What's New in Antibiotics

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Disclosures

- I have no conflicts of interest to disclose pertinent to this presentation.
- I have been a consultant for Gilead, Astellas, Cempra and BMS, and was on the speaker's bureau for Gilead and Astellas.

Objectives

- Participant will be able to describe new long-acting antibiotics for MRSA.
- Participant will be able to list the differences between tedizolid and linezolid as well as the contraindications for prescribing these antibiotics.
- Participant will be able to select an appropriate antibiotic for treatment of skin and soft tissue infection.

Does every soft tissue infection need treatment for MRSA?

Case

- 46 y/o previously healthy man presents with history of fever and chills. He states that he woke up with rigors, then noticed pain in his leg. He developed redness and swelling of the left leg. He tried to go to work, but had increasing pain, and eventually presented to the hospital. On admission, temp was 102.3 F, BP 90/60, P 102, R 18, exam significant for erythema/edema of left leg.
- How many people would order an antibiotic with MRSA activity?

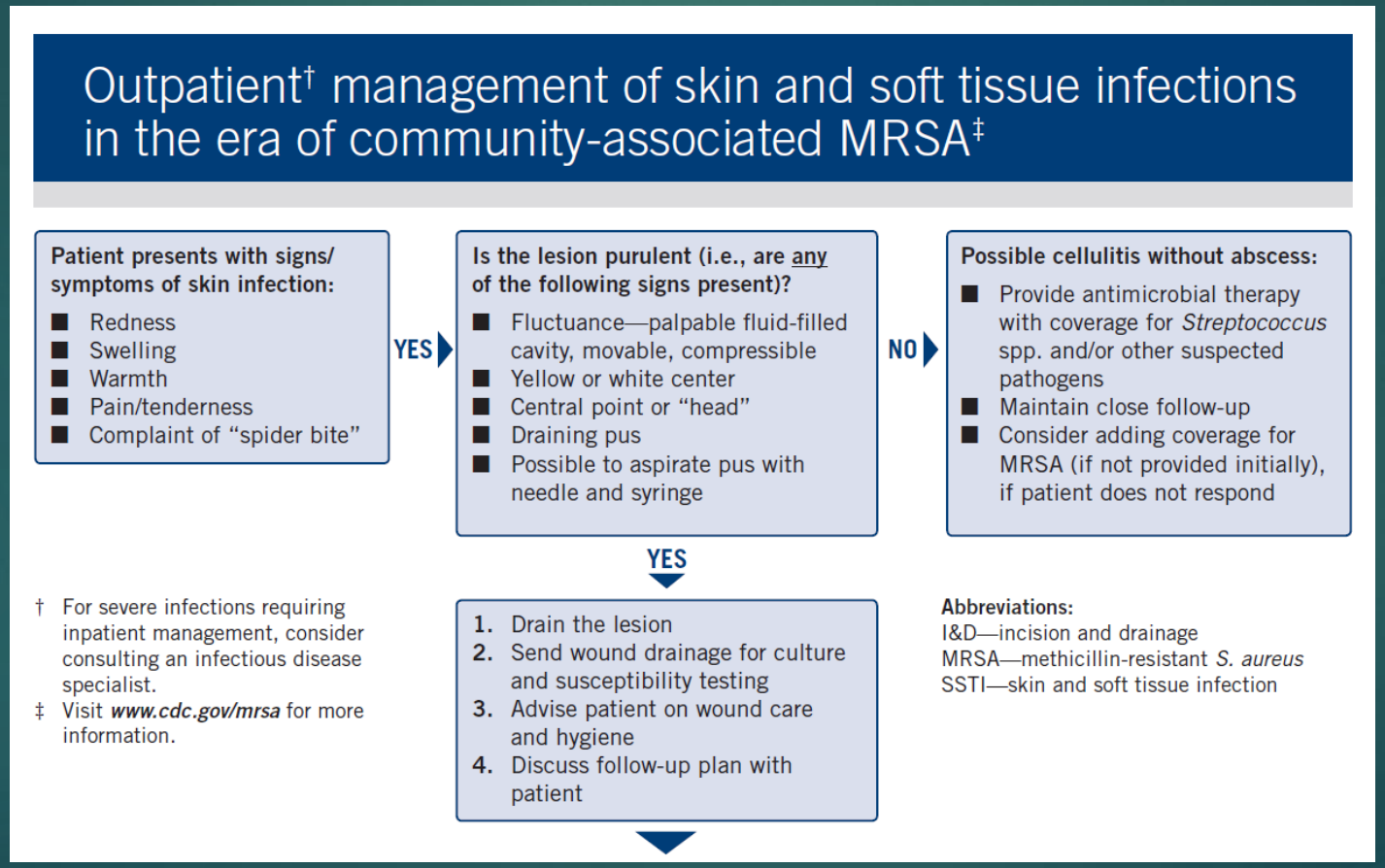
Case #2

- 30 y/o previously healthy man presents with c/o spider bite. He woke up in the middle of the night and noticed a spider walking across his sheets. The next morning he noticed the spider bite on his leg and some redness. This increased in size and became more painful. After several days, he presented to the ED with above complaint. He had a temp 102.3 F, BP 120/80, P 96, R18 and on exam there was a necrotic eschar on the foot with erythema extending up the leg.

Which antibiotic would you give this patient?

- Oral TMP/SMX
- IV Clindamycin
- IV Vancomycin
- Linezolid IV or po
- Tedizolid IV or po
- Dalbavancin
- Oritavancin
- Ceftaroline

CDC Guidelines For Treatment of SSTI



CDC Treatment Guidelines for MRSA SSTI

If systemic symptoms, severe local symptoms, immunosuppression, or failure to respond to I&D, consider antimicrobial therapy with coverage for MRSA in addition to I&D. (See below for options)

Options for empiric outpatient antimicrobial treatment of SSTIs when MRSA is a consideration*

Drug name	Considerations	Precautions**
Clindamycin	■ FDA-approved to treat serious infections due to *S. aureus* ■ D-zone test should be performed to identify inducible clindamycin resistance in erythromycin-resistant isolates	■ *Clostridium difficile*-associated disease, while uncommon, may occur more frequently in association with clindamycin compared to other agents.
Tetracyclines ■ Doxycycline ■ Minocycline	■ Doxycycline is FDA-approved to treat *S. aureus* skin infections.	■ Not recommended during pregnancy. ■ Not recommended for children under the age of 8. ■ Activity against group A streptococcus, a common cause of cellulitis, unknown.
Trimethoprim-Sulfamethoxazole	■ Not FDA-approved to treat any staphylococcal infection	■ May not provide coverage for group A streptococcus, a common cause of cellulitis ■ Not recommended for women in the third trimester of pregnancy. ■ Not recommended for infants less than 2 months.
Rifampin	■ Use only in combination with other agents.	■ Drug-drug interactions are common.
Linezolid	■ Consultation with an infectious disease specialist is suggested. ■ FDA-approved to treat complicated skin infections, including those caused by MRSA.	■ Has been associated with myelosuppression, neuropathy and lactic acidosis during prolonged therapy.

■ MRSA is resistant to all currently available beta-lactam agents (penicillins and cephalosporins)
■ Fluoroquinolones (e.g., ciprofloxacin, levofloxacin) and macrolides (erythromycin, clarithromycin, azithromycine) are not optimal for treatment of MRSA SSTIs because resistance is common or may develop rapidly.

* Data from controlled clinical trials are needed to establish the comparative efficacy of these agents in treating MRSA SSTIs. Patients with signs and symptoms of severe illness should be treated as inpatients.
** Consult product labeling for a complete list of potential adverse effects associated with each agent.

Treatment of MRSA SSTI

- Most CA-MRSA are susceptible to multiple classes of antibiotics other than β-lactams
- Treatment options include clindamycin for susceptible strains, TMP/SMX, doxycycline, quinolones, plus IV medications
- Keep in mind that resistance to quinolones and TCN can develop on therapy
- Do not prescribe rifampin by itself
- Decolonization is short-lived

http://www.cdc.gov/mrsa/community/photos/photo-mrsa-8.html

http://www.cdc.gov/mrsa/community/photos/photo-mrsa-1.html

http://www.cdc.gov/mrsa/community/photos/photo-mrsa-3.html

When to think about MRSA:

- Most MRSA skin infections appear as pustules or boils
- The area is usually swollen and red
- May be very painful
- Patient often refers to a “spider bite”
- infections commonly occur at sites of visible skin trauma, such as cuts and abrasions; may also occur with minor skin trauma
- Often in areas of the body covered by hair

Treatment of MRSA or ABSSSI

- When pus is present, I+D should be done
- Antibiotics may not be needed if adequate debridement performed
- Multiple different choices of IV antibiotics available
- All have different side effects, drug interactions and spectra of activity

When should I consider some of the newer antibiotics for MRSA?

Oritavancin (Orbactiv)

- Semisynthetic lipoglycopeptide analogue of vancomycin
- It has 3 separate mechanisms of action for activity against bacteria
- Indications: treatment of ABSSSI caused by gram positive organisms including: MRSA, staph aureus, strep pyogenes, strep dysgalactiae, strep anginosus group and vancomycin susceptible isolates of enterococcus
- Should not be given to patients with vancomycin allergy
- Approved for patients ages 18 and older
- Pregnancy category C

Oritavancin (Orbactiv)

- May prolong aPTT for up to 48 hours and PT for up to 24 hours
- May increase warfarin levels
- Does not include an indication for osteomyelitis; more osteomyelitis seen in oritavancin arm than in comparator arm in clinical trial
- Adverse reactions: headache, nausea, vomiting, diarrhea
- Dose: 1200 mg via single infusion over 3 hours; must be infused in D5W

SOLO I and II Study

- Studies of single dose oritavancin 1200 mg vs. 7-10D of IV vancomycin 1g or 15 mg/kg, dose adjustment allowed per local standards)
- Metronidazole and Aztreonam were allowed if deemed necessary
- Double-blind randomized trial, international
- Study endpoints:
  - No worsening at 48-72 hours (no increase in area, no fever, no need to change antibiotic
  - Investigator-assessed cure at 7-14D after treatment
  - 20% decrease in size of skin involvement at 48-72h
  - 60 D safety f/u

SOLO I and II

- Pts were age 18 and older
- Had to require at least 7D IV antibiotic therapy per investigator judgment
- At 75 cm^2 area of erythema/induration
- Primary efficacy endpoints: cessation of spreading of lesion or decrease in size, absence of fever, no rescue antibiotic needed
- Secondary endpoint was cure at post-therapy evaluation

SOLO-II

Table 2. Primary Efficacy Outcome at Early Clinical Response by Baseline Pathogen[a] (Microbiological Intent-to-Treat Population)

Baseline Pathogen	Oritavancin (n = 285), no./No. (%)	Vancomycin (n = 296), no./No. (%)	Difference (95% CI)
No. of patients with at least 1 pathogen	234/285 (82.1)	252/296 (85.1)	–3.0 (–9.0 to 3.0)
Staphylococcus aureus	208/250 (83.2)	219/258 (84.9)	–1.7 (–8.1 to 4.7)
MRSA	82/100 (82.0)	82/101 (81.2)	0.8 (–9.9 to 11.5)
MSSA	126/150 (84.0)	137/157 (87.3)	–3.3 (–11.1 to 4.6)
Streptococcus species	36/48 (75.0)	50/57 (87.7)	–12.7 (–27.6 to 2.2)
S. anginosus group[b]	14/18 (77.8)	24/27 (88.9)	–11.1 (–33.7 to 11.5)
S. pyogenes	16/23 (69.6)	18/22 (81.8)	–12.3 (–37.0 to 12.5)
S. dysgalactiae	5/6 (83.3)	3/3 (100.0)	
S. agalactiae	1/1 (100.0)	4/4 (100.0)	
Enterococcus faecalis	5/6 (83.3)	6/7 (85.7)	

Patients with multiple pathogens are counted once in the rows for each pathogen. Only pathogens that appeared in both treatment arms are listed.

Abbreviations: CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

[a] Includes only gram-positive pathogens known to cause acute bacterial skin and skin structure infections, whether isolated from infection site culture or blood culture.

[b] Includes *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*.

Corey et al. Single-Dose Oritavancin for Treatment of ABSSSIs • CID 2015:60 (15 January) • 259

SOLO I and II Outcomes

- Anyone with missing endpoint data was considered a treatment failure; most of the treatment "failures" were due to missing data
- Outcomes were similar for Oritavancin and Vancomycin; Oritavancin is non-inferior to Vancomycin
- There were more drug (placebo) discontinuations in the oritavancin group than in the vancomycin group
- AE's were similar: nausea, HA, emesis

Dalbavancin

- Also indicated for ABSSSI for susceptible organisms: MRSA, staph aureus, strep pyogenes, strep dysgalactiae, strep anginosus group
- 2 dose regimen: 1000 mg IV on day 1 followed by 500 mg IV day 8
- Dose decreased in patients with CrCl <30
- Should not be given to patients with hypersensitivity to glycopeptides
- Administered IV over 30 minutes
- Most common adverse reactions were headache, nausea and diarrhea

Dalbavancin

- More frequent ALT elevations were seen in dalbavancin group than in comparator group
- Pregnancy category C
- Can cause red man syndrome if infused too rapidly

Dalbavancin

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Once-Weekly Dalbavancin versus Daily Conventional Therapy for Skin Infection

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ABSTRACT

BACKGROUND

Dalbavancin, a lipoglycopeptide antibiotic agent that is active against gram-positive pathogens, has a long plasma half-life, allowing for once-weekly dosing. DISCOVER 1 and DISCOVER 2 were identically designed noninferiority trials of dalbavancin for the treatment of acute bacterial skin and skin-structure infection.

METHODS

We randomly assigned patients to receive dalbavancin intravenously on days 1 and 8 or vancomycin intravenously for at least 3 days with the option to switch to oral linezolid to complete 10 to 14 days of therapy. The primary end point, early clinical response, required the cessation of spread of infection-related erythema and the absence of fever at 48 to 72 hours. Secondary end points at the end of therapy in-

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DISCOVER I and II

- Double-blind, international multi-center RCT (54 and 86 sites)
- Participants had to have erythema 75 cm^2, needing at least 3D of IV antibiotics per judgment of investigator, and one or more systemic sign of infection: fever, WBC >12K and or more than 10% band forms; also purulent drainage, fluctuance, warmth, swelling and induration
- Patients who had 14D of antibiotic treatment prior to randomization were excluded
- Patients were given dalbavancin on days 1 and 8 or vancomycin 1g IV q 12 hours or 15 mg/kg q 12 h for at least 3 D, with option to switch to oral linezolid to complete 10-14D therapy

DISCOVER

- Patients for whom there was missing data were considered treatment failures; failure to record temperature within the designated time period was the biggest reason for treatment failure
- The dalbavancin group received oral placebo if the decision was made to change to oral medication to complete therapy
- Outcomes were similar in both groups for pooled ITT data 90.7% vs. 92.1% at D14; DISCOVER I had less resolution of infection in the dalbavancin group than the vanco-linezolid group
- Of note, in patients who had bacteremia at baseline and had f/u blood cultures, 23/23 in dalbavancin group were negative, whereas 12/14 in the vanco/linezolid group were negative (85.7%) at end ot treatment

Adverse Events

- Adverse events were lower with dalbavancin than with vancomycin/linezolid (32.8% vs 37.9%)
- There was 1 death in dalbavancin group; 7 in vancomycin/linezolid group
  - Pt in dalbavancin group died at D32 of sepsis and prior fracture
  - In vanco/linezolid group, 2 pts died from cardiopulmonary failure, 1 from PE, 1 from CHF, 1 from acute heart failure, 1 from SLE, and one sudden death
- Serious AE's: 1 in dalbavancin group with anaphylactoid reaction; one in vancomycin group with cellulitis, GI disorder, toxic nephropathy, and AKI in vancomycin-linezolid group

Dalbavancin

- Not inferior to vancomycin-linezolid
- More adverse events in vancomycin-linezolid group; median duration of adverse events longer in vancomycin-linezolid group than in dalbavancin group (4D vs 3D)

Tedizolid phosphate IV/PO

- Drug is indicated for treatment of ABSSSI with susceptible organisms including MRSA
- It is administered either orally or IV, 200 mg once daily for 6 days
- FDA approval based on two trials, ESTABLISH 1+2
- One trial was all oral therapy vs, linezolid twice daily
- Other trial was IV/PO in hospital and outpatient setting, also vs. linezolid
- Trials were randomized, placebo-controlled trials in patients >18 years old with ABSSSI

ESTABLISH Trials

- Endpoints were early clinical response at 48-72 hours, and post-therapy evaluation at days 18-25
- Patients in ESTABLISH 2 had to receive at least one day of IV tedizolid, and also could have received aztreonam and /or metronidazole if polymicrobial infection was suspected
- Trials demonstrated that drug was noninferior to llinezolid for the primary and secondary endpoints

Tedizolid

- Oxazolidinone for treatment of ABSSSI caused by: MRSA, MSSA, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus Group and Enterococcus faecalis
- Available as IV or PO once daily 200 mg for patients 18 and older
- Pregnancy category C
- Safety in patients with ANC less than 1000 is unknown
- Most common adverse events: nausea, diarrhea, headache, vomiting and dizziness

Other Effects

- Myelosuppression was seen in both linezolid and tedizolid arm
- Possible drug effect beyond the 6D of treatment with tedizolid
- Optic and peripheral neuropathy have been reported with other oxazolidinone when used more than 28D, unknown with this drug as not used more than 6D; rates of both were similar in clinical trial
- It is a reversible MAO inhibitor; effect on MAO inhibitors not studied as those patients excluded from clinical trial
- Patients taking SSRI's were excluded from trials

ESTABLISH I and II

- Multi-center RCT
- Included pts age 18 and older with 75 cm^2 erythema and local, regional or systemic sign of infection and documented or suspected gram positive infection
- Exclusions: uncomplicated ABSSSI, CLBSI, thrombophlebitis, and surgical site infection resulting from anything other than clean surgery; >96 hours of antibiotic prior to randomization or prior antibiotic failure
- ESTABLISH I was a trial of po tedizolid 200 mg po daily for 6D vs. po linezolid 600 mg bid for 10D
- ESTABLISH II was a trial of IV tedizolid vs. IV linezolid with option to change to oral to complete therapy

ESTABLISH I and II

- Patients over age 12 were included in ESTABLISH II
- Treatment response was defined as 20% or more decrease in size of area of infection, no other antibiotic receipt with similar gram positive activity, and no death within 72 h of first dose of drug
- More patients in the tedizolid group had ALT elevations, but still completed 6D therapy; no long-term consequences
- Less thrombocytopenia (2.3% vs. 4.9%)
- Less leukopenia in tedizolid vs. linezolid arm

Caveats

- These trials are difficult to conduct, and are not like the real world.
- We don't know the actual outcomes because of missing data.
- Patients with MSSA were not changed to beta-lactams as they would be in the real world.
- Much more data is needed about how to use these drugs.

Cost of Drugs Active Against MRSA

Drug	Dose (for normal renal function)	Cost per dose	Approx Cost per Course of Treatment
Vancomycin	20 mg/kg IV q 12h	1000 mg $7.46	$150.00
Ceftaroline	600 mg IV q 12h	$151.62	$1516-4245
Tigecycline	100 mg IV once, then 50 mg q 12h	50 mg $136	$2856
Linezolid	600 mg IV or po q12	IV $294, po $182	IV $5880, po $3640
Tedizolid	200 mg IV or po for 6D	PO $354 IV $282	PO $2124 IV $1692
Dalbavancin	1000 mg, then 500 mg a week later	$1788 for 500 mg	$5364
Oritavancin	1200 mg once	$1160 for 400 mg	$3480
Daptomycin	4 mg/kg or 6 mg/kg	$455.04 for 500 mg	$3185-6370

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Randomized non-inferiority trial to compare trimethoprim/sulfamethoxazole plus rifampicin versus linezolid for the treatment of MRSA infection

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Objectives: The therapeutic arsenal for MRSA infections is limited. The aim of this study was to assess the non-inferiority of a combination of trimethoprim/sulfamethoxazole plus rifampicin versus linezolid alone for the treatment of MRSA infection.

Methods: We conducted a randomized, open-label, single-centre, non-inferiority trial comparing trimethoprim/sulfamethoxazole (160 mg/800 mg three times daily) plus rifampicin (600 mg once a day) versus linezolid (600 mg twice a day) alone in adult patients with various types of MRSA infection. Patients were allocated 1:1 to either regimen. The primary outcome was clinical cure at 6 weeks after the end of treatment (non-inferiority margin 20%) assessed by both ITT and PP analyses. Secondary outcomes included the microbiologically documented persistence of MRSA in clinical cultures, mortality and adverse events. The study protocol has been registered with ClinicalTrials.gov (NCT00711854).

Results: Overall, 150 patients were randomized to one of the two treatment arms between January 2009 and December 2013 and were included in the ITT analysis. Of these 56/75 (74.7%) in the linezolid group and 59/75 (78.7%) in the trimethoprim/sulfamethoxazole and rifampicin group experienced clinical success (risk difference 4%, 95% CI −9.7% to 17.6%). The results were confirmed by the PP analysis, with 54/66 (81.8%) cured patients in the linezolid group versus 52/59 (88.1%) in the trimethoprim/sulfamethoxazole and rifampicin group (risk difference 6.3%, 95% CI −6.8% to 19.2%). There were no statistically significant differences between the two groups in any of the secondary outcomes, including microbiologically documented failure. Four adverse drug reactions attributed to the study medication occurred in the linezolid group versus nine in the trimethoprim/sulfamethoxazole and rifampicin group.

Conclusions: Compared with linezolid, trimethoprim/sulfamethoxazole and rifampicin seems to be non-inferior in the treatment of MRSA infection.

When to consider newer MRSA treatments:

- Nice alternative to hospitalization when good follow-up can be assured and insurance will cover the antibiotic
- Role is not yet clearly defined
- Downside is cost, and not clear that there is any benefit over currently available medications
- Useful when trying to avoid longterm IV antibiotics

And one more piece of advice…

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY AUGUST 2006, VOL. 27, NO. 8

ORIGINAL ARTICLE

Nose Picking and Nasal Carriage of *Staphylococcus aureus*

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OBJECTIVE. Nasal carriage of *Staphylococcus aureus* is an important risk factor for *S. aureus* infection and a reservoir for methicillin-resistant *S. aureus*. We investigated whether nose picking was among the determinants of *S. aureus* nasal carriage.

SETTING AND PARTICIPANTS. The study cohort comprised 238 patients who visited the ear, nose, and throat (ENT) disease outpatient clinic of a tertiary care hospital and did not have a nose-specific complaint (defined as ENT patients) and 86 healthy hospital employees (including medical students and laboratory personnel).

A few words about other antibiotics recently approved

Why do we need more antibiotics?

- Few choices currently available for MDRO gram negative organisms
- Most of the antibiotics available are beta-lactams
- For patients who cannot tolerate beta-lactams, not many other options
- Fluoroquinolone resistance increasing
- Carbapenem resistance is increasing
- Colistin and aminoglycosides have multiple side effects

ESBL

- Found in enterobacteriaceae (klebsiella, E.coli, enterobacter, salmonella, etc.
- ESBLs are bacteria that produce ESBL enzymes that mediate resistance to extended-spectrum (third generation) cephalosporins (eg. ceftazidime, cefotaxime, and ceftriaxone) and monobactams (eg. aztreonam) but do not affect cephamycins (eg. cefoxitin and cefotetan) or carbapenems

KPC

- This is the most common carbapenemase and was initially identified in North Carolina in Klebsiella but has spread world-wide
- KPC Enterobacteriaceae are becoming more common in hospitals and longterm care facilities
- Patients often have multiple comorbidities
- Long-term care facilities often have patients colonized with these organisms
- Prior antibiotic exposure is often present
- The plasmid that harbors KPC resistance has been transferred to other gram negatives: E.coli, enterobacter, serratia, pseudomonas, etc.
- Very limited treatment options
- Mortality rate high

CRE

- High mortality rates (as high as 50%)
- Limited treatment options
- Often carry genes that confer resistance to other antibiotics
- CRE was rare prior to 1992, now increasing
- Once one facility in an area has CRE, it often spreads

MDRO Acinetobacter

- CDC uses resistance to more than one class of antibiotics as MDRO, but in reality these organisms are usually resistant to multiple classes of antibiotics
- Usual definition is resistance to carbapenems or more than 3 classes of antibiotics
- Some define multidrug-resistant Acinetobacter as an isolate that is susceptible to no more than one class of antimicrobial agents, excluding colistin
- Strains that are resistant to all antibiotics including polymyxin have been reported

MDR-GNB

- Increased LOS
- Increased mortality
- Environmental transmission
- Limited treatment options

Everything old is new again: Minocycline

- Minocycline is a semisynthetic tetracycline that was available as an oral medication, now available in IV formulation
- It is primarily bacteriostatic, and works by inhibiting protein synthesis
- It is a broad-spectrum antibiotic with activity against:
  - Gram positives: listeria, bacillus, staph and strep
  - Gram negatives: enterobacter, klebsiella, E.col, acinetobacter, shigella, H.flu, vibrio, Yersinia pestis, F. tularensis, bartonella, brucella
  - Anaerobes: clostridia, actinomyces, fusobacterium, propionibnacterium
  - Other: chlamydia, rickettsiae, syphilis, etc.

Minocycline: Indications

- RMSF, Q fever, infections caused by Rickettsiae
- Mycoplasma pneumonia infections
- Lympohogranuloma venereum
- Psittacosis
- NGU caused by Ureaplasma or Chlamydia trachomatis
- Long list of indications
- One of the preferred drugs for MDRO Acinetobacter

Contraindications

- Should not be used in pregnant women after formation of teeth (10 weeks gestation to 8 years of age)
- Can cause dose related retardation of skeletal development in animal studies
- DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) has been reported with minocycline
- Tetracyclines can cause an increase in BUN, especially in patients with severe CKD- dose should not exceed 200 mg in 24 hours
- Photosensitivity occurs with TCN's
- Lightheadedness, dizziness and vertigo can occur transiently

Ceftazidime/avibactam (Avycaz)

- Fixed combination of ceftazadime and avibactam
- Avibactam is a non-beta-lactam beta-lactamase inhibitor
- Avibactam protects ceftazadime from breakdown by beta-lactamases
- It is indicated for complicated IAI and complicated UTI
- Limited clinical data currently available, so only to be used for patients with limited treatment options

Ceftazidime/avibactam

- Must be given with metronidazole for IAI
- Dose reduction for patients with reduced CrCL 30-50
- Dose is 2.5 grams IV q 8 hours for 5-14D

Indications

- Complicated Intra-Abdominal Infections (cIAI) -in combination with Metronidazole
- Complicated Urinary Tract Infection (cUTI)
- ESBL producing Gram negatives
- CRE (carbapenem resistant Enterobacteriaceae)
- MDR Pseudomonas aeruginosa

Adverse Reactions

- Most Common AE: Nausea, Vomiting, Constipation, Anxiety
- In renal impairment, decreased efficacy, seizures, and other neurologic events
- Not for use in those with known PCN or cephalosporin sensitivity
- CNS effects noted in patients receiving ceftazidime: seizures, encephalopathy, coma, asterixis, myoclonus
- Increased mortality in patients with decreased CrCl vs. meropenem

Ceftolozane/tazobactam (Zerbaxa)

- Indicated for cIAI and cUTI
- 1.5 g IV q 8 hours for adults 18 and older
- Dose reduced for CrCl <50
- Used in combination with metronidazole for cIAI
- Active against: gram negatives, strep anginosus group, bacteroides

Ceftolozane/tazobactam

- Clinical cure rates lower in patients with CrCl 30-50 compared to >50
- Compared to meropenem for cIAI and to levofloxacin for cUTI
- AE's were similar for meropenem in IAI study and similar to levofloxacin in cUTI study

Ceftolozane/tazobactam

- Not active against carbapenemases or metallo-beta lactamases
- Unknown whether there is clinical activity against acinetobacter
- Active against MDRO Pseudomonas; has activity against many pseudomonas resistance determinants
- Active against most ESBL-producing Enterobacteriaceae, but does not have activity against KPC

Cost

Drug	Approx Cost per dose	Approx Cost per Day
Ceftolozane/tazo	$99.60	$298.80
Meropenem	$18.48 (1g)	$55.44
Ceftazidime/avibactam	$285	$855
Piperacillin/tazobactam	$12.24-27.40 (3.375g)	$49.60-109.60
Cefepime	$8.45 (2g)	$25.35

Peramivir

- Neuraminidase inhibitor
- Given IV as a single dose
- Non-inferior to oseltamivir when given to patients with uncomplicated seasonal influenza
- Pregnancy category C
- Safety in pediatrics not established
- Cost is $950 for a single dose vs. $115-230 for 5-10D of oseltamivir
- Symptoms resolved a mean of 21h sooner in treatment group than in placebo group
- Cross-resistance expected

Conclusions

- Multiple new drugs available
- Benefit of these drugs over those currently available not yet clear
- More data is needed except in situations where treatment options are limited
- All of the new drugs are very expensive