UPDATES IN INFECTIOUS DISEASES

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Disclosures

- Nothing to disclose

Objectives

Pharmacist:

1. Recall infectious diseases guideline updates from 2018 and understand major differences from previous version.
2. Review recent changes in antimicrobial resistance.
3. Review other major ID publications and findings from past year.

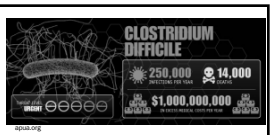
Technician:

1. List risk factors for *C. difficile* infection.
2. List antimicrobial agents that are currently recommended for treatment of *C. difficile* infection in adults.

Outline

1. *C. difficile* treatment guideline update
2. Recent updates/additions to other infectious diseases guidelines
3. Review of recent and significant infectious diseases publications

C. difficile Refresher



apua.org

- Anaerobic, spore-forming, Gram-positive rod
- Disease causing strains can produce toxin A and B, as well as binary toxin
  - Produces inflammatory response → diarrhea, erosion of mucosa, formation of pseudomembranes
- Particularly common in healthcare environments
- Risk factors:
  - Antibiotics !!! – most important risk factor, all classes carry risk
  - PPIs and histamine-2 blockers (lesser association)
  - Hospitalization, nursing home resident, admission to LTCF
  - Age > 65 y
  - Immunosuppression, neutropenia, advanced HIV
  - GI disease/surgery/invasive procedure
  - Chemotherapeutic agents
- Recurrence occurs in ~25% of patients

Clinical Infectious Diseases

IDSA GUIDELINE

Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

L. Clifford McDonald,[1] Dale N. Gerding,[2] Stuart Johnson,[2,3] Johan S. Bakken,[4] Karen C. Carroll,[5] Susan E. Coffin,[6] Erik R. Dubberke,[7] Kevin W. Garey,[8] Carolyn V. Gould,[1] Ciaran Kelly,[9] Vivian Loo,[10] Julia Shaklee Sammons,[1] Thomas J. Sandora,[11] and Mark H. Wilcox[12]

Clin Infect Dis. 2018;66(7):e1-e48.

Clostridiodes difficile Infection Updates

- Inclusion of specific pediatric guidelines
- Discussion on laboratory guided diagnosis in adults
- Removal of metronidazole for first-line therapy in adults
- Discussion on fecal transplantation utilization
- Consideration of prophylaxis techniques

- Also, just to ensure that we keep the medical field confusing, *Clostridium difficile* has been changed to ***Clostridiodes difficile . . .*** but, we can still call it *C diff* ☺

Pharmacy Times: Practice Pearls from the 2018 Clostridium Difficile Treatment Guidelines. March 6, 2018.
Int J Syst Evol Microbiol. 2017 Sep;67(9):3140-3143.

C. difficile in the Pediatric Population

- From 1991 to 2009, increase in incidence of CDI among pediatric residents from 2.6 to 32.6 per 100000
- 71% of pediatric CDI identified by positive *C. difficile* stool testing arose from the community
- Colonization rates decrease with increasing age
  - Nontoxigenic strains are more common than toxigenic strains among colonized infants, but colonization is transient and different strains are found to colonize the same infant at different times
- Colonization is less frequent among breastfed as compared with bottle-fed infants
- Risk factors for CDI in children mirror those for adults

Clin Infect Dis. 2018;66(7):e1-e48.

Treatment in Pediatric Patients

Clinical Definition	Recommended Treatment	Pediatric Dose	Maximum Dose	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	• Metronidazole × 10 days (PO), OR • Vancomycin × 10 days (PO)	• 7.5 mg/kg/dose tid or qid • 10 mg/kg/dose qid	• 500 mg tid or qid • 125 mg qid	Weak/Low Weak/Low
Initial episode, severe/ fulminant	• Vancomycin × 10 days (PO or PR) with or without metronidazole × 10 days (IV)[a]	• 10 mg/kg/dose qid • 10 mg/kg/dose tid	• 500 mg qid • 500 mg tid	Strong/Moderate Weak/Low
First recurrence, non-severe	• Metronidazole × 10 days (PO), OR • Vancomycin × 10 days (PO)	• 7.5 mg/kg/dose tid or qid • 10 mg/kg/dose qid	• 500 mg tid or qid • 125 mg qid	Weak/Low
Second or subsequent recurrence	• Vancomycin in a tapered and pulsed regimen[a], OR • Vancomycin for 10 days followed by rifaximin[b] for 20 days, OR • Fecal microbiota transplantation	• 10 mg/kg/dose qid • Vancomycin: 10 mg/kg/dose qid; rifaximin: no pediatric dosing • --	• 125 mg qid • Vancomycin: 500 mg qid; rifaximin: 400 mg tid • --	Weak/Low Weak/Low Weak/Very low

Abbreviations: IV, intravenous; PO, oral; PR, rectal; qid, 4 times daily; tid, 3 times daily.
[a]In cases of severe or fulminant *Clostridium difficile* infection associated with critical illness, consider addition of intravenous metronidazole to oral vancomycin.
[a]Tapered and pulsed regimen: vancomycin 10 mg/kg with max of 125 mg 4 times per day for 10–14 days, then 10 mg/kg with max of 125 mg 2 times per day for a week, then 10 mg/kg with max of 125 mg once per day for a week, and then 10 mg/kg with max of 125 mg every 2 or 3 days for 2–8 weeks.
[b]No pediatric dosing for rifaximin; not approved by the US Food and Drug Administration for use in children <12 years of age.

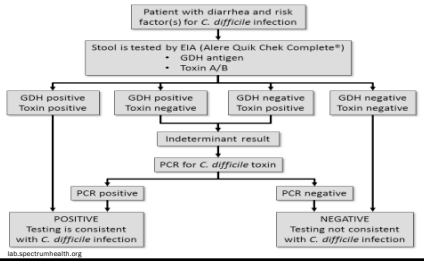
Clin Infect Dis. 2018;66(7):e1-e48.

Treatment in Pediatric Patients

- Fidaxomicin
  - A preliminary study in children suggests that it is safe with little gastrointestinal absorption
  - RCT comparing fidaxomicin and vancomycin in children with *C. difficile* infection is underway
- Fecal microbiota transplant (FMT)
  - Consider FMT for pediatric patients with multiple recurrences of CDI following standard antibiotic treatments
  - Limited evidence
  - In most reported cases, fecal sample donation was from the child's mother or father
  - Potential benefits of FMT must be balanced against theoretical risks
    - Metabolic or immune-based disorders

J Pediatric Infect Dis Soc. 2018;7(3):210.
ClinicalTrials.gov Identifier: NCT02218372
Clin Infect Dis. 2018;66(7):e1-e48.

Laboratory Guided Diagnosis



Other Laboratory Considerations

- Only test patients likely to have *C. difficile* disease!
- Avoid testing (if possible) in patients with laxatives within previous 48 hours
- Reject specimens that are not liquid or soft (take the shape of the container)
- Collaborate with Quality Improvement, Infection Control, and Antibiotic Stewardship to assess appropriateness of testing
- Do not perform repeat testing (within 7 days) during the same episode of diarrhea

Clin Infect Dis. 2018;66(7):e1-e48.

First-line Therapy

- Initial episode (severe or non-severe): vancomycin OR fidaxomicin x10 days
  - Metronidazole for non-severe cases where access to other therapies is limited
- Fulminant (hypotension, shock, ileus):
  - high dose vancomycin, +/- IV metronidazole OR rectal vancomycin
- First Recurrence: based on initial treatment regimen
  - Vancomycin x10 days if metronidazole used first
  - 6-12 week vancomycin taper/pulse OR fidaxomicin if standard vancomycin regimen used first
- Subsequent Recurrence:
  - Vancomycin taper/pulse OR vanco x10 days then rifaximin x20 days OR fidaxomicin OR FMT

Agent	Adult Dose	Cost[a]	Initial Treatment Response[b]	Recurrence Risk[c]	Resistance in Clinical Isolates	Adverse Events	Evidence Supporting Efficacy
Proven efficacy							
Vancomycin	125 mg PO qid × 10 days	$$$$ $ (Liq)	+++	++	Not reported	Minimally absorbed	Multiple RCTs; US FDA approved
Fidaxomicin	200 mg PO bid × 10 days	$$$$	+++	+	One clinical isolate with increased MIC	Minimally absorbed	Two phase 3 RCT comparisons to vancomycin; US FDA approved
Metronidazole	500 mg PO tid × 10 days	$	++	++	Increased MIC reported in some studies; hetero-resistance also reported	Neuropathy, nausea	Multiple RCTs

Clin Infect Dis. 2018;66(7):e1-e48.

RIP Metronidazole

Outcomes	No. of Participants (No. of Studies)	Percentage Resolution	Relative Effect[a] (95% CI)	*P* Value
Direct comparisons of metronidazole and vancomycin				
Resolution of diarrhea at end of (10 days) treatment	RCTs prior to 2000: 156 (2)	95 (MTR) 98 (VAN)	RR, 0.97 (.91–1.03)	.4
	RCTs since 2000: 687[c] (3)	75 (MTR) 85 (VAN)	RR, 0.89 (.82–.96)	.002
	All RCTs: 843 (5)	78 (MTR) 87 (VAN)	RR, 0.89 (.85–.96)	.0008
Resolution of diarrhea at end of treatment without CDI recurrence –1 month after treatment	RCTs prior to 2000: 156 (2)	85 (MTR) 84 (VAN)	RR, 1.0 (.90–1.2)	1.0
	RCTs since 2000: 687[c] (3)	59 (MTR) 70 (VAN)	RR, 0.84 (.74–.94)	.002
	All RCTs: 843 (5)	63 (MTR) 73 (VAN)	RR, 0.87 (.79–.96)	.003

Clin Infect Dis. 2018;66(7):e1-e48.

Fecal Microbiota Transplant

- Fecal microbiota transplantation is recommended for patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments
- Appropriate antibiotic treatments for at least 2 recurrences (3 CDI episodes) should be tried prior to FMT
- Oral vancomycin for 3–4 days prior to FMT administration to reduce the burden of vegetative *C. difficile*
- Rate of success varies with the route of instillation (77-94%), but highest success with instillation via colon
- Blood and feces screening of stool donors

Clin Infect Dis. 2018;66(7):e1-e48.

CDI Prophylaxis Considerations

- Insufficient data at this time to recommend extending the length of anti–*C. difficile* treatment beyond the recommended treatment course
- Insufficient data at this time to recommend administration of probiotics for primary prevention of CDI
  - Probiotic trials limited by significant study heterogeneity and reproducible efficacy
  - Potential for organisms in probiotic formulations to cause infections

Clin Infect Dis. 2018;66(7):e1-e48.

Role of Antibiotic Stewardship

- Minimize the frequency and duration of high-risk antibiotic therapy and the number of antibiotic agents prescribed
- Implement an antibiotic stewardship program
- Antibiotics to be targeted should be based on the local epidemiology and the *C. difficile* strains presents
  - Restriction of fluoroquinolones, clindamycin, and cephalosporins (except for surgical antibiotic prophylaxis) should be considered

Clin Infect Dis. 2018;66(7):e1-e48.

Research Gaps

- We know a great deal about *C. difficile*, but we still have much to learn…
  - What is the best treatment for recurrent CDI?
  - What is the best method to prevent recurrent CDI?
  - What is the best way to restore colonization resistance of intestinal microbiota?
  - When should fecal transplant be considered?
  - Should specific commensal bacteria be administered in place of minimally screened fecal specimens from donors?
  - What is the role of adjunctive therapy as new agents become available?
  - What preventive measures can be taken to reduce the incidence of CDI?
  - What is the best method to identify patients at risk of primary or recurrent CDI?
  - Can administration of probiotics or biotherapeutic agents effectively prevent CDI?
  - What are the most effective antibiotic stewardship strategies to prevent CDI?
  - What are the most effective transmission prevention strategies (ie, environmental management and isolation) to prevent CDI in inpatient settings?

Clin Infect Dis. 2018;66(7):e1-e48.

Penicillin Allergy and *C. difficile*

- Objective: Evaluate the relation between penicillin allergy and development of MRSA and *C. difficile*
- Participants: 301399 adults without previous MRSA or *C. difficile*
  - 64 141 with penicillin allergy and 237258 matched comparators
- Outcomes:
  - Primary: risk of incident MRSA and *C. difficile*
  - Secondary: use of β-lactam antibiotics and β-lactam alternative antibiotics
- Results:
  - 1365 developed MRSA (442 with penicillin allergy and 923 comparators)
    - Adjusted hazard ratio for MRSA was 1.69 (95% CI 1.51 to 1.90)
  - 1688 developed *C. difficile* (442 with penicillin allergy and 1246 comparators)
    - Adjusted hazard ratio for *C. difficile* was 1.26 (95% CI 1.12 to 1.40)
  - Adjusted incidence rate ratios for antibiotic use among patients with penicillin allergy were 4.15 (95% CI 4.12 to 4.17) for macrolides, 3.89 (3.66 to 4.12) for clindamycin, and 2.10 (2.08 to 2.13) for fluoroquinolones
  - Increased use of β-lactam alternative antibiotics accounted for 55% of the increased risk of MRSA and 35% of the increased risk of *C. difficile*

BMJ. 2018;361:k2400.

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2017 UPDATE

A CLINICAL PRACTICE GUIDELINE

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline.

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: clinical providers' supplement.

Pre-Exposure Prophylaxis (PrEP)

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI† High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI‡ High number of sex partners History of inconsistent or no condom use Commercial sex work In high HIV prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 3-6 months, test for bacterial STIs		
	Do oral/rectal STI testing	For women, assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update

Randy A. Taplitz, Erin B. Kennedy, Eric J. Bow, Jennie Crews, Charise Gleason, Douglas K. Hawley, Amelia A. Langston, Loretta J. Nastoupil, Michelle Rajotte, Kenneth V. Rolston, Lynne Strasfeld, and Christopher R. Flowers

Antimicrobial Prophylaxis in Cancer Immunosuppression

Type of Prophylaxis	Population	Recommendation	Timing of Prophylaxis
Antibacterial	Patients at high risk of febrile neutropenia (Table 2) or profound, protracted neutropenia	Fluoroquinolone prophylaxis is recommended	During period of expected neutropenia
Antifungal	Patients at high risk of febrile neutropenia (Table 2) or profound, protracted neutropenia Patients with GVHD[14]	Oral triazole or parenteral echinocandin prophylaxis is recommended; a mold-active triazole is recommended when the risk of invasive aspergillosis is > 6%, such as in patients with AML/MDS or during treatment of GVHD[7-9]	During period of expected neutropenia
	Patients receiving chemotherapy regimens associated with > 3.5% risk for pneumonia from *Pneumocystis jirovecii* (eg, those with ≥ 20 mg prednisone equivalents daily for ≥ 1 month or those on the basis of purine analogs)	Prophylaxis, eg, trimethoprim-sulfamethoxazole (TMP-SMX), is recommended	Postmyeloid reconstitution or engraftment after stem-cell transplantation, particularly in the setting of postengraftment augmented immunosuppression (for the treatment of GVHD)

Antimicrobial Prophylaxis in Cancer Immunosuppression

Type of Prophylaxis	Population	Recommendation	Timing of Prophylaxis
Antiviral	HSV-seropositive patients undergoing HSCT or leukemia induction therapy	Antiviral prophylaxis with a nucleoside analog is recommended (eg, acyclovir)	Until recovery of the WBC count or resolution of mucositis, whichever occurs later; duration can be extended for persons with frequent recurrent HSV infections or those with GVHD, or can be continued as VZV prophylaxis for up to 1 year
	Patients at substantial risk of reactivation of HBV infection	Treatment with a nucleoside reverse transcription inhibitor (eg, entecavir or tenofovir) is recommended	See updated ASCO HBV Provisional Clinical Opinion[15]
	Any individuals treated with chemotherapy for malignancy and family and household contacts	Administration of inactivated influenza vaccine is recommended for household contacts and health care providers	Optimal timing of vaccination for patients being treated for cancer is not established, but serologic responses may be best between chemotherapy cycles (> 7 days after the last treatment) or > 2 weeks before chemotherapy starts[1] Patients with cancer and their household contacts should be immunized annually[1] Influenza vaccination response seems to be best in HSCT recipients if vaccinated > 6 months after transplantation[1]
	Immunosuppressed adult oncology patients	The Expert Panel also supports other vaccination recommendations for immunosuppressed adult oncology patients that are contained within the IDSA guideline for vaccination of the immunosuppressed host[16]	Not applicable

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JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America Clinical Practice Guideline Update

Randy A. Taplitz, Erin B. Kennedy, Eric J. Bow, Jennie Crews, Charise Gleason, Douglas K. Hawley, Amelia A. Langston, Loretta J. Nastoupil, Michelle Rajotte, Kenneth Rolston, Lynne Strasfeld, and Christopher R. Flowers

Updates in Progress

- Community-acquired pneumonia
- Intra-abdominal infections
- Vancomycin
- Others:
  - Influenza
  - Management of catheter-related infections
  - New fever in critically ill patients
  - Asymptomatic bacteriuria
  - Outpatient parenteral anti-infective therapy (OPAT)
  - Nontuberculous Mycobacterial (NTM) diseases
  - Prevention of healthcare-associated infections in acute care hospitals
  - Lyme disease
  - Nervous system Lyme disease

MRSA Bacteremia Combination Therapy

- Open-label, multicenter, RCT
- Primary outcome: duration of bacteremia
- 60 patients with MRSA bacteremia enrolled
  - 31 received combination therapy (CT) (vancomycin + flucloxacillin x7days)
  - 29 standard therapy (ST) (vancomycin alone)
- Results:
  - Mean duration of bacteremia 1.94 days vs. 3 days in CT and ST groups, respectively
    - 65% faster resolution in CT group (95% CI 41%-102%, p=0.06)
  - Non-significant differences in 28 and 90-day mortality, metastatic infection, nephrotoxicity
    - CT group had higher rate of SCr increase >50% (28% vs 11%)
- Mechanism of synergy unclear, but may be related to "see-saw" effect
- Take away message:
  - Combining an antistaphylococcal beta-lactam with vancomycin may shorten the duration of MRSA bacteremia
  - Further trials with a larger sample size and objective clinically relevant end points are warranted

Clin Infect Dis. 2016;62(2):173-180.

C. difficile Infection and Antibiotics in Patients Occupying the Same Bed

- Retrospective, multicenter, cohort study
- Primary end point: CDI in the subsequent patient occupying the same bed
- 100615 pairs of patients enrolled
  - Prior patients must have spent 24 hours in the same bed and left the bed <1 week before subsequent patient
  - Subsequent patients excluded if CDI in previous 90 days or positive CDI test w/in 48 hours of admission
- Results:
  - 576 pairs (0.57%) had subsequent patient CDI
    - Subsequent patient CDI incidence higher when prior patient received antibiotics (0.72% vs. 0.43%, p<0.01)
- Take away message:
  - Antibiotics given to one patient may alter local microenvironment and potentially cause harm to subsequent patients
  - Further emphasizes need for judicious antibiotic use

JAMA. 2016;176(12):1801-1808.

Clinical Impact of Beta-Lactam Allergy

- Multicenter, prospective, cohort study
- Primary outcome: composite end point of treatment-related adverse events (AKI, CDI, ADR, readmission)
- 507 patients enrolled
  - Group 1 (n=412): patients without beta-lactam allergy (BLA)
  - Group 2 (n=23): patients with BLA and beta-lactam therapy not preferred
  - Group 3 (n=47): patients with BLA and beta-lactam therapy preferred and administered
  - Group 4 (n=25): patients with BLA and beta-lactam therapy preferred but not administered
- Results:
  - Primary outcome more likely in group 4 than in group 1 (40% vs. 16%, p<0.05)
    - Driven by infection-related readmission and ADRs
  - ADRs were also more common in group 3 than in group 1
- Take away message:
  - Highlights the need to thoroughly evaluate BLA
  - Promotes prescribing of beta-lactams where preferred, especially without severe allergic reaction
  - Consider penicillin skin testing when possible

Clin Infect Dis. 2016;63(7):904-910.

Vancomycin Combinations and AKI

- Retrospective, matched, cohort study
- Primary outcome: incidence of AKI
- 279 pairs of patients enrolled
  - Vancomycin + piperacillin/tazobactam (VPT)
  - Vancomycin + cefepime (VC)
  - 20% admitted to ICU
  - Exclusion criteria: patients with SCr > 1.2 mg/dL or renal replacement therapy
- Results:
  - AKI higher in VPT group (29%) than VC group (11%), (HR= 4.0, 95% CI 2.6 – 6.2)
    - VPT was an independent predictor of AKI
  - Onset of AKI more rapid in VPT group compared to VC group (3 vs. 5 days, p <0.0001)
  - Vancomycin trough level and AKI:
    - In VPT group, AKI incidence similar across varying trough levels
    - In VC group, Incidence of AKI increased with increasing trough level
- Take away message:
  - Need to evaluate risk/benefit ratio when initiating VPT as empiric therapy
  - Discontinue vancomycin (or both agents) when appropriate

Clin Infect Dis. 2017;64(2):116-123.

More Effective ASP Intervention

- Multiple ASP interventions for inpatient use, including:
  - IV to PO conversion
  - Dose optimization
  - Syndrome specific interventions
  - Rapid diagnostics interventions
  - Other pharmacy-driven interventions
  - Education and research

  - **Pre-prescription authorization (PPA)** – requires approval prior to first dose
  - **Post-prescription review with feedback (PPRF)** – assesses appropriateness after ≥ 1 dose received

More Effective ASP Intervention

- Quasi-experimental, crossover study
- Primary outcome: days of antibiotic therapy (DOT) per patient
  - Length of therapy (LOT), days of therapy regardless of number of antimicrobials, was secondary outcome
- 1508 inpatients prescribed >24h of antibiotic therapy were enrolled
  - PPA (n=778)
  - PPRF (n=730)
  - 4 different medical teams saw all patients
    - 2 teams assigned to each PPA and PPRF initially; following washout period, teams reassigned to the opposite group
- Results:
  - Fewer patients in PPA group has inappropriate therapy on day 1 (33.7% vs. 41.1%, p<0.01)
  - By day 3, PPRF was associated with fewer inappropriate regimens, fewer antibiotics without indication, and fewer broad-spectrum antibiotics
  - DOT/1000 PD decreased in PPRF group, and remained stable after PPA implemented (p<0.01)
  - DOT/1000 PD was steady in PPA group initially, then decreased following PPRF implementation (p=0.02)
- Take away message:
  - PPRF may have more of an impact on decreasing antibiotic DOTs compared with PPA.

Clin Infect Dis. 2017;64(5):537-543.

CAP Duration of Therapy

- Multicenter, non-inferiority, RCT
- Primary outcome: clinical success at day 10 and day 30
- 312 patients enrolled
  - Intervention group (n=162): minimum 5 days antibiotics and treatment cessation when afebrile x48 hours and ≤ 1 CAP-associated sign of instability
  - Control group (n=150): duration of treatment at discretion of physician
  - Exclusion criteria: immunocompromised, ICU admission, risk of MDRO
- Results:
  - Clinical success rate at day 10 was 48.6% in control group and 56.3% in intervention group (p=0.18)
    - Clinical success rate at day 30 was 88.6% in control group and 91.9% in intervention group (p=0.33)
  - Median duration of antibiotic treatment longer in the control group (10 vs. 5 days, p < 0.001)
  - No difference in 30 day mortality
- Take away message:
  - Duration of antibiotic therapy for CAP should be based on clinical response
  - Supports shorter treatment duration for CAP is effective and safe
- Approximately 80% of patients in both groups treated with fluoroquinolones

JAMA. 2016;176(9):1257-1265.

Switching From TDF to TAF

- Randomized, active-controlled, open-label, multicenter, noninferiority study
- Primary efficacy endpoint: virologic success (HIV RNA <50 copies/mL) at 48 weeks
- 1436 patients enrolled
  - Tenofovir alafenamide (TAF) (n=959): switch from TDF regimen to TAF/EVG/FTC/cobi
  - Tenofovir disoproxil fumarate (TDF) (n=477): stay on TDF containing regimen
- Results:
  - Virologic success was achieved in 97% and 93% of patient in TAF and TDF groups, respectively
  - TAF group achieved 12% noninferiority margin and demonstrated superiority with 4.1% difference
  - Mean spine and hip BMD increased in the TAF group and decreased in the TDF group
  - Median eGFR increased by 1.2 mL/min in the TAF group and decreased by 3.7 mL/min in the TDF group
- Take away message:
  - Virologic suppression is maintained when switching from TDF to TAF based regimens
  - BMD and eGFR may improve when switching from TDF to TAF based regimens

Lancet Infect Dis. 2016;16(1):43-52.

Antibiotics for Aspiration Pneumonitis

- Retrospective, cohort study
- Primary outcome: in-hospital mortality w/in 30 days of aspiration event
- 200 patients enrolled
  - **Antibiotic prophylaxis** during first 2 days following aspiration event (n=76)
    - Ceftriaxone (46%), piperacillin/tazobactam (26%), resp. fluoroquinolone (9%)
  - **Supportive care only** during first 2 days following aspiration event (n=124)
- Results:
  - Antibiotic prophylaxis was not associated with any improvement in mortality (OR= 0.9, 95%CI 0.4 – 1.7)
  - No significant difference in rate of ICU transfer
  - Antibiotic prophylaxis resulted in more frequent antibiotic escalations and fewer antibiotic free days
- Take away message:
  - Prophylactic antibiotics for acute aspiration pneumonitis do not offer clinical benefits
  - Prophylactic antibiotics may generate antibiotic selective pressures that result in need for escalation of antibiotic therapy

Clin Infect Dis. 2018;67:513-518.

Treatment of ESBL Bacteremia

- Noninferiority, parallel group, RCT
- Primary outcome: all-cause mortality at 30 days
- 391 patients with ceftriaxone nonsusceptible *Klebsiella* spp or *E coli* bacteremia
  - Piperacillin/tazobactam 4.5 g every 6 hours (n = 188) (PTZ)
  - Meropenem 1 g every 8 hours (n = 191) (MER)
- Results:
  - 12.3% in the PTZ group met primary outcome of mortality w/in 30 days
  - 3.7% in the MER group met met primary outcome of mortality w/in 30 days
  - Nonfatal serious ADEs occurred in 2.7% and 1.6% of patients in PTZ and MER groups, respectively
- Take away message:
  - Use of PTZ compared to MER did not result in noninferior 30-day mortality
  - Use of PTZ not supported for treatment of ESBL-producing *Enterobacteriaceae* bacteremia

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

New Antimicrobials

- Eravacycline (Xerava) – tetracycline, approved 8/2018
- Plazomicin (Zemdri) – "next generation" aminoglycoside, approved 6/2018
- Ibalizumab (Trogarzo) – CD4-directed post-attachment HIV-1 inhibitor, approved 3/2018
- **Bictegravir**/TAF/emtricitabine (Biktarvy) – integrase inhibitor combination, approved 2/2018
- Letermovir (Pervymis) – CMV DNA terminase inhibitor, approved 11/2017
- Recombinant zoster vaccine (Shingrix) – approved 10/2017
- Secnidazole (Solosec) – 5-nitroimidazole, approved 9/2017
- Meropenem/vaborbactam (Vabomere) – carbapenem + beta-lactamase inhibitor, approved 8/2017
- Delafloxacin (Baxdela) – fluoroquinolone, approved 6/2017

Infectious Diseases Resources

- Twitter
  - Fastest way to stay current with ID updates (in my opinion)
  - CDC, Sanford Guide, CIDRAP, DASON, CLSI
  - Jason Gallagher, Tim Gauthier, Debbie Goff, Jamie Kisgen, Monica Mahoney
- Persiflagers Infectious Disease PusCast – Mark Crislip MD
- IDStewardship: Top ID/stewardship Journal Articles
- ECHO – Antimicrobial Stewardship
  - Fridays at noon
- IDSA

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Conclusions

- Download and review the new guidelines for the treatment of *C. difficile* infection
  - Now pediatric specific recommendations
  - Ensure laboratory is utilizing an appropriate testing algorithm
  - Avoid metronidazole when other therapies are available
  - Consider FMT in patients with multiple recurrences
- Know where to find new PrEP guidelines as well as oncology guidelines for prophylaxis and outpatient febrile neutropenia
- New antimicrobials!
  - Evaluate supporting data and utilize ONLY where appropriate
- Identify a user-friendly resource to help keep up-to-date in ID, review at regular intervals