

Hot Topics in Infectious Diseases

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Disclosures

- I have research funding from Cidara, Mundipharma, F2G, Scynexis, GSK and Elion
- I have been a consultant for Pfizer, Takeda and Treeline biosciences

What's New in Infectious Diseases?

- Formidable New & Old Bugs
 - Measles
 - Resistant dermatophyte—*Trichophyton indotineae*
 - Powassan and other vector-borne illnesses
- New Antimicrobials
 - Zoliflodacin 2025
 - Gepotidacin 2025
 - Sulopenem etzadroxil+probenecid 2024
- New Problems
 - Impact of climate change on infection
- New Infectious Diseases Guidelines
 - Surviving sepsis 2026
 - Complicated UTI 2025
 - Histoplasmosis 2025
 - Antimicrobial resistance 2024
- New Approach to Old Problems
 - Oral antibiotics for serious invasive infection
 - Shorter antimicrobial courses for bloodstream infection

Learning objectives

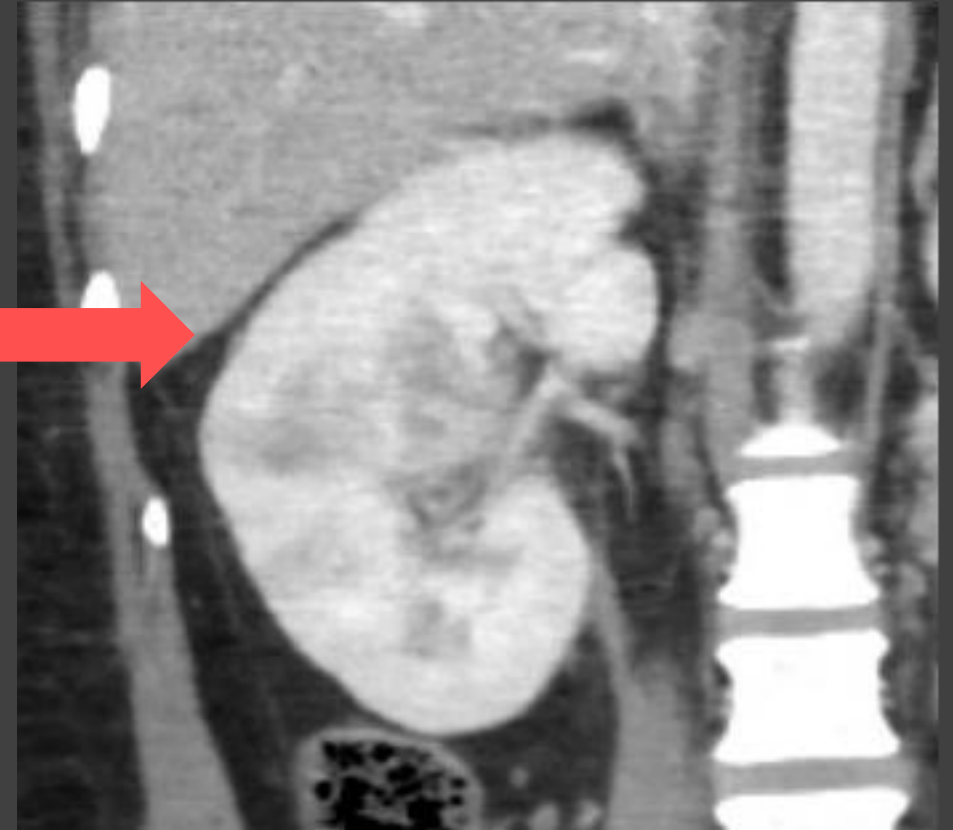
1. To learn when it is appropriate and safe to use oral antibiotics for gram negative bacteremia and to learn the best antibiotic choices
2. To learn when it is appropriate to treat bacteremia with a short (7 day) course of antibiotics
3. To develop an understanding of the current and potential impact of climate change on infection risk
4. To learn the basic epidemiology, presentation and treatment of *Trichophyton indotineae* (antifungal-resistant dermatophyte)

New Approach to Old Problems:

Oral antibiotics for serious invasive infections

Clinical Question

- A 35-year-old woman with obesity and recurrent UTI presents with fever to 103F, tachycardia, hypotension and right flank pain
 - CT imaging consistent with pyelonephritis
- She is admitted to the ICU where she requires pressors for <12 hours
- Improves on empiric cefepime
- 4 of 4 **Blood cultures** and **urine culture** from admission grow **E coli**
 - Subsequent blood cultures negative
- She is afebrile, normotensive and ready for discharge 3 days later



What's the best antibiotic regimen for discharge home on hospital day 4?

- E coli urine susceptibilities
 - Ampicillin resistant
 - Cefazolin susceptible
 - Cefepime susceptible
 - Ceftriaxone susceptible
 - Ciprofloxacin resistant
 - Levofloxacin resistant
 - Nitrofurantoin susceptible
 - Trimethoprim-sulfamethoxazole susceptible

- A. Oral nitrofurantoin x5 days
- B. IV ceftriaxone x6 days
- C. Oral trimethoprim-sulfa x6 days
- D. Oral amoxicillin x10 days
- E. Oral cephalexin x10 days

A shift to oral antibiotics for serious infection?

- Historically serious invasive infections in adults have been treated with parenteral antibiotics
- However, benefits of avoiding long term IV therapy make oral therapy appealing
 - Oral therapy can reduce length of hospital stay, improve mobility, reduce cost
 - Complications of IV therapy include catheter-related infection, line-associated DVT, cost associated with line care
- Areas where there is increasing interest in using oral antibiotics as “step-down” therapy includes
 1. Gram-negative bacteremia (GNB)
 2. Endocarditis
 3. Bone and joint infection in adults

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 1. **Gram-negative bacteremia (GNB)**
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 3. Bone and joint infection in adults

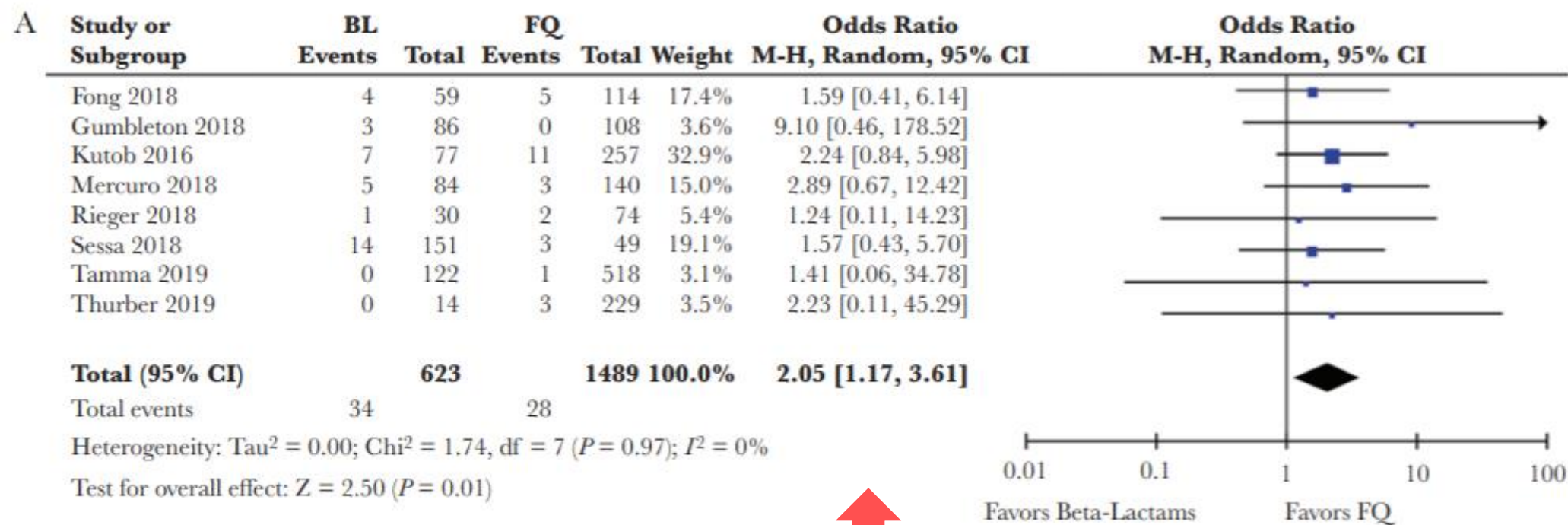
Important studies have demonstrated the feasibility. Oral step-down antibiotics for these infections is an area of emerging practice change and study!

Oral Antibiotics: Basic Principles

- Certain antibiotics have excellent oral bioavailability such that oral therapy achieves similar concentrations to IV (eg. levofloxacin)
 - In some cases where oral bioavailability is less, increased dose of oral agent can overcome lower bioavailability (eg. Ciprofloxacin → 400 IV = 750mg po)
 - In some cases oral bioavailability is good, but oral dosing is limited by side effects (eg. Clindamycin IV is given at higher doses than can be given orally)
- Oral antibiotics at standard dose with similar concentrations to IV:
 - Levofloxacin, Ciprofloxacin, Moxifloxacin
 - Trimethoprim-Sulfamethoxazole (TMP-SMX)
 - Metronidazole
 - Linezolid
 - Clindamycin (but hard to tolerate at appropriate dose)

Oral Antibiotics: Gram-Negative Bloodstream Infection

- Tamma, et al. studied a propensity score-matched cohort of 1478 patients with **Enterobacteriaceae** and adequate source control at 3 hospitals
 - GNB sources: Urinary tract (40%), GI tract (20%) catheter-associated (18%), pulmonary (4%), SSTI (3%)
 - Microbiology: *E. coli* 44%, *Klebsiella spp.* 36%, *Enterobacter spp.* 12%
- No difference in 30-day mortality or recurrent bacteremia between those treated with oral 'step-down' therapy within 5 days vs. parenteral therapy
 - Recurrent bacteremia was rare in both groups (<1% in both groups)
- Median time from bacteremia to hospital discharge was significantly shorter in the oral therapy group (5 days vs. 7 days, HR 0.98)
- 84% in the oral step-down group were treated with antibiotics with high oral bioavailability → the large majority of which were fluroquinolones
 - Low number of patients treated with low bioavailability oral antibiotics limited statistical power to address the importance of bioavailability
 - Minority of patients were immunocompromised



- Punjabi et al. performed a meta-analysis of studies assessing oral step-down therapy for **Enterobacteriaceae bacteremia**
 - No difference in 30-day mortality
 - BUT infection recurrence at primary site or bloodstream more common in oral beta-lactam group vs. fluroquinolone/TMP-SMX (5.46% vs. 1.98%)
 - Unclear if some of this is related to suboptimal beta-lactam dosing

Impact of oral Bioavailability on GNB Therapy

- Daneman et al. studied outcomes in 2012 patients with **GNB** who were >65 years old and treated with high oral bioavailability antibiotics (TMP-SMX, quinolones) versus low oral bioavailability (beta-lactams) in a propensity score matched analysis

Table 3

Adjusted propensity-matched analysis of the primary and secondary outcomes among patients with gram-negative bloodstream infection treated with highly versus less-bioavailable drugs at discharge

Outcomes	Less bioavailable, n (%)	Highly bioavailable, n (%)	p	Highly (vs. Less) bioavailable, odds ratio (95% CI)
90-d outcome				
Primary composite of mortality, recurrent BSI, or re-admission	216 (21.5)	171 (17.0)	0.01	0.74 (0.59–0.93)
90-d secondary outcomes				
Mortality	49 (4.9)	43 (4.3)	0.52	0.87 (0.57–1.32)
Recurrent BSI	100 (9.9)	62 (6.2)	0.00	0.59 (0.42–0.82)
Re-admission	141 (14.0)	121 (12.0)	0.19	0.84 (0.65–1.09)
ER visit	107 (10.6)	110 (10.9)	0.83	1.03 (0.78–1.37)
Repeat outpatient antibiotic use	140 (13.9)	122 (12.1)	0.23	0.86 (0.66–1.11)
Development of antibiotic resistance	<6 ^a	<6 ^a	0.71	0.75 (0.17–3.35)

- Geyer et al. studied outcomes in 194 patients with **Enterobacteriales** bacteremia due to UTI treated with quinolone or TMP-SMX vs. **high dose oral cephalexin (1 g PO TID) or amoxicillin (1 g po TID)**
 - No difference in composite of mortality or recurrent bacteremia with in 30 days

Practical Conclusions: Oral therapy for GNB

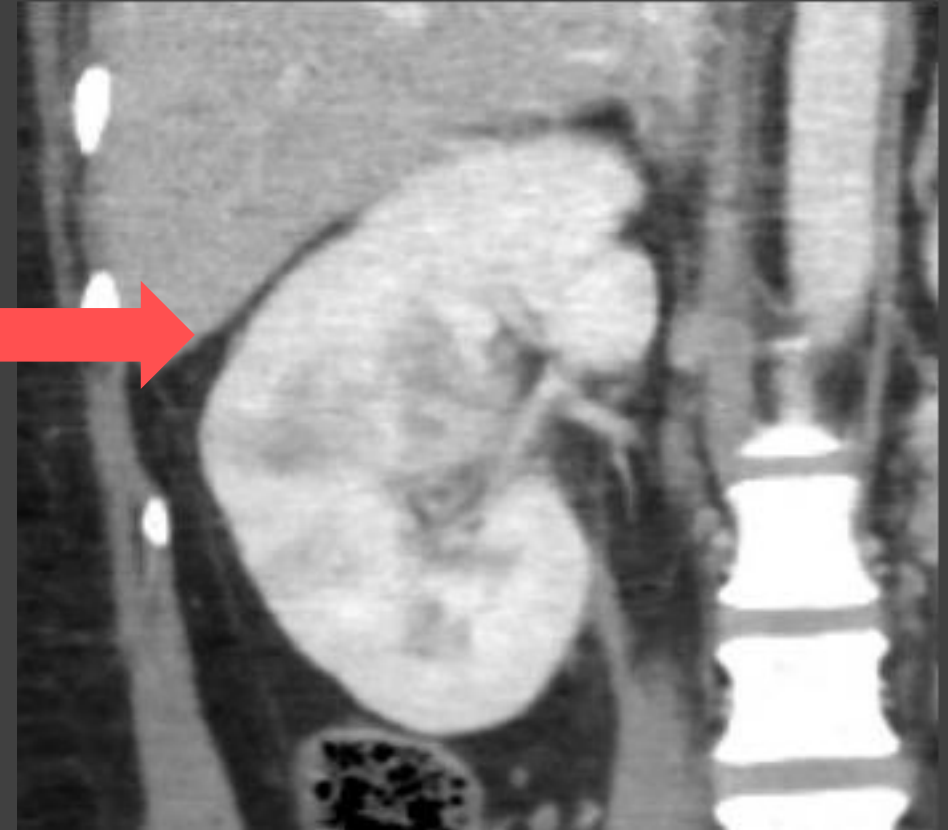
- While studies suggest quinolones/TMP-SMX appear to perform better than oral beta-lactams for **Enterobacterales**, both groups have important toxicities
 - Limitations: Most studies left out non-**Enterobacterales** and had limited immunocompromised patients
- Reasons we don't like quinolones
 - Multiple warnings issued by FDA for risk of tendonopathy, neuropsychiatric side effects and possibly increased risk of aneurysms
 - Overuse has led to relatively frequent resistance among gram-negative organisms
 - Quinolones have been associated with increased C. diff risk in some studies
- Challenges with TMP-SMX
 - Risks include reversible impact on creatinine, hyperkalemia, abnormal LFTs and rash
- When and how to try beta-lactams
 - **When:** In cases where resistance precludes use of drugs with high oral bioavailability and IV therapy is not a reasonable option
 - **How:** With careful attention to optimized dosing....

New Approach to Old Problems:

Shorter course of antibiotics for
bloodstream infection

Similar Clinical Question– different choices

- A 35-year-old woman with obesity and recurrent UTI presents with fever to 103F, tachycardia, hypotension and right flank pain
 - CT imaging consistent with pyelonephritis
- She is admitted to the ICU where she needs pressors for 12 hours but quickly improves on empiric cefepime
- 4 of 4 **Blood cultures** and **urine culture** from admission grow **E coli**
 - Subsequent blood cultures negative
- She is afebrile and normotensive 4 days later



What's the best antibiotic regimen for her on hospital day 4?

- Allergies: Sulfa causes throat swelling and wheezing
- E coli urine susceptibilities
 - Ampicillin resistant
 - Cefazolin resistant
 - Cefepime susceptible
 - Ceftriaxone susceptible
 - Ciprofloxacin resistant
 - Levofloxacin resistant
 - Nitrofurantoin susceptible
 - Trimethoprim-sulfamethoxazole susceptible
- A. Oral cephalexin x 10 days
- B. IV ceftriaxone x 3 more days
- C. IV cefepime x 6 more days
- D. Trimethoprim-sulfa desensitization, then give x 6 more days
- E. IV cefepime x 3 more days

A shift to shorter courses of antibiotics for bloodstream infection?

- Bloodstream infection affects over half a million people per year in North America
- Historically bloodstream infection has been treated with long courses of antibiotics (>10 days) due to concerns about recurrence
 - Optimal duration studies for organ-specific infections often exclude bacteremic patients
- However, with increasing awareness of the importance of antimicrobial stewardship several recent studies have explored the performance of short courses of antibiotics for GNB relative to longer courses

Study Details	Comparison	Outcomes	Limitations	Exclusions
<ul style="list-style-type: none"> • Yahav et al. CID 2019 • Type: Randomized clinical trial • Where: 2 Israeli and 1 Italian academic medical centers • When: 2013-2017 • Patients: 604 patients with aerobic GNB 	7d (306) vs. 14d (298) of antibiotics	<ul style="list-style-type: none"> • Clinical failure (all-cause mortality at 90d, relapse, suppurative, or distant complications; readmission or extended hospitalization) was similar in the two groups: 45.8% in 7d vs 48.3% in 14d group (risk difference, – 2.6% [95% CI –10.5% to 5.3%]) 	<ul style="list-style-type: none"> • Treatment assignment not blinded • 68% of patients had urinary source • ~10% of patients had non enteric GNB 	<ul style="list-style-type: none"> • Hemodynamic instability of fever w/in 48 hours • Uncontrolled focus of infection • Immunosuppression • Polymicrobial GNB
<ul style="list-style-type: none"> • Von Dach et al. JAMA 2020 • Type: Partially–blinded randomized clinical trial • Where: 3 Swiss tertiary care hospitals • When: 2017-2019 • Patients: 504 Adults with GNB 	CRP-guided antibiotic duration* (170) vs. 7d antibiotics (169) vs. 14d antibiotics (165)	<ul style="list-style-type: none"> • 2.4% in the CRP arm vs. 6.6% in the 7d arm vs. 5.5% in the 14d arm had <i>clinical failure</i> (defined as: recurrent GNB, local or distant bacterial complication, restart of antibacterials, 30d mortality) • Both CRP-guided and 7d arm were non-inferior to 14d arm 	<ul style="list-style-type: none"> • Low rate of clinical failure limits interpretation • 69% of patients had urinary source • 75% of bacteremias were <i>E coli</i> 	<ul style="list-style-type: none"> • Hemodynamic instability or fever w/in 24 hours • Immunosuppression • Recurrent, non-fermenting GNB or polymicrobial bacteremia
<ul style="list-style-type: none"> • Molina et al. CMI 2022 • Type: Randomized clinical trial • Where: 5 Spanish medical centers • When: 2014-2016 • Patients: 248 Adults with <i>Enterobacterales</i> bacteremia 	7d (119) vs. 14d (129) of antibiotics	<ul style="list-style-type: none"> • Primary endpoint: total number of antibiotic days from positive blood culture to day 28→ median was 7 (7-14) in 7d arm vs. 14 (14-16) 14d arm • There was no difference in clinical outcomes including mortality, relapse of bacteremia, relapse of fever or drug-related adverse events 	<ul style="list-style-type: none"> • Treatment assignment not blinded • ~60% of isolates <i>E coli</i> • 55% related to UTI • Endpoint (antibiotics days) close to intervention 	<ul style="list-style-type: none"> • Uncontrolled bacteremia • Neutropenia anticipated for >7d • Infection that requires prolonged treatment • Carbapenemase-producing organism

*CRP arm stopped antibiotics when CRP 75% reduced from peak

BALANCE (Bacteremia Antibiotic Length Actually Needed for Clinical Effectiveness) Trial 2024

- Multicenter open-label randomized trial that compared 7 vs 14 days of antibiotics to treat bacteremia in **3608** hospitalized patients
 - **Important details**
 - Antibiotic choice, dose & delivery mode up to investigator
 - Investigators blinded to the arm of treatment **until day 7**
 - **Important exclusions**
 - Immunocompromise (solid organ or stem cell transplant, neutropenia)
 - Prosthetic heart valve
 - Endovascular graft
 - Suspected syndrome that requires long treatment (e.g. osteomyelitis)
 - Suspected contaminant blood culture
 - Staph aureus bacteremia
 - Fungemia
- Primary outcome was death from any cause at 90 days after bacteremia

Balance Trial Results

- Key characteristics were balanced between arms:
 - **Level of illness:** 55% in ICU, 45% on hospital ward, 22% on mech ventilation
 - **Comorbidities:** 32% diabetes, 22% solid tumor cancer
 - **Bacteremia source:** 42% urinary, 19% GI or biliary, 13% pulmonary

Most commonly isolated pathogens in blood cultures — no. (%)

<i>Escherichia coli</i>	1582 (43.8)
<i>Klebsiella</i> species	552 (15.3)
<i>Enterococcus</i> species	250 (6.9)
Coagulase-negative staphylococci	174 (4.8)
<i>Pseudomonas</i> species	170 (4.7)

Daneman N, et al. N Engl J Med 2025;392:1065-78

Table 2. Primary and Secondary Outcomes.

Outcome	7-Day Group (N=1814)	14-Day Group (N=1794)	Difference (95% CI)* percentage points
Primary outcome, death from any cause by 90 days — no./total no. (%)			
Primary analysis, intention-to-treat population	261/1802 (14.5)	286/1779 (16.1)	−1.6 (−4.0 to 0.8)
Secondary analysis, per-protocol population	178/1370 (13.0)	222/1483 (15.0)	−2.0 (−4.5 to 0.6)
Modified intention-to-treat analysis, survival ≥7 days	247/1788 (13.8)	272/1765 (15.4)	−1.6 (−3.9 to 0.7)
Secondary outcomes			
Death in hospital — no. (%)†	168 (9.3)	184 (10.3)	−1.0 (−2.9 to 0.9)
Death in ICU — no./total no. (%)‡	91/1014 (9.0)	97/1008 (9.6)	−0.6 (−3.2 to 1.9)
Median no. of days in hospital (IQR)	10 (6–21)	11 (6–22)	−1 (−1.5 to −0.5)
Median no. of hospital-free days by day 28 (IQR)	17 (0–21)	15 (0–21)	2 (0.8 to 3.2)
Median no. of days in ICU (IQR)§	5 (3–11)	5 (3–11)	0 (−0.4 to 0.4)
Median no. of days of vasopressor use (IQR) ¶	3 (2–5)	3 (2–4)	0
Median no. of days of mechanical ventilation (IQR)	6 (3–14)	5 (2–12)	1 (−0.6 to 2.6)
Relapse of bacteremia — no. (%)	47 (2.6)	39 (2.2)	0.4 (−0.6 to 1.4)
Median no. of antibiotic-free days by day 28 (IQR)**	19 (11–21)	14 (11–14)	5 (4.6 to 5.4)
Antimicrobial-related adverse outcomes — no. (%)			
Allergy	14 (0.8)	19 (1.1)	−0.3 (−0.9 to 0.3)
Anaphylaxis	1 (0.1)	1 (0.1)	0 (−0.2 to 0.2)
Acute kidney injury	15 (0.8)	17 (0.9)	−0.1 (−0.7 to 0.5)
Acute hepatitis	2 (0.1)	4 (0.2)	−0.1 (−0.4 to 0.2)
<i>Clostridioides difficile</i> infection — no. (%)	31 (1.7)	35 (2.0)	−0.2 (−1.1 to 0.6)
Secondary infection or colonization with antibiotic-resistant organisms — no. (%)	173 (9.5)	152 (8.5)	1.1 (−0.8 to 2.9)
Secondary infection or colonization with antibiotic-resistant organisms in sterile culture — no. (%)	20 (1.1)	24 (1.3)	−0.2 (−1 to 0.5)

Practical Conclusions: How long to treat bacteremia?

- Recent studies show that 7 days of antibiotics are likely equally as effective as 14 days to treat bacteremia *in the right patient population*
 - Studies largely excluded several specific issues including
 - Patients with complicated infection (e.g. undrained abscess, osteomyelitis, endocarditis)
 - Certain types of bacteria → Pseudomonas and non-fermenters excluded or underrepresented
 - Only BALANCE trial assessed gram positive organisms, but excluded Staph aureus and Staph lugdunensis
 - Certain types of hosts → transplant and neutropenic patients largely excluded
 - Data suggest this may be safe for critically ill patients → Balance trial did include ICU patients

Von Dach E, et al. JAMA. 2020;323:2160-9.

Yahav D, et al. Clin Infect Dis 2019; 69:1091–8.

Molina J, et al. Clin Microbiol Infect 2022;28:550-7.

Daneman N, et al. N Engl J Med 2025;392:1065-78.

New Problems:

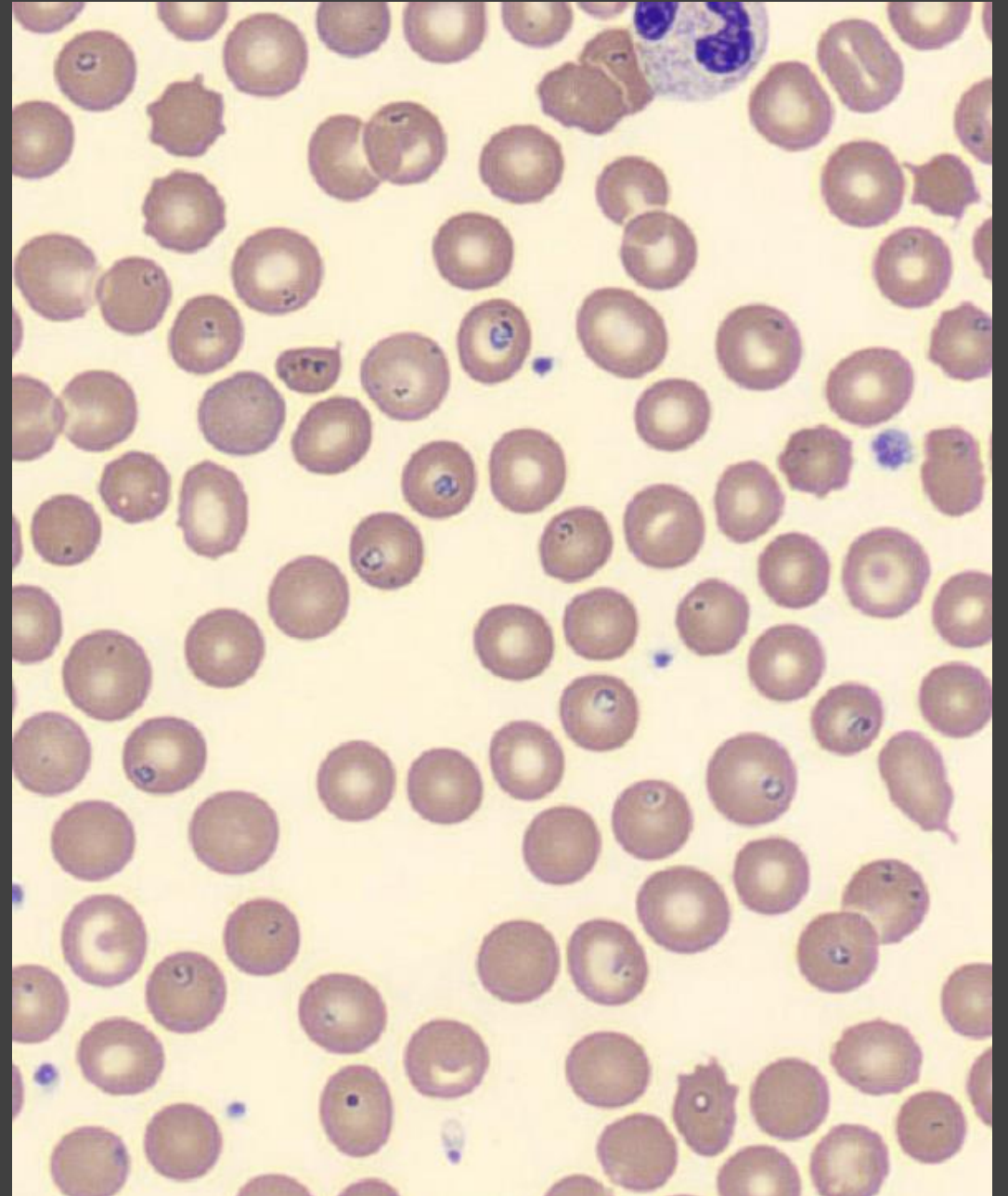
Impact of climate change on infection

Clinical Case

- 68-year-old man with diffuse large B cell lymphoma s/p 6 cycles of R-CHOP chemotherapy 4 months ago presents the first week of January with malaise, dyspnea on exertion and sweats that have progressed for the last 2 weeks
 - His daughter notes that he looks yellow
- Past medical history is notable for lymphoma as above, hypertension, hyperlipidemia and asplenia (MVA at age 18)
- Medications include atorvastatin, amlodipine and lisinopril
- Social history is notable for living in the suburbs of Boston. Retired engineer. Two pet Labradors that he walks in a nearby nature reserve daily. Just returned from a holiday vacation to Hawaii for 10 days.

Examination & Labs

- Exam
 - Notable for a fatigued appearing man with pale conjunctiva
 - Mild tachycardia with regular rhythm
 - Clear lungs but is tachypneic
- Labs
 - WBC 4.2, HCT 24, PLT 301
 - Differential sent...
 - Cr 1.4, AST 111, ALT 34, T Bili 2.9
 - LDH 1102



The likely cause of his illness is:

- A. Malaria
- B. Leptospirosis
- C. Babesia
- D. Oroyo fever (*Bartonella bacilliformis*)
- E. Dengue fever

Climate change and Infection

- Climate change has the potential to have broad reaching impacts on human infection
- Knowledge of some changes we see now can help with prevention and early diagnosis

Table. Impact of Climate-Related Changes on Infectious Disease Epidemiology

Disease type	Climate-related change	Effect on infectious disease epidemiology	Examples
Vector-borne diseases	Shorter, warmer winters Longer summers Expanding range of vectors, eg, mosquitoes and ticks Changes in precipitation patterns	Increased disease incidence Expanding seasonality into winter months Expanding geographic range, primarily northward and westward Increased likelihood of onward transmission	Babesiosis Lyme disease Anaplasmosis Powassan virus Ehrlichiosis Dengue Zika virus Chikungunya virus Malaria
Zoonotic diseases	Changes in animal migration patterns, natural ranges, and population density Habitat destruction Increased interaction between different animal species Increased human-animal interaction	Increased cross-species transmission events Emergence of novel human pathogens Increased disease incidence Expanding geographic range	Avian influenza (H5N1) Plague Hantavirus Tularemia Emerging coronaviruses
Fungal diseases	Expanded thermotolerance in fungal organisms New favorable environments for endemic fungi	Emergence of novel human pathogens Expanding geographic range of endemic mycoses	<i>Candida auris</i> <i>Sporothrix brasiliensis</i> <i>Coccidioides</i> <i>Histoplasma</i> <i>Blastomyces</i>
Waterborne diseases	Rise of sea level Extreme weather events Flooding-induced strain on water infrastructure Changes in precipitation patterns Changes in coastal water temperature	Increased disease incidence after storms Expanding seasonality Expanding geographic range, primarily northward	<i>Campylobacter</i> <i>Escherichia coli</i> <i>Cryptosporidium</i> <i>Vibrio</i> species

How might climate change impact fungal infection?

- Humans have two major defenses against invasive fungal infection:
 1. Relatively high body temperature (we're warm-blooded!)
 2. Immune defenses
- Warm ambient temperatures and particularly the number of days with excessive heat can select for environmental fungi that rapidly adapt to survive at warmer temperatures
 - Fungi that survive at warmer temperatures can be better suited to cause human infection
 - The first potential example of this: *Candida auris*, which has significant thermotolerance (grows well at 37°C), emerged on different continents ~2010
 - This organism can cause difficult-to-treat infection in a vulnerable population (ICU in particular) and is typically multidrug resistant
 - Other fungi not known to cause human infection now could adapt and cause new syndromes

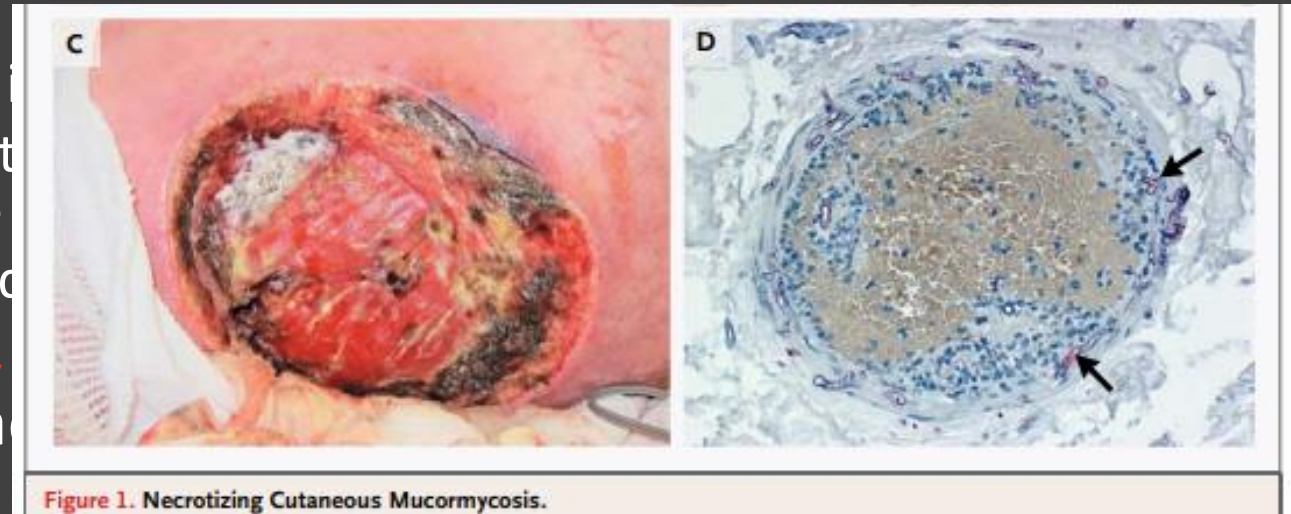
Climate change & Fungi: Distribution & Disasters

- Distribution

- The distribution of endemic mycoses
- Modeling studies have suggested that the Ohio river valley has expanded to
- Modelling studies have also suggested the Northwest US

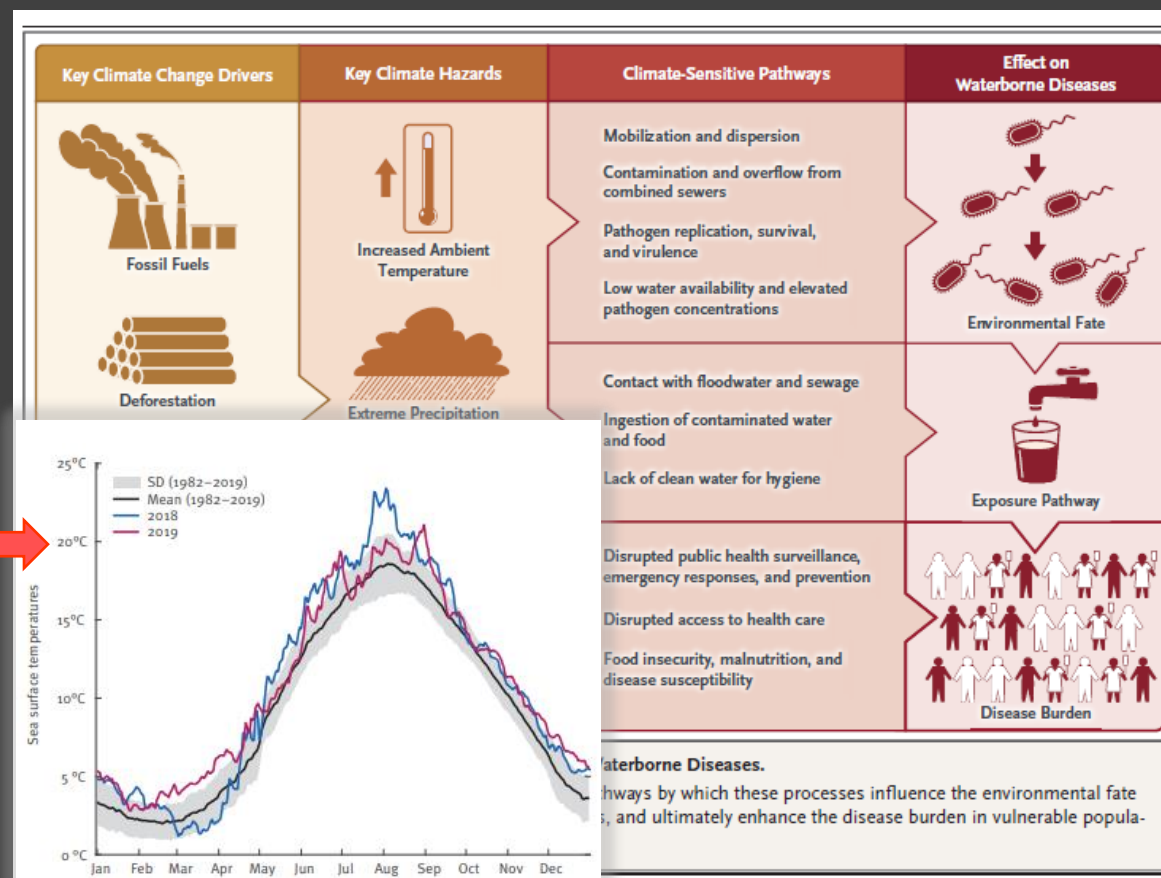
- Increased natural disasters make it difficult to detect invasive fungal infection

- **Tornado eg:** Joplin, Missouri 2011: following a severe tornado (winds >200 miles per hour) a cluster of cutaneous mucormycosis was reported in 13 injured individuals due to *Apophysomyces trapeziformis*
- **Wildfire eg:** Wildfire smoke contains microbes including fungal spores
 - Mulliken et al. studied the association between wildfire smoke and California hospital admissions for *Coccidioides* and *Aspergillus* and found that *Coccidioides* admissions rose 20% in the month following smoke exposure based on smoke plume data



Waterborne Infection and Climate Change

- Climate change has impacted movement of water between earth & atmosphere
 - Increased evaporation has increased atmospheric water vapor
- This can favor certain waterborne pathogens:
 - Some thrive with increased flooding or sea level surges due to dispersion and contamination (fecal pathogens, leptospirosis)
 - Some thrive in warmer water directly (Salmonella, vibrio, amoeba) or indirectly (Legionella in air conditioning units)
- Eg: Vibrio infection has increased globally
 - Outbreak of domestically acquired infections in Germany in 2018-2019 associated with increased temperatures in Baltic Sea
 - In Maryland there was 39% increase in average Vibrio infection incidence from 2006-12 vs. 2013-19
 - Same research group showed linear relationship between water temperature and *V. vulnificus* presence in Chesapeake



Semenza JC, Ko AL. N Engl J Med 2023;389:2175-87
 Brehm TT et al. Euro Surveill 2021; doi: 10.2807/1560-7917.ES.2021.26.41.2002041
 Brumfield KD et al. Appl Environ Microbiol. 2023; doi: 10.1128/aem.00307-23
 Morgado ME, et al. Environ Res 2024; doi: 10.1016/j.envres.2023.117940.

Summary thoughts on climate and infection

- How does it help us to understand how climate change may impact infectious diseases risk?
 - Climate change literature can feel heavy and leave providers feeling helpless
 - However, regardless of one's stance on climate change, knowledge is helpful!
 - Natural disasters can be associated with increased waterborne and invasive fungal infection so knowledge can lead to earlier diagnosis and better outcomes
 - Travel advice with awareness of shifting epidemiology (e.g. increased vibrio risk in areas previously with cooler water) can be helpful for infection prevention and earlier recognition of infection
 - This includes checking available public health resources about infection risk in certain locations even domestically

Formidable New & Old Bugs:

Trichophyton indotineae

Clinical Case

- 27-year-old woman with no medical history presents with a rash on the inner thighs, mons and buttocks for a few months
 - The rash started on the thighs then spread
 - She initially went to an urgent care where she was prescribed topical steroids and topical terbinafine
 - The rash has continued to spread since starting these and may be a little itchier
 - Her social history is notable for having a new male partner for the last 3 months who frequently travels throughout Southeast Asia for work
 - She notes that he has a similar rash on the buttocks



Caplan AS, et al. MMWR 2023;72:526-7.

After taking a skin scraping for culture what is the best treatment for this infection?

- A. Topical 2% miconazole cream until the rash resolves
- B. Prednisone pulse 40 mg po daily x5 days and fluconazole 150 mg po daily x14 days
- C. Stop topical steroids and continue topical terbinafine by itself
- D. Topical nystatin cream
- E. Econsult a dermatologist and/or ID physician because this looks bad

Trichophyton indotineae

- Trichosporon species (dermatophytes) are the cause of Tinea, a contagious superficial infection that can involve hair, skin and nails
- In last 15 years an epidemic of severe **treatment-refractory** dermatophytosis due to a new species, *T. indotineae*, has been reported in Southeast Asia
 - In India outbreak has been associated with OTC combination topical antifungal/antibacterials + high potency steroids (e.g. clobetasol)
- By late 2010's cases were reported in Europe...
- Caplan et al. described first two cases in US noted by a dermatologist in NYC in 2023
 - Both cases were severe widespread pruritic eruptions, only one of whom travelled recently (Bangladesh)
- Reference lab study of Trichophyton isolates in US sent for susceptibility testing 2021-22 showed *T. indotineae* accounted for 8%
 - Three additional isolates identified 2001-2020 starting in 2017



Uhrlass S, et al. J. Fungi 2022, 8, 757.
Bishnoi A, et al. Lancet Inf Dis 2018;18:250-1
Caplan AS, et al. MMWR 2023;72:526-7.
Canete-Gibas CF, et al. J Clin Microbiol 2023;61:e00562-23

Primary Characteristics of *T. indotineae* in the US

1. Severe and extensive rash even in normal adult & pediatric hosts

- Rash can be severe involving large areas of the body
- Notably, US patients are also often prescribed topical steroids before diagnosis is made which may exacerbate the infection
 - 7 patients among a recent series of 11 cases were treated with topical steroids



Caplan AS, et al. MMWR 2023;72:526-7.
Caplan AS, et al. JAMA dermaol. 2024;160:701-9.
Canete-Gibas CF, et al. J Clin Microbiol 2023;61:e00562-23
Gold JAW, et al. Emerg Infect Dis 2024;30:1978-80.

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2. Transmissible through familial and sexual contact

- Household transmission suspected in many reported US cases
- Sexual transmission reported in US, but difficult to track since it is not a reportable infection

3. Treatment refractory due to frequent antifungal resistance

- It is typically resistant to terbinafine and is not reliably susceptible to fluconazole or griseofulvin → obtaining culture and susceptibilities is important
- Itraconazole is the most reliable active systemic therapy and clinically the most effective (drug interactions, oral absorption, and tolerability can be an issue)

4. Knowledge among providers is poor

- Recent survey of ID providers showed only 65% knew about the problem and 39% knew how to get antifungal susceptibility testing on fungal species from culture

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Summary

- **Oral antibiotics for GNB**

- Oral antibiotics with high bioavailability like quinolones and TMP-SMX perform as well as IV antibiotics for GNB but have important toxicities
- Risk of worse outcome may be higher with oral beta lactams

- **Shorter course of antibiotics for bacteremia**

- 7 days of antibiotics may work as well as 14 days for bacteremia therapy
- Role of short course antibiotics is less clear in certain populations and with gram positive infections

- **Climate change and infection**

- Climate change is impacting human infection risk through changes in vector-borne, zoonotic, fungal and water-borne infection patterns
- Knowledge of changes can help with improved diagnosis and avoidance

- ***Trichophyton indotineae***

- Emerging in US since 2017
- Severe often extensive dermatophyte infection that is typically antifungal-resistant and can spread among families and between sexual contacts

Disclosures

- I have research funding from Cidara, Mundipharma, F2G, Scynexis, GSK and Elion
- I have been a consultant for Pfizer, Takeda and Treeline biosciences

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