UTIs: Wee have the will and the way

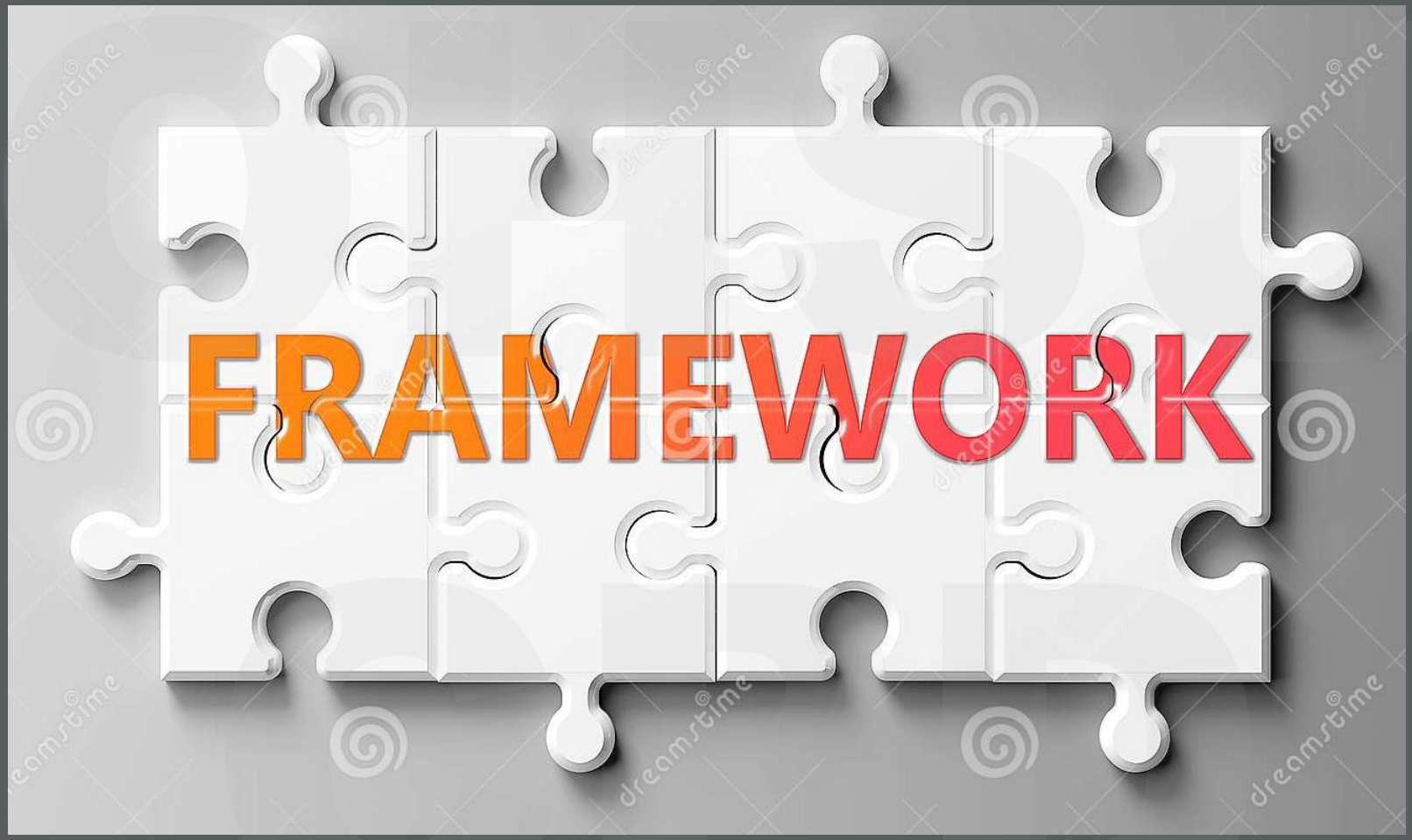
How to treat the toughest bugs and prevent recurrence

DATE: June 2025 PRESENTED BY: Erin Bonura MD, MCR

Objectives

By the end of this session, the audience will be able to

- Describe a framework for categorizing UTIs
- State the empiric treatment of choice for UTIs
- State treatment options for drug resistant UTIs in the inpatient and outpatient settings
- Describe prevention options for recurrent UTIs



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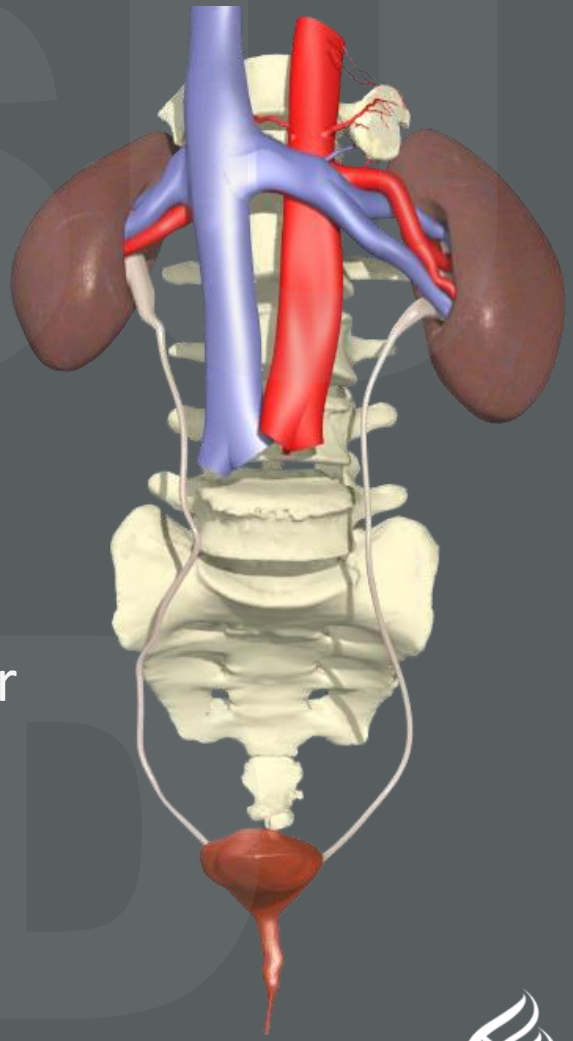
~COMPLICATED~

Symptoms

- Pyelonephritis
  - Fever
  - Flank pain
  - +/- frequency, dysuria, urgency
- Cystitis
  - Frequency
  - Dysuria
  - Urgency
  - Suprapubic discomfort
- Prostatitis
  - Acute: pain, fever, obstructive symptoms
  - Chronic: subtle
- Urethritis
  - Dysuria

Upper tract

Lower tract



Complicating Factors

- History of MDR Urine Isolate
- Use of Quinolone, Bactrim, BSBL
- Travel to area with high rates MDR
- Inpatient stay at HC Facility

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Case 1: E.C.

Ms. EC is a 45 yo cisgender woman with a past medical history of hypertension presents with 3 days of dysuria, frequency, hesitancy and fever. On exam she has a temp of 102F, HR98, BP 160/94, pO2 98%. She has suprapubic and flank tenderness. Urinalysis shows 50 WBC, + leuk esterase, + nitrite, no squames. Urine culture grows >100k e.coli (Resistant to cefazolin). What is the best treatment choice?

A. TMP-SMX x 5 days
B. Ciprofloxacin x 7 days
C. Nitrofurantoin x 10 days
D. Ceftriaxone x 14 days

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Table 1: EMPIRIC MANAGEMENT OF URINARY TRACT INFECTIONS

Uncomplicated/ Lower		Complicated/ Upper	
Cystitis		Pyelonephritis	
Low risk MDR	High risk MDR	Low risk MDR Mild-Mod Illness	High risk MDR Critical Illness*
Culture ***Optional***	**Culture**	**Culture**	**Culture**
Nitrofurantoin x 5 d	Nitrofurantoin	Quinolone	Pip-tazo
Bactrim x 3 d (if resistance <20%)	Fosfomycin	Bactrim if susceptible	Cefepime
Fosfomycin x 1		Ceftriaxone	Carbapenem (don't forget ERTA)

Always tailor regimen based on culture data!

* May consider double coverage until culture results return

§ History of MDR urine isolate; Inpatient stay at health care facility; Use of quinolone, bactrim or broad spectrum betalactam; Travel to area with high rates of MDR organisms (India, Israel, Spain, Mexico)

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EMPIRIC MANAGEMENT OF URINARY TRACT INFECTIONS

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Bactrim x 3 d (if resistance <20%)	Fosfomycin	Bactrim if susceptible x 7-10	Cefepime x 10-14
Fosfomycin x 1		Ceftriaxone x 10-14	Carbapenem (don't forget ERTA) x 10-14
Always tailor regimen based on culture data!			

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OHSU OUTPATIENT ADULTS (January 1, 2020 – December 31, 2020)

	Gram Negative Aerobes						Gram Positiv	
	Pseudomonas aeruginosa (123)	Enterobacter cloacae complex (51)	E.coli (1221)	Proteus mirabilis (103)	Klebsiella pneumoniae (152)	Klebsiella oxytoca (33)	Enterococcus faecalis (154)	All Staphylococcus aureus (583)
Ampicillin	-	-	65	85	-	-	99	-
Amoxicillin/clavulanate	-	-	88	98	95	88	-	-
Cefazolin	-	-	94	91	97	41	-	75
Cefepime	98	100	99	99	99	100	-	-
Ceftriaxone	-	88[b]	96	99	97	88	-	-
Ciprofloxacin	90	98	89	92	98	100	89[a]	-
Clindamycin	-	-	-	-	-	-	-	79
Erythromycin	-	-	-	-	-	-	-	-
Gentamicin	89	100	96	96	99	97	-	-
Levofloxacin	90	100	89	92	98	100	91[a]	-
Meropenem	95	98	100	100	100	100	-	-
Nitrofurantoin[a]	-	35	97	-	30	76	99	-
Oxacillin (nafcillin)	-	-	-	-	-	-	-	75
Piperacillin/tazobactam	96	94	98	100	96	91	-	-
Tetracycline	-	85	82	-	84	91	31[a]	95
Tobramycin	97	98	97	96	97	97	-	-
Trimethoprim/ sulfamethoxazole	-	88	82	85	90	91	-	95

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OHSU INPATIENT ADULTS (January 1, 2020 – December 31, 2020)

	Gram Negative Aerobes									Gram P		
	Serratia marcescens (38)	Pseudomonas aeruginosa (184)	Enterobacter cloacae (116)	Klebsiella aerogenes (34) (formerly Enterobacter aerogenes)	E.coli (572)	Proteus mirabilis (78)	Klebsiella pneumoniae (186)	Klebsiella oxytoca (75)	Stenotrophomonas maltophilia (48)	Streptococcus pneumoniae (35)[c]	Enterococcus faecalis (248)	Enterococcus faecium (58)
Trimethoprim/ sulfamethoxazole	100	-	85	97	73	83	91	92	98	80	-	-
Vancomycin	-	-	-	-	-	-	-	-	-	-	100	71

Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial

Torsten Sandberg, Gunilla Skoog, Anna Bornefalk Hermansson, Gunnar Kahlmeter, Nils Kuylenstierna, Anders Lannergård, Gisela Otto, Bo Settergren, Gunilla Stridh Ekman

	7 days N (%)	14 days N (%)	Difference (90% CI)	P value
E. coli	64 (88)	79 (95)	-	-
Bacteremia	16 (22)	26 (32)	-	-
Cure	68 (93%)	78 (93%)	-0.3% (-7.4 to 7.2)	0.015
Clinical failure or recurrent UTI sx	5 (7%)	6 (7%)	-	-

Sandberg T, et al. *Lancet* 2012;380:484-90.

Clinical Infectious Diseases

MAJOR ARTICLE

Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

Dafna Yahav,[1,2] Erica Franceschini,[3] Fidi Koppel,[4] Adi Turjeman,[2,5] Tanya Babich,[2,5] Roni Bitterman,[4] Ami Neuberger,[4,6] Nesrin Ghanem-Zoubi,[4] Antonella Santoro,[3] Noa Eliakim-Raz,[1,2] Barak Pertzov,[5] Tali Steinmetz,[5] Anat Stern,[4] Yaakov Dickstein,[4] Elias Maroun,[4] Hiba Zayyad,[4] Jihad Bishara,[1,2] Danny Alon,[7] Yonatan Edel,[2,8] Elad Goldberg,[9] Claudia Venturelli,[3] Cristina Mussini,[3] Leonard Leibovici,[2,5] Mical Paul[4,6]; for the Bacteremia Duration Study Group[a]

Included:

- GNB bacteremia at day 7 IF afebrile and stable x 48hrs
- UTI, Intraabdominal, CVC
- SSTI, unknown source
- Community or Hospital Acquired

Excluded:

- Other sources
- Uncontrolled source
- Polymicrobial growth
- Brucella, salmonella
- Neutropenia, HSCT
- HIV

GNB Bacteremia 7 vs 14 days

	7 days	14 days
Bacteria type	**N (%)**	**N (%)**
- E.coli	186 (60.8)	194 (65)
- Klebsiella spp	47 (15.3)	33 (11.1)
- Other enterobacteriaceae	40 (13.1)	43 (14.4)
- Acineto/Pseudomonas spp	30 (9.9)	34 (8.0)
Source of Bacteremia		
- UTI	212 (69.3)	199 (66.8)
- Primary bacteremia	23 (7.5)	28 (9.4)
- Abdominal	37 (12.1)	34 (11.4)
- Respiratory	14 (4.6)	10 (3.4)
- Other	20 (6.5)	27 (8)

Yahav et al. Clinical Infectious Diseases. 2019;69(7):1091–8

Primary Outcomes for GNB Bacteremia 7 vs 14 d

Outcome	7d 306 (%)	14d 296 (%)	P Value
Primary Outcome	140 (45.8)	144 (48.3)	.527
90d all cause mort	36 (11.8)	32 (10.7)	.702
Readmissions	119 (38.9)	127(42.6)	.363
Distant complications	2	1	
Relapse	8 (2.6)	8 (2.7)	.957
Suppurative complications	16 (5.2)	10 (3.4)	.257
14 d mortality	7 (2.3)	4 (1.3)	2.88
28 d mortality	15 (4.9)	13 (4.4)	.753

What Antibiotics Were Used?

Type of IV antibiotics [a]	Short arm (306 patients)	Long arm (298 patients)
Cephalosporins	157 (51.3)	167 (56.0)
Beta-lactam beta-lactamase inhibitors	72 (23.5)	63 (21.1)
Quinolones [b]	15 (4.9)	14 (4.7)
Aminoglycosides	39 (12.7)	36 (12.1)
Carbapenems	23 (7.5)	16 (5.4)
Trimethoprim-sulfamethoxazole	0	2 (0.7)

Type of ORAL antibiotics [a]	Short arm (196 patients)	Long arm (242 patients)*
Quinolones	151 (77.0)	172 (71.1)
Beta-lactams	28 (14.3)	50 (20.7)
Trimethoprim-Sulfamethoxazole	17 (8.7)	20 (8.3)

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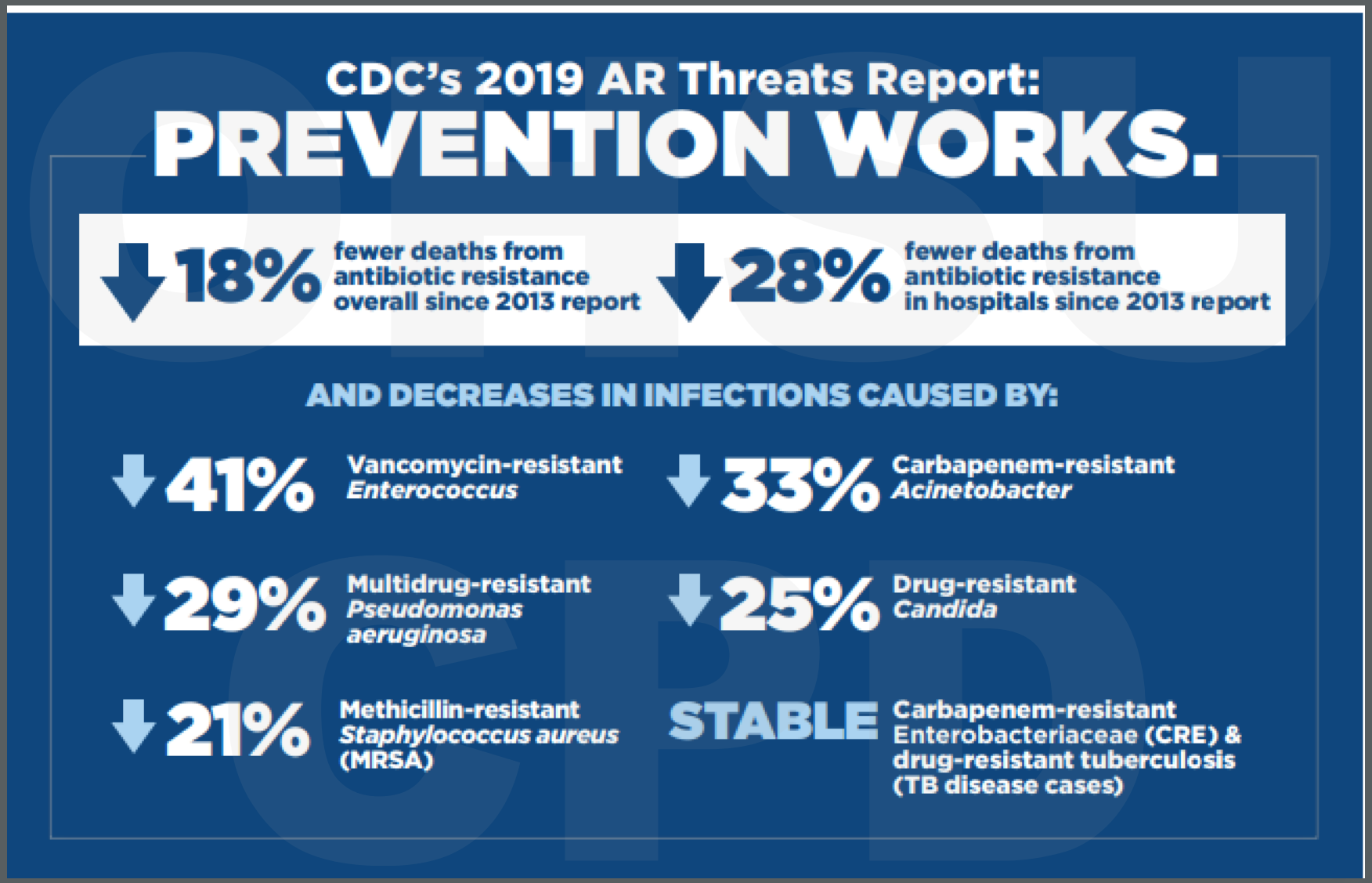
Treatment Take home

- UTI categorization is now lower vs upper tract with MDR considerations
- Upper tract infections can be treated for 7 days (quinolones)
- Enterobacteriaceae bacteremia in setting of UTI can be treated for 7 days

Case 2: Mr. M.DR

Mr. Michael Don Rivera is a 65 year old cisgender man with a history of BPH who presents with dysuria, frequency, and flank tenderness. He has a temp of 101.3F, HR 85, BP 146/84, RR12, Pox1000% RA. Exam is notable for suprapubic and flank tenderness. Labs show a WBC of 16, Hb 15, Plt 450k, Creat 1.0 and all others within normal limits. Urinalysis shows +25WBC, no RBC and culture grows e.coli resistant to cefazolin and ceftriaxone. What is the best option below.

A. Treat with pip-tazo x 14 days
B. Treat with Trimethoprim-sulfamethoxazole x 10 days
C. Treat with nitrofurantoin x 5 days


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)

Despite these gains, CDC's 2019 AR Threats Report shows additional actions are needed to protect people.

2.8M+ antibiotic-resistant infections each year

35k+ deaths from antibiotic resistance each year

Plus: 223,900 cases and 12,800 deaths from *Clostridioides difficile*

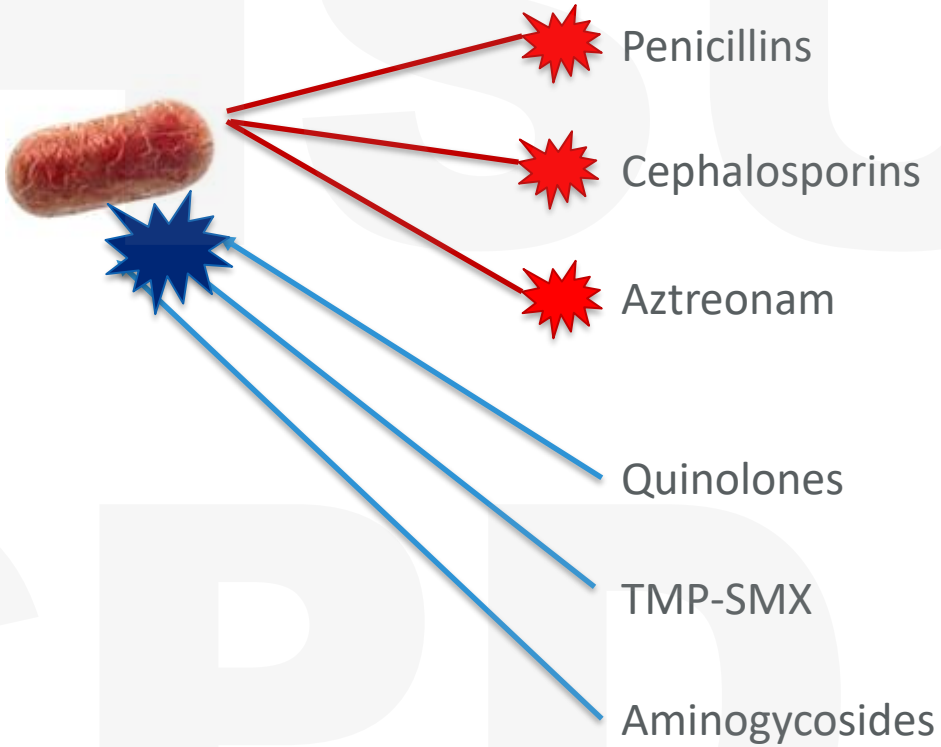
AND INCREASES IN INFECTIONS CAUSED BY:

- ↑ **315%** Erythromycin-resistant invasive group A strep
- ↑ **124%** Drug-resistant *Neisseria gonorrhoeae*
- ↑ **50%** ESBL-producing Enterobacteriaceae

Let's Talk about ESBLs

53%

2012-2017



www.idsociety.org/practice-guideline/amr-guidance/

What to use for Lower Track UTI with ESBL?

EMPIRIC MANAGEMENT OF URINARY TRACT INFECTIONS			
Uncomplicated		**Complicated**	
Cystitis		**Pyelonephritis**	
Low risk MDR	**High risk MDR**	**Low risk MDR Mild-Mod Illness**	**High risk MDR Critical Illness***
Culture ***Optional***	**Culture**	**Culture**	**Culture**
Nitrofurantoin x 5 d	Nitrofurantoin	Quinolone x 7d	Pip-tazo x 10-14
Bactrim x 3 d (if resistance <20%)	----------	Bactrim if susceptible x 7-10	Cefepime x 10-14
Fosfomycin x 1	Fosfomycin	Ceftriaxone x 10-14	Carbapenem (don't forget ERTA) x 10-14
Pivmecillinam	Pivmecillinam??		
Always tailor regimen based on culture data!			

What about Fosfomycin?

JAMA | Original Investigation

Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women

A Randomized Clinical Trial

Angela Huttner, MD; Anna Kowalczyk, MS; Adi Turjeman, MSc; Tanya Babich, MSc; Caroline Brossier, RN; Noa Eliakim-Raz, MD; Katarzyna Kosiek, MD, PhD; Begoña Martinez de Tejada, MD, PhD; Xavier Roux, MD; Shachaf Shiber, MD; Ursula Theuretzbacher, PhD; Elodie von Dach, PhD; Dafna Yahav, MD; Leonard Leibovici, MD; Maciek Godycki-Ćwirko, MD, PhD; Johan W. Mouton, MD, PhD; Stephan Harbarth, MD

- Clinical response: 70% with Nitrofurantoin vs 58% Fosfomycin
- Microbiologic resolution: 74% (nitro) vs 63% fos
- Cost: $5 Nitro course vs $75 for one sachet Fosfomycin

Huttner A, et al. JAMA 2018;319:1781

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The Newby: Pivmecillinam

- Penicillin with extended GM spectrum
- Only for UTI - Acute simple cystitis
- Low risk of selecting for resistant organisms
- Agent of choice in many Nordic countries due to low resistance
- Some activity against ESBL and carbapenemases
- Well tolerated – mild GI AE
- Dose varies by region/country – 185mg PO TID x 3-7days

Treatment for Upper UTI due to ESBL-E

Carbapenems

- Ertapenem
- Meropenem
- Imipenem

Quinolones

- Levofloxacin
- Ciprofloxacin

TMP-SMX

Why not Pip-tazo??

Research

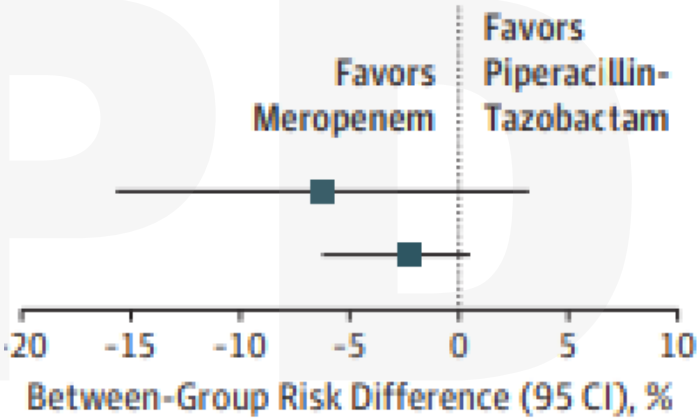
JAMA | Original Investigation

Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance

A Randomized Clinical Trial

30d mortality:

12.3% P-T vs 3.7% Mero



JAMA. 2018 Sep 11;320(10):984-994.

What if it is CRE (run away?)

Upper UTI

- Quinolones
- Bactrim
- Extended inf mero?
- Ceftaz-Avi, mero-vabor, imi-rel, cefiderocol
- Aminoglycosides (ami and plazo)

Lower UTI

- Quinolones
- Bactrim
- Nitrofurantoin
- Aminoglycoside

Key Points

- We still need to be mindful of drug resistance
- For ESBL-E (resistance to Ceftriaxone), **Bactrim** and nitrofurantoin are great for lower track
- Pivmecillinam is a **NEW** option in the US for cystitis
- For ESBL-E upper tract – **Bactrim** and quinolones
- For CRE – **Bactrim** and quinolones (if lucky) then think about the newbies (but consider an ID consult first)

Case 3: Ms. De L'eau

Ms. De l'eau is an 65 year old cisgender woman with a history of recurrent urinary tract infections. She is currently on nitrofurantoin daily but continues to have UTIs. She had a urologic evaluation and does not have any anatomic abnormality to address. What would you suggest?

A. She should start vaginal estrogen
B. She should start 20mg of Proanthocyanidin daily
C. She should drink a liter of water a day
D. She should switch to cephalexin prophylaxis

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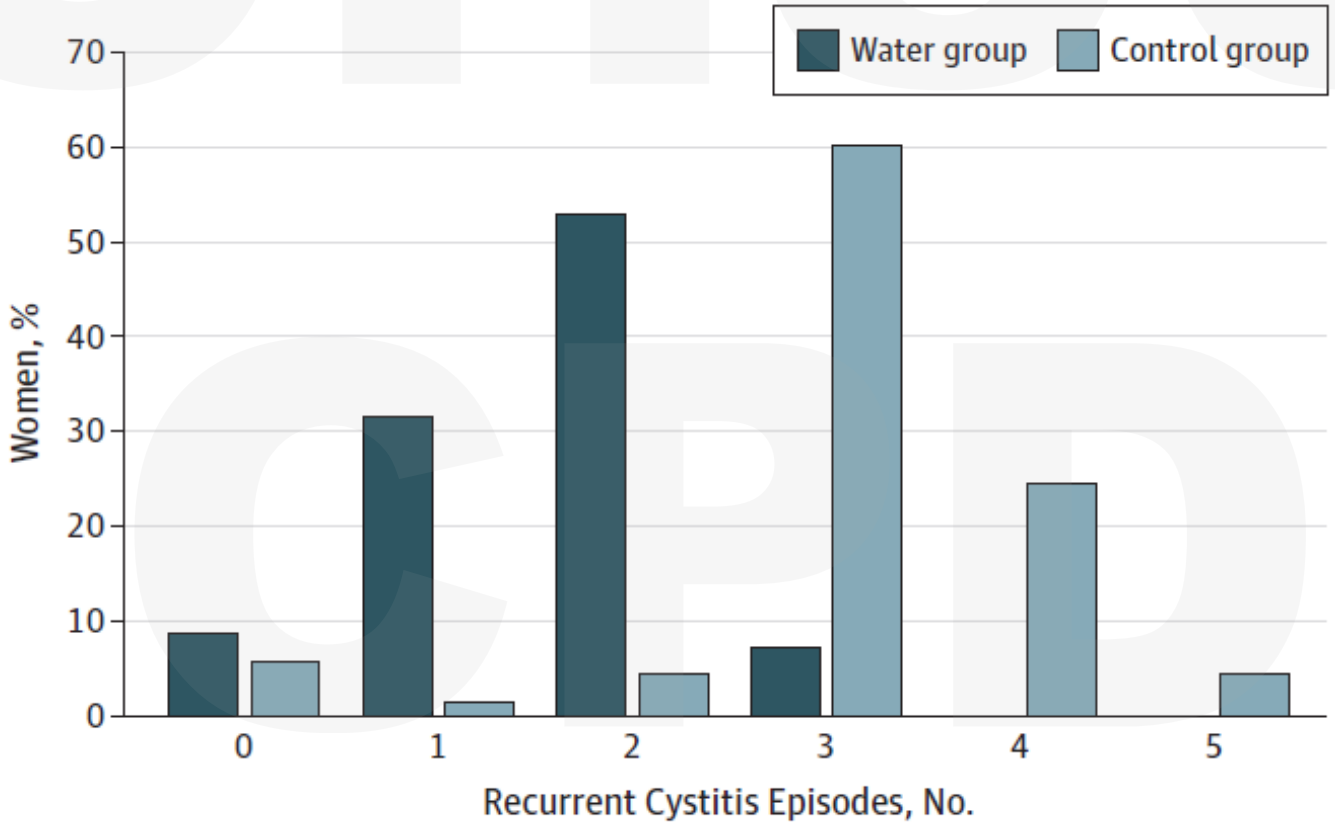
Increased water decreased UTI

Figure 2. Recurrent Cystitis Episodes by Study Group



AMA Intern Med. 2018;178(11):1509-1515.

Vaginal estrogen

- Raz et al., NEJM 1993:

  estrogen (0.5) vs placebo (5.9) episodes/person/year

- FPMRS 2021:

UTI events	Placebo	Estrogen	P value
Intention to Treat	16/17	9/18	0.041
Per Protocol	10/11	8/15	0.036

NEJM. 1993;329:753-6

Female Pelvic Med Reconstr Surg 2021;27: 112–117

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MAJOR ARTICLE

Effectiveness of Estriol-Containing Vaginal Pessaries and Nitrofurantoin Macrocrystal Therapy in the Prevention of Recurrent Urinary Tract Infection in Postmenopausal Women

R. Raz,[1,4] R. Colodner,[2] Y. Rohana,[5] S. Battino,[3] E. Rottensterich,[5] I. Wasser,[5] and W. Stamm[6]

- 9 months; 86 pessary vs 85 nitrofurantoin
- 85 episodes in pessary group vs 30 with NM
- 2 episodes per person/yr vs 0.8 in NM group
- Pessary may not be as effective as cream

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Efficacy of different antibiotics

Organism	No drug	Sulfa	Methenamine	TMP-SMX
E.Coli	24	10	10	0
Klebsiella	2	2	1	0
Citrobacter	1	0	0	0
Enterococcus	5	9	2	1
GBS	1	1	0	0
Totals	33	22	13	1

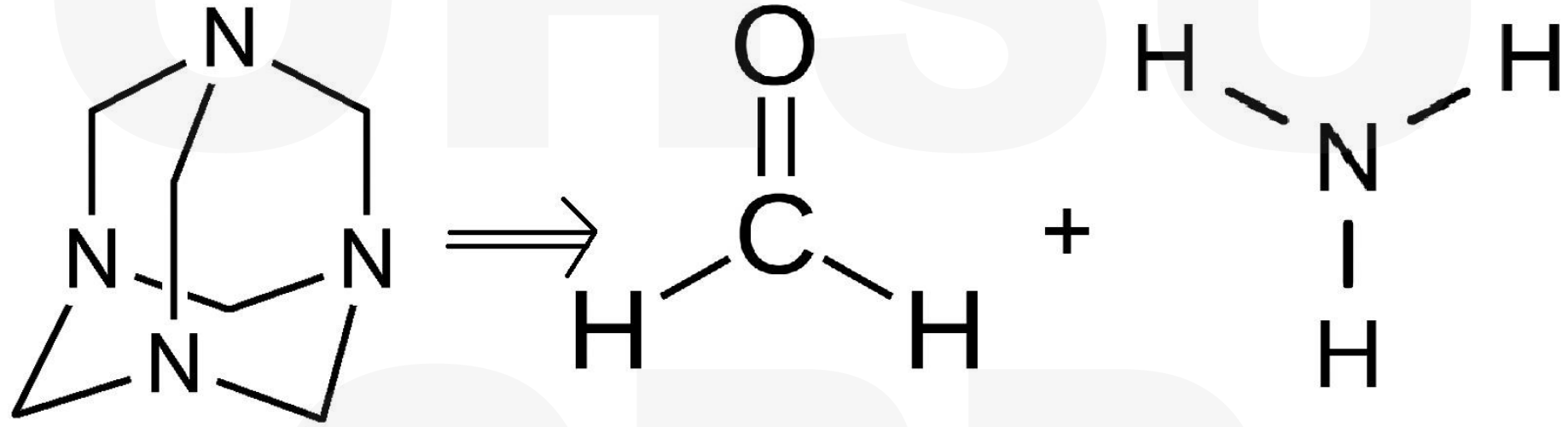
Engl J Med. 1974 Sep 19;291(12):597-601.

Efficacy of different antibiotics

Organism	No drug	Sulfa	Methenamine	TMP-SMX
E.Coli	24	10	10	0
Klebsiella	2	2	1	0
Citrobacter	1	0	0	0
Enterococcus	5	9	2	1
GBS	1	1	0	0
Totals	33	22	13	1

Engl J Med. 1974 Sep 19;291(12):597-601.

Now back up, what is methenamine?



Methenamine Formaldehyde Ammonia

Methenamine vs Placebo

	Methenamine hippurate	Placebo
Cases	11	41
Organisms	E.coli, Proteus, GBS	E.coli, Proteus, Klebsiella, Enterobacter, Enterococcus

Br Med J (Clin Res Ed). 1987 Jun 13;294(6586):1507-8.

Tools & Tricks for UTI Prevention

Tool	Mechanism	Evidence It Works?	Considerations
Increased H2O	Flush the system	*Maybe*	Need more studies
Cranberry Juice	Proanthocyanidin 36mg	**YES**	
Vaginal Estrogen	Replacement	**YES**	No increased AE
Methenamine	Formaldehyde	**YES**	No incontinence, good function
D Mannose	Inhibit adhesion to bladder cells	**NO**	Too variable
Post-coital or continuous Abx	Bactericidal	**YES** – sort of	Balance risk of MDR selection, AE
Probiotics	Improve vaginal flora	**NO**	Too variable

Key Points

- Drinking an additional 1.5L water can reduce UTI frequency
- Vaginal estrogen cream can reduce UTI frequency
  - Possibly more than pessaries
  - No increased AE
- Methenamine 1gram BID can be considered
- The active ingredient in Cranberry juice DOES have evidence
- Ultimately, antibiotic prophylaxis does work… for a time

Take Home Points

- Nitrofurantoin is **only** for cystitis
- Bactrim is a great drug for upper, lower, and MDR UTIs
- ESBLs do not necessarily need a carbapenem, use erta if you do need one
- CREs can get tricky – feel free to call an ID friend
- Prevention does not have to mean antibiotics
  - Increase water consumption
  - Vaginal estrogen
  - Consider methenamine (check contraindications first)

Key References

IDSA GNR Guidelines

JAMA UTI 2024 Guidance

Thank You


WHEN YOU FINALLY GET A
MEDICINE THAT WORKS.