobial usage was highest, thus demonstrating the importance of the selective pressure of antimicrobial usage on the emergence and spread of resistant organisms.

Resistance

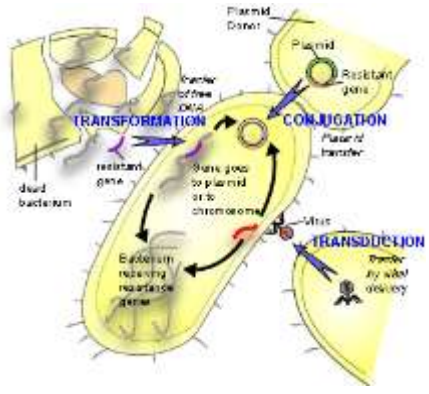
- Resistance is caused by the convergence in an environment or host of an antimicrobial agent which inhibits susceptible organisms and selects the resistant clones and the genetic resistance determinant in microorganisms selected by the antimicrobial drug
- Then microorganisms with selected resistance genes propagate and spread to other hosts or environments

Cont…

- If the selective pressure by the presence of the antimicrobial agent is again exerted, the resistant organisms will become dominant
- This problem is confounded by the fact that antimicrobial resistance is TRANSFERABLE!!

Transferance

- A gene conferring ABX resistance (usually to a single class) can be transferred to different strains & species by means of mobile genetic elements
  - Bacteriophages
  - Plasmids
  - Naked DNA
  - Transposons
- Such genes usually confer high levels of resistance



What resistance does…

- Leads to inappropriate empiric ABX therapy & delay in treatment
- Associated with a higher proportion of treatment failures
- Increased morbidity & mortality
- Prolonged hospitalizations & cost

- Global impact!

Educating your Patients

- ABX worked Last Time!
- "If I give you ABX you'll be better in 7 days, if I don't it'll take you a week to recover"
- PostABX era
- Moms with sick kiddos
- VACCINES

Dealing with Crappy Colleagues

- Physicians have a vital and unavoidably necessary role to play in ensuring socially optimal access to antibiotics.
- Physicians' management of the antibiotic supply has been poor and their defense of population health tepid at best.
- Physicians face limited incentives for antibiotic conservation from other sources, such as malpractice liability, regulatory standards, and reimbursement systems.

Dealing with Crappy Colleagues

- Acting as a prudent steward of the antibiotic supply often seems to be at odds with a physician's commonly understood fiduciary duties, ethical obligations, and professional norms, all of which traditionally emphasize the individual health paradigm as opposed to population health responsibilities.
- While multifaceted efforts are needed to combat antibiotic resistance effectively, physician gate-keeping behavior should become a priority area of focus.

Questions?