Antimicrobial Stewardship

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Antimicrobial Stewardship

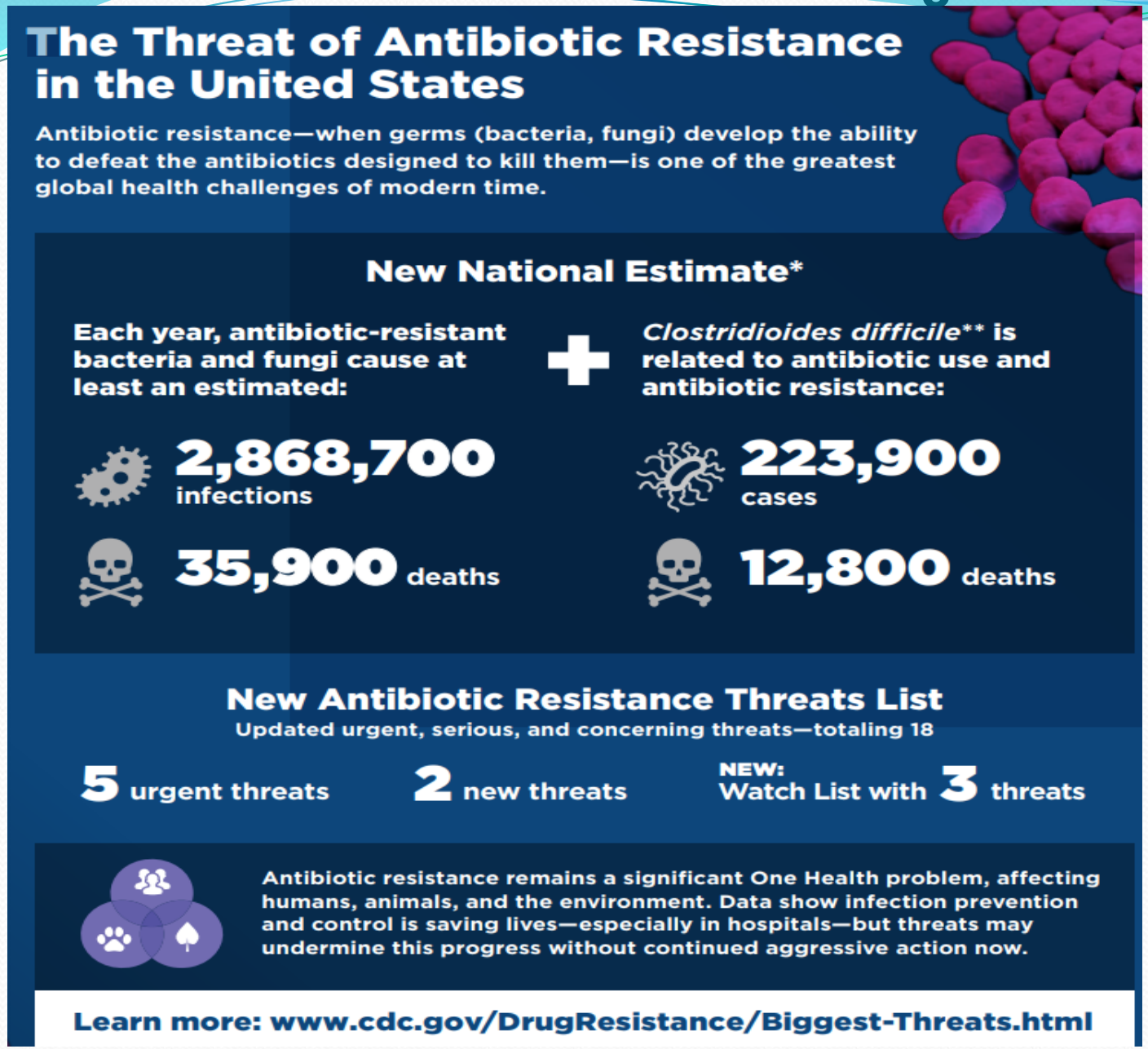
- Studies have estimated that **30-50% of antibiotics prescribed in acute-care hospitals are unnecessary or inappropriate**[1]

- **Antimicrobial stewardship definition:** Coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration[2]

- **Objectives of stewardship:** Achieving the best clinical outcomes related to antimicrobial use while minimizing toxicity and other adverse events, thereby limiting the selective pressures that drive the emergence of antimicrobial-resistant strains of bacteria

1. National Quality Forum. Antimicrobial Stewardship in Acute Care: A Practical Playbook. Accessed 10 June 2016.
2. Infectious Diseases Society of America. http://www.idsociety.org/Stewardship_Policy/. Accessed 27 March 2017.

Antibiotic Resistance: A Growing Crisis



CDC. Antibiotic Resistance Threats in the United States, 2019 https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

CDC's 2019 AR Threats Report:
PREVENTION WORKS.

↓ 18% fewer deaths from antibiotic resistance overall since 2013 report

↓ 28% fewer deaths from antibiotic resistance in hospitals since 2013 report

AND DECREASES IN INFECTIONS CAUSED BY:

- **↓ 41%** Vancomycin-resistant *Enterococcus*
- **↓ 33%** Carbapenem-resistant *Acinetobacter*
- **↓ 29%** Multidrug-resistant *Pseudomonas aeruginosa*
- **↓ 25%** Drug-resistant *Candida*
- **↓ 21%** Methicillin-resistant *Staphylococcus aureus* (MRSA)
- **STABLE** Carbapenem-resistant Enterobacteriaceae (CRE) & drug-resistant tuberculosis (TB disease cases)

CDC strategies that work in healthcare:

Preventing device- and procedure-related infections, such as from urinary catheters or central lines

Stopping the spread of resistant germs within and between healthcare facilities

Containing emerging threats through early detection and aggressive response

Tracking and improving appropriate antibiotic use

Infection prevention and control in non-hospital settings, such as long-term care facilities

CDC strategies that work in communities:

Widespread use of vaccines to prevent infections and spread

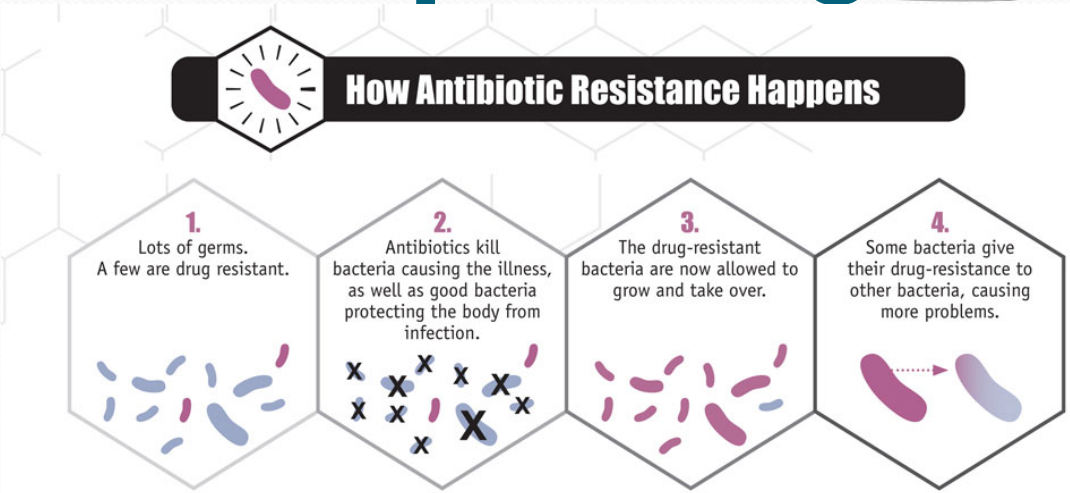
Routine tuberculosis and gonorrhea screening for at-risk groups and prompt treatment

Using safer sex practices (e.g., condoms)

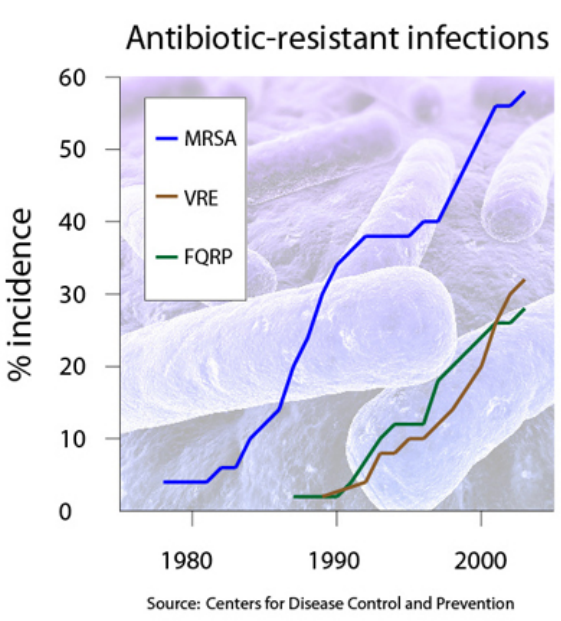
Safe food handling and preparation

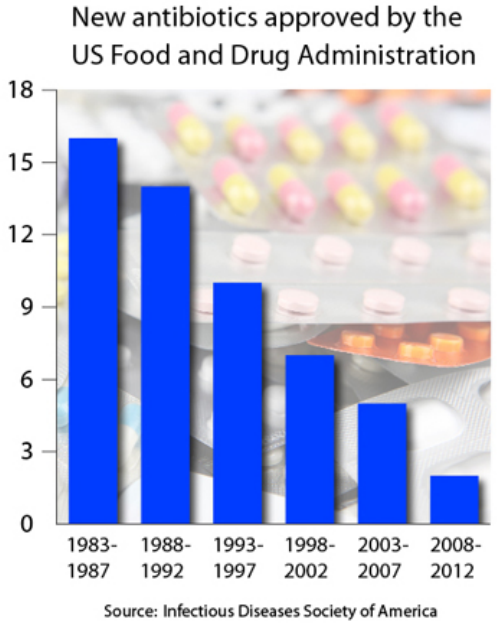
Improving antibiotic use everywhere

Superbugs

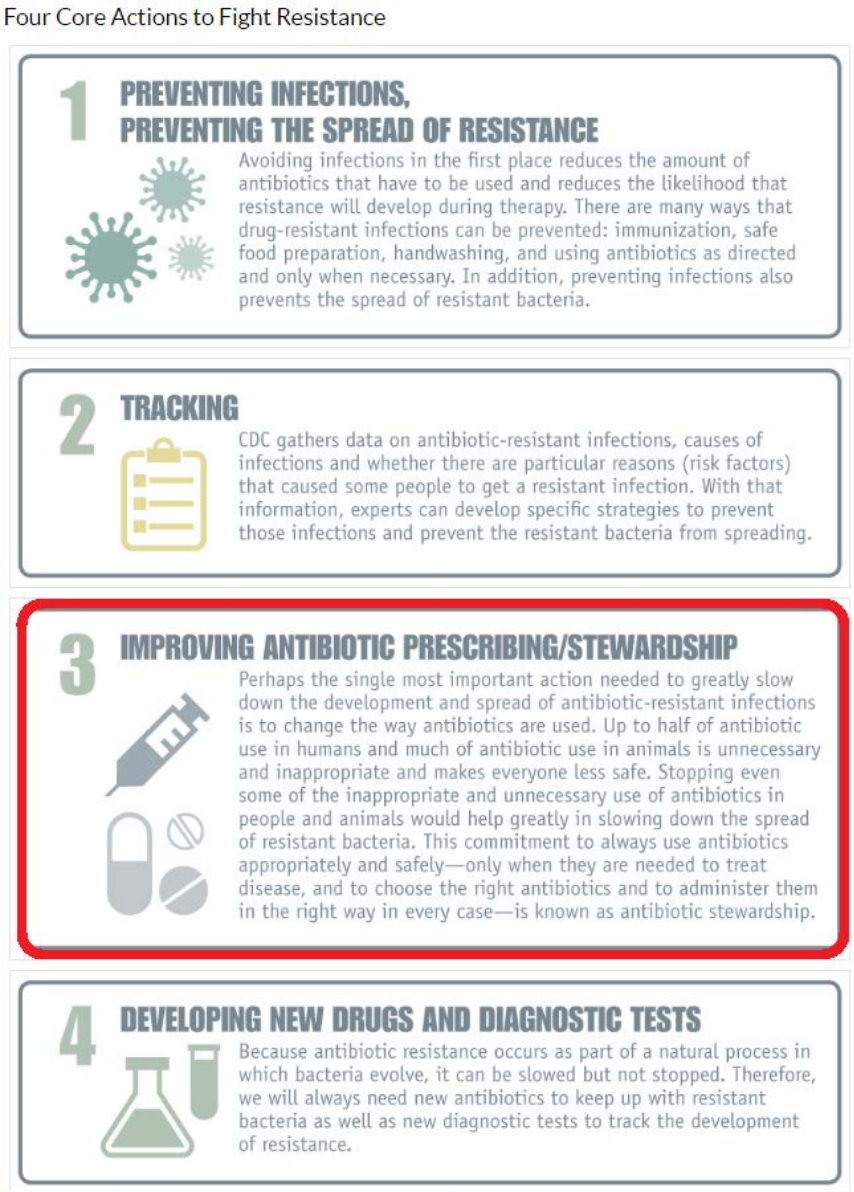


- Antibiotic resistance is outpacing new antibiotic development





CDC: Four Core Actions



The critical role of the staff nurse

- Antibiotic first responders
- Central communicators for the multidisciplinary care team
- Coordinators of patient care
- 24-hour monitors of patient status, safety, and response to antibiotic therapy

Clin Infect Dis. 2016 Jan 1;62(1):84-9.

Nursing Interventions

- Ensure that cultures are drawn **before** antibiotics are started so that there's guidance for effective antibiotic therapy
- **Timely administration** of first-dose antibiotics.

- Patient monitoring
  - Patient response to antibiotics
  - Laboratory results
  - Microbiology culture and sensitivity reports
  - Adverse effects
- Being a patient advocate for appropriate antibiotic use
  - Ensuring good hand hygiene and isolation practices to decrease risks of infection and the spread of infections
  - If no signs of infection, ask providers/pharmacists if antibiotics are really needed and if they can be stopped
  - Asking if antibiotics can be tailored based on culture and sensitivity results
  - Advocating for IV to PO conversions

Antimicrobial Stewardship at Salinas Valley Memorial Healthcare

- SVMH has developed a multi-disciplinary, evidence-based stewardship program

- SVMH's team
  - Infectious Disease specialists
  - Pharmacy
  - Microbiology
  - Infection Prevention
  - Nursing
  - Quality Improvement
  - Informatics

Pharmacist managed antibiotic dosing and blood levels

Antibiotic	Blood level timing	Therapeutic goal mcg/mL	Toxic level mcg/mL	notes
IV Vancomycin	1 hour before next dose	10-15	>20	Levels are not indicated for Oral vancomycin formulation
Gentamicin Tobramycin	Trough-30 minutes before next dose Peak-30 minutes after end of infusion	Trough <1 Peak varies depending on indication 4-6 Up to 8-12	Trough>2	Trough for extended infusion; Peak and trough for conventional dosing
Amikacin	Trough-30 minutes before next dose Peak-30 minutes after end of infusion	Trough 1-8 Peak 20-30		

SVMH Stewardship Interventions

- Pre-authorization of restricted and broad-spectrum antibiotics
- Audit and feedback
  - ICU multidisciplinary rounds
  - House-wide antibiotic reviews with ID and pharmacy
  - Pharmacy review of cultures and sensitivity results
- Rapid testing of blood cultures that yields results within hours (Verigene)
- IV to PO conversions
- Informal and formal ID consults generated from stewardship
- Pharmacokinetic dosing and monitoring of high-risk antimicrobials

Strategies for Improved Antimicrobial Prescribing

1. Ensure antibiotics are indicated

2. Select an appropriate antibiotic with a **narrow spectrum** if possible, to minimize collateral damage

3. Ensure that antibiotic durations are evidence-based and take into account clinical response. Use the **shortest** appropriate **length of therapy**

4. Remember to **re-evaluate** therapy based on culture results, laboratory data, clinical status, etc. **De-escalate** therapy, convert IV to PO, and discontinue therapy when appropriate

Are Antibiotics Needed?

Illness	Usual Cause		Antibiotic Needed
	Viruses	Bacteria	
Cold/Runny Nose	✓		NO
Bronchitis/Chest Cold (in otherwise healthy children and adults)	✓		NO
Whooping Cough		✓	Yes
Flu	✓		NO
Strep Throat		✓	Yes
Sore Throat (except strep)	✓		NO
Fluid in the Middle Ear (otitis media with effusion)	✓		NO
Urinary Tract Infection		✓	Yes

https://www.cdc.gov/features/getsmart/

For Clean Surgeries, Avoid Continuing Prophylactic Antibiotics after Surgical Closure

- Surgeries are generally considered “clean” if respiratory, alimentary, genital, or urinary tracts are not entered

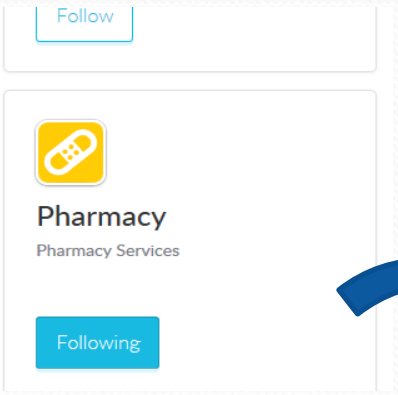
- Examples of clean procedures that usually do not require continuing antibiotics after the procedure: orthopedic surgeries, ophthalmic surgeries, plastic surgeries, laminectomies, spinal fusions, pacemaker surgeries, etc.

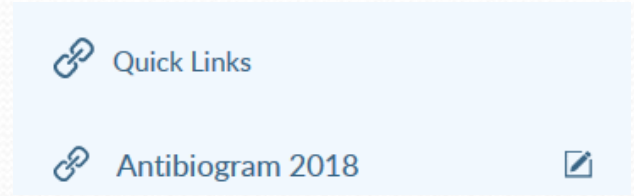
- Exclusions (cases that may require post-op antibiotics)
  - Non-clean cases in which respiratory, alimentary, genital or urinary tracts are entered
  - Cardiothoracic surgeries
  - Antibiotics not used for peri-operative prophylaxis (e.g. initiated for treatment of active infections)

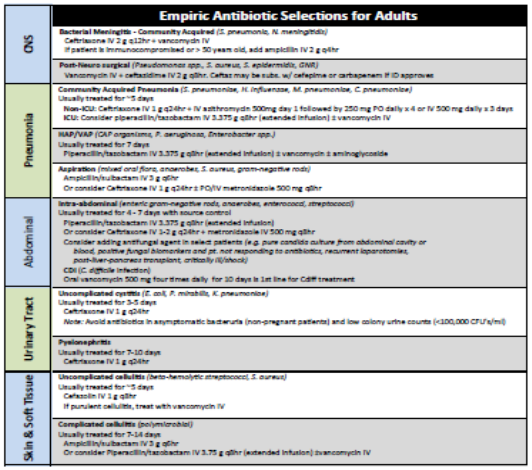
https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf

SVMH Antibiogram

- Includes SVMH antibiotic susceptibility information, empiric therapy recommendations, tailored therapy recommendations for Verigene results, and antibiotic stewardship clinical pearls
- Available on STARnet Pharmacy Page, in physician's lounge, or contact Microbiology Department for a copy







Antibiogram 2018
Data is Percent Susceptible

	ORGANISM	Total No. Isolates	AMPICILLIN	AMPICILLIN-SULBACTAM	CEFAZOLIN	CEFTAZIDIME	CEFTRIAXONE	CLINDAMYCIN	COTRIMOXAZOLE	ERYTHROMYCIN	GENTAMICIN	GENTAMICIN 120	LEVOFLOXACIN	MINOCYCLINE	NITROFURANTOIN	METHICILLIN	PENICILLIN - ORAL	PENICILLIN - IV	STREPTOMYCIN	TETRACYCLINE	TOBRAMYCIN	PIPERACILLIN-TAZOBACTAM	VANCOMYCIN
			AM	SAM	CZ	CAZ	CRO	CC	SXT	E	GM	GMI	LVX	MI	FD#	M	PO	PIV	ST1	TE	NN	TZP	VA
Gram-Negative	*CITROBACTER*	78			32	87	87		85		96		96		87						95	89	
	ENTEROBACTER	140				86	86		93		96		94		20						97	82	
	E. COLI	1688	54	62	79	87	87		73		88		76		95						87		
	KLEBSIELLA	322		86	88	93	93		90		94		95		32						93	95	
	P. MIRABILIS	177	86	92	92	94	94		74		90		76								91	99	
	S. MARCESCENS	29				100	100		100		100		97								97	100	
	P. AERUGINOSA	169				86					95		84								97	91	
Gram-Positive	*ENTEROCOCCUS*	335	94									65	77		94				90				96
	S. AUREUS	467						80	97							67				94			100
	S. AGALACTIAE	126						41		34							100	100					100
	S. PNEUMONIAE	40					100		78	79			98				88	88					100

Clinical Pearls

- If patients clinically respond to therapy, use the shortest recommended duration of therapy to reduce risk of *C. difficile* and other adverse effects.
- Avoid all proton pump inhibitors during CDI management.
- In non-pregnant and non-neutropenic patients, avoid antibiotics for asymptomatic bacteruria and low colony urine counts (< 100,000 CFU's/mL). Take into account urinalysis results.
- Double-anaerobic coverage is not needed: pip/taz (Zosyn), amp/sulbactam (Unasyn), and carbapenems have great anaerobic coverage.
- For *S. aureus* bacteremia, use IV therapy.
- Double gram-negative coverage usually not needed based on our susceptibility data. If used, de-escalate with final sensitivities result.
- Avoid Quinolones unless severe PCN allergy or no alternative treatment options in uncomplicated respiratory/urinary infections.
- Avoid quinolones due to increased risks of aortic rupture, hypoglycemia, and CNS effects.

Verigene Result Recommendations

Genus	Species	Resistance Markers		Treatment of Choice
Staphylococci	*S. aureus*	-mecA	MSSA	Cefazolin or nafcillin
		+mecA	MRSA	Vancomycin
	S. epidermidis	-mecA	MSSE	Possible contaminant if only one blood cx positive. If not, treat w/ vanco
		+mecA	MRSE	
Streptococci	*S. pyogenes* (Grp A)	-	-	Penicillin, cefazolin
	S. agalactiae (Grp B)	-	-	Penicillin, cefazolin
	S. anginosus grp	-	-	Penicillin, ampicillin, ceftriaxone
	S. pneumoniae	-	-	Ceftriaxone
Enterobacteriaceae	*E.coli, Proteus spp., K. pneumoniae*	-CTX-M	-	Ceftriaxone
		+CTX-M	+ESBL	Meropenem w/ ID approval
Enterococci	*E. faecalis*	-VanA/B	-	Ampicillin
		+VanA/B	VRE	Dapto or linezolid w/ID approval
	E. faecium	-VanA/B	-	Ampicillin
		+VanA/B	VRE	Dapto or linezolid w/ID approval

Consider using PO instead of IV formulations for the following antibiotics:

Azithromycin *(35-50% oral bioavailability)*
Clindamycin *(~90% oral bioavailability)*
Doxycycline *(~90% oral bioavailability)*
Fluconazole *(>90% oral bioavailability)*
Levofloxacin *(~99% oral bioavailability)*
Linezolid *(~100% oral bioavailability)*
Metronidazole *(~80% oral bioavailability)*
Rifampin *(~90-95% oral bioavailability)*
Sulfamethoxazole/trimethoprim *(90-100% oral bioavailability)*

Tailored Therapy Based on Verigene

- New molecular blood culture test implemented at SVMH
- Rapidly identifies gram-positive and gram-negative bacteria in a few hours
- Improved turnaround time of blood culture tests by 30-40 hours compared to standard methods
- These tests, **when acted upon in a timely manner**, have been shown to improve patient outcomes (decreased lengths of stay, cost-savings)

Verigene

- Verigene detects 12 different gram-positive and 8 gram-negative organisms as well as genetic markers for antibiotic resistance
- Differentiates methicillin-sensitive staphylococcus aureus (MSSA) from methicillin-resistant Staphylococcus aureus (MRSA) by identifying the resistance-conferring mecA gene
- Differentiates vancomycin-sensitive Enterococci from vancomycin-resistant Enterococci (VRE)
- Detects genetic resistance markers such as those associated with extended-spectrum beta-lactamases (ESBL)

Verigene Result Recommendations				
Genus	**Species**	**Resistance Markers**		**Treatment of Choice**
Staphylococci	*S. aureus*	**-mecA**	**MSSA**	Cefazolin or nafcillin
		+mecA	**MRSA**	Vancomycin
	S. epidermidis	**-mecA**	**MSSE**	Possible contaminant if only one blood cx positive. If not, treat w/ vanco
		+mecA	**MRSE**	
Streptococci	*S. pyogenes (Grp A)*	-	-	Penicillin, cefazolin
	S. agalactiae (Grp B)	-	-	Penicillin, cefazolin
	S. anginosus grp	-	-	Penicillin, ampicillin, ceftriaxone
	S. pneumoniae	-	-	Ceftriaxone
Enterobacter-eceae	*E.coli, Proteus K. pneumoniae*	**-CTX-M**	-	Ceftriaxone
		+CTX-M	**+ESBL**	Meropenem w/ ID approval
Enterococci	*E. faecalis*	**-VanA/B**	-	Ampicillin
		+VanA/B	**VRE**	Dapto or linezolid w/ID approval
	E.faecium	**-VanA/B**	-	Ampicillin
		+VanA/B	**VRE**	Dapto or linezolid w/ID approval

SVMH Antibiogram. Published 2017

Intravenous to Oral Therapy

Converting IV to PO maintains efficacy while

- Supporting earlier ambulation
- Decreasing complications from IV lines (thrombophlebitis, infections)
- Decreasing lengths of stay
- Decreasing equipment and drug costs
- Saving personnel time (nursing administration time, pharmacy compounding time)

IV to PO Conversions

Patients can be considered for IV to PO conversions when they are:

- Taking other oral medications
- Improving clinically (normal vital signs, hemodynamically stable, improving WBC, etc.)
- Have no conditions that might affect GI absorption of medications (e.g. persistent nausea/vomiting, ileus, active GI bleed, etc.)

Examples of IV to PO Conversions

Sequential Therapy (same agent but changing from IV to PO dosage form with the same or orally equivalent dose)	**Step-Down Antimicrobial Therapy** (conversion to a different agent that offers a similar spectrum of activity)
▪ **Azithromycin** *(35-50% oral bioavailability but has excellent distribution to the lungs)* ▪ **Clindamycin** *(~90% oral bioavailability)* ▪ **Doxycycline** *(~90% oral bioavailability)* ▪ **Famotidine** *(~50% oral bioavailability)* ▪ **Fluconazole** *(>90% oral bioavailability)* ▪ **Levofloxacin** *(~99% oral bioavailability)* ▪ **Levothyroxine** *(~50% oral bioavailability)* ▪ **Linezolid** *(~100% oral bioavailability)* ▪ **Metronidazole** *(~80% oral bioavailability)* ▪ **Pantoprazole** *(~80% oral bioavailability)* ▪ **Rifampin** *(~90-95% oral bioavailability)* ▪ **Sulfamethoxazole/trimethoprim** *(90-100% oral bioavailability)*	▪ **Ampicillin** → amoxicillin ▪ **Ampicillin/sulbactam** → amoxicillin/clavulanate ▪ **Aztreonam** → ciprofloxacin or levofloxacin ▪ **Cefazolin** → cephalexin ▪ **Cefotaxime or ceftriaxone** → cefpodoxime or cefuroxime axetil ▪ **Ceftazidime or cefepime** → ciprofloxacin or levofloxacin ▪ **Piperacillin/tazobactam** → levofloxacin + metronidazole, or levofloxacin + amoxicillin/clavulanate

Shorter Durations of Therapy

- Recent studies have shown that shorter antibiotic courses often work just as well, and may be preferred to longer courses due to a reduced risk of developing resistance and developing superinfections

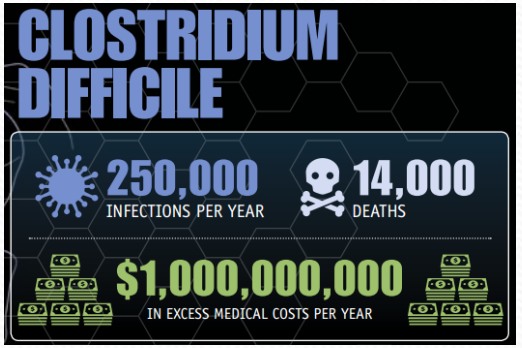
INFECTIONS	DIAGNOSTIC CONSIDERATIONS	EMPIRIC THERAPY	DEFINITIVE THERAPY Tailor to culture results and define duration, including discharge prescription.
Skin and soft tissue infection	Develop diagnostic criteria to distinguish purulent and non-purulent infections and severity of illness (i.e., mild, moderate and severe) so that skin and soft tissue infections can be managed appropriately according to guidelines.	Avoid empiric use of antipseudomonal beta-lactams and/or anti-anaerobic agents unless clinically indicated. Use of therapy specific for MRSA may not be necessary in uncomplicated non-purulent cellulitis [53].	Guidelines suggest that most cases of uncomplicated bacterial cellulitis can be treated for 5 days if the patient has a timely clinical response [53].

INFECTIONS	DIAGNOSTIC CONSIDERATIONS	EMPIRIC THERAPY	DEFINITIVE THERAPY Tailor to culture results and define duration, including discharge prescription.
Community-acquired pneumonia[54]	Review cases after initiation of therapy to confirm pneumonia diagnosis versus non-infectious etiology.	Avoid empiric use of antipseudomonal beta-lactams and/or MRSA agents unless clinically indicated.	Guidelines suggest that in adults, most cases of uncomplicated pneumonia can be treated for 5 days when a patient has a timely clinical response [55, 56]. Data also suggest that negative results of MRSA nasal colonization testing can help guide decisions to discontinue empiric therapy for MRSA pneumonia [57]

INFECTIONS	DIAGNOSTIC CONSIDERATIONS	EMPIRIC THERAPY	DEFINITIVE THERAPY Tailor to culture results and define duration, including discharge prescription.
Urinary tract infection (UTI)	Implement criteria for ordering urine cultures to ensure that positive cultures are more likely to represent infection than bladder colonization [58]. **Examples include:** • Order a urine culture only if the patient has signs and symptoms consistent with UTI such as urgency, frequency, dysuria, suprapubic pain, flank pain, pelvic discomfort or acute hematuria. • For patients with urinary catheters, avoid obtaining urine cultures based solely on cloudy appearance or foul smell in the absence of signs and symptoms of UTI. Nonspecific signs and symptoms such as delirium, nausea and vomiting should be interpreted with caution as, by themselves, they have a low specificity for UTI.	Establish criteria to distinguish between asymptomatic and symptomatic bacteriuria. Avoid antibiotic therapy for asymptomatic bacteriuria except in certain clinical situations where treatment is indicated, such as for pregnant women and those undergoing an invasive genitourinary procedure.	Use the shortest duration of antibiotic therapy that is clinically appropriate.

Reducing Clostridium Difficile Infections

- Prevention
  - Hand hygiene
  - Isolation
  - Environmental decontamination



- Improve prescribing
  - Minimize the use of excessively broad-spectrum antimicrobials when treating infections to lessen the disruption of gastrointestinal normal flora. Minimize the use of drugs commonly associated with c. diff (clindamycin, levofloxacin and other fluoroquinolones, etc.)
  - Minimize antibiotic exposures to the shortest reasonable duration
  - Avoid gastric acid suppression, such as with Proton-Pump-Inhibitors, unless clinically indicated (e.g. mechanical ventilation, coagulopathy, high dose corticosteroids, sepsis, history of GI bleed, traumatic brain, spinal cord, or burn injury, etc.)