Strategic Use of ABX for Improved Patient Outcomes

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Infectious Diseases

EXPLORE HEALTHCARE SUMMIT

Objectives

- identify new antibiotics that have been developed in the past 10 years
- Be more comfortable with antibiotic choices
- Be aware of updated CMS/TJC antimicrobial stewardship recommendations & requirements
- Understand the limitations of antimicrobials in certain patient populations

Case Based Discussion

I chose this format to be more discussive in nature, rather than a dry lecture
I want you to realize 2 things:

1. ABX are not easy and there is rarely ONE correct answer or choice
2. Never be afraid to be wrong & change your mind

Failure in the ID realm

I have a mantra of 3 as to why treatments in the ID world fail:

- Wrong bug
- Wrong drug
- Wrong (or incomplete) diagnosis

Case #1

- 82 yo female comes to the ER with low abdominal pain & fever
- UA done
- BCx drawn
- Given empiric ceftriaxone & IVF
- Feels better
- ER dx her with a UTI & sends her out on Keflex 500mg PO BID

Discussion

Concerns I have at this point

- No abdominal CT (how do we know it's not complicated? Or pyelo?)
- Cephalosporins for UTI's should really be based on susceptibility proven data, especially with E. Coli, K. Pneumoniae & P. Mirabilis
- While q12 is in the guidelines for uncomplicated UTI's, it's T1/2 is 1 hour & there is ample literature to suggest that q6 hour dosing is needed to be effective & to overcome an innoculum effect

Next day

- I get a call from the ER doc (not the same one who saw her)
  - They are sure this is a quick question & overkill on their part, but….
  - UA shows 9 WBC per HPF & UCx shows CoNS, so clearly a UTI & the Keflex is correct
  - Interestingly, her BCx have 1 of 4 bottles with a listeria contamination….

Discussion

Concerns I have now

- A UA with <15 WBC per HPF is not a UTI (exceptions)
- CoNS (or any staph for that matter) is not a urinary pathogen
- Listeria is NEVER a contaminant (be happy you found it in any bottles!)

New recommendations

- Admission
- repeat BCx
- ABX choices?

The Patient (in more detail)

- CKD stage 3 with baseline Cr of 1.35
- IPF on inhalers & occ O2 use
- Her adult kids bring her LO's often & she says they aren't always the freshest (she throws a lot of it away) - I asked her about fruit salads
- This is all in Green Bay, WI

Discussion

ABX I put her on

- Ampicillin q8
- Gentamicin 1mg/kg IV q24 for synergy
- Gentle IVF for the gent, making sure she doesn't get volume overloaded on them with her IPF
- Other options?

Take away points

- Know what is/is not contaminants
- Never be afraid to use the right ABX, even for the wrong pt
- Know your local outbreak alerts!

Case #2

- A 62 yo farmer you know well comes to you with complaints of fever, HA, fatigue - its mid August
- He has a hx of DM2 & his last A1C was 8.9%
- You know he hunts too & is often in the woods
- You check his labs & as suspected, his Na is low & AST/ALT are a bit elevated
- You get a tick panel (since you have a high clinical suspicion) & start him on doxycycline

Discussion

Continued

- You get the tick panel back & it's negative
- You call the patient to see how he is doing
  - He felt a bit better for a day or 2 & then back to having a dull headache, more progressive fatigue & general malaise
- You tell him to come back in

Now what?

- Labs?
- Anything else to ask him?
- Scans?

New info

- You forgot he was an airplane fanatic & he went to Oshkosh this year
- A CBC with manual diff shows
  - A hemolytic anemia
  - intracellular forms and the tech reports a parasite level of 13%

Discussion

- Diagnosis?
- Any new labs?
- Treatment?

What I did

- I made the dx of babesiosis based on the parasite forms
- I checked a new set of tick infections
  - Most labs here in OK test for: Ehrlichia, RMSF, tularemia
  - I ordered Anaplasma & Lyme to make sure a concomitant infection not present
- I got him admitted to the hospital & consulted on him (parasitemia >10% in an immunocompromised patient)
  - I left him on the doxy until the other tick tests came back
  - I started him on IV azithromycin 1g q24 & PO atovaquone 750mg BID
  - Checked CBC with diff daily - when parasite level <4% (& he clinically felt better) we changed to PO regimen - he will take it for 6 weeks! (Normally its just a 7-10 day treatment for low level parasitemia & immunocompetent host)

Take away points

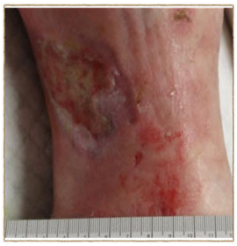
- Always get a good hx, even if you think you know them
- Understand how other dx affect the immune system
- Even though you are right, you may be wrong
- Know what to admit & what you can manage in the clinic

Case #3

- 93 yo male with HTN on lisinopril
- Has PAD & CVI with ulcers
- Sees the wound care clinic often (he enjoys the visits)
- Non-compliant with wound recommendations (in order to keep coming to the clinic?)
- Lives with a daughter who has addiction problems

Continued

- He comes into the wound clinic with complaints of
  - Increased pain (doesn't normally have any pain)
  - Increased wound drainage
  - No erythema



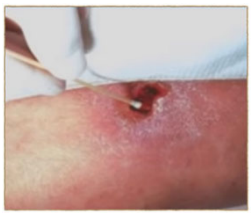
Next steps?

Continued

- Wound swab obtained (properly! - more on that in a bit)
- Application of Drawtex dressing for the drainage
- Discussion about empiric ABX vs bacterial overload therapy

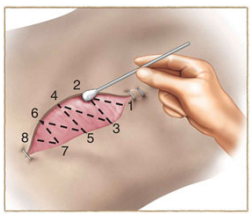
Levine's Technique

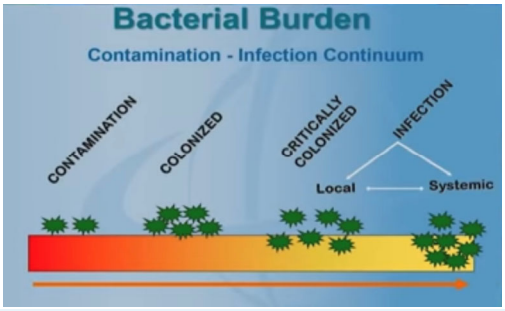
- Clean wound
- Find a cm of clean tissue
- Rotate swab with pressure to express fluid to cx
- Place in culture media containers & label WHERE YOU GOT IT FROM



Z swab

- Clean the wound
- Run swab along the surface of the wound
- Less optimal than Levine's
- Run the risk of getting necrotic tissue contamination or touching the skin at the wound edges





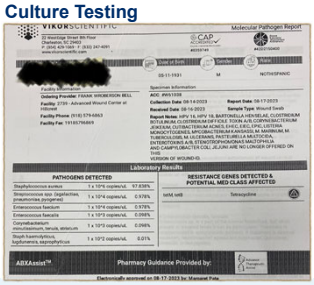
Continued…

- The wound culture comes back
  - "Mixed skin flora"

WTH?

Quantitative Culture Testing

- Can help to distinguish who is the biggest player in the field
- Can also tell you who might be a runner up if initial therapy stalls
- Can tell you what they are colonized with (better empiric choices for the next time)
- Can take up to 4 days to get the results back


VIKORSCIENTIFIC

Molecular Pathogen Report

Laboratory Results

PATHOGENS DETECTED

RESISTANCE GENES DETECTED & POTENTIAL MED CLASS AFFECTED

ABXAssist™

Pharmacy Guidance Provided by:

Discussion on Rx

What he did

- Cleaned the wound, added the absorbable dressing & a silver dressing to decrease the bioburden since there was no systemic s/s of infection & no localized erythema
- Gentle compression with wraps 3x per week
- Once the Vikor cx results came back he started him on cephalexin 500mg PO QID (on ACE-i)

Case #4

- 46 yo male veteran who has been battling major depressive d/o polysubstance abuse, suicidal ideation & suicide attempts for years (going back as far as 2009 from the medical records).
- He has also had mildly elevated LFT's since that time as well (etOH abuse, hepatic steatosis found on CT scan in 2015) & has been checked multiple times for HCV over the years (see micro/serology section below) and have all been NR since 2015.
- He was diagnosed with secondary syphilis in January & given a shot of PCN IM
- He admits to being very promiscuous – 20-40 partners in a 90-day time period, ~40% compliance with condoms, on PrEP but admits to remembering to take 2-3 x per week
- He had little GI symptomatology until early this summer when he noted some bloody diarrhea in June. Dx with GC/chlam a few times in the preceding months, positive again for chlam & rx with ceftriaxone & doxy
- In late July he presented to the ER in NTX for acute abdominal pain. CT of the abdomen & pelvis on 7/22/23 was unremarkable.
- He came to us last week for inpatient recovery to our Domiciliary program
- We do a battery of screening tests upon entry, HCV is now reactive

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Past Serology Testing

- 3/27/2015 HCV NR, HBV NR, HIV NR
- 7/20/2015 HCV NR, HBV NR, HIV NR
- 10/6/2015 HCV NR, HBV NR, HIV NR
- 11/28/2018 HCV NR, HBV NR
- 5/10/22 NP swab - RSV neg, Flu A/B neg, COVID neg
- 6/28/22 HIV NR, HSV 1/2 NR, Urine & rectal swab for GC+, chlamydia neg
- 7/20/22 HCV NR, HIV NR
- 8/25/22 HBV NR, HIV NR, HAV reactive (vaccine 2017), urine GC +, urine chlamydia +
- 1/4/23 HIV NR, pharynx GC +, HCV NR, HBV NR
- 1/18/23 HIV NR, RPR 1:16
- 5/19/23 HBV sAb reactive, HBV coreAb NR, HBV sAg NR, HIV NR, HCV NR, Urine chlamydia +
- 6/8/23 RPR 1:8, HIV NR
- 7/31/23 HCV reactive - VL 16 mil
- 7/31/23 HIV NR,
- 7/31/23 NP swab - RSV neg, flu A/B neg, COVID neg
- 8/14/23 HBV sAb NR
- 8/17/23 RPR reactive (titer pending)
- 8/17/23 Urine for GC/chlamydia - drawn & pending

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Next steps?

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What we ordered

- We had no confidence in the compliance with PCN (it looked like only one shot was given) & subsequent doxycycline Rx that was sent to him. Initial titer on diagnosis was 1:16, repeat titer 6 months later was 1:8. Repeat RPR with reflex to titer was ordered
- HCV genotype & VL ordered
- Liver US ordered

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Results

- RPR reactive, titer 1:8
- HCV
  - genotype pending
  - VL 16,078,500
  - HCVsAg+, HCV Ab + , anti-HCV Ig neg
- Liver enzymes elevated: AST 540 ALT 1350
- LFT's OK (INR 1.1, Tbili 1.7)
- Liver US fatty liver with a 7x7 mm density, rec MRI to eval for HCC

- Great, now what....

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diagnoses

- HCV
  - Acute
    - We have a negative test in May (a little over 2 months ago)
    - High VL
    - No anti-HCV Ig yet
  - Genotype pending
  - Liver US with a suspicious lesion
    - MRI ordered, set for today
    - Risk of HCC in this patient?
  - Do we treat?

- Syphilis
  - Repeat titer is stable
  - No rash on exam
  - What do we do about this?

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Treatment options for ACUTE HCV

- No treatment was previously recommended for acute HCV as data suggests that 20-30% of patients will naturally clear the infection on their own & a repeat testing algorithm in 3-6 months was standard of care (and still can be if he wants to do this)
- however, with his high risk behavior & the potential for him to spread the infection, HCV treatment can be offered, if he desires, based on 2020 guidelines for "treatment as prevention" of new HCV infections in the high risk population
- HCV universal genotype therapy with Mavyret (glecaprevir/pibrentasvir) 100/40 Mg 3 PO qday for 8-12 weeks
  - Problem with some of the new meds (especially Mavyret) is they are contraindicated with high Child-Pugh scores & HCC
    - We will have to await MRI & genotype
    - Problem – all the MELD scores & Child-Pugh algorithms are geared toward chronic HCV & detecting fibrosis
- We do need to eval for other causes of liver disease (autoimmune, etc…)

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Syphilis

- Treatment recommendations
  - Primary – benzathine PCN 2.4 MU IM x1
  - Secondary – benzathine PCN 2.4 MU IM x1
  - Early latent – benzathine PCN 2.4 MU IM x1
  - Late latent – benzathine PCN 2.4 MU IM x3 weeks (1 per week)
  - Tertiary – benzathine PCN 2.4 MU IM x3 weeks (1 per week)
    - With normal CSF exam
  - Neurosyphilis – aqueous crystalline PCN-G 18-24 MU IV per day divided
    - I remember the 4's
      - 4MU IV q4 hrs for 14 days
- PCN allergy – doxycycline for 1/2/EL/LL, tertiary or neuro – desensitize
  - True percentage of PNC allergy?
- Some are now recommending a second shot for 1/2/EL in pregnant patients
- Don't forget JH reactions
- Repeat titer in 3-6 months should drop by how much?

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Chronic HCV has changed dramatically, this could be its own lecture

Test often in rural OK, you WILL find it!

Update yourself on the new treatment options

Buddy up with a pharmacist that can help with education

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Case #5

- 61 yo female well known to the ID group
  - She is a kidney transplant patient because of PCK Dz
  - Kidney is from her sister & was placed in 2007
  - Multiple UTI's: 2013, 2016 x2, 5/2022, 7/2023, 8/2023
- she had a recent brief admission in July for an ESBL Klebsiella UTI & improved on ertapenem therapy & was discharged home after just 2 day stay in the hospital to complete a 10-day course of ABX at the outpt infusion center.
- Unfortunately, she developed recurrent symptoms within a few days of stopping the ABX.
- She presented back to the ER for evaluation & a UCx showed GNR.
- We assumed the same Klebsiella with perhaps more of a pyelonephritis picture based on CT scan & re-started ertapenem

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- Discussion….

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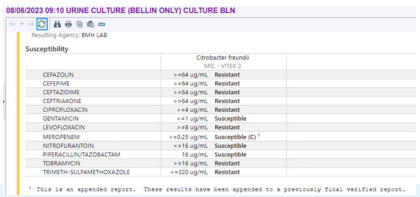
What went wrong

- Our mantra of 3
  - Wrong bug, so wrong drug, incomplete dx
- She did not feel better after 24 hours of ABX like she did last time
- Cx was slower to grow for us and came back as a Citrobacter freundii



08/06/2023 09:10 URINE CULTURE (BELLIN ONLY) CULTURE BLN

Resulting Agency: BMH LAB

Susceptibility

	Citrobacter freundii MIC - VITEK 2	
CEFAZOLIN	>=64 ug/mL	Resistant
CEFEPIME	>=64 ug/mL	Resistant
CEFTAZIDIME	>=64 ug/mL	Resistant
CEFTRIAXONE	>=64 ug/mL	Resistant
CIPROFLOXACIN	>=4 ug/mL	Resistant
GENTAMICIN	<=1 ug/mL	Susceptible
LEVOFLOXACIN	>=8 ug/mL	Resistant
MEROPENEM	<=0.25 ug/mL	Susceptible (C) †
NITROFURANTOIN	<=16 ug/mL	Susceptible
PIPERACILLIN/TAZOBACTAM	16 ug/mL	Susceptible
TOBRAMYCIN	>=16 ug/mL	Resistant
TRIMETH-SULFAMETHOXAZOLE	>=320 ug/mL	Resistant

† This is an appended report. These results have been appended to a previously final verified report.

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Now what?

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Interpreting Vitek or Phoenix reports

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Susceptibility

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TRIMETH-SULFAMETHOXAZOLE	>=320 ug/mL	Resistant

[1] This is an appended report. These results have been appended to a previously final verified report.

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BLOOD CULTURE, ANAEROBIC (BELLIN ONLY)

Status: Final result Visible to patient: No (inaccessible in MyChart)

Specimen Information: Blood, peripheral draw

0 Result Notes

Culture — Staphylococcus Aureus (MSSA) !

Resulting Agency: BMH LAB

Susceptibility

	Staphylococcus Aureus (MSSA) MIC - VITEK 2	
CLINDAMYCIN	0.25 ug/mL	Susceptible
OXACILLIN	<=0.25 ug/mL	Susceptible
TETRACYCLINE	<=1 ug/mL	Susceptible
TRIMETH-SULFAMETHOXAZOLE	<=10 ug/mL	Susceptible
VANCOMYCIN	1 ug/mL	Susceptible

ABSCESS CULTURE (BELLIN ONLY)

Status: Final result Visible to patient: Yes (not seen) Doc Abscess

Specimen Information: PNA,Psoas Muscle; Fluid

0 Result Notes

Culture — Many Methicillin Resistant Staph Aureus !

NOTE: This is a Methicillin Resistant Staph (MRSA)

CEFTAROLINE Susceptibility testing = Susceptible

Resulting Agency: BMH LAB

Susceptibility

	Methicillin Resistant Staph Aureus MIC - VITEK 2	
CLINDAMYCIN	0.25 ug/mL	Susceptible
DAPTOMYCIN	4 ug/mL	Susceptible
OXACILLIN	>=4 ug/mL	Resistant
TETRACYCLINE	>=16 ug/mL	Resistant
TRIMETH-SULFAMETHOXAZOLE	<=10 ug/mL	Susceptible
VANCOMYCIN	2 ug/mL	Susceptible

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08/02/2023 2142 | 08/03/2023 2048 | Blood Culture ID: PCR [45606540] (Abnormal) Blood, peripheral draw | Final result

Component	Value
ENTEROCOCCUS FAECALIS BY PCR	Not Detected
ENTEROCOCCUS FAECIUM BY PCR	Not Detected
LISTERIA MONOCYTOGENES BY PCR	Not Detected
STAPHYLOCOCCUS AUREUS BY PCR	Detected †
STAPHYLOCOCCUS EPIDERMIDIS BY PCR	Not Detected
STAPHYLOCOCCUS LUGDUNENSIS BY PCR	Not Detected
STREPTOCOCCUS BY PCR	Not Detected
STREPTOCOCCUS AGALACTIAE BY PCR	Not Detected
STREPTOCOCCUS PNEUMONIAE BY PCR	Not Detected
STREPTOCOCCUS PYOGENES BY PCR	Not Detected
ACINETOBACTER CALCOACETICUS-BAUMANII COMPLEX BY PCR	Not Detected
BACTEROIDES FRAGILIS BY PCR	Not Detected
ENTERC BACTERIA BY PCR	Not Detected
ENTEROBACTER CLOACAE COMPLEX BY PCR	Not Detected
ESCHERICHIA COLI BY PCR	Not Detected
KLEBSIELLA AEROGENES BY PCR	Not Detected
KLEBSIELLA OXYTOCA BY PCR	Not Detected
KLEBSIELLA PNEUMONIAE BY PCR	Not Detected
PROTEUS BY PCR	Not Detected
SALMONELLA BY PCR	Not Detected
SERRATIA MARCESCENS BY PCR	Not Detected
HAEMOPHILUS INFLUENZAE BY PCR	Not Detected
NEISSERIA MENINGITIDIS BY PCR	Not Detected
PSEUDOMONAS AERUGINOSA BY PCR	Not Detected
STENOTROPHOMONAS MALTOPHILIA BY PCR	Not Detected
CANDIDA ALBICANS BY PCR	Not Detected
CANDIDA AURIS BY PCR	Not Detected
CANDIDA GLABRATA BY PCR	Not Detected
CANDIDA KRUSEI BY PCR	Not Detected
CANDIDA PARAPSILOSIS BY PCR	Not Detected
CANDIDA TROPICALIS BY PCR	Not Detected
CRYPTOCOCCUS NEOFORMANS/GATTII BY PCR	Not Detected
MEC A/C AND MREJ (MRSA)	*Detected* (Methicillin resistant) †

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Back to our lady…

- We got an US to eval for any stones
- CT scan from ER showed an abdominal hernia over the transplanted kidney (gut bacteria translocation?)
- The note at the end of the culture made me pause…
- We changed her over to meropenem-vaborbactam (Vabomere)
  - She improved withing 36 hours
- Other alternatives (in the USA, where we have mostly KPC's & occ OXA-48's):
  - Avycaz (ceftazidime-avibactam)
  - Recarbrio (Imipenem-relebactam)
  - Zerbaxa (Ceftolazone-tazobactam)
- Problems with these meds?

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IV Preparation
Reconstitute with 20 mL of 0.9% NaCl per vial; and then further dilute

Mixed gently to dissolve; reconstituted solution concentration equals 0.05 g/mL (meropenem) and 0.05 g/mL (vaborbactam)

Reconstituted solution must be immediately diluted further in a 0.9% NaCl infusion bag

After dilution, final infusion concentration of meropenem/vaborbactam should be 2-8 mg/mL

Visually inspect the diluted solution for particulate matter and discoloration prior to administration (the infusion solution for administration should appear colorless to light yellow); discard unused portion after use

See prescribing information for further information

IV Administration
Infuse diluted solution IV over 3 hr

Infusion must be completed within 4 hr if stored at room temperature or 22 hr if stored refrigerated at 2-8°C (36-46°F)

Storage
Unopened vial: Store at room temperature 20-25°C (68-77°F); excursions are permitted to 15-30°C (59-86°F)

Reconstituted vial/diluted solution: 4 hr at room temperature; 22 hr if refrigerated at 2-8°C (36-46°F)

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- Lightning round
- Quick cases ☺

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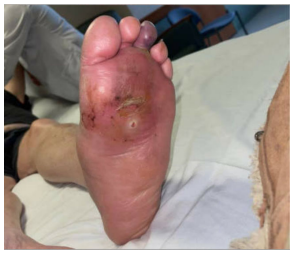
Quick case #1

- 63 yo with poorly controlled DM2 comes into your office with a foul smell about him
- Family visiting for the summer noted the smell & insisted he get "it taken care of"
- This has been going on for 3 months according to him
- He is otherwise asymptomatic
  - No fevers
  - No chills
  - BP normal



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Discussion

- Inpt or outpt?
- Is this an emergency?
- What to do when?
- ABX
  - Empiric
  - Pathogen directed
  - LOT?
- Surgery
- Pathology

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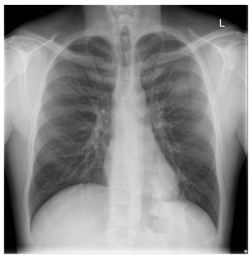
Quick Case #2

- 42 yo smoker comes into your office in October with a cough & fatigue with chills
- VS in your office:
  - 100.6 F 116 21 125/89 92% on RA
- You get a CXR.....



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Discussion

- Diagnosis
- Tests to order
- Inpt or outpt
- ABX needed?

- Things to consider
  - Age
  - Meds
  - Underlying conditions

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Quick Case #3

- 55 yo homeless man who presented to the ER for a worsening itchy rash over his face, arms, & trunk that started about 5 days ago.
- He presented to the ER at that time & was diagnosed with folliculitis & put on cephalexin & anti-histamines - he said taking these meds did not improve the condition.
- He also noted fevers, and a cough that started becoming blood tinged.
- He had some abdominal pain & had been avoiding food. Imaging in the
- ER showed severe interstitial lung infiltration with reactive LAN.

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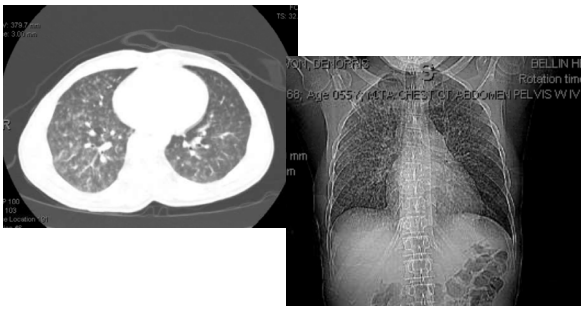

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Discussion

- Differential?
- Empiric ABX?
- Next tests?

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ABX Stewardship

- The right drug, at the right dose, for the right patient, for the right LOT
- Started in the hospital
- Now going to ER
- Will be going to outpt clinics in the next few years (we are already doing it in the VA)
- It will be critical for the rest of your career to know as much as you can about ABX & how to use them properly….

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CMS requirements

485.640 requires the following goals for an antibiotic stewardship program be met:

1. Coordination among all components of the CAH responsible for antibiotic use and resistance, including, but not limited to:
   - the infection prevention and control program
   - the QAPI program
   - the medical staff
   - nursing
   - pharmacy services;
2. Document the evidence-based use of antibiotics in all departments and services of the CAH

3. Demonstration of improvements, including sustained improvements, in proper antibiotic use, such as through reductions in, CDI and antibiotic resistance in all departments and services of the hospital.

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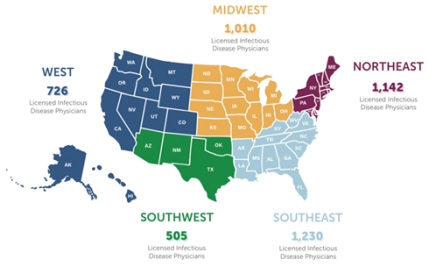
INFECTIOUS DISEASE PHYSICIANS BY REGION



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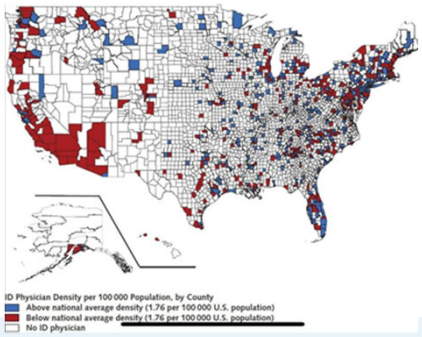

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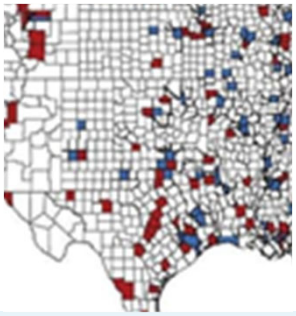

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The future of ID

- Understand the ID physician pipeline
- Lack of training for PA/NP's in ID
- Fellowship fill rates
- ID physicians across the nation - the sad statistics

ABX Pearls

- Not all FQ are equal
- Learn the new ABX options
- Infections are regional
- Sometimes people need a dx, not more ABX
- A fever might be good
- "Double coverage"
- New LOT guidelines
- Asymptomatic bactiuria
- FUO
- Get used to MAb use & increased OI's

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